OMB No. 0990-0115 Electronic Request for Proposal SECTION A – SOLICITATION/CONTRACT FORM
OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE CMB WEBSITE AT
http://www.niaid.nih.gov/contract/default.htm FOR ANY SOLICITATION AMENDMENTS THAT MAY BE ISSUED. THIS OFFICE WILL PROVIDE NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS.

<table>
<tr><td colspan="4">Purchase Authority: Public Law 92-218, as amended.
NOTE: The issuance of this solicitation does not commit the government to an award.</td></tr>
<tr><td>RFP Number:

NIH-NIAID-DMID-03-39</td><td>Just In Time:

[ ] Yes
[X] No</td><td>Small Bus. Set-Aside [ ]Yes [X]No
8(a) Set-Aside [ ]Yes [ ]No
NAICS Code: 54171
Size Standard: 500 employees</td><td>Level of Effort:
[ ] Yes [X] No
Total Effort:
[ ]</td></tr>
<tr><td colspan="4">TITLE: In Vitro and Animal Models for Emerging Diseases and Biodefense</td></tr>
<tr><td colspan="2">Issue Date:
September 30, 2002</td><td colspan="2">Due Date: February 4, 2003
Time: 4:00 PM, EST</td><td>Technical Proposal Page Limits:
[X] Yes (See “How to Prepare and Submit Electronic Proposals”)
[ ] No</td></tr>
<tr><td colspan="2" rowspan="2">ISSUED BY:
Paul D. McFarlane
Contracting Officer
CMB, DEA, NIAID, NIH
6700-B Rockledge Drive
Room 2230, MSC 7612
Bethesda, MD 20892-7612</td><td colspan="3">[X] NIAID reserves the right to make awards without discussion.</td></tr>
<tr><td>NO. OF AWARDS:
[ ] Only 1 Award
[X] Multiple Awards</td><td colspan="2">PERIOD OF PERFORMANCE:

7 years beginning on or about 09/30/2003</td></tr>
<tr><td colspan="5">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 SECTION J - Attachments)</td></tr>
<tr><td colspan="5">The Official Point of Receipt for the purpose of determining timely delivery is the Contract Management Branch as stated above. The paper copy with original signatures is the official copy for recording timely receipt. If the 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 HHSAR 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation. FACSIMILE SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.</td></tr>
<tr><td colspan="5">POINT OF CONTACT -- Paul D. McFarlane --COLLECT CALLS WILL NOT BE ACCEPTED--

Telephone: Direct 301-496-0349 Main 301-496-0612 | Fax 301-402-0972 | E-Mail pm24v@nih.gov</td></tr>
</table>

Updated thru FAC 97-25 (05/02/01)

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BACKGROUND / STATEMENT OF WORK / NOTES TO OFFERORS
In Vitro and Animal Models for Emerging Diseases and Biodefense
DMID-03-39

BACKGROUND

As concern grows about the use of biological agents in acts of terrorism or war, Federal health agencies are evaluating and accelerating measures to protect the public from the health consequences of such an attack. Recent events have reminded us that bioterrorism can be a major contributor in disease emergence. Basic and applied research supported by the National Institutes of Health (NIH) complements the efforts of other Federal agencies by developing the essential tools—diagnostics, therapeutics, and vaccines—that are needed by physicians, nurses, epidemiologists, and other public health workers to prevent and control a disease outbreak. NIAID is the primary NIH Institute that supports and conducts research on the diagnosis, prevention, and treatment of infections caused by a wide variety of emerging pathogens, including agents that could be intentionally introduced.

In vitro and animal models are needed to ensure development and testing of vaccines, therapeutics, and diagnostics, and preclinical safety testing will be required to speed the development of new generation products. Animal models will be critical to FDA approval of BioDefense therapies and vaccines since in most cases clinical trials to test efficacy are not possible.

Given the current level of interest in developing additional therapies and prevention strategies, particularly for organisms with potential use in bioterrorism, NIAID must expand current capacity for therapeutics and vaccine development. There is little private sector interest in developing therapies and preventions related to BioDefense because of the lack of market potential.

Moreover, a number of promising candidate therapies and vaccines have been identified for bioterrorism organisms/diseases. However, development has been delayed because of the lack of validated animal models in which to test these candidates. New models need to be developed, particularly for non-human primates where the shortage of rhesus macaques is severely limiting development of new vaccines and therapies.

This contract will facilitate NIAID's development of therapeutics and preventive measures related to BioDefense. Offerors may submit proposals in response to one or more of the six parts described below.

INTRODUCTION

The "In Vitro and Animal Models for Emerging Infectious Diseases, including Bioterrorism Agents" contract will provide targeted screening to identify potential therapeutic and preventive modalities, as well as resources to characterize additional antimicrobial activities of already licensed antimicrobial agents, small animal and non-human primate models to test the safety and efficacy of therapeutic and preventive modalities that target emerging infectious agents including, Bioterrorism Category A-C agents as outlined in the CDC website http://www.bt.cdc.gov/Agent/Agentlist.asp. A list of priority organisms is also available on the NIAID website http://www.niaid.nih.gov/dmid/biodefense/bandc_priority.htm.

The objective of this contract is to provide a range of developmental resources to bring new therapies and preventive measures from the laboratory to initial clinical testing in humans. The contract consists of six parts, listed below, which each contribute to the overall development effort. These contracts will provide a ready capacity in a number of needed areas and will be utilized as products become available for testing. Test articles that are found to have activity in Part A may progress through development using contractors from other parts. For Parts C, D, E and F, various vaccine concepts may be tested based on the following categories: (a) synthetic peptides, (b) recombinant subunits, (c) vector based vaccines, (d) virus-like particles/replicons, or (e) nucleic acid based vaccines.

Part A: In Vitro Screens for Antimicrobial Activity. Part A will provide the capacity to screen test articles for antimicrobial activity against emerging infectious agents including, Bioterrorism Category A-C agents. Materials for testing will be obtained by NIAID and provided to the contractor for testing. This activity is not intended to cover antiviral screening against viral hemorrhagic fevers or poxviruses, which is covered by a separate contract.

Part B: Clinical Isolate Panels for Selected Bacterial Pathogens. Part B will provide the capacity to perform antimicrobial activity determination against clinical panels of bacterial pathogens to arrive at tentative susceptibility breakpoints. This activity is to be performed using bacterial pathogens classified as emerging infectious agents, including Bioterrorism Category A-C agents. Antimicrobial agents to be tested under this contract will be selected on the basis of their activity against select genera and species of bacterial pathogens using reference strains.

Part C: Small Animal Models for Selected Pathogens, including GLP Studies. Part C will support the development, validation and use of various small animal models to screen new therapeutic, diagnostic and preventive agents or test the efficacy of therapeutics, immunotherapies, diagnostics, and vaccines with activity against emerging infectious agents including, Bioterrorism Category A-C agents.

Part D: Non-human Primate Models for Selected Pathogens, including GLP Studies. Part D will support the development, validation and use of various non-human primate models to screen new therapeutic, diagnostic and preventive agents or test the efficacy of therapeutics, immunotherapies, diagnostics, and vaccines with activity against emerging infectious agents including, Bioterrorism Category A-C agents.

Part E: Safety and Immunogenicity Testing for Vaccines. Part E will support the testing of vaccine preparations as required prior to initial clinical evaluation (under GLP). This includes testing candidate products for safety and immunogenicity (both cellular and humoral) in small animals and, if appropriate, in non-human primates.

Part F: Safety/Toxicology and Pharmacology Testing for Therapeutics. Part F will support the testing of candidate products for safety, including reproductive toxicology and other appropriate tests, in small and large animal, and if necessary, in non-human primates. This activity includes all such tests as are required to support clinical use in humans; testing must be sufficient to meet requirements for IND filing (GLP).

DEFINITIONS:

Clinical panels: standardized, defined panels of clinical or isolates of infectious agents.

Infectious agent or agents: Organisms responsible for causing the diseases listed in the Bioterrorism Category A-C agent list or the NIAID Priority Pathogens list.

Test article or articles or products: materials that are supplied to be tested in the contract. The test articles/products may include, but are not limited to, vaccines (of several types), therapeutic vaccines, antibodies, biological products, antitoxins, drugs, other therapeutic modalities, diagnostic materials or assays.

CONTRACT TYPE:

An Indefinite Delivery – Indefinite Quantity (IDIQ) type contract is planned. It is anticipated that multiple awards will be made for each part of this IDIQ Solicitation. The Contract will be in effect for seven (7) years. An IDIQ contract provides for an indefinite quantity, within stated limits, of supplies or services to be furnished during a fixed period, with deliveries or performance to be scheduled by placing orders with the contractor. Task orders will be issued to the pre-qualified pool of contractors for parts A, B, C, D, E or F based on the specific requirements of the task order. NIAID reserves the right to award to any contractor in the pool and to solicit to expand this pool as necessary throughout the seven (7) year period of this effort.

In response to this RFP, potential Offerors may submit proposals for one or more of the six (6) Parts described above. For Parts A and B, Offerors should propose as many organisms or groups of organisms as possible. Within Parts C, and D Offerors may submit proposals for one or more of the models using the same organisms/disease or models for more than one organism/disease. Offerors for Parts E and F should propose a comprehensive services to cover all aspects of the Statement of Work. Proposals will undergo peer review based on the evaluation criteria and awards will be made to the most qualified proposals. Each Offeror awarded a contract under a given Part or Category, will receive a guaranteed minimum dollar award over the term of the Contract. The following scale sets forth the guaranteed minimum dollar awards per Part:

Part A $ 75,000
Part B $ 75,000
Part C $100,000
Part D $150,000
Part E $100,000
Part F $100,000

Statement of Work
In Vitro and Animal Models for Emerging Diseases and Biodefense
RFP DMID-03-39

Independently, and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, materials, equipment, and facilities, not otherwise provided by the Government under the terms of this contract, directly or through subcontractors and/or consultants, as needed to undertake targeted research essential to the development of therapeutics, diagnostics, and preventive measures for emerging infectious diseases, including bioterrorism agents.

This Statement of Work is divided into six Parts: A) In vitro screening, B) Clinical isolate panels, C) Small animal models, D) Non-human primate models, E) Safety and immunogenicity testing, and F) Toxicology and Pharmacology testing. Each Contractor will be responsible for the General Statement of Work for all parts and for one or more of the six Parts. Contractors for each Part will fully and formally cooperate with the relevant other Part Contractors and with the Project Officer.

General Statement of Work for All Parts:

Independently, and not as an agent of the Government, the Contractor shall exert its best efforts to furnish all necessary services, qualified professional and technical personnel, materials, equipment, and facilities, not otherwise provided by the Government under the terms of this contract as needed to perform the work set forth below. All Contractors shall perform the work described below in addition to one or more sections A – F.

Specifically as directed by the Project Officer, the Contractor shall:

1. Receive, Store, and Record Compounds. Develop and maintain efficient, effective procedures for documentation of receipt of compound/test article shipments from the acquisition contractor or the Project Officer. Provide for a computerized inventory of compound/test article identifiers, amounts available, storage locations, and standardized microbiological activity.

2. Organize, maintain, and transfer information on protocols and test results, as well as provide reports of these, to the Project Officer. Establish electronic message and document transfer capability with the Project Officer.
a. The Contractor shall report data generated under this contract to the Project Officer in the form of progress reports as described in the contract Reporting Requirements (written reports and computer files). To facilitate timely transmission of data and information, the Contractor shall establish and maintain an efficient data management system and electronic communication (electronic mail) with the Project Officer's office.
b. The Contractor's Principal Investigator and key personnel shall meet with the Project Officer at periodic intervals, to be scheduled after contract award, to review progress, anticipated or existing problems, and discuss the work to be performed.

3. Abide by terms of the Confidentiality Agreement with drug sponsors signed by the NIAID. Copies will be provided to the Contractor prior to or simultaneous with the delivery of the therapeutic agents covered by the agreements. Provide specific procedures to safeguard proprietary information to maintain all confidential data and information in files accessible only to the Project Officer, Principal Investigator, and involved staff.

4. The Contractor shall provide advance copies of draft manuscripts for publication (including abstracts and public presentations) based on data generated under this contract to the Project Officer, and obtain clearance from the Project Officer before submitting for publication or presentation. Support from the Government must be acknowledged in all abstracts, presentations, and publications.

5. Provide safe facilities and resources and conduct work in accordance with the Biosafety in Microbiological and Biomedical Laboratories guidelines. Ensure that all requirements to store and process select agents are followed. Conduct work in accordance with the clause outlined under SAFETY CONTROLS AND STANDARDS, attached to this RFP.
a. Conduct work under this contract under Biosafety Level 3 or 4 guidelines, when appropriate and in accordance with all applicable Federal, state and local laws, codes, ordinances and regulations, and with basic references and related modifications. (See SAFETY CONTROLS AND STANDARDS, attached to this RFP.)
b. Provide facilities and equipment to receive, store, and manipulate infectious viral and bacterial agents and potentially hazardous compounds and maintain their stability; provide systems to track stocks of infectious agents, access to those stocks, their use, and disposal.
c. Provide protective garments, equipment, and sufficient monitoring to assure safe handling of potentially hazardous microorganisms and materials. Specifically, the Contractor shall comply with all applicable health and safety regulations while conducting the work set forth herein.

d. Insure that no identifiable data on the compounds or products and the results of testing will be kept in files open to the public, and that facilities for computer operation, data entry, and file storage are secure from unauthorized access. Only those contract employees or government employees directly engaged in this project shall have access to the files of information regarding source and nature of confidential or proprietary materials and results of testing.

PART A: IN VITRO SCREENS FOR ANTIMICROBIAL ACTIVITY

The first activity under this contract is the capacity to screen test articles for antimicrobial activity against emerging infectious agents including Bioterrorism Category A-C agents. Materials for testing will be obtained by NIAID and provided to the contractor for testing. This activity is not intended to cover antiviral screening against viral hemorrhagic fevers and poxviruses, which is covered by a separate contract.

Independently, and not as an agent of the government, the contractor shall develop, validate, and use in vitro assays to screen test substances for activity against emerging infectious agents.

Specifically as directed by the project officer, the contractor shall:

1. Maintain quality controlled stocks of bacterial pathogens, control and test substances:
   a) Receive stocks of select BioDefense bacterial strains through the Project Officer.

b) Provide stocks of reference/quality control strains of non-BioDefense pathogens as required for quality control assurance of control antibiotics.
c) Maintain quality controlled, viable frozen or lyophilized stocks of all strains under appropriate conditions.
d) Assure identity of stocks at least to the species level using appropriate assay methods.
e) Maintain and document current inventory, purity and identity assessment for each strain.
f) Provide detailed accounting for pathogen stock use and disposal.
g) Maintain stocks of appropriate quality control antibiotics under recommended conditions as described in the relevant NCCLS standards.
h) Maintain stocks of test substances under conditions specified by the Project Officer.
i) Provide detailed and routine quality control assessment for the performance of all bacterial stains, control antibiotics and test substances using appropriate published testing guidelines, wherever available.

2. Perform evaluation of antimicrobial activity of test substances against panels of standard reference strains of selected bacterial pathogens. Determine the inhibitory effect on bacterial replication and/or infectivity based on meaningful endpoints, such as, but not limited to, Minimum Inhibitory Concentration Determinations. Evaluations shall incorporate both the substance under investigation, a positive control agent, and an untreated control. Document preparation, lots, and use of test substances, bacterial growth media, and control antibiotics.

3. Perform special studies as directed by the Project Officer which shall include, but are not restricted to, evaluation and development of new assay systems, combination drug testing, mechanism of action studies targeting specific steps in bacterial life cycle, and other more detailed testing.

PART B: CLINICAL ISOLATE PANELS FOR SELECTED BACTERIAL PATHOGENS

The second activity to be supported under this contract is the capacity to perform antimicrobial activity determination against clinical panels of bacterial pathogens to determine ranges of activity and arrive at tentative susceptibility breakpoints. These determinations are to be performed including, but not limited to, bacterial pathogens classified as emerging infectious agents, including Bioterrorism Category A-C agents.

These contracts will provide a ready capacity in a number of needed areas and be utilized as agents become available for testing. Antimicrobial agents to be tested under this contract will have been selected on the basis of their activity against select genera and species of bacterial pathogens using reference strains (see Part A of this solicitation), and are to be evaluated in Part B of this contract against clinical isolates of the same genera and species of bacterial pathogens to establish their range of activity (MIC50/90) and tentative susceptibility breakpoints.

Screening of currently licensed and marketed antibiotics, as well as promising new chemical entities for antibacterial activity against Bacillus anthracis, Yersinia pestis and other bacterial pathogens that are causative agents of emerging and reemerging infections or have the potential to be used in bioterrorism are a priority for the NIAID. Activity data against clinical panels, as well as establishment of tentative susceptibility breakpoints, should be suitable for inclusion in an IND.

Independently and not as an agent of the Government, the contractor shall, as directed by the Project Officer:

1. Maintain quality controlled stocks of bacterial pathogens, control and test reagents (this shall be done under GLP as requested):
    a) Receive stocks of select clinical and reference bacterial strains through the Project Officer.
    b) Provide stocks of reference/quality control strains of non-bioterrorism pathogens as required for quality control assurance of control antibiotics.
    c) Maintain quality controlled, viable frozen or lyophilized stocks of select clinical and reference bacterial strains under appropriate conditions.
    d) Assure identity of stocks at least to the species level using appropriate assay methods.
    e) Maintain and document current inventory, purity and identity assessment for each clinical isolate and reference/quality control strain.
    f) Provide detailed accounting for pathogen stock use and disposal.
    g) Maintain quality controlled, viable frozen or lyophilized stocks of quality control strains to be included in all activities.
    h) Characterize antimicrobial susceptibility profile for each clinical strain against a panel of antibiotics as directed and approved by the Project Officer. This antibiogram will include both licensed and investigational antimicrobial agents.
    i) Prepare, when required for testing, fresh viable cultures of reference/quality select pathogen strains in or on appropriate culture medium.
    j) Maintain stocks of appropriate quality control antibiotics under recommended conditions as described in the relevant NCCLS standards.
    k) Maintain stocks of test products under conditions specified by the Project Officer.
    l) Provide detailed and routine quality control assessment for the performance of all bacterial stains, control antibiotics and test products using appropriate published testing guidelines.

2. Perform evaluation of antibacterial activity of test agents against panels of clinical isolates for selected bacterial pathogens under GLP.

    a) Conduct all MIC determinations according to the relevant NCCLS standards, where available or as directed by the Project Officer, in liquid or on solid medium.
    b) Document preparation, lots, and use of test products, bacterial growth media, and control antibiotics.
    c) Conduct appropriate standard format MIC evaluations with test products against clinical isolates of selected bacterial pathogens and at least one standard strain of the same species.
    d) Include in each standard MIC evaluation the appropriate number of reference/quality control strains for each control antibiotic.
    e) Conduct MIC50 and MIC90 determinations using at least the minimum acceptable number of clinical isolate strains to derive MIC50 and MIC90 values.
    f) Provide documentation of all primary test results.
    g) As part of quality control assurance, provide documentation of performance and results of test antibiotics and reference/quality control strains for same day experiments, as well as for experiments done on different days for the same strain/antibiotic combination.

h) Provide documentation of physical appearance (such as, but not limited to, cloudiness or precipitation in solution, etc) of test and control agents, as well as documentation of any observations made during testing (such as, but not limited to, unexpected bacterial growth behavior, etc.)
i) Determine tentative clinical breakpoints for the test agents.
j) If requested by the Project Officer, activity of combinations of test products and/or antibiotics against selected panels of strains shall be evaluated using a standard checkerboard format.

3. Perform special studies, as directed by the Project Officer, which may include but are not limited to standardization of assay conditions proposed and developed by the NCCLS for bioterrorism agents and reference organisms.

PART C: SMALL ANIMAL MODELS FOR SELECTED PATHOGENS INCLUDING GLP STUDIES

The third activity area to be supported under this contract is the development, validation and use of various small animal models to screen new therapeutic, diagnostic and preventive agents or test the efficacy of therapeutics, immunotherapies, diagnostics, and vaccines with activity against emerging infectious agents including, Bioterrorism Category A-C agents.

These contracts will provide a ready capacity in a number of needed areas and be utilized as products become available for testing. Other studies such as disease pathogenesis and natural history are not intended for this contract. In vivo safety testing, pharmacokinetics, pharmacodynamics, and toxicity testing are covered under Part E and F of this solicitation.

Models for testing of Rift Valley Fever vaccine, Plague vaccine, and screening of currently licensed and marketed antibiotics for anthrax and pneumonic plague are a priority for the NIAID. Offerors are also encouraged to propose models for other important emerging and/or rare viral and bacterial agents as well. Not intended for this solicitation are animal models for infection with Pox viruses, Filoviruses, and Viral Hemorrhagic Fever agents specifically: Punta Toro, Pichinde, Benzi, and Semlicki Forest viruses, TB, influenza, and botulinum toxin.

Independently, and not as an agent of the government, the Contractor shall develop small animal models to be used for screening and efficacy testing of new products including therapeutics, immunotherapies, diagnostics, and vaccines. Conduct all in vivo testing as are required for approval of a product for human administration. Testing must be sufficient to meet requirements for IND filing.

Specifically as directed by the Project Officer, the contractor shall:

1. Utilize or provide one or more well-characterized and validated animal models(s) of human infection and/or disease mediated by Category A-C disease agents to evaluate candidate diagnostics, drugs, vaccines and immunotherapies for preliminary efficacy. (A validated model is one that has shown correlation of results with human clinical trials or trials conducted in NHP, or with the natural history of human infection and is suitable to provide data relevant for obtaining FDA approval for an IND, licensure, or specific indication. The Project Officer will provide guidance for these models.) For infection models, the infection of animals should be efficiently established. For other models, for example, mice transgenic with the human virus receptor gene or mice implanted with virus-infected human tissues, provide and use animals for evaluation of candidate therapies. For all models, the process and dosage level of infection and challenge and/or disease pathogenesis should resemble the corresponding human disease as closely as possible. Standardized protocols, when provided by the Project Officer, shall be incorporated.

2. Perform preclinical evaluations of experimental therapies, diagnostic, and preventive agents for infections as specified by the Project Officer. The test agents shall be evaluated for efficacy. When appropriate, conduct studies to evaluate novel strategies for drug delivery and dosing, including combination and sequential drug administration. These studies shall include appropriate uninfected and untreated controls and may involve aerosol challenge of some agents requiring specialized testing facilities. Federal guidelines for care and use of laboratory animals must be followed as well as requirements for approval of animal use protocols. Unless directed otherwise, submit each proposed protocol/experiment/effort to the Project Officer for review, prioritization, and approval. Agents for evaluation will be provided by the NIAID Project Officer.

Some, but not all studies will require that they be performed in accordance with Good Laboratory Practice (GLP) regulations.

Evaluation capabilities of the animal model shall include, but not be limited to, the following:

a. Quantitative assessments, which detect differences, with at least a minimal level of statistical confidence, between treatment groups of animals, with specific indicators including confirmation of infection, quantitation of organisms present in tissues of infected animals, markers of disease progression, and selected indicators of morbidity.
b. Microbiological and histological analyses, including but not limited to special stains and cultures, to document the purity, severity, pathology, and location of the animal infection. Necropsy/pathology support shall be available as needed.
c. Appropriate observations and measures of general toxicity, to include body weight, blood chemistries, hematologic measures, body temperature, behavior, and other indicators of general health.
d. Immunogenicity and/or immune responses when appropriate for the test article.
e. Limited pharmacokinetic determinations. Offerors will be required only to have the capability of collecting and preparing blood, cell, and tissue samples for shipment to another site for analysis.

3. Perform further studies to characterize and refine the proposed model(s) and to develop new models. The contractor may be required, as directed by the Project Officer, to use animal models other than the one proposed if well-characterized animal models become available. As directed by the Project Officer, develop and evaluate new assays and models that may be required for new/emerging agents and models.

4. Conduct work with animals in accordance with NIH guidelines for animal care and use. Maintain awareness of evolving regulatory requirements for animal research and with the FDA regulatory guidelines for animal studies in support of licensure, such as the 21 CFR Parts 314 and 601 "New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical of Feasible." When efficacy studies are intended to support the clinical use of a test article in humans, the contractor shall also:

a. Provide all data, information, and records required for the writing and submission of the Masterfile, Investigators Brochure, and all other documents related to IND submission and maintenance to the Project Officer or to a designated third party.

b. Retain all records, samples, histopathological slides, etc. and make them available as directed by the Project Officer and as indicated under GLP guidelines.

c. Maintain awareness of evolving regulatory requirements for preclinical toxicologic evaluations for chemicals or biologics, and develop new test systems or models as required to meet new needs.

d. Participate as necessary in discussions with the FDA during pre-IND, IND, and pre-NDA meetings.

PART D: NON-HUMAN PRIMATE MODELS FOR SELECTED PATHOGENS, INCLUDING GLP STUDIES

This activity will support the development, validation and use of various non-human primate models to screen new therapeutic, diagnostic and preventive agents or test the efficacy of therapeutics, immunotherapies, diagnostics, and vaccines with activity against emerging infectious agents including, Bioterrorism Category A-C agents. These contracts will provide a ready capacity in a number of needed areas and be utilized as products become available for testing. Other studies such as disease pathogenesis, small proof of principle studies, and natural history are not intended for this contract. In vivo safety testing, pharmacokinetics, pharmacodynamics, and toxicity testing are covered under Part E and F of this solicitation.

Models for testing of Rift Valley Fever vaccine, Plague vaccine, and screening of currently licensed and marketed antibiotics, as well as new therapeutics and vaccines, for anthrax, pneumonic plague, pox viruses, and viral hemorrhagic fevers are a priority for the NIAID. Offerors are encouraged to propose models for other important emerging and/or rare viral and bacterial agents as well and to propose models that utilize animals other than rhesus macaques. Not intended for this solicitation are animal models for infection with TB or influenza. Models using baboons or chimpanzees should not be proposed.

Independently, and not as an agent of the Government, the Contractor shall develop non-human primate animal models to be used for screening and efficacy testing of new products including therapeutics, immunotherapies, diagnostics, and vaccines. Conduct in vivo testing in an infection model as is required for approval of a product for human administration. Testing must be sufficient to meet requirements for IND filing.

Specifically as directed by the Project Officer, the Contractor shall:

1. Utilize or provide one or more well-characterized non-human primate models(s) of Category A-C disease agents for experimental use for evaluation of candidate diagnostics, drugs, vaccines, and immunotherapies. The process of infection and/or disease pathogenesis should resemble the corresponding human disease as closely as possible. If validated models are available, they should be included. A validated model is one that has shown correlation of results with human clinical trials or trials conducted in NHP.

2. Perform preclinical evaluations of experimental therapies, diagnostic, and/or preventive agents/vaccines for infections as specified by the Project Officer. The test agents shall be evaluated for efficacy. When appropriate, conduct studies to evaluate novel strategies for drug delivery and dosing, including combination and sequential drug administration. These studies shall include appropriate uninfected and untreated controls and may involve aerosol challenge of some agents requiring specialized testing facilities. Unless directed otherwise, each proposed protocol/experiment/effort shall be submitted to the Project Officer for review, prioritization, and approval. Agents for evaluation will be provided by the NIAID Project Officer.

   Some, but not all studies will require that they be performed in accordance with Good Laboratory Practice (GLP) regulations.

   Evaluation capabilities of the animal model shall include, but not be limited to, the following:
   a. Quantitative assessments, which detect statistically valid differences between treatment groups of animals, with specific confirmation of infection, quantitation of infection, markers of disease progression, selected indicators of morbidity, and other measures as are appropriate for the model.
   b. Microbiological and histological analyses, including but not limited to special stains and cultures, to document the purity of stocks and severity, pathology, and location of the animal infection.
   c. Appropriate observations and measures of general toxicity, to include but not limited to body weight, blood chemistries, hematologic measures, body weight, and other indicators of general health. Necropsy/pathology support shall be available as needed.
   d. Limited pharmacokinetic determinations. Offerors will be required only to have the capability of collecting and preparing blood, cell, and tissue samples for shipment to another site for analysis.

3. Perform further studies to characterize and refine the proposed model(s) and to develop new models. The contractor may be required to use animal models other than the one proposed if well-characterized animal models become available. As directed by the Project Officer, develop and evaluate new assays and models that may be required for new/emerging agents and models.

4. Conduct work with animals in accordance with NIH guidelines for animal care and use. Maintain awareness of evolving regulatory requirements for animal research and with the FDA regulatory guidelines for animal studies in support of licensure, such as the 21 CFR Parts 314 and 601 “New Drug and Biological Drug Products: Evidence Needed to

Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical of Feasible." When efficacy studies are intended to support the clinical use of a test article in humans, the contractor shall also:

a. Provide all data, information, and records required for the writing and submission of the Masterfile, Investigators Brochure, and all other documents related to IND submission and maintenance to the Project Officer or to a designated third party.

b. Retain all records, samples, histopathological slides, etc. and make them available as directed by the Project Officer and as indicated under GLP guidelines.

c. Maintain awareness of evolving regulatory requirements for preclinical toxicologic evaluations for chemicals or biologics, and develop new test systems or models as required to meet new needs.

d. Participate as necessary in discussions with the FDA during pre-IND, IND, and pre-NDA meetings.

PART E: SAFETY AND IMMUNOGENICITY TESTING for VACCINES

The fifth activity area to be supported under this contract is the testing of vaccine preparations as required prior to initial clinical evaluation. This includes testing candidate products for safety and immunogenicity (both cellular and humoral) in small animals and, if appropriate, in non-human primates.

Independently, and not as an agent of the Government, the Contractor shall test candidate products for safety and immunogenicity (both cellular and humoral) in small animals and, if necessary, in non-human primates, and other appropriate tests, including reproductive toxicology. Perform all such tests as are required to support clinical use in humans of a vaccine product. Testing must be sufficient to meet requirements for IND filing.

Specifically, the contractor shall:

1. At the request of the Project Officer, contractor shall perform all tests required to qualify a vaccine product for human administration or to qualify relevant cell substrates for vaccine production, including but not limited to the list below. Such testing must also include all tests required for Investigational New Drug (IND) and Masterfile submission. All studies must be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) unless specified by the Project Officer in writing.

a. Preclinical immunogenicity evaluation: The preclinical studies shall be designed to assess the immune response including seroconversion rates, antibody levels, and cell mediated immune responses in vaccinated animals.

b. Preclinical safety evaluations shall include but are not limited to the following:

1) Systemic toxicity: Preclinical studies shall include dose-ranging and dose escalation studies of systemic toxicity as well as toxicity to potential target organs, including hematopoietic and immune systems, and histological evaluation of organs.
2) Local reactogenicity: Local site reactivity studies to include detailed clinical observations and histological evaluation of tissue at the injection site or other visible lesions from biopsies or term necropsy samples.
3) Genetic toxicity: In the case of DNA and vector-based vaccines the pivotal GLP preclinical study shall focus on assessment for the potential for the nucleic acid vaccine to recombine with endogenous host DNA sequences and integrate into cell chromosomes. Studies designed to address the potential for integration shall use the most sensitive methods available.
4) Tumorigenicity studies: Tumorigenicity studies may be appropriate under certain conditions, such as if the preclinical genetic testing demonstrates evidence of integration activity and/or broad tissue distribution, or to qualify cell substrates used in vaccine production. Such studies shall be performed when necessary.
5) Reproductive toxicity studies.
Reproductive toxicity studies must be performed prior to the use of these vaccines in pregnant women. Such studies shall include but are not limited to fertility, general reproductive performance, teratology, and developmental toxicity.
6) All other safety tests as may be required for a particular vaccine type.

c. Adjuvant testing: The use of adjuvants and/or facilitators for the administration of a vaccine will necessitate specific preclinical evaluation procedures to ensure the safety of the candidate formulation to include but not limited to the evaluations listed in b) above.

2. In addition, the contractor shall:

a. Provide all data, information, and records required for the writing and submission of the Masterfile, Investigators Brochure, and all other documents related to IND submission and maintenance to the Project Officer or to a designated third party.
b. Retain all records, samples, histopathological slides, etc. and make them available as directed by the Project Officer and as indicated under GLP guidelines.
c. Maintain awareness of evolving regulatory requirements for preclinical immunogenicity and safety evaluations for vaccines, and develop new test systems or models as required to meet new needs.
d. Participate as necessary in discussions with the FDA during pre-IND, IND, and pre-NDA meetings.

PART F: SAFETY/TOXICOLOGY AND PHARMACOLOGY TESTING for THERAPEUTICS

The sixth activity under this contract is the testing of candidate products for safety, including reproductive toxicology and other appropriate tests, in small and large animal, and if necessary, in non-human primates. This activity includes all such tests as are required to support clinical use in humans; testing must be sufficient to meet requirements for IND filing (GLP).

Independently, and not as an agent of the Government, the Contractor shall test candidate products for safety/toxicity and perform pharmacology studies. Perform all such tests as are required to support clinical use in humans of a therapeutic or vaccine product.

Specifically, the contractor shall:

1. At the request of the Project Officer, contractor shall perform all tests required to qualify a therapeutic product for human administration including but not limited to the list below. Such testing must also include all tests required for Investigational New Drug (IND) and Masterfile submission. All studies must be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) unless specified by the Project Officer in writing.

a. Preclinical toxicity evaluations of experimental anti-infective therapies or other test articles in small animals, to include but not limited to:
1) Determination in rodents of the maximally tolerated dose (MTD) of experimental therapies.
2) Determination in rodents of the acute and subchronic systemic toxicity of experimental therapies,
3) Determination of relevant pharmacokinetic/toxicokinetic parameters of experimental therapies in these species.

b. Preclinical toxicity and pharmacology evaluations of experimental anti-infective therapies or other test articles in large animals (non-rodents), to include but not limited to:
1) Determination in a non-rodent large animal (e.g. dog or non-human primate) of the acute and subchronic systemic toxicity of experimental therapies, and establishment of relevant pharmacokinetic parameters in this species.
2) Determination of the pharmacokinetics/pharmacodynamics of experimental therapies in non-human primates.

c. Other preclinical toxicity/safety studies, using appropriate animal and in vitro assays, to include, but not limited to:
1) Genetic toxicity of experimental therapies or test articles: Genetic toxicity studies must be performed for most therapies. Such studies shall include but are not limited to the ability of the test article to produce genetic damage in mammalian cells as indicated by the ability to induce mutations at the thymidine kinase locus (tk) in L5178Y mouse lymphoma cells and the ability of the test article to induce genetic damage in the Salmonella/ E.coli test system.
2) Tumorigenicity studies: Tumorigenicity studies may be appropriate under certain conditions, such as when agents are expected to be administered for extended periods of time. Such studies shall be performed when necessary.
3) Reproductive toxicity studies: Reproductive toxicity studies must be performed prior to the use of these therapies in pregnant women. Such studies shall include but are not limited to fertility, general reproductive performance, teratology, and developmental toxicity.
4) Immunotoxicity studies: Immunotoxicity studies to determine in rodents the toxicity of experimental therapies to the immune system, or other specialized target organ system.
5) Biotransformation assays: Assays, conducted in vitro to evaluate the potential of experimental therapies to undergo biotransformation in test animals and humans.
6) Additional pharmacologic assays: Assays and studies to determine additional pharmacologic parameters of experimental therapies, such as but not limited to: tissue distribution, mass balance, etc. May require use of radiolabeled material that would be provided by NIAID.
7) All other safety and pharmacology assays and studies that may be required for a particular therapeutic agent.

2. In addition, the contractor shall:
a. Evaluate the data resulting from the conduct of the above studies and draw relevant conclusions about pharmacokinetics, target organ(s) of toxicity, and likely human adverse reactions to the evaluated therapies.
b. Provide all data, information, and records required for the writing and submission of the Masterfile, Investigators Brochure, and all other documents related to IND submission and maintenance to the Project Officer or to a designated third party.
c. Retain all records, samples, histopathological slides, etc. and make them available as directed by the Project Officer and as indicated under GLP guidelines.
d. Maintain awareness of evolving regulatory requirements for preclinical toxicologic evaluations for chemicals or biologics, and develop new test systems or models as required to meet new needs.
e. Participate as necessary in discussions with the FDA during pre-IND, IND, and pre-NDA meetings.

STATEMENT OF WORK
PART A (1)
IN VITRO SCREENS FOR ANTIMICROBIAL ACTIVITY

The activity to be supported under this contract is screen compounds for antimicrobial activity against infectious agents listed below. Materials for testing will be provided by NAID.

[NOTE #1 to Offerors: Include all steps necessary to establish and perform standardized screening assays for the organisms listed below. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. Assume up to 500 compounds for testing within the first year, to be sent in groups of approximately 50 compounds.

Offerors may propose studies using pathogens from those listed below. The proposal should clearly indicate exactly what work is proposed.]

1. Specifically, the contractor shall develop, validate, and use in vitro assays to screen compounds for antimicrobial activity against one or more of the following pathogens:
a. Category A : Bacillus anthracis, Francisella tularensis, Yersinia pestis
b. Category B bacteria: Burkholderia pseudomallei, Coxiella burnetti, Brucella species, Burkholderia mallei,
c. Other Category B pathogens: Staphylococcus enterotoxin B, Typhus fever (Rickettsia prowazekii), diarrheagenic E.coli, pathogenic Vibrios, Shigella species, Salmonella, Listeria monocytogenes, Campylobacter jejuni, Yersinia enterocolitica
d. Category B protozoa: Cryptosporidium parvum, Cyclospora cayatanensis, Giardia lamblia, Entamoeba histolytica, Toxoplasma, Microsporidia

2. Maintain quality controlled stocks of bacterial pathogens, control and test substances: as outlined in the Statement of Work for Part A of "In Vitro Screens for Antimicrobial Activity"

3. Perform evaluation of antimicrobial activity of test substances against panels of standard reference strains of selected bacterial pathogens. Determine the inhibitory effect on replication and/or infectivity based on MIC values. Evaluations shall incorporate both the substance under investigation, a positive control agent, and an untreated control. Document preparation, lots, and use of test substances, bacterial growth media, and control antibiotics.

4. Provide all data, information, and records required to support labeling to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

5. Complete all tasks as outlined in the "General Statement of Work" for "In Vitro and Animal Models for Emerging Diseases and Biodefense."

STATEMENT OF WORK
PART B (1)
CLINICAL ISOLATE PANELS FOR SELECTED BACTERIAL PATHOGENS

The activity to be supported under this contract is to determine the range of antimicrobial activity of already licensed antimicrobial agents, as MIC50 and MIC90 values against clinical panels of pathogens. Materials for testing and clinical isolates will be provided by NAID.

[NOTE #1 to Offerors: Include all steps necessary to establish and perform standardized antimicrobial activity assays for the organisms listed below to determine MIC50 and MIC90 values, as well as tentative susceptibility breakpoints for each antibiotic. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. Assume that panels will be comprised of approximately 20 strains of each pathogen.]

1. Specifically, the contractor shall determine the antibacterial activity of antibiotics against panels of clinical strains of Bacillus anthracis, Francisella tularensis, Yersinia pestis and shall be available to participate in the establishment of testing standards for the bacterial pathogens and antibiotics. Antibiotics to be tested include: gentamicin, doxycycline, ciprofloxacin, levofloxacin, ceftriaxone, amoxicillin, amoxicillin clavulanate, azithromycin, and clarithromycin. Conduct all evaluations as outlined in the Statement of Work for Part B of "In Vitro and Animal Models for Emerging Diseases and Biodefense, RFP DMID-03-39

2. Maintain quality controlled stocks of bacterial pathogens, control and test substances: as outlined in the Statement of Work for Part B of "In Vitro and Animal Models for Emerging Diseases and Biodefense, RFP DMID-03-39.

3. Provide all data, information, and records required to support labeling to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes this request.

4. Complete all tasks as outlined in the "General Statement of Work" for "In Vitro and Animal Models for Emerging Diseases and Biodefense".

STATEMENT OF WORK
PART C (1)
SMALL ANIMAL MODELS FOR SELECTED PATHOGENS – ANTHRAX

The activity to be supported under this contract is the testing of various FDA-approved antibiotics for activity against anthrax in a small animal model. This includes testing that may support licensure/labeling of these drugs for use against anthrax under the FDA's "animal rule".

[NOTE #1 to Offerors: Include all testing required to support labeling of these drugs for treatment of anthrax. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Offeror should obtain USP drugs from a pharmacy and include information about the source in the proposal.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not, may propose to do the studies but should clearly indicate that the work cannot be performed according to GLP.

Offerors who are proposing a model for anthrax by other than aerosol exposure may respond, but must address how the model differs from aerosol exposure.]

1. Specifically, the contractor shall perform all tests required to qualify the antibiotics for labeled use to treat inhalational anthrax in humans, including but not limited to the list below. Such testing shall be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) where possible. Antibiotics to be tested include: amoxicillin, azithromycin, clarithromycin, levofloxacin, and amoxicillin clavulanate, with ciprofloxacin as a positive control and saline as a negative control.

a. Pharmacokinetic studies, if necessary to determine doses to be used in efficacy studies.
b. Efficacy of the antibiotics listed above against anthrax.
c. Other tests as may be necessary for completion of the efficacy study.

2. Provide all data, information, and records required to support labeling to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

3. Complete all tasks as outlined in the "General Statement of Work" for "In Vitro and Animal Models for Emerging Diseases and Biodefense."

STATEMENT OF WORK
PART C (2)
SMALL ANIMAL MODELS FOR SELECTED PATHOGENS – PLAGUE

The activity to be supported under this contract is the testing of various FDA-approved antibiotics for activity against plague in a small animal model. This includes testing that may support licensure/labeling of these drugs for use against pneumonic plague under the FDA's "animal rule".

[NOTE #1 to Offerors: Include all testing required to support labeling of these drugs for plague treatment. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Offeror should obtain USP drugs from a pharmacy and include information about the source in the proposal.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not, may propose to do the studies but should clearly indicate that the work cannot be performed according to GLP.

Offerors who are proposing a model for bubonic, rather than pneumonic, plague may also respond, but must address how the model differs from pneumonic plague.]

1. Specifically, the contractor shall perform all tests required to qualify the antibiotics for labeled use to treat plague in humans, including but not limited to the list below. Such testing shall be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) where possible. Antibiotics to be tested include: gentamicin, doxycycline, ciprofloxacin, levofloxacin, and ceftriaxone, with saline as a negative control.

a. Pharmacokinetic studies, if necessary to determine doses to be used in efficacy studies.
b. Efficacy of the antibiotics listed above against plague.
c. Other tests as may be necessary for completion of the efficacy study.

2. Provide all data, information, and records required to support labeling to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

3. Complete all tasks as outlined in the "General Statement of Work" for "In Vitro and Animal Models for Emerging Diseases and Biodefense."

STATEMENT OF WORK
PART D (1)
NON-HUMAN PRIMATE MODELS FOR SELECTED PATHOGENS – ANTHRAX

The activity to be supported under this contract is the testing of various FDA-approved antibiotics for activity against anthrax in a non-human primate animal model. This includes testing that may support licensure/labeling of these drugs for use against anthrax under the FDA's "animal rule".

[NOTE #1 to Offerors: Include all testing required to support labeling of these drugs for treatment of anthrax. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Offeror should obtain USP drugs from a pharmacy and include information about the source in the proposal.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not, may propose to do the studies but should clearly indicate that the work cannot be performed according to GLP.

Offerors who are proposing a model for anthrax by other than aerosol exposure may respond, but must address how the model differs from aerosol exposure.]

1. Specifically, the contractor shall perform all tests required to qualify the antibiotics for labeled use to treat inhalational anthrax in humans, including but not limited to the list below. Such testing shall be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) where possible. Antibiotics to be tested include: amoxicillin, azithromycin, clarithromycin, levofloxacin, and amoxicillin clavulanate, with ciprofloxacin as a positive control and saline as a negative control.

a. Bridging studies to move from rhesus macaques to cynomolgus macaques. These studies should include, at a minimum, untreated (or saline treated) groups and groups treated with ciprofloxacin.
b. Pharmacokinetic studies, if necessary to determine doses to be used in efficacy studies.
c. Efficacy of the antibiotics listed above against anthrax.
d. Other tests as may be necessary for completion of the efficacy study.

2. Provide all data, information, and records required to support labeling to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

3. Complete all tasks as outlined in the "General Statement of Work" for "In Vitro and Animal Models for Emerging Diseases and Biodefense."

STATEMENT OF WORK
PART D (2)
NON-HUMAN PRIMATE MODELS FOR SELECTED PATHOGENS – PLAGUE

The activity to be supported under this contract is the testing of various FDA-approved antibiotics for activity against plague in a non-human primate model. This includes testing that may support licensure/labeling of these drugs for use against pneumonic plague under the FDA's "animal rule".

[NOTE #1 to Offerors: Include all testing required to support labeling of these drugs for plague treatment. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Offeror should obtain USP drugs from a pharmacy and include information about the source in the proposal.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not, may propose to do the studies but should clearly indicate that the work cannot be performed according to GLP.

Offerors who are proposing a model for bubonic, rather than pneumonic, plague may also respond, but must address how the model differs from pneumonic plague.]

1. Specifically, the contractor shall perform all tests required to qualify the antibiotics for labeled use to treat plague in humans, including but not limited to the list below. Such testing shall be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) where possible. Antibiotics to be tested include: gentamicin, doxycycline, ciprofloxacin, levofloxacin, and ceftriaxone, with saline as a negative control.

a. Pharmacokinetic studies, if necessary to determine doses to be used in efficacy studies.
b. Efficacy of the antibiotics listed above against plague.
c. Other tests as may be necessary for completion of the efficacy study.

2. Provide all data, information, and records required to support labeling to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

3. Complete all tasks as outlined in the "General Statement of Work" for "In Vitro and Animal Models for Emerging Diseases and Biodefense."

STATEMENT OF WORK
PART D (3)
NON-HUMAN PRIMATE MODELS FOR SELECTED PATHOGENS – WEST NILE VIRUS

The activity to be supported under this contract is the development and validation of a non-human primate model for West Nile virus infection and disease suitable for future testing of candidate vaccines and therapeutics.

[NOTE #1 to Offerors: Include all tests/studies that would be used to develop and validate the model. The proposal should be structured in terms of specific milestones to be accomplished. Provide a timeline. Offerors who have a model that is partially developed or who have developed models for other flaviviruses should include information about the model. Offerors should also include information about the approach to be used to develop a reproducible, standard model. If the Offeror will require assistance in obtaining strains of the virus, please indicate this in the proposal.]

1. Specifically, the contractor shall develop and standardize a non-human primate model of West Nile virus infection and disease suitable for screening and efficacy testing of new products including therapeutics, immunotherapies, diagnostics, and vaccines. Studies/measure may include, but are not limited to:

a. Microbiological, histological, and immunologic analyses
b. Disease progression and pathogenesis; clinical parameters
c. Titration of viral stocks in animals; determination of infectious doses
d. Optimization of model for endpoints such as encephalitis

2. Optimize and standardize the model to meet the needs of testing efficacy of therapeutics and vaccines under the FDA's "animal rule": 21 CFR Parts 314 and 601 "New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible"

3. Provide all data, information, and records required to support regulatory filings to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

4. Complete all tasks as outlined in the "General Statement of Work" for "In Vitro and Animal Models for Emerging Diseases and Biodefense."

STATEMENT OF WORK
PART E (1)
SAFETY AND IMMUNOGENICITY TESTING FOR VACCINES – RECOMBINANT PROTEIN VACCINE

The activity to be supported under this contract is the testing of a recombinant protein vaccine, such as anthrax protective antigen (rPA), as required prior to initial clinical evaluation and for continued clinical development. This includes testing candidate products for safety and immunogenicity (both cellular and humoral).

[NOTE #1 to Offerors: Include all testing required for an IND and for advanced clinical development (Phase II trials and including special populations) for this type of product. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Government will provide the test vaccine.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not, may propose to do the studies but should clearly indicate that the work cannot be performed according to GLP. The Offeror should clearly identify the types of animal(s) that will be used in each study.]

1. Specifically, the contractor shall perform all tests to qualify a vaccine product for human administration including but not limited to the list below. Such testing must also include all tests required for Investigational New Drug (IND) and Masterfile submissions. In addition, include all testing that will be necessary to expand clinical development to special populations. All studies must be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58).

a. Preclinical immunogenicity evaluation: The preclinical studies shall be designed to assess the immune response including seroconversion rates, antibody levels, and cell mediated immune responses in vaccinated animals. Studies should also be designed to establish a model for determining potency.

b. Preclinical safety evaluations may include but are not limited to the following:

1) Systemic toxicity: Preclinical studies shall include dose-ranging and dose escalation studies of systemic toxicity as well as toxicity to potential target organs including hematopoietic and immune systems.
2) Local reactogenicity: Local site reactivity studies to include detailed clinical observations and histological evaluations of tissue of the injection site or other visible lesions from biopsies or term necropsy samples.
3) All other safety tests as may be required for a particular vaccine type and for advanced clinical development, such as genetic toxicity, tumorigenicity, and reproductive toxicity studies.
4) Provide all data, information, and records required to support regulatory filings to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.
5) Complete all tasks as outlined in the “General Statement of Work” for “In Vitro and Animal Models for Emerging Diseases and Biodefense.”

STATEMENT OF WORK
PART E (2)
SAFETY AND IMMUNOGENICITY TESTING FOR VACCINES – LIVE ATTENUATED VIRUS VACCINE

The activity to be supported under this contract is the testing of a live virus vaccine, such as Modified Vaccinia Ankara (MVA), as required prior to initial clinical evaluation and for continued clinical development in special populations. This includes testing candidate products for safety and immunogenicity (both cellular and humoral).

[NOTE #1 to Offerors: Include all testing required for an IND and for advanced clinical development (Phase II trials and including special populations) for this type of product. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Government will provide the test vaccine.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not, may propose to do the studies but should clearly indicate that the work cannot be performed according to GLP. The Offeror should clearly identify the types of animal(s) that will be used in each study.]

1. Specifically, the contractor shall perform all tests to qualify a vaccine product for human administration including but not limited to the list below. Such testing must also include all tests required for Investigational New Drug (IND) and Masterfile submissions. In addition, include all testing that will be necessary to expand clinical development to special populations. All studies must be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58).

a. Preclinical immunogenicity evaluation: The preclinical studies shall be designed to assess the immune response including seroconversion rates, antibody levels, and cell mediated immune responses in vaccinated animals. Studies should also be designed to establish a model for determining potency.

b. Preclinical safety evaluations may include but are not limited to the following:

1) Systemic toxicity: Preclinical studies shall include dose-ranging and dose escalation studies of systemic toxicity as well as toxicity to potential target organs including hematopoietic and immune systems.
2) Local reactogenicity: Local site reactivity studies to include detailed clinical observations and histological evaluations of tissue of the injection site or other visible lesions from biopsies or term necropsy samples.
3) All other safety tests as may be required for a particular vaccine type and for advanced clinical development, such as genetic toxicity, tumorigenicity, and reproductive toxicity studies.

4. Provide all data, information, and records required to support regulatory filings to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

5. Complete all tasks as outlined in the “General Statement of Work” for “In Vitro and Animal Models for Emerging Diseases and Biodefense.”

STATEMENT OF WORK
PART F (1)
SAFETY/TOXICOLOGY AND PHARMACOLOGY TESTING FOR THERAPEUTICS

The activity to be supported under this contract is providing pharmacokinetics and safety data for various FDA-approved antibiotics that will be tested for activity against plague and/or anthrax in small animal and/or non-human primate models.

[NOTE #1 to Offerors: Include all testing required to support efficacy studies in animal models . This information will support labeling of these drugs for plague and/or anthrax treatment. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Offeror should obtain USP drugs from a pharmacy and include information about the source in the proposal.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not, may propose to do the studies but should clearly indicate that the work cannot be performed according to GLP.

Offerors may propose studies in small animal models, non-human primates, or both. The proposal should clearly indicate exactly what work is proposed.]

1. Specifically, the contractor shall perform all tests to determine the pharmacokinetics of the antibiotics listed below after a single parenteral administration in mice and rabbits. Such testing shall be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) where possible. Antibiotics to be tested include: gentamicin, doxycycline, ciprofloxacin, levofloxacin, ceftriaxone, amoxicillin, amoxicillin clavulanate, azithromycin, and clarithromycin.

2. Perform all tests to determine the pharmacokinetics of the antibiotics after a single parenteral administration in non-human primates as listed below. Such testing shall be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) where possible. Antibiotics to be tested include:

a. gentamicin, doxycycline, ciprofloxacin, levofloxacin, and ceftriaxone in African green monkeys
b. amoxicillin, amoxicillin clavulanate, azithromycin, clarithromycin, levofloxacin, and ciprofloxacin in rhesus and cynomolgus macaques.

3. Perform such safety studies as may be deemed necessary to support use of these antibiotics (listed above) in efficacy studies in mice, rabbits, and/or non-human primates. Safety/toxicity studies should be based on a review of available literature.

4. Provide all data, information, and records required to support labeling to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

5. Complete all tasks as outlined in the “General Statement of Work” for “In Vitro and Animal Models for Emerging Diseases and Biodefense.”

Notes To Offerors Organized by RFP Part
In Vitro and Animal Models for Emerging Diseases and Biodefense
DMID-03-39
General Statement of Work for All Parts

[NOTE #1 TO ALL OFFERORS: Offerors that receive awards for more than one Part will be eligible for Minimum Awards for each Part. Offerors that receive awards for models of more than one organism or more than one model Parts A, C or D will be eligible for a single minimum award for that part. It is anticipated that the maximum total funding under this Contract will be between $25 - 40 million per year. When a need is established for any of the products or services under this Contract, a Task Order will be submitted to one or more Contractor(s) qualified under that Part. Contractor(s) will submit a detailed proposal with milestones to perform the work stated in the Task Order together with a detailed budget proposal within 30 calendar days. Resulting awards will include specifics on deliverables and reports.]

[NOTE #2 TO ALL OFFERORS: Because the Parts A - F of this solicitation are not highly related, single institutions may not have the expertise and facilities required to perform all requirements in the Statement of Work. Thus it is acceptable for an Offeror to submit a proposal for Part A, B, C, D, E, or F or any combination of the six. See evaluation criteria. Each Part will be independently evaluated so that the Offeror will only be evaluated based on the specific Part(s) for which it applies. Lack of expertise in one Part will not affect the evaluation of other Parts.

Separate review committees will likely be involved in the review of Parts A - F. Therefore, responses should be packaged as separate, stand-alone entities for each Part.

If the Offeror wishes to include in his/her proposal Parts or specific tasks for which he/she does not have direct expertise, then Offeror may propose a subcontract in order to fulfill the requirements of activities in Parts A - F. The Contractor shall be directly responsible for all work performed under this contract, including work done by any subcontractor. If a subcontractor is proposed, similar technical information should be provided as part of the proposal as that required of the Contractor, i.e., technical approach, methods, experience, personnel qualifications, facilities, resources, etc., and cost details should also be provided by the subcontractor.

In responding to this RFP, Offerors should describe in detail the responsibilities and level of effort of all proposed personnel who will be assigned to the contract. In addition, Offerors should describe an administrative framework showing clear lines of authority.

Documentation should be provided on the qualifications, experience, education, competence, and availability of the Principal Investigator, Research, Technical and Administrative Support staff; the extent to which outside consultants shall be used as well as assurance of their availability. If a subcontractor is proposed, similar technical information should also be provided as part of the Technical Proposal. Proposed subcontractors should also provide cost details.

Technical proposals must describe specifically how the Offeror will fulfill each of the items in the Statement of Work below. The technical proposal should include:

* qualifications, experience, education, competence, availability, and specific assignment of each proposed member of the research team (include resumes/CVs); how they will interact regarding lines of authority (provide an administrative framework in flow chart format); the decision-making authority of the Principal Investigator in relation to the rest of the organization
* specific levels of effort proposed for each individual (hours/percentages of time) and availability in relation to other commitments
* procedures for initiation of this contract's projects in a timely manner (describe how other projects in general are prioritized within their organization and the level of priority this contract will receive)

* all instrumentation, equipment, and laboratory space to be used to fulfill the work requirements (indicate what equipment and resources are under the control of the Principal Investigator and which are to be shared; if shared, indicate who is responsible for controlling access and how determination of priority usage is made). Indicate specifically which space, equipment, resources are to be used in completion of the proposed work. Documentation of BSL3/4 certification should be provided.
* documentation of access to animals as required by the statement of work; documentation of AALAC-accreditation.

[NOTE #3 TO ALL OFFERORS] The handling and transportation of all reagents and government-owned property under this contract should be in accordance with all applicable local, state, and federal regulations including health and safety standards.

(See the attached HHS Safety and Health clause, the Safety Controls and Standards and item #4 of the General Work Statement.)

[NOTE #4 TO ALL OFFERORS: The Offeror should propose a plan for data management, analysis, and electronic digital communication with the Project Officer. Communications should include the ability to transmit and receive electronic mail with the Division of Microbiology and Infectious Diseases (DMID) computer network system. The Government will not authorize purchase of stand-alone computers under this contract for this purpose. The NIAID is connected to the Internet and uses IBM-compatible computer hardware for data management and communications. The Offeror should supply an IBM-compatible computer and should submit electronic reports in Microsoft Word^{tm} for Windows and Microsoft Excel^{tm} for Windows. In the Technical Proposal, please list and describe existing computer hardware and software resources available to or planned to be specifically dedicated this project. For the purpose of preparing a cost proposal, assume 1 visit of one key personnel per study to Bethesda MD to meet with the Project Officer and other key DMID personnel.]

[NOTE #5 TO ALL OFFERORS: Data, Data Rights, Copyrights, Confidentiality of Information, Publication, Patents -- The information required by the Government will be obtained through the required contract reports. The original data shall remain with the Contractor and shall be subject to certain contract clauses. HHSAR clause 352.224-70 Confidentiality of Information (April 1984), HHSAR clause 352.270-6 Publications and Publicity (July 1991), FAR clause 52.227-11 Patent Rights - Retention by the Contractor (Short Form) (June 1997) and FAR clause 52.227-14 Rights in Data - General (June 1987) will be incorporated by reference (or in full text) into any resultant contract. Most of the data provided to or generated by the Contractor shall require confidential treatment. It is not anticipated that this contract will result in the award of a patent to the Contractor. In addition, the Government may require the use of Screening Agreements or Material Transfer Agreements between the NIAID and providers of compounds in order to protect the intellectual property rights of third party compound suppliers. A sample DMID Screening Agreement is provided with this solicitation and shall be included in any resultant contract as a means of informing potential Offerors and Contractors.]

[NOTE #6 TO ALL OFFERORS: PLANNED DEVIATIONS TO REQUIRED GENERAL CONTRACT CLAUSES FAR 52.227-11 AND FAR 52.227-14 The NIAID plans to seek a deviation from FAR clause 52.227-11, Patent Rights-Retention by the Contractor (Short Form) (June 1989). Pursuant to a Determination of Exceptional Circumstances (DEC) as required by FAR 27.303, the NIAID plans to modify clause at FAR 52.227-11, Patent Rights-Retention by the Contractor (Short Form) (June 1989) to restrict the contractor's rights to subject inventions arising under the contract. Specifically, the contractor will be required to assign to the Government or, if deemed appropriate by the NIAID and subject to certain rights reserved to the Government, to a collaborating party designated by the Government the entire right, title and interest throughout the world to each subject invention, except to the extent that rights are retained by the Contractor under the Greater Rights Determination provision of the clause. The contractor may request greater rights to an identified invention, and the NIH will consider whether granting the requested rights will interfere with rights of the Government or any collaborating party or otherwise impede the ability of the Government or others to develop new candidates for therapies, disease prevention and diagnosis as well as potential enabling technologies that may result from data ensuing from evaluations performed under this contract useful for antimicrobial discovery and development. Contractors are encouraged to request greater rights where inventions relate to technology outside NIAID's program and where the contractor has negotiated with a supplier of a proprietary composition for the disposition of patent rights concerning a subject invention related to the composition.

Furthermore, the timing of data publication will need to be restricted to allow adequate time for patent applications to be filed on inventions arising from the contracts. This would be accomplished by a deviation from FAR clause 52.227-14, Rights in Data-General (June 1987). Specifically, although NIAID encourages the publication of articles on research results, FAR 52.227-14 Rights in Data-General (June 1987) will be narrowly modified to restrict the Contractor's right to use, release to others, reproduce, distribute, and publish data produced or used by the contractor in the performance of this contractor allow adequate time for the filing of patent applications and to protect data that will be submitted as part of a regulatory filing. NIAID will reserve the right to coordinate the timing of data publication so that appropriate domestic and international invention applications may be filed as appropriate.

Because these clause deviations are not yet approved, their text is not available for publication. However, it is NIAID's intention that the finalized versions of the deviated FAR clauses will be available before award of any contract resulting from this initiative. Instead, the aforementioned description of how these clause deviations will be practiced under the resultant contract is provided. Potential Offerors are afforded an opportunity to comment on their understanding of what NIAID is planning and to identify what impact these deviations may have on their conduct of the work should they be awarded a contract. Responses should be provided, in writing, to the Point of Contact for this RFP. See the bottom of the front page of this RFP for this individual's name and contact information. Comments should be provided within 30 days of the issue date of this RFP. Thereafter, NIAID will consider this input and determine whether alternative courses of action may be necessary. Decisions regarding these deviations will be made in consideration of the success of this NIAID requirement.]

[NOTE #7 TO ALL OFFERORS: A copy of the applicable Biosafety guidelines can be obtained from NIAID upon request. These guidelines will apply to all animal models, which may apply to this RFC. The experience of the Offeror in working with potential biohazards such as viruses and animals, as well as toxic chemicals and radioisotopes should be addressed. The Offeror shall include a Safety and Health Plan for compliance with Biosafety Level 3/4 guidelines in the Technical proposal and include a summary of the Offertory's safety and health operating procedures manual. The Offeror should also include in his/her proposal a summary of contingency plans in the case of accidental exposure to an infectious agent. The summary should include plans and timelines for reporting to the safety officer, evacuation of exposed personnel, and decontamination procedures. In addition, procedures for the care of experimental animals should be discussed if animal use is proposed.

The DHHS Safety and Health Clause (Jan 2001) 352.223-70 and the Safety Controls and Standards (attached) will become part of any resultant contract. Written documentation from a Biosafety Officer (or equivalent) should be provided (e.g., a safety management program) to assure compliance with all safety guidelines and regulations, training and monitoring of personnel for exposure to infectious or hazardous reagents, and safe disposal of such agents.]

PART A: IN VITRO SCREENS FOR ANTIMICROBIAL ACTIVITY

[NOTE A-1 TO OFFEROR: It is expected that 500 experimental antimicrobial substances will be evaluated annually. The Project Officer will provide the substances, which will come from NIAID's acquisition and coordination facility (contract N01-AI-95364, Southern Research Institute), NIAID staff contacts with drug sponsors, and contractors' contacts with drug sponsors. These substances may be irritating, toxic, and/or potentially carcinogenic or hazardous.

The Offeror shall provide validated screening systems for all of the designated bacteria selected. Methods of screening shall be appropriate for the assessment of the efficacy and toxicity of potential therapeutic and/or prevention approaches against the proposed bacteria. Assays can be manual or automatic format. Offerors shall justify the choice of method(s) proposed.

[NOTE A-2 TO OFFEROR: More detailed testing will generally be required when the initial screening shows that a substance has a substantial level of activity. The technical proposal shall describe preliminary screening procedures, the criteria used to select compounds recommended for further evaluation, and procedures for the special studies. Offerors may propose subcontractors for special studies.

Each special study will have distinctive evaluation needs; thus, the Project Officer will designate specific assays after consultation with the Contractors. As requested by the Project Officer, assays pertinent to special studies shall be designed, developed, compared to existing assays, standardized, validated and performed, as necessary. The Offeror should include documentation of qualifications, expertise, and strategies to modify systems or develop new systems for such studies.]

[NOTE #A-2 TO OFFEROR: Stocks of bacterial pathogens of BioDefense will be transferred to the contractor through the Project Officer. As part of the proposal, the Offeror shall provide an outline of typical operating procedures to identify and maintain primary stocks and working stocks of bacterial pathogens and to prepare cultures for testing. This shall include description of a timetable for when and how often new working stocks and cultures for testing are prepared. Quality control procedures to assure and track viability, purity and identity of bacterial pathogens shall be described in the proposal. The Offeror shall list all appropriate NCCLS standards for preparing cultures of reference/quality control strains for testing. Where no specific NCCLS standards are available, the Offeror shall describe which standards will be employed and provide a rationale for this selection. The Offeror shall provide discussion of any problems or issues anticipated for the use of strains of select agents for testing. As part of the cost proposal, assume that stocks of up to 10 aliquots of each pathogen strain shall be maintained by the contractor, that strain identity shall be determined upon receipt and when strains are used for testing. Assume that about 20 selected strains will be provided by the Project Officer for storage and use. Furthermore, assume that quality control assessment for working stocks shall be performed only when strains are used for testing.]

[NOTE #A-3 TO OFFEROR: As part of the proposal, the Offeror shall describe, as a sample protocol, typical standard operating procedures for conducting growth inhibition assays. This sample protocol may not be the final protocol employed for testing but will serve as a means to evaluate the proposal. This protocol shall also include examples of documentation that will be provided for each test, description of quality control assurance and expected performance of quality control standards. The Offeror shall describe limits for acceptable and unacceptable control performance. The Offeror shall list all appropriate NCCLS standards for MIC determination for bacterial pathogens listed in the CDC agents of BioDefense and for quality control strains. Where no specific NCCLS standards are available, the Offeror shall describe which standards will be employed and provide a rationale for this selection. The Offeror shall also provide discussion of any problems or issues anticipated for the use of strains of select agents for testing. The Offeror is to assume that test agents will be provided by NIAID while provision of control antibiotics and non-bioterrorism reference/control strains will be the responsibility of the contractor.]

PART B: CLINICAL ISOLATE PANELS FOR SELECTED BACTERIAL PATHOGENS

[NOTE #B-1 TO OFFEROR: Stocks of clinical isolates of relevant bacterial pathogens will be transferred to the contractor through the Project Officer. As part of the proposal, the Offeror shall provide an outline of typical operating procedures to identify and maintain primary stocks and working stocks of bacterial pathogens and to prepare cultures for testing. This shall include description of a timetable for when and how often new working stocks and cultures for testing are prepared. Quality control procedures to assure and track viability, purity and identity of bacterial pathogens shall be described in the proposal. The Offeror shall list all appropriate NCCLS standards, where available, for preparing cultures of reference, clinical and quality control strains for testing. The Offeror shall provide discussion of any problems or issues anticipated for the use of clinical strains of select agents for testing. As part of the cost proposal, assume that stocks of up to 10 aliquots of each pathogen strain shall be maintained by the contractor, that strain identity shall be determined upon receipt and when strains are used for testing. Assume that about 200 strains of selected clinical and reference strains will be provided by the Project Officer for storage and use. Furthermore, assume that quality control assessment for working stocks shall be performed only when strains are used for testing.]

[NOTE #B-2 TO OFFEROR: As part of the proposal, the Offeror shall describe, as a sample protocol, typical standard operating procedures for conducting MIC50 and MIC90 evaluations, as well as tentative breakpoint determinations. This sample protocol may not be the final protocol employed for testing but will serve as a means to evaluate the proposal. This protocol shall also include examples of documentation that will be provided for each test, description of quality control assurance and expected performance of quality control standards. The Offeror shall describe limits for acceptable and unacceptable control performance. The Offeror shall also provide discussion of any problems or issues anticipated for the use of clinical strains of select agents for testing. The Offeror shall provide, as part of the cost proposal, a cost estimate for MIC50 and MIC90 determinations for one test agent against 20 clinical strains, one reference/quality control strain with 2 control antibiotics. The Offeror is to assume that test agents will be provided by NIAID while provision of control antibiotics and non-bioterrorism reference/control strains will be the responsibility of the contractor. The Offeror shall describe how many test agents and bacterial strains can be maximally evaluated per unit time (week or month) and per FTE. It is estimated that about 20 test products will be evaluated against about 200 clinical strains of bacterial pathogens per year (this number is an estimate and may be exceeded).]

[NOTE #B-3 TO OFFEROR: The Offeror shall provide documentation as to his/her expertise in working with pathogenic bacterial pathogens, as well as potentially hazardous or toxic chemicals. The Offeror shall include in the proposal a Safety and Health Plan for compliance with Biosafety Level 2/3 guidelines and shall include a summary of the Offeror's safety and health operating procedures manual.]

PART C: SMALL ANIMAL MODELS FOR SELECTED PATHOGENS INCLUDING GLP STUDIES

[NOTE C-1 TO OFFEROR: The purpose of this solicitation is to obtain animal model systems to evaluate the clinical potential of experimental agents and to facilitate the entry of these agents into human clinical trials. The model system(s) employed should have features similar to the corresponding infection in humans and these should be described. The pathologic and immunologic aspects of the model in association with infection should be discussed in detail and relate to the ability to use this model to predict clinical effectiveness of experimental agents. If a non-infection model is proposed the Offeror should explain in detail why the model is suitable. The infectious agent should be either a human infectious agent or an animal agent with considerable homology to the comparable bioterrorism agent. Background, history and available data that correlate with data produced by the model with regard to comparison with human disease/protection should be provided.

Documentation of availability of animals and animal holding space must be included. Offerors should have capacity to house a minimum of 1000 rodents and/or 200 large animals concurrently; capacity in excess of this requirement is strongly suggested, and may be through documented access of off-site facilities or subcontracts. Capability to perform aerosol challenge studies should be included.

For the purposes of providing a cost proposal, Offeror(s) shall provide a detailed budget based on the development and validation of one rodent model and one large animal model. Include documentation for personnel costs and all specific animal, supply, and equipment costs.]

[NOTE C-2 TO OFFEROR: Documentation of assays to monitor the effect of the study agent on the disease process shall be provided. The Offeror should describe in detail his/her technical approach for evaluating therapies by providing a sample protocol. This protocol should include a description of the experimental design (sequence in which various types of studies will be carried out, number of arms per study, number of animals per group, number of doses to be explored, potential routes

of administration, controls, etc.) and a description of the methods to be used to carry out evaluations; to quality assure/control test agents and to analyze the data. A rationale for the design should be included, based on statistical considerations. A discussion of the logistical problems associated with the implementation of the protocol should be provided. A schedule showing the time required to analyze a therapeutic agent should be provided with an estimate of the total number of agents that could be examined at one time. Schedules will provide for acquisition of study animals, animal protocol preparation, review and approval, study execution, data analysis, draft report preparation, review of draft reports by the NIAID Project Officer and final report preparation.

Some but not all studies will require that they be conducted in accordance with Good Laboratory Practices (GLP). For example, proof of concept or pilot studies will not require GLP, while some studies submitted under the FDA's proposed "animal rule" may. Thus, Offerors should provide documentation of their experience conducting GLP studies. If available, Offerors should provide examples of recent studies that have been presented to the FDA.

It is understood that some Offerors may propose evaluations of therapeutics or vaccines, or both. For purposes of the cost proposal, each Offeror should include a protocol for non-GLP evaluation of a recombinant protein vaccine (such as rPA for anthrax) and/or a protocol to evaluate a new antibiotic (injectible form). Include documentation for personnel costs and all specific animal, supply, assay, and equipment costs. Offerors with the capacity to perform studies under GLP should separately provide costs for the same study(ies) done according to GLP.

The capability to conduct pharmacokinetic studies, safety, and toxicology evaluation is not a requirement, but may be included in the proposal; this should not be included in the budget. It is anticipated that the experimental therapeutic agents will include conventional organic chemical molecules and some biological therapies such as nucleic acids, antibodies, or proteins. Vaccine candidates may come from each of the four general vaccine Categories. Test Article acquisition usually results from NIAID staff contact with drug sponsors, Contractor contacts with drug sponsors, and from identification of in vitro activity in NIAID screening facilities. These agents may be irritating, toxic, and/or potentially carcinogenic or hazardous.]

[NOTE C-3 TO OFFEROR: These studies may include the characterization and definition of the model system in terms of the disease pathogenesis and host response. Delineation of the role of agent gene expression and replication, agent and host strain differences, and the significance of agent resistance may be included in these studies.]

[NOTE C-4 TO OFFEROR: The final "animal rule" is available at: http://www.fda.gov/cber/rules/humeffic.pdf]

PART D: NON-HUMAN PRIMATE MODELS FOR SELECTED PATHOGENS, INCLUDING GLP STUDIES

[NOTE D-1 TO OFFEROR: The purpose of this solicitation is to obtain animal model systems to evaluate the clinical potential of experimental agents and to facilitate the entry of these agents into human clinical trials. The model system(s) employed should have features similar to the corresponding infection in humans and these should be described. The pathologic and immunologic aspects of the model in association with infection should be discussed in detail and relate to the ability to use this model to predict clinical effectiveness of experimental agents. If a non-infection model is proposed the Offeror should explain in detail why the model is suitable. The infectious agent should be either a human infectious agent or an animal agent with considerable homology to the comparable bioterrorism agent.

Documentation of availability of animals and animal holding space must be included. Offerors should have capacity to house a minimum of 70 animals/year; larger capacity should be proposed if possible.]

[NOTE D-2 TO OFFEROR: Documentation of assays to monitor the effect of the study agent on infection and/or the disease process should be provided. The Offeror should describe in detail his/her technical approach for evaluating the test agent (therapeutic, vaccine, antibody, etc.) by providing a sample protocol. This protocol should include a description of the experimental design (sequence in which various types/parts of studies will be carried out, number of arms per study, number of animals per group, number of doses/schedules to be explored, potential routes of administration, etc.) and a description of the methods and assays to be used to carry out evaluations, to quality assure/control test agents, and to analyze the data. A rationale for the design should be included, based on statistical considerations. A discussion of the logistical problems associated with the implementation of the protocol and proposed alternatives should be provided. A schedule showing the time required to analyze a therapeutic agent and/or vaccine should be provided with an estimate of the total number of agents that could be examined at one time. Documentation of availability of animals for these evaluations should be included.

Some but not all studies will require that they be conducted in accordance with Good Laboratory Practices (GLP). For example, proof of concept studies will not require GLP, while some studies submitted under the FDA's proposed "animal

rule" may. Thus, Offerors should clearly indicate their experience conducting GLP studies. If available, Offerors should provide examples of recent studies that have been presented to the FDA.

It is understood that some Offerors may propose evaluations of therapeutics or vaccines, or both. For purposes of the cost proposal, each Offeror should include a protocol for non-GLP evaluation of a recombinant protein vaccine (such as rPA for anthrax) and/or a protocol to evaluate a new antibiotic (injectible form). Include documentation for personnel costs and all specific animal, supply, assay, and equipment costs. Offerors with the capacity to perform studies under GLP should separately provide costs for the same study(ies) done according to GLP.

The capability to conduct pharmacokinetic studies, safety, immunogenicity, and toxicology evaluation is not a requirement but may be included in the proposal; this should not be included in the budget. It is anticipated that the experimental therapeutic agents will include conventional organic chemical molecules and some biological therapies such as nucleic acids, antibodies, or proteins. Vaccine candidates may come from each of the four general vaccine Categories. Agent acquisition usually results from NIAID staff contacts with drug sponsors, Contractor contacts with drug sponsors, and from identification of in vitro activity in NIAID screening facilities. These agents may be irritating, toxic, and/or potentially carcinogenic or hazardous.]

[NOTE D-3 TO OFFERORS: These studies may include the characterization and definition of the model system in terms of the disease pathogenesis and host response. Delineation of the role of agent gene expression and replication, agent and host strain differences, and the significance of agent resistance may be included in these studies. Offerors should provide examples of previous model development activities.]

[NOTE D-4 TO ALL OFFERORS: The final "animal rule" is available at: http://www.fda.gov/cber/rules/humeffic.pdf]

PART E: SAFETY AND IMMUNOGENICITY TESTING for VACCINES

[NOTE #E-1 TO OFFERORS: Documentation of experience in preclinical safety and evaluation of immune response testing should be provided. It is anticipated that the contractor will have the capacity to perform testing for each type of vaccine candidate covered by this contract, including each of the four general vaccine Categories. Offeror should outline in detail the tests and procedures it will use to qualify each type of vaccine product for human administration. Provide an appropriate model for determining the cellular and humoral immunogenicity of vaccine in small animals and, if necessary, in non-human primates. Offeror(s) should provide documentation of models/protocols that have been used successfully in previous investigations. Offeror(s) may propose subcontracts for any specific testing procedure (e.g., primate studies). Documentation of available equipment and access to an AAALAC-accredited (or equivalent) animal facility and the capacity for testing the safety and immunogenicity of products should be included.

For the purposes of providing a cost proposal, Offeror(s) should provide a detailed budget based on the preclinical safety and immunogenicity evaluation of one recombinant protein vaccine product. Assume that tumorigenicity and reproductive toxicity studies are not required for the cost estimate. Include documentation for personnel costs and all specific animal, supply, and equipment costs.]

[NOTE #E-2 TO OFFERORS. Specific requirements listed in the Statement of Work are not meant to limit the scope or specifics of preclinical vaccine testing. Such testing will include all of the tests required to qualify a vaccine product for human administration.]

[NOTE #E-3 TO OFFERORS. In addition to the CFR, the FDA also provides "Points to Consider" (PTC) Documents. Testing should be conducted consistent with these guidelines. Examples of relevant guidelines include:
a) Points to consider in the Production and Testing of New Drugs and Biologicals
Produced by Recombinant DNA Technology (4/10/85). Supplement (4/6/92).
b) Points to Consider in Human Somatic Cell Therapy and Gene Therapy (8/29/91).
c) Points to Consider in the Characterization of Cell Lines Used to Produce
Biologicals (7/12/93).
d) Points to Consider for Plasmid DNA Vaccines for Preventive Infectious Disease Indications (10/96)

These documents, as well as additional guidelines relating to testing and manufacture, are available from the Division of Congressional and Public Affairs. To receive copies call 888-223-7329 then dial 999 to get a list of documents and their number. Consumer information number is 301-827-2000. On the Internet go to www.cber.fda.gov.]

PART F: SAFETY/TOXICOLOGY AND PHARMACOLOGY TESTING for THERAPEUTICS

[NOTE #F-1 TO OFFERORS: Documentation of experience in preclinical toxicology and pharmacology testing should be provided. It is anticipated that 'therapies' will mainly be conventional organic chemical molecules. However, it is likely that some non-chemical (biological) therapies such as nucleic acids, antibodies, or proteins also will be studied. The Offeror should clearly describe their experience evaluating either or both conventional organic chemical molecules or/and biological therapies (e.g. nucleic acid plasmids, antibodies, or proteins). The Offeror should include any experience conducting GLP toxicology and pharmacokinetic studies using these biological therapeutics.

Documentation of available equipment and access to an AAALAC-accredited (or equivalent) animal facility and the capacity for testing the toxicology and pharmacology of products should be included.

Although every effort will be made by the NIAID to provide analytical methods for the detection of experimental therapeutics for use in the pharmacokinetic portion of these and other protocols, there may be instances where this information will not be available. In those cases, it is expected that the Contractor will have the ability to develop these techniques or modify existing literature techniques using their own internal chemistry support resources.

For the purposes of providing a cost proposal, Offeror(s) should provide a detailed budget based on the preclinical safety and pharmacology/pharmacodynamic of one drug (new small molecular entity) and one biological product including tumerogenicity. Assume that reproductive toxicity studies are not required and that analytical methods will be provided by NIAID. Include documentation for personnel costs and all specific animal, supply, and equipment costs.]

[NOTE #F-2 TO OFFERORS. Specific requirements listed in the Statement of Work are not meant to limit the scope or specifics of preclinical testing for therapeutics or other test articles. Such testing will include all of the tests required to qualify a therapeutic product for human administration.]

[NOTE #F-3 TO OFFERORS. In addition to the CFR, the FDA also provides “Points to Consider” (PTC) Documents. Testing should be conducted consistent with these guidelines. These documents, as well as additional guidelines relating to testing and manufacture, are available from the Division of Congressional and Public Affairs. To receive copies call 888-223-7329 then dial 999 to get a list of documents and their number. Consumer information number is 301-827-2000. On the Internet go to www.cber.fda.gov. or www.fda.gov/cder]

[NOTE #F-4 TO OFFERORS: The FDA has not published specific protocols to be used for determining immunotoxicity of anti-infective agents, nor for the in vitro determination of metabolic potential. Therefore the Offeror should provide sample protocols, including rationale for use that might be utilized in such studies, and document experience in routinely conducting and evaluating these studies on anti-infective therapies. Sufficient detail should be provided to permit evaluation of experience, expertise, and competence in routine use of these protocols.]

Reporting Requirements and Deliverables
In Vitro and Animal Models for Emerging Diseases and Biodefense
RFP DMID-03-39

In addition to those reports required by the Statement of Work and other terms of this Contract the Contractor shall prepare and submit the following reports in the manner stated below. Reports will be required for Contractors with active Task Orders throughout the period of work.

Milestone Reports (each task order will include guidelines for milestone reports).
Upon the completion of each milestone as indicated in the Task Order, the Contractor shall submit three (3) copies of a milestone report as described below. Two (2) copies should be submitted to the Project Officer and one (1) copy to the Contracting Officer. The milestone report should be factual and concise and consist of the following:

1) A title page containing:
a. Contract number and title
b. Sequence of report; e.g., "Year 1, 2nd Milestone Report"
c. Period of performance being reported
d. Contractor's name and address
e. Date of submission

2) Reports shall include, but are not limited to the following information:
a. A report detailing the actions taken to achieve the milestone.
b. A report listing all specifics about the tests/studies as outlined in the Task Order.
c. Graphs and tables of primary, and summarized data obtained.
d. Description of any current technical or substantive technical or performance problems encountered, along with proposed corrective action.
e.Financial information as outlined in the task
f.Other information as may be required by the Project Officer.

II. Final Report
At the end of each Task, the contractor shall submit three (3) copies of the final report documents, two (2) copies to the Project Officer and one (1) copy to the Contracting Officer, which will summarize the results of the entire contract work for the complete performance period. This report will be in sufficient detail to explain comprehensively the results achieved and will be submitted no later than the completion date of the Task Order. The final report shall contain:

1) Title Page as described above in paragraph I.1)
2) Introduction covering the purpose and scope of the contract effort.
3) Description of the overall progress, plus a separate description of each protocol, assay, and subcontract employed and modifications and performance on the contract during the period of performance. Descriptions will include pertinent primary and summarized data in tables or graphs as appropriate to present significant results achieved, conclusions resulting from analysis, and a scientific evaluation of the data accrued under the contract.
4) A cumulative list of all studies and test products tested to date, including number of bacterial strains tested, and dates for beginning and completion of studies.
5) Copies of any abstracts, manuscripts, and publications.
6) A cumulative listing of all publications.

III. Other Deliverables.

1) The Contractor shall deliver to the Government or its designee by the completion date of the Task Order, the following items:
   a. All data obtained from contract studies.
   b. All test products remaining from these studies.
   c. Other deliverables as may be outlined in the Task Order

PART I - THE SCHEDULE

SECTIONS B - H -- UNIFORM CONTRACT FORMAT - GENERAL

A Sample Uniform Contract Format may be found at the following website:

http://www4.od.nih.gov/ocm/contracts/rfps/sampkt.htm

[Disregard SECTION I and J of this sample. Those SECTIONS have been incorporated as part of this RFP.]

PART II – CONTRACT CLAUSES

SECTION I - CONTRACT CLAUSES

THE FOLLOWING PAGES CONTAIN A LISTING(S) OF GENERAL CLAUSES WHICH WILL BE APPLICABLE TO MOST CONTRACTS RESULTING FROM THIS RFP. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR(S) WILL DETERMINE THE SPECIFIC GENERAL CLAUSES LISTING TO BE CONTAINED IN THE CONTRACT(S) AWARDED FROM THIS RFP.

ARTICLE I.1. GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT – FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

This contract incorporates the following clauses 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. Also, the full text of a clause may be accessed electronically at this URL: http://www.arnet.gov/far/.

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

FAR Clause No.	Date	Title
52.202-1	Dec 2001	Definitions
52.203-3	Apr 1984	Gratuities (Over $100,000)
52.203-5	Apr 1984	Covenant Against Contingent Fees (Over $100,000)
52.203-6	Jul 1995	Covenant Against Contingent Fees (Over $100,000)
52.203-7	Jul 1995	Anti-Kickback Procedures (Over $100,000)
52.203-8	Jan 1997	Cancellation, Rescission, and Recovery of Funds for Illegal or Improper Activity (Over $100,000)
52.203-10	Jan 1997	Price or Fee Adjustment for Illegal or Improper Activity (Over $100,000)
52.203-12	Jun 1997	Limitation on Payments to Influence Certain Federal Transactions (Over $100,000)
52.204-4	Aug 2000	Printing/Copying Double-Sided on Recycled Paper (Over $100,000)
52.209-6	Jul 1995	Protecting the Governments Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment (Over $25,000)
52.215-2	Jun 1999	Audit and Records - Negotiation (Over $100,000)
52.215-8	Oct 1997	Order of Precedence – Uniform Contract Format
52.215-10	Oct 1997	Price Reduction for Defective Cost or Pricing Data
52.215-12	Oct 1997	Subcontractor Cost or Pricing Data (Over $500,000)
52.215-14	Oct 1997	Integrity of Unit Prices (Over $100,000)
52.215-15	Dec 1998	Pension Adjustments and Asset Reversions
52.215-18	Oct 1997	Reversion or Adjustment of Plans for Post-Retirement Benefits (PRB) Other Than Pensions

52.215-19	Oct 1997	Notification of Ownership Changes
52.215-21	Oct 1997	Requirements for Cost or Pricing Data or Information Other Than Cost or Pricing Data - Modifications
52.216-7	Feb 2002	Allowable Cost and Payment
52.216-8	Mar 1997	Fixed Fee
52.219-8	Oct 2000	Utilization of Small Business Concerns (Over $100,000)
52.219-9	Jan 2002	Small Business Subcontracting Plan (Over $500,000)
52.219-16	Jan 1999	Liquidated Damages - Subcontracting Plan (Over $500,000)
52.222-2	Jul 1990	Payment for Overtime Premium (Over $100,000) (NOTE: The dollar amount in paragraph (a) of this clause is $0 unless otherwise specified in the contract.)
52.222-3	Aug 1996	Convict Labor
52.222-26	Apr 2002	Equal Opportunity
52.222-35	Dec 2001	Equal Opportunity for Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans
52.222-36	Jun 1998	Affirmative Action for Workers with Disabilities
52.222-37	Dec 2001	Employment Reports on Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans
52.223-3	Jan 1997	Hazardous Material Identification and Material Safety Data, Alternate I (Jul 1995)
52.223-6	May 2001	Drug-Free Workplace
52.223-14	Oct 2000	Toxic Chemical Release Reporting
52.225-1	May 2002	Buy American Act - Supplies
52.225-13	Jul 2000	Restrictions on Certain Foreign Purchases
52.227-1	Jul 1995	Authorization and Consent, Alternate I (Apr 1984)
52.227-2	Aug 1996	Notice and Assistance Regarding Patent and Copyright Infringement (Over $100,000)
52.227-11	Jun 1997	Patent Rights - Retention by the Contractor (Short Form) (NOTE: In accordance with FAR 27.303 (a) (2), paragraph (f) is modified to include the requirements in FAR 27.303 (a) (2) (i) through (iv). The frequency of reporting in (i) is annual.
52.227-14	Jun 1987	Rights in Data – General
52-232-9	Apr 1984	Limitation on Withholding of Payments
52.232-17	Jun 1996	Interest (Over $100,000)
52.232-20	Apr 1984	Limitation of Cost
52.232-23	Jan 1986	Assignment of Claims
52.232-25	Feb 2002	Prompt Payment

52.232-34	May 1999	Payment by Electronic Funds Transfer--Other Than Central Contractor Registration
52.233-1	Dec 1998	Disputes
52.233-3	Aug 1996	Protest After Award
52.242-1	Apr 1984	Notice of Intent to Disallow Costs
52.242-3	May 2001	Penalties for Unallowable Costs (Over $500,000)
52.242-4	Jan 1997	Certification of Final Indirect Costs
52.242-13	Jul 1995	Bankruptcy (Over $100,000)
52.243-2	Aug 1987	Changes - Cost Reimbursement, Alternate V (Apr 1984)
52.244-2	Aug 1998	Subcontracts, Alternate II (Aug 1998) *If written consent to subcontract is required, the identified subcontracts are listed in ARTICLE B., Advance Understandings.
52.244-5	Dec 1996	Competition in Subcontracting (Over $100,000)
52.245-5	Jan 1986	Government Property (Cost-Reimbursement, Time and Material, or Labor Hour Contract)
52.246-23	Feb 1997	Limitation of Liability (Over $100,000)
52.249-6	Sep 1996	Termination (Cost-Reimbursement)
52.249-14	Apr 1984	Excusable Delays

DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR)
(48 CFR CHAPTER 3) CLAUSES

HHSAR Clause No.	Date	Title
352.202-1	Jan 2001	Definitions - with Alternate paragraph (h) (Jan 2001)
352.228-7	Dec 1991	Insurance - Liability to Third Persons
352.232-9	Apr 1984	Withholding of Contract Payments
352.233-70	Apr 1984	Litigation and Claims
352.242-71	Apr 1984	Final Decisions on Audit Findings
352.249-14	Apr 1984	Excusable Delays
352.270-5	Apr 1984	Key Personnel
352.270-6	Jul 1991	Publication and Publicity

[END OF GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT – Rev. 05/2002]

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:

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

FAR 52.216-18, Ordering (OCTOBER 1995).

"(a) ....Such orders may be issued from ____ through ____ [Insert dates upon award]..."

FAR 52.216-22, Indefinite Quantity (OCTOBER 1995).

"(d) ...the Contractor shall not be required to make any deliveries under this contract after [INSERT DATE IN CONTRACT] ..."

FAR 52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns (MAY 2001).

"(b) Evaluation adjustment. (1) The Contracting Officer will evaluate offers by adding a factor of 10% percent to the price of all offers, except--..."

FAR 52.227-14, Rights in Data - General (JUNE 1987)

DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION/PUBLIC HEALTH SERVICE ACQUISITION REGULATION (HHSAR)/(PHSAR) (48 CHAPTER 3) CLAUSES:

HHSAR 352.223-70, Safety and Health (JANUARY 2001) This clause is provided in full text in SECTION J - ATTACHMENTS.

HHSAR 352.224-70, Confidentiality of Information (APRIL 1984).

HHSAR 352.270-9, Care of Live Vertebrate Animals (JANUARY 2001).

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

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

NIH (RC)-7, Procurement of Certain Equipment (APRIL 1984) (OMB Bulletin 81-16).

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:

FAR Clause 52.244-6, SUBCONTRACTS FOR COMMERCIAL ITEMS (MAY 2002)

Definitions. As used in this clause--

Commercial item, has the meaning contained in the clause at 52.202-1, Definitions.

Subcontract, includes a transfer of commercial items between divisions, subsidiaries, or affiliates of the Contractor or subcontractor at any tier.

To the maximum extent practicable, the Contractor shall incorporate, and require its subcontractors at all tiers to incorporate, commercial items or non-developmental items as components of items to be supplied under this contract.

(1) The Contractor shall insert the following clauses in subcontracts for commercial items:

52.219-8, Utilization of Small Business Concerns (OCT 2000) (15 U.S.C. 637(d)(2) and (3)), in all subcontracts that offer further subcontracting opportunities. If the subcontract (except subcontracts to small business concerns) exceeds $500,000 ($1,000,000 for construction of any public facility), the subcontractor must include 52.219-8 in lower tier subcontracts that offer subcontracting opportunities.
52.222-26, Equal Opportunity (APR 2002) (E.O. 11246).
52.222-35, Equal Opportunity for Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans (DEC 2001) (38 U.S.C. 4212(a)).
52.222-36, Affirmative Action for Workers with Disabilities (JUN 1998) (29 U.S.C. 793).
52.247-64, Preference for Privately Owned U.S.-Flag Commercial Vessels (JUN 2000) (46 U.S.C. Appx 1241) (flowdown not required for subcontracts awarded beginning May 1, 1996).

While not required, the Contractor may flow down to subcontracts for commercial items a minimal number of additional clauses necessary to satisfy its contractual obligations.

The Contractor shall include the terms of this clause, including this paragraph (d), in subcontracts awarded under this contract.

PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

SECTION J - LIST OF ATTACHMENTS

The following Attachments are provided in full text with this Solicitation:

PACKAGING AND DELIVERY OF PROPOSALS (Attached to this listing)

HOW TO PREPARE AN ELECTRONIC PROPOSAL: (Attached to this listing)

PROPOSAL INTENT RESPONSE SHEET [SUBMIT ON/BEFORE: December 5, 2002] (Attached to this listing)

[NOTE: Your attention is directed to the "Proposal Intent Response Sheet". If you intend to submit a proposal, you must complete this form and return it to this office via fax or e-mail on or before the date identified above. The receipt of this form is critical as it contains information essential for CMB's coordination of the electronic submission and review of proposals.]

RFP FORMS AND ATTACHMENTS:

THE RFP FORMS/ATTACHMENTS LISTED BELOW ARE AVAILABLE IN A VARIETY OF FORMATS AND MAY BE VIEWED OR DOWNLOADED DIRECTLY FROM THIS SITE:

http://www.niaid.nih.gov/contract/ref.htm

APPLICABLE TO TECHNICAL PROPOSAL (INCLUDE THESE DOCUMENTS/FORMS WITH YOUR TECHNICAL PROPOSAL):

- **Technical Proposal Cover Sheet**
- **Summary of Related Activities**
- **Government Notice for Handling Proposals**
- **Project Objectives, NIH 1688-1**

APPLICABLE TO BUSINESS PROPOSAL (INCLUDE WITH YOUR BUSINESS PROPOSAL):

- **NIH-2043, Proposal Summary and Data Record**
- **Small Business Subcontracting Plan Format *[if applicable]***
- **Offeror's Points of Contact**

TO BECOME CONTRACT ATTACHMENTS (INFORMATION ONLY):

- **NIH(RC)-1: Invoice/Financing Request Instructions for NIH Cost-Reimbursement Type Contracts**
- **NIH(RC)-7: Procurement of Certain Equipment, (OMB Bulletin 81-16)**
- **Safety and Health, HHSAR Clause 352.223-70 (Copy is attached to this solicitation.)**
- **Disclosure of Lobbying Activities, OMB Form LLL**

PACKAGING/DELIVERY/ELECTRONIC SUBMISSION OF THE PROPOSAL

Listed below are delivery instructions for the submission of both PAPER and ELECTRONIC COPIES of your proposal.

PAPER SUBMISSION: The paper copy is the official copy for recording timely receipt of proposals. You are required to submit one original paper copy of your proposal along with the number of extra copies required below.

ELECTRONIC SUBMISSION: In addition to the paper submission, you are required to submit your proposal electronically through the CRON (Contracts Review Online) in accordance with the instructions provided below. If you experience difficulty or are unable to transmit, you should submit your proposal on a CD-Rom or ZipDisk by an express delivery service. We can then upload your proposal into the electronic system. You must certify that both the original paper and electronic versions of the proposal are identical.

SUBMISSION OF PROPOSALS BY FACSIMILE IS NOT ACCEPTABLE.

Shipment and marking of paper copies shall be as indicated below:

A. EXTERNAL PACKAGE MARKING:

In addition to the address cited below, mark each package as follows:

"RFP NO. NIH-NIAID-03-39 TO BE OPENED BY AUTHORIZED GOVERNMENT PERSONNEL ONLY"

B. NUMBER OF COPIES:

The number of copies required of each part of your proposal are as specified below.

Technical Proposal: One (1) unbound signed original and five (5) unbound copies. Ten (10) copies of all material NOT available electronically (i.e. SOPs, Pertinent Manuals, Non-scannable Figures or Data, and Letters of Collaboration/Intent, etc.). Offerors should strictly limit such materials.

Business Proposal: One (1) unbound signed original and 5 unbound copies.

C. PAPER COPIES and CD-Rom or ZipDisk to:

If Hand Delivery or Express Service	**If using U.S. Postal Service**
Paul McFarlane, Contracting Officer Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230 Bethesda, Maryland 20817	Paul McFarlane, Contracting Officer Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230, 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).

HOW TO PREPARE AND SUBMIT AN ELECTRONIC PROPOSAL

PAGE LIMITS -- THE TECHNICAL PROPOSAL IS LIMITED TO NOT-TO-EXCEED 150 PAGES MAXIMUM INCLUSIVE OF APPENDICES, ATTACHMENTS, OPERATING MANUALS, NON-SCANNABLE FIGURES OR DATA, LETTERS OF INTENT, ETC. ANY PORTIONS OF YOUR PROPOSAL NOT AVAILABLE ELECTRONICALLY ARE ALSO CONSIDERED TO BE INCLUDED IN THE TOTAL PAGE LIMITATION. PROVIDE TEN (10) COMPLETE (UNBOUND) COPIES OF ANY NON-ELECTRONIC DOCUMENTS. IN DETERMINING WHETHER OR NOT TO INCLUDE ANY TECHNICAL PROPOSAL CONTENT, CONSIDER WHETHER OR NOT YOU BELIEVE THE NIAID WOULD REQUIRE THE DOCUMENTATION IN ORDER TO MAKE A COMPLETE EVALUATION OF THE PROPOSAL PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE PROPOSAL AND WILL NOT BE READ OR EVALUATED.

Note that although no page limit has been placed on the Business Proposal, Offerors are encouraged to limit its content to only those documents necessary to provide adequate support for the proposed costs.

ELECTRONIC SUBMISSION – To submit a proposal electronically under this RFP, Offerors will need to prepare the proposal on a word processor or spreadsheet program (for the business portion) and convert them to Adobe Acrobat Portable Document Format (.pdf). THE TECHNICAL PROPOSAL AND BUSINESS PROPOSAL MUST BE CONTAINED ON SEPARATE FILES which must be identified as either TECHNICAL or BUSINESS and include some recognizable portion of the ORGANIZATION NAME.

Please note that the electronic submission does not replace the requirement to submit a signed, unbound original paper copy of both your Technical and Business Proposal, along with any required unbound duplicate copies. These paper originals should be mailed or hand-delivered to the address provided in this attachment and must be received on/before the closing date and time.

There is no limit to the size (MB) of the two electronic PDF files to be submitted; however, the size of the technical proposal is limited to the page limitation language outlined above. For purposes of assessing compliance with the page count, technical proposals will be viewed using the print function of the Adobe Acrobat Reader, Version 4.0 (or higher).

Formatting Requirements:
Do not embed sound or video (e.g., MPEG) files into the proposal documents. The evaluation system does not have the capability to read these files.
Keep graphics embedded in documents as simple as possible. Complex graphics require longer periods for the computers used in the evaluation system to draw, and redraw these figures and scrolling through the document is slowed significantly.
Type density and size must be 10 to 12 points. If constant spacing is used, there should be no more than 15 cpi, whereas proportional spacing should provide an average of no more than 15 cpi. There must be no more than six lines of text within a vertical inch. Margins must be set to 1 inch around.
Paper size should not exceed 8-1/2 x 11. Larger paper sizes will be counted as 2 pages.
Limit colors to 256 colors at 1024 x 768 resolution; avoid color gradients.
Simplify the color palette used in creating figures.
Be aware of how large these graphics files become. Large files are discouraged.
Limit scanned images as much as possible.
Limit appendices and attachments to relevant technical proposal information (e.g., SOPs, pertinent manuals, non-scannable figures or data, resumes, letters of commitment/intent).

SUBMISSION OF "PROPOSAL INTENT TO RESPOND SHEET":

Upon receipt by the Contracting Officer of the "Proposal Intent Response Sheet", Offerors will be provided, via e-mail correspondence, specific electronic access information and electronic proposal transmission instructions. For this reason, it is imperative that all Offerors who are intending to submit a proposal in response to this RFP contact the Contract Specialist identified in this RFP and complete and submit the attached "Proposal Intent Response Sheet" by the date provided on that Attachment.

CREATE ADOBE PDF ONLINE -- Adobe will allow you to create 5 documents on a trial for free. If you want to use the site regularly it costs $10/month or $100/year. Please link to the following URL for information:

https://createpdf.adobe.com/index.pl/3847995518.39272?BP=IE

LOG-IN / TRANSMISSION INSTRUCTIONS:

1. Log-in Site: Will be provided by the Contract Specialist after receipt of the "Proposal Intent Response Sheet"
2. Log-in Name: Will be provided by the Contract Specialist.
3. Log-in Password: Will be provided by the Contract Specialist.
4. Procedure -- When your proposal is completed and converted to a PDF file using Adobe Acrobat, it is ready to be transmitted electronically. You must upload separate Technical and Business Proposal Files. It is recommended that proposals be transmitted a few days before the due date so that you will have sufficient time to overcome any transmission difficulties.

You must have Explorer 3.1 or higher.
It is essential that you use antiviral software to scan all documents.
Click on "Sign On" and enter your log-in name and password.
Click on "Browse" to locate your saved files on your computer.
Click on "Upload Proposal" after you have located the correct file.
After a file is uploaded, a link to the file will appear under "Upload Files" at the bottom of the screen. Click on that link to view the uploaded file.
If you experience difficulty in accessing your documents, please contact the appropriate NIH contracts office immediately.
If you wish to revise your proposal before the closing date and time, simply log in again and re-post.

USER ACCESS TO THE POSTING SITE WILL BE DENIED AFTER THE RFP CLOSING DATE AND TIME PROVIDED WITH THIS RFP OR ITS MOST RECENT AMENDMENT(S).

PROPOSAL INTENT RESPONSE SHEET

RFP No.: NIH-NIAID-DMID-03-39
RFP Title: In vitro and Animal Models for Emerging Diseases and Biodefense

Please review the attached Request for Proposal. Furnish the information requested below and return this page by Thursday, December 5, 2002. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

Since your proposal will be submitted electronically, please include the name and e-mail of the individual to whom the electronic proposal instructions, login code, and password should be provided.

[ ] 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:
CMB, NIAID, NIH
Attn: Paul D. McFarlane, Contracting Officer
Ref: RFP-NIH-NIAID- DMID-03-39
6700-B Rockledge Drive
MSC 7612, Room 2230
Bethesda, MD 20892-7612
FAX# (301) 402-0972
Email : pm24v@nih.gov

PART IV – REPRESENTATIONS AND INSTRUCTIONS

SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

Representations, Certifications, and Other Statements of Offerors or Quoters (Negotiated).

REPRESENTATIONS AND CERTIFICATIONS

The Representations and Certifications required by this particular acquisition can be accessed electronically from the INTERNET at the following address:

http://rcb.cancer.gov/rcb-internet/forms/rcneg.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 THE REPRESENTATIONS AND CERTIFICATIONS AND SUBMIT THEM AS PART OF YOUR BUSINESS PROPOSAL.

SECTION L - INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS

1. GENERAL INFORMATION

Alternate I (October 1997). As prescribed in 15.209(a)(1), substitute the following paragraph (f)(4) for paragraph (f)(4) of the basic provision:

> (f) (4) The Government intends to evaluate proposals and award a contract after conducting discussions with Offerors whose proposals have been determined to be within the competitive range. 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. Therefore, the offeror's initial proposal should contain the offeror's best terms from a price and technical standpoint.

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.

The North American Industry Classification System (NAICS) code for this acquisition is 541710.
The small business size standard is 500 Employees.

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 System (NAICS) Code and corresponding size standard which best describes the nature of the requirement in the solicitation.

NOTICE OF PRICE EVALUATION ADJUSTMENT FOR SMALL DISADVANTAGED BUSINESS CONCERNS

In accordance with FAR Clause 52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns, incorporated in Section I.3., Offerors will be evaluated by adding a factor of 10% percent to the price of all offers, except offers from small disadvantaged business concerns that have not waived the adjustment. (Note: A listing of other Offerors who are excepted and will not have this evaluation factor added to their offer may be found in subparagraph (b) of FAR Clause 52.219-23.

A small disadvantaged business concern may elect to waive the adjustment, in which case the factor will be added to its offer for evaluation purposes. The agreements in paragraph (d) of FAR Clause 52.219-23 do not apply to Offerors that waive the adjustment.

AN OFFEROR WHO ELECTS TO WAIVE THIS EVALUATION ADJUSTMENT MUST SPECIFICALLY INDICATE WITH A STATEMENT TO THIS EFFECT ON THE COVER PAGE OF ITS BUSINESS PROPOSAL.

TYPE OF CONTRACT AND NUMBER OF AWARD(S)

It is anticipated that multiple awards will be made from this solicitation and that the award(s) will be made on/about September 30, 2003.

It is anticipated that the awards from this solicitation will be multiple-year cost reimbursement type completion contract with a period of seven years (or as many years are necessary to complete specific efforts). Incremental funding will be used. See Section L.2.c. Business Proposal Instructions.

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 following year-1 (only) labor estimates are provided for each part of the work statement. This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

SOW PART	LABOR CATEGORY	ESTIMATED YEAR-1 EFFORT
A	Principal Investigator	15%
	Professional Staff	50%
	Senior Technician	100%
	Technical Support	200%
	Clerical Support	20%
	TOTAL	385%

SOW PART	LABOR CATEGORY	ESTIMATED YEAR-1 EFFORT
B	Principal Investigator/Project Director	15%
	Professional Staff	50%
	Senior Technician	100%
	Technical Support	200%
	Clerical Support	15%
	TOTAL	380%

SOW PART	LABOR CATEGORY	ESTIMATED YEAR-1 EFFORT
C	Principal Investigator/Project Director	20%
	Professional Staff	100%
	Animal Supervisor	80%
	Technical Support	100%
	Clerical Support	100%
	TOTAL	400%

SOW PART	LABOR CATEGORY	ESTIMATED YEAR-1 EFFORT
D	Principal Investigator/Project Director	25%
	Professional Staff/Veterinarian	75%
	Senior Laboratory Investigator	50%
	Animal Supervisor	50%
	Technical Support	150%
	Clerical Support	200%
	TOTAL	550%

SOW PART	LABOR CATEGORY	ESTIMATED YEAR-1 EFFORT
E	Principal Investigator/Project Director	25%
	Project Leader/Veterinarian	40%
	Professional Staff	75%
	Senior Technician	100%
	Technical Support	300%
	Clerical Support	20%
	TOTAL	560%

SOW PART	LABOR CATEGORY	ESTIMATED YEAR-1 EFFORT
F	Principal Investigator/Project Director	30%
	Project Leader/Veterinarian	40%
	Professional Staff	100%
	Senior Technician	100%
	Technical Support	400%
	Clerical Support	30%
	TOTAL	700%

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.

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.

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.

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/approximately equal to cost or price/significantly less important than cost or price]. The relative importance of the evaluation factors is 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.

PREPARATION COSTS

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

SERVICE OF PROTEST (AUGUST 1996) - FAR 52.233-2

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 General Accounting Office (GAO), shall be served on the Contracting Officer (addressed as follows) by obtaining written and dated acknowledgment of receipt from:

Brenda J. Velez
Contracting Officer
Contract Management Branch, DEA
National Institute of Allergy and Infectious Diseases
6700-B Rockledge Drive, Room 2230, MSC 7612
BETHESDA MD 20892-7612

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)

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)

USE OF INTERNET WEB SITE ADDRESSES (URLs) IN PROPOSALS

Unless otherwise specified or required in NIAID solicitations, internet Web Site addresses (URLs) may not be used to provide information necessary to the conduct of the review of the proposal. Direct access to an internet site by a Reviewer who is examining and reviewing the proposal on behalf of the NIAID could compromise their anonymity during the review process. If a URL contains information pertinent to the proposal content, the Offeror must provide access to the website via a temporary website portal which allow reviewers the capability to view and interact with the site.

The proposal must clearly identify the URLs to be accessed and the procedure for accessing the temporary website portal. Access must not require the identity of the individual.

2. INSTRUCTIONS TO OFFERORS

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.

Contract Type and General Clauses

It is contemplated that a [cost-reimbursement (completion/level of effort)/fixed price] 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.

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 addressees, 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, identification of the proposal part, and indicate whether the proposal is an original or a copy.

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:"**

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.

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.

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).

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 INFORMATION/SUMMARY OF LABOR AND DIRECT COSTS).) 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.

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.

Evaluation of Proposals

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

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 procurements, 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.

Care of Live Vertebrate Animals

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

> Notice to Offerors of Requirement for Adequate Assurance of Protection of Vertebrate Animal Subjects - (SEPTEMBER 1985)

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. 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.

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.

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.

Selection of Offerors

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.

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

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.

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

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.

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 this Institute's policy to conduct discussions with all Offerors in the competitive range, the Institute 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 sources in accordance with HHSAR 315.370.

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.

The Institute 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 the Institute's requirements. Synopses of awards exceeding $25,000 will be published in the Commerce Business Daily and FedBizOpps.

Small Business Subcontracting Plan

If the proposed contract exceeds a total estimated cost of $500,000 for the entire period of performance, the 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.

THIS PROVISION DOES NOT APPLY TO SMALL BUSINESS CONCERNS.

a) *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.*

b) The Offeror understands that:

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.

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.

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.

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.

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.

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.

Each plan must contain the following:

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.

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.

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.

A description of the method used to develop the subcontracting goals.

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

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.

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

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.

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.

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.

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.

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.

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 Industry 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. Credit under this evaluation factor is not available to SDB concerns that receive a Price Evaluation Adjustment (PEA) under FAR 19.11. Therefore, an SDB will be evaluated on this factor only if that SDB concern waives the PEA. Waiver of the price evaluation adjustment shall be clearly stated in the proposal.

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

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

Offerors shall include with their offers, SDB targets, expressed as dollars and percentages of total contract value, in each of the applicable, authorized NAICS Industry Subsector(s). The applicable authorized NAICS Industry 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 Industry 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.

Reimbursement of Costs for Independent Research and Development Projects (Commercial Organizations Only)

The primary purpose of the Public Health Service (PHS) is to support and advance independent research within the scientific community. This support is provided in the form of contracts and grants totaling approximately 7 billion dollars annually. PHS has established effective, time tested and well recognized and accepted procedures for stimulating and supporting this independent research by selecting from multitudes of proposals those research projects most worthy of support within the constraints of its appropriations. The reimbursement of independent research and development costs not incidental to product improvement, through the indirect cost mechanism, would circumvent this competitive process.

To ensure that all research and development projects receive similar and equal consideration, all Offerors may compete for direct funding for independent research and development projects they consider worthy of support by submitting those projects to the appropriate Public Health Service grant and/or contract office for review. Since these projects may be submitted for direct funding, the successful Offeror agrees that no costs for any independent research and development project, including applicable indirect costs, will be claimed under any contract resulting from this solicitation.

Salary Rate Limitation in Fiscal Year 2002 **

> Offerors are advised that pursuant to P.L. 107-116, no NIH Fiscal Year 2002 (October 1, 2001 - September 30, 2002) 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. 107-116 applies only to Fiscal Year 2002 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. 107-116 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 extramural mechanism at a rate in excess of Executive Level I."

Information regarding the FY-2002 rate can be found at: **http://www.opm.gov/oca/02tables/ex.pdf**

It should be noted that a similar public law may be enacted in Fiscal Year 2003, at which time that public law will be incorporated into any resultant contract(s).

Institutional Responsibility Regarding Conflicting Interests of Investigators

EACH INSTITUTION MUST:

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.

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

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.

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.

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.

Establish adequate enforcement mechanisms and provide for sanctions where appropriate.

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

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;

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;

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

the Institution will otherwise comply with the regulations.

INSTITUTIONAL MANAGEMENT OF CONFLICTING INTERESTS

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:

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

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.

(1) **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:

1. 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

2. 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 .

Prohibition on Contractor Involvement with Terrorist Activities

The Offeror/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.

- **Office of Health and Safety – Laboratory Registration / Select Agent Transfer Program**

The awardee is responsible for ensuring that all work under this grant, cooperative agreement, or contract complies with all Federal requirements related to select agents including CDCs that can be found at http://www.cdc.gov/od/ohs/lrsat.htm and NIH's OBA that can be found at http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html .

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):

Submission of Offers in the English Language, FAR Clause 52.214-34, (April 1991).

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

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

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

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.

Technical Discussions

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

Statement of Work

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.

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.

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.

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.

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.

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.

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.

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.

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.

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).

Additional Technical Proposal Information

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.

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.

Other Considerations

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

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.

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

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

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

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

BUSINESS PROPOSAL INSTRUCTIONS

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.

Proposal Cover Sheet

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

Solicitation, contract, and/or modification number;
Name and address of Offeror;
Name and telephone number of point of contact;
Name, address, and telephone number of Contract Administration Office, (if available);
Name, address, and telephone number of Audit Office (if available);
Proposed cost and/or price; profit or fee (as applicable); and total;
The following statement: By submitting this proposal, the Offeror, if selected for discussions, grants the contracting officer or an authorized representative the right to examine, at any time before award, any of those books, records, documents, or other records directly pertinent to the information requested or submitted.
Date of submission; and
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.

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."

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.

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.

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.

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.

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.

Other Administrative Data

Property

It is DHHS policy that Contractors will provide all equipment and facilities necessary for performance of contracts. Exception may be granted to furnish Government-owned property, or to authorize purchase with contract funds, only when approved by the Contracting Officer. If the Offeror is proposing that the Government provide any equipment, other than that specified under Government Furnished Property in the RFP, the proposal must include comprehensive justification which includes:

An explanation that the item is for a special use essential to the direct performance of the contract and the item will be used exclusively for the purpose. Office equipment such as desks, office machines, etc., will not be provided under a contract except under very exceptional circumstances.

No practical or economical alternative exists (e.g., rental, capital investment) that can be used to perform the work.

The Offeror shall identify Government-owned property in its possession and/or Contractor titled property acquired from Federal funds, which it proposes to use in the performance of the prospective contract.

The management and control of any Government property shall be in accordance with DHHS Publication (OS) 686 entitled, "Contractors Guide for Control of Government Property (1990)," a copy of which will be provided upon request.

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.

The solicitation number (or other procurement identification number).
The offeror's name and remittance address, as stated in the offer.
The signature (manual or electronic, as appropriate), title, and telephone number of the offeror's official authorized to provide this information.
The name, address, and 9-digit Routing Transit Number of the offeror's financial agent.
The offeror's account number and the type of account (checking, savings, or lockbox).
If applicable, the Fedwire Transfer System telegraphic abbreviation of the offeror's financial agent.
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.

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.

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)

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

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

Facilities capital cost of money [(see FAR 15.408(h)] will be an allowable cost under the contemplated contract, if the criteria for allowability in subparagraph 31.205-10(a)(2) of the Federal Acquisition Regulation are met. One of the allowability criteria requires the prospective Contractor to propose facilities capital cost of money in its offer.

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.

Subcontractors

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

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

What priority the work will be given and how it will relate to other work.

The amount of time and facilities available to this project.

Information on their cognizant field audit offices.

How rights to publications and patents are to be handled.

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/PDPclausecover.htm

Proposer's Annual Financial Report

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

Representations and Certifications

One copy of the Representations and Certifications attached as Section K shall be completed and be signed by an official authorized to bind your organization. Additionally, a completed copy of the Representations and Certifications shall be submitted from any proposed subcontractor. You may find this document at:
http://www.niaid.nih.gov/contract/forms.htm

Travel Costs/Travel Policy

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.

Certification of Visa's 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 performed in the United States and its territories, then the Offeror must indicate in the proposal that these individuals have the required visas.

SECTION M - EVALUATION FACTORS FOR AWARD

In Vitro and Animal Models for Emerging Diseases and Biodefense
DMID-03-39
SECTION M - EVALUATION FACTORS FOR AWARD

1. GENERAL

The technical proposal will receive paramount consideration in the selection of the Contractors for this acquisition. All evaluation factors, other than cost or price, when combined are significantly more important than cost or price. However, cost/price may become a critical factor in source selection in the event that two or more Offerors are determined to be essentially equal following the evaluation of all factors other than cost/price. In any event, the Government reserves the right to make an awards to those Offerors whose proposals 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. MANDATORY QUALIFICATION CRITERIA

The following mandatory qualification criteria establish conditions that MUST be met at the time of receipt of Final Proposal Revisions by the Contracting Officer in order for the proposal to be considered any further for award:

A. The Offeror must have documented access to BSL2 and/or 3 and/or 4 facilities as required to fulfill the statement of work and must fully document capacity for testing the products as proposed.
B. The Offeror must document availability of appropriate storage space to maintain necessary infectious agents and test articles.
C. If working with animals, the Offeror must document access to an AAALAC-accredited (or equivalent) animal facility and the capacity (appropriate cage space, etc.) needed for testing the products (drugs, vaccines, etc.) as proposed.
D. If working with animals, the Offeror must document availability of animals sufficient for the proposed model(s) and number of studies and meeting the requirements of the Statement of Work
E. For Parts E and F, the Offeror must document prior successful completion and submission to the FDA of preclinical studies performed under GLP. Include an indication of FDA acceptance of studies.

3. 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 of commitment to use SDB concerns
(b) Complexity and variety of the work SDB concerns are to perform
(c) Extent of participation of SDB concerns in terms of the value of the total acquisition

4. 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.

Part A – In Vitro Screens for Antimicrobial Activity

CRITERA	WEIGHT
A. Technical Approach Weight	**40**

1) Overall understanding of the project and adequacy and feasibility of plans to address all items in the Work Statement. This includes the detailed description of specific tasks to be performed, including controls, quality control measures and tracking, methods and resources to be used and the discussion of problems likely to occur with plans for addressing them. 15 pts.

2) Technical approach, including SOPs for determination of antimicrobial activity, development of new assay systems, and mechanism of action studies as requested in the Statement of Work, including logistics and coordination. 25 pts

B. Experience and Qualification of Personnel **35**

1) Documented availability, expertise, and proficiency of the Principal Investigator, in the performance of antimicrobial testing/screening and in managing a project of comparable size and complexity. 15 pts

2) Documented availability, experience, and capabilities of other professional and technical staff in the performance of antimicrobial testing and/or screening and documented availability. 10 pts

3) Previous institutional expertise and proven track record in the antimicrobial testing. 10 pts

C. Facilities and Resources **25**

1) Availability of adequate facilities, equipment, and resources necessary to safely and efficiently accomplish the work described in the Statement of Work. Adequacy of detailed floor plan, indicating space to be committed and documented for performance of this project. Adequacy of Biosafety containment, safety plans and accident contingency plans. 15 pts

2) Capacity to perform required testing in a timely and efficient manner (resources dedicated to this project). 10 pts

Part B -- Clinical Isolate Panels for Selected Bacterial Pathogens

CRITERA	WEIGHT
A. Technical Approach Weight	**40**

1) Overall understanding of the project and adequacy and feasibility of plans to address all items in the Work Statement. This includes the detailed description of specific tasks to be performed, including controls, quality control measures and tracking, methods and resources to be used and the discussion of problems likely to occur with plans for addressing them. 15 pts.

2) Technical approach, including appropriateness of NCCLS standards and SOPs for determination of antimicrobial activity, MIC50/90 and tentative MIC breakpoints as requested in the Statement of Work, including logistics and coordination. 25 pts

B. Experience and Qualification of Personnel **35**

1) Documented availability, expertise, and proficiency of the Principal Investigator, in the performance of antimicrobial testing using large panels of clinical strains and in managing a project of comparable size and complexity. 15 pts

2) Documented availability, experience, and capabilities of other professional and technical staff in the performance of antimicrobial testing using large panels of clinical strains and documented availability. 10 pts

3) Previous institutional expertise and proven track record in the antimicrobial testing in general and specifically to evaluate activities against clinical stains; previous experience in conducting work under GLP. 10 pts

C. Facilities and Resources **25**

1) Availability of adequate facilities, equipment, and resources necessary to safely and efficiently accomplish the work described in the Statement of Work. Adequacy of detailed floor plan, indicating space to be committed and documented for performance of this project. Adequacy of Biosafety containment, safety plans and accident contingency plans. 15 pts

2) Capacity to perform required testing in a timely and efficient manner (resources dedicated to this project). 10 pts

TOTAL POINTS: 100

Part C: Small animal models for selected pathogens, including GLP studies

CRITERA	**WEIGHT**
A. Technical Approach Weight	**40**

1) Overall understanding of the project and adequacy and feasibility of plans to address all items in the Work Statement. This includes the detailed description of specific tasks to be performed, methods and resources to be used, and the discussion of problems likely to occur and plans for addressing them. 10 pts.

2) Technical approach for efficacy testing of vaccines and/or therapeutics as requested in the Statement of Work including logistics and coordination. 20 pts

3) Model development: Scientific and technical potential of the proposed animal model to be developed or modified to enhance its usefulness in the evaluation of therapies/strategies and topical microbicides. Scoring will be based on the requested discussion of how the Offeror could further extend or adapt the proposed model(s). 10 pts

B. Experience and Qualification of Personnel **35**

1) Documented expertise and proficiency of the Principal Investigator, in the performance of safety and immunogenicity testing suitable for vaccines destined for human trials and in managing a project of comparable size and complexity and documented availability. 15 pts

2) Documented experience and capabilities of other professional and technical staff in the performance of safety and immunogenicity testing and documented availability. 10 pts

3) Previous institutional expertise and proven track record in the evaluation of vaccines and/or therapeutics. 10 pts

C. Facilities and Resources **25**

1) Availability of adequate facilities, animals, equipment, and resources necessary to safely and efficiently accomplish the work described in the Statement of Work. Adequacy of detailed floor plan, indicating space to be committed for performance of this project. Adequacy of animal facilities. Adequacy of safety plans and accident contingency plans. 15 pts

2) Capacity to perform required testing in a timely and efficient manner (resources dedicated to this project). 10 pts

TOTAL POINTS: 100

Part D: Non-human primate models for selected pathogens, including GLP studies.

CRITERA **WEIGHT**

A. Technical Approach Weight **40**

1) Overall understanding of the project and adequacy and feasibility of plans to address all items in the Work Statement. This includes the detailed description of specific tasks to be performed, methods and resources to be used, and the discussion of problems likely to occur and plans for addressing them. 10 pts.

2) Technical approach for efficacy testing of vaccines and/or therapeutics as requested in the Statement of Work including logistics and coordination. 20 pts

3) Model development: Scientific and technical potential of the proposed animal model to be developed or modified to enhance its usefulness in the evaluation of therapies/strategies and topical microbicides. Scoring will be based on the requested discussion of how the Offeror could further extend or adapt the proposed model(s). 10 pts

B. Experience and Qualification of Personnel **35**

1) Documented expertise and proficiency of the Principal Investigator, in the performance of efficacy testing in non-human primates and in managing a project of comparable size and complexity and documented availability. 15 pts

2) Documented experience and capabilities of other professional and technical staff in the performance of safety and immunogenicity testing and documented availability. 10 pts

3) Previous institutional expertise and proven track record in the evaluation of vaccines and/or therapeutics; expertise in performing studies under GLP, if appropriate. 10 pts

C. Facilities and Resources **25**

1) Availability of adequate facilities, animals, equipment, and resources necessary to safely and efficiently accomplish the work described in the Statement of Work. Adequacy of detailed floor plan, indicating space to be committed for performance of this project. Adequacy of animal facilities. Adequacy of safety plans and accident contingency plans. 15 pts

2) Capacity to perform required testing in a timely and efficient manner (resources dedicated to this project). 10 pts

TOTAL POINTS: 100

Part E: Safety and Immunogenicity Testing for Vaccines

CRITERA **WEIGHT**

Technical Approach Weight **40**

1) Overall understanding of the project and adequacy and feasibility of plans to address all items in the Work Statement. This includes the detailed description of specific tasks to be performed, methods and resources to be used, and the discussion of problems likely to occur and plans for addressing them. 15 pts.

2) Technical approach for efficacy testing of vaccines and/or therapeutics as requested in the Statement of Work including logistics and coordination. 25 pts

B. Experience and Qualification of Personnel **35**

1) Documented expertise and proficiency of the Principal Investigator, in the performance of safety and immunogenicity testing suitable for vaccines destined for human trials and in managing a project of comparable size and complexity and documented availability. 15 pts

2) Documented experience and capabilities of other professional and technical staff in the performance of safety and immunogenicity testing and documented availability. 10 pts

3) Previous institutional expertise and proven track record in the evaluation of vaccines and/or therapeutics; previous experience in conducting work under GLP. 10 pts

C. Facilities and Resources **25**

1) Availability of adequate facilities, animals, equipment, and resources necessary to safely and efficiently accomplish the work described in the Statement of Work. Adequacy of detailed floor plan, indicating space to be committed for performance of this project. Adequacy of animal facilities. 15 pts

2) Capacity to perform required testing in a timely and efficient manner (resources dedicated to this project). 10 pts

TOTAL POINTS: 100

Part F: Safety/Toxicology and Pharmacology Testing for Therapeutics

CRITERA	**WEIGHT**
Technical Approach Weight	**40**

1) Overall understanding of the project and adequacy and feasibility of plans to address all items in the Work Statement. This includes the detailed description of specific tasks to be performed, methods and resources to be used, and the discussion of problems likely to occur and plans for addressing them. 15 pts.

2) Technical approach for efficacy testing of therapeutics as requested in the Statement of Work including logistics and coordination. 25 pts

B. Experience and Qualification of Personnel **35**

1) Documented expertise and proficiency of the Principal Investigator, in the performance of toxicology and pharmacology testing suitable for therapeutics destined for human trials and in managing a project of comparable size and complexity and documented availability. 15 pts

2) Documented experience and capabilities of other professional and technical staff in the performance of toxicology and pharmacology testing and documented availability. 10 pts

3) Previous institutional expertise and proven track record in the evaluation of therapeutics; previous experience in conducting work under GLP. 10 pts

C. Facilities and Resources **25**

1) Availability of adequate facilities, animals, equipment, and resources necessary to safely and efficiently accomplish the work described in the Statement of Work. Adequacy of detailed floor plan, indicating space to be committed for performance of this project. Adequacy of animal facilities. 15 pts

2) Capacity to perform required testing in a timely and efficient manner (resources dedicated to this project). 10 pts

TOTAL POINTS: 100

PHS 352.223-70 SAFETY AND HEALTH (JANUARY 2001)

(a) To help ensure the protection of the life and health of all persons, and to help prevent damage to property, the Contractor shall comply with all Federal, State and local laws and regulations applicable to the work being performed under this contract. These laws are implemented and/or enforced by the Environmental Protection Agency, Occupational Safety and Health Administration and other agencies at the Federal, State and local levels (Federal, State and local regulatory/enforcement agencies).

(b) Further, the Contractor shall take or cause to be taken additional safety measures as the Contracting Officer, in conjunction with the project or other appropriate officers, determines to be reasonably necessary. If compliance with these additional safety measures results in an increase or decrease in the cost or time required for performance of any part of work under this contract, an equitable adjustment will be made in accordance with the applicable "Changes" clause set forth in this contract.

(c) The Contractor shall maintain an accurate record of, and promptly report to the Contracting Officer, all accidents or incidents resulting in the exposure of persons to toxic substances, hazardous materials or hazardous operations; the injury or death of any person; and/or damage to property incidental to work performed under the contract and all violations for which the Contractor has been cited by any Federal, State or local regulatory/enforcement agency. The report shall include a copy of the notice of violation and the findings of any inquiry or inspection, and an analysis addressing the impact these violations may have on the work remaining to be performed. The report shall also state the required action(s), if any, to be taken to correct any violation(s) noted by the Federal, State or local regulatory/enforcement agency and the time frame allowed by the agency to accomplish the necessary corrective action.

(d) If the Contractor fails or refuses to comply with the Federal, State or local regulatory/enforcement agency's directive(s) regarding any violation(s) and prescribed corrective action(s), the Contracting Officer may issue an order stopping all or part of the work until satisfactory corrective action (as approved by the Federal, State or local regulatory/enforcement agencies) has been taken and documented to the Contracting Officer. No part of the time lost due to any stop work order shall be subject to a claim for extension of time or costs or damages by the Contractor.

(e) The Contractor shall insert the substance of this clause in each subcontract involving toxic substances, hazardous materials, or hazardous operations. Compliance with the provisions of this clause by subcontractors will be the responsibility of the Contractor.

(End of clause)

SAFETY CONTROLS AND STANDARDS

In order to provide safety controls for protection of the life and health of employees and other persons; for prevention of damage to all property, and for avoidance of work interruptions in the performance of the contract, the Contractor and any subcontractors shall comply with the following standards or subsequent issues or any supplements. In addition, the Contractor shall comply with all applicable Federal, state and local laws, codes, ordinances and regulations, including obtaining of all required licenses and permits in connection with biological and hazardous materials.

1. The Biosafety Microbiological and Biomedical Laboratory Guidelines, Centers for Disease Control and Prevention and the National Institutes of Health, third edition, HHS Pub. No. (CDC) 93-8395 published by the U.S. Government Printing Office, May 1993, stock number 17-040-00523-7.
2. The DHHS regulations regarding the transfer of select agents (42 CFR Part 72) http://www.cdc.gov/od/ohs/lrsat/regmat.htm
3. Recommendations for the Safe Handling of Cytotoxic Drugs, NIH Publication No. 92-2621.
4. NIH Guidelines for the Laboratory Use of Chemical Carcinogens, NIH Publication No. 81-2385.

Copies of the above may be obtained from the Government Printing Office or:
Division of Safety
Office of Research Services
National Institutes of Health
Building 31 - Room 1C02
Bethesda, Maryland 20892
301-496-2960

Agreement for Submitting Products to the Division of Microbiology and Infectious Diseases, NIAID, NIH for Antiviral Screening

The Division of Microbiology and Infectious Diseases of the National Institute of Allergy and Infectious Diseases (DMID, NIAID), an institute of the National Institutes of Health, which is a component of the U.S. Public Health Service, an agency of the U.S. Government, offers antiviral screening services, through contract testing laboratories, to for-profit and non-profit organizations to help facilitate the rapid development and commercialization of products for the treatment of viral diseases other than AIDS. The COMPANY would like to submit its product(s) for antiviral screening. Therefore, the COMPANY and DMID, NIAID agree as follows:

1. **Restricted Use of COMPANY Product(s).** COMPANY may submit product(s), patented or unpatented, to DMID, NIAID for the purpose of being evaluated for antiviral activity *in vitro* by one or more testing laboratories under contract with the DMID, NIAID (hereinafter "contractor(s)"). DMID, NIAID agrees that the product(s) will be evaluated only in accordance with known testing protocol(s) by its contractor(s), as approved by COMPANY, as agents with potential for the treatment or prevention of infectious diseases and for no other purpose. The product(s) will not be transferred to any party other than the approved contractor(s). In addition, the product(s) will not be chemically modified, replicated, derivatized or reverse engineered unless required by the approved testing protocol or otherwise approved in writing by COMPANY.

2. **Confidentiality.** Information, data and records will be handled as follows:

   a. COMPANY shall forward to the Virology Branch (VB) or Enteric and Hepatic Diseases Branch (EHDB) of the DMID, NIAID or, as directed by either the VB or the EHDB, to the contractor(s) the data sheet(s) on the product(s) to be evaluated, marked "confidential". COMPANY shall provide duplicate copies of the data sheet(s) for each product, which shall include all pertinent available data as to chemical composition, solubility, toxicity, etc. and any precautions that should be followed in handling, storing and shipping the product. For those products in which COMPANY has a proprietary interest but does not yet have adequate patent protection, COMPANY may, in rare cases and with approval by DMID, NIAID, submit a product(s) under code number(s) only. In these cases, COMPANY agrees to reveal to DMID, NIAID and its contractor(s) the structures or identities of the coded product(s), marked "confidential", which subsequently turn out to be positive in any one of the test systems. The structures or identities of such product(s) will remain confidential in accordance with Section 2b below.

   b. COMPANY may provide to DMID, NIAID and/or its contractor(s) any scientific, business or financial information relevant to the product(s) that COMPANY deems to be its proprietary and confidential information. COMPANY must identify such information as confidential. To the extent permitted by law, this information will remain confidential for five (5) years from the date of disclosure unless:

      (1) the information is known by the public or becomes known by the public through no fault of DMID, NIAID or its contractor(s);

      (2) the information was obtained by DMID, NIAID or its contractor(s) from a third party having no confidentiality obligation to COMPANY;

      (3) the information was made available to DMID, NIAID or its contractor(s) by COMPANY without a confidentiality obligation;

      (4) the information has been independently developed by DMID, NIAID or its contractor(s) without reference to COMPANY's information; or

      (5) the information is required to be disclosed by law, regulation or court order provided that COMPANY has been notified and DMID, NIAID and/or its contractor(s) have taken reasonable efforts to minimize the extent of the required disclosure.

c. DMID, NIAID agrees that information or data about the product(s), including the evaluation results, will be kept in restricted-access files by DMID, NIAID and the contractor(s). Only employees of DMID, NIAID or its contractor(s) will have access to the files containing information about the product(s) including the evaluation results. COMPANY acknowledges that the evaluation results are not its confidential information and may be disclosed by DMID, NIAID and/or its contractor(s) *only* in accordance with Section 3b below.

d. The contracts between DMID, NIAID and the testing laboratories require the contractor(s) to abide by the terms of this Agreement.

e. DMID, NIAID will use its best efforts to assure rapid ongoing communication of the evaluation results to COMPANY and, in turn, COMPANY will use its best efforts to keep DMID, NIAID up-to-date on COMPANY's own ongoing concomitant studies.

3. **Intellectual Property and Publications.** COMPANY recognizes that the exchange of biological data and other information is generally desirable in the field of antiviral treatment, and DMID, NIAID recognizes that COMPANY, is entitled to protection for its research and development work on the product(s) and its related technical information. Therefore:

a. Intellectual Property. DMID, NIAID agrees that all right, title and interest in and to all products and information provided by COMPANY to DMID, NIAID under this Agreement will remain with COMPANY. DMID, NIAID acknowledges that this Agreement may not be construed as a grant by COMPANY of a license or any other right or interest beyond those expressly set forth herein. The contracts between DMID, NIAID and its testing laboratories require the contractor(s) to assign to COMPANY all right, title and interest in and to any invention made during the evaluation that directly relates to COMPANY's product(s). For purposes of this Agreement the phrase "directly relates to" means "contains, in whole or in part, COMPANY's product(s)" and/or any new use of COMPANY's product(s).

b. Publications. COMPANY and DMID, NIAID agree that the publication of biological data on COMPANY's product(s) evaluated under this Agreement is worthwhile and to be encouraged. Therefore:

(1) COMPANY agrees that DMID, NIAID and/or its contractor(s) may publish or otherwise publicly disclose the evaluation results after a period of six (6) months from the date the evaluation results are reported to COMPANY. Publication of data within the six (6) month period will require COMPANY'S prior consent, which shall not be unreasonably withheld. DMID, NIAID and/or its contractor(s) shall not publish information identifying COMPANY as the source of the product(s) without COMPANY's prior written approval.

(2) As soon as the evaluation(s) is/are completed and reported by the contractor(s) to the VB or EHDB of DMID, NIAID, COMPANY will receive a full report of the evaluation(s). COMPANY agrees to consult the VB or EHDB of DMID, NIAID whenever COMPANY desires to include the evaluation results in any publication or other public disclosure such as a press release, and shall give appropriate credit to the U.S. Public Health Service and the DMID, NIAID's contractor(s) that performed the evaluation(s). COMPANY shall not construe the involvement of DMID, NIAID or its contractor(s) in the evaluation(s) as an endorsement of the product(s) by the U.S. Government or any of its agencies or employees.

4. **Liability and Indemnification.** Each Party shall be liable for any loss, claim, damage, or liability that it incurs as a result of its activities under this Agreement except that the NIAID, as an agency of the U.S. Government, assumes liability only to the extent provided under the Federal Tort Claims Act, 28 U.S.C. Ch. 171. No indemnification is provided by either Party under this Agreement. The NIAID is prohibited under statute, the Anti-Deficiency Act, 31 U.S.C. § 1341, from indemnifying any party, absent other specific statutory authorization.

If COMPANY agrees to the terms above, please have an authorized representative countersign below and return one fully signed original to the Division of Microbiology and Infectious Diseases, NIAID.

National Institute of Allergy and Infectious Diseases

Carole Heilman, Ph.D.
Director, Division of Microbiology & Infectious Diseases
NIAID, NIH

Date

COMPANY

Signature of Authorized Representative

Printed/Typed Name

Name of Company

Address of Company

Date