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

NIH-NIAID-DAIDS-07-24
Safety Evaluation of Anti-Infective Agents

OMB control number 0990-0115

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

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

3. **Issue Date:**	4. **Due Date:**	5. **Small Bus. Set-Aside:**
July 24, 2006	October 11, 2006 **Time:** 3:00 p.m., EST	[ ]Yes [X] No **8(a) Set-Aside:** [ ]Yes [X] No **NAICS #:** 541720 (See Part IV, Section L.)

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

9. **Issued By:**
Joshua J. LaVine, Contract Specialist
Office of Acquisitions, DEA
NIAID, NIH, DHHS
6700-B Rockledge Drive
Room 3214, MSC 7612
Bethesda, MD 20892-7612

10. [X] **NIAID reserves the right to make awards without discussions.**

11. **Options:**
[X] No
[ ] Yes (See Part IV, Section L.)

12. **Period of Performance:**
Up to 7 years beginning on or about June 29, 2007

13. Primary Point of Contact:
Name : Joshua J. LaVine
Phone: 301-496-2509 via TTY Relay #711
Fax: 301-402-0972
E-Mail: JLaVine@niaid.nih.gov

14. **Secondary Point of Contact:**
Name: Eileen Webster-Cissel
Phone: 301-496-0349
Fax: 301-402-0972
E-Mail: Webstere@mail.nih.gov

15. **Protest Officer:**
Charles W. Grewe
Director, Office of Acquisitions
Address (See block 9.)

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

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

DELIVERY ADDRESS INFORMATION

18. **Hand Delivery or Overnight Service:**
Joshua J. LaVine
Office of Acquisitions, DEA
NIAID, NIH, DHHS
6700-B Rockledge Drive, Room 3214
Bethesda, MD 20817

19. **U.S. Postal Service or an Express Delivery Service**
Joshua J. LaVine
Office of Acquisitions, DEA
NIAID, NIH, DHHS
6700-B Rockledge Drive, Room 3214, MSC 7612
Bethesda, MD 20892-7612

20. The **Official Point of Receipt** for the purpose of determining timely delivery is the address provided in Block 19, above. The original paper copy with original signatures is the official copy for recording timely receipt. If the original paper copy of your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with HHSAR 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation. FACSIMILE SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.

DETAILED TABLE OF RFP CONTENTS

PART I - THE SCHEDULE

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

SECTION B - SUPPLIES OR SERVICES AND PRICES/COSTS

ARTICLE B.1. BRIEF DESCRIPTION OF SUPPLIES OR SERVICES

The Division of AIDS, NIAID, maintains a portfolio of drug development contracts to assist academic investigators and small pharmaceutical firms by providing the preclinical resources necessary to support submission of an Investigational New Drug (IND) application to the Food and Drug Administration (FDA). The objective of this contract is to support the National Institute of Allergy and Infectious Diseases (NIAID) in its mission to develop safe and effective therapies for the treatment of infectious diseases caused by Human Immunodeficiency Virus (HIV), Mycobacterium tuberculosis, Plasmodium sp., opportunistic pathogens that infect AIDS patients, and others. The NIAID requires a Safety Evaluation Contract to assess the health and safety potential of new therapies under development by, or with the support of, the Division of AIDS, NIAID. The scope of this effort is to evaluate the toxicity and pharmacokinetics of potential chemical and biological therapies for AIDS and other infectious diseases in various laboratory animal species.

ARTICLE B.2. PRICES/COSTS

The final contract will contain the price/cost provisions agreed upon by the Government and the Offeror.

ARTICLE B.3. PROVISIONS APPLICABLE TO DIRECT COSTS

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

ARTICLE B.4. ADVANCE UNDERSTANDINGS

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

SECTION C - DESCRIPTION/SPECIFICATIONS/WORK STATEMENT

ARTICLE C.1. STATEMENT OF WORK

a. Independently and not as an agent of the Government, the Contractor shall be required to furnish all the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the Statement of Work, dated July 10, 2006, attached hereto and made a part of this Solicitation (See Section J - List of Attachments).

ARTICLE C.2. REPORTING REQUIREMENTS

a. Technical Progress Reports

1. In addition to the required reports set forth elsewhere in this Schedule, the preparation and submission of regularly recurring Technical Progress Reports will be required in any contract resulting from this solicitation. These reports will require descriptive information about the activities undertaken during the reporting period and will require information about planned activities for future reporting periods. The frequency and specific content of these reports will be determined prior to contract award.

   For proposal preparation purposes only, it is estimated that 3 copies of these reports will be required as follows:

(X) Quarterly
(X) Annually
(X) Final - Upon final completion of the contract

2. Summary of Salient Results

The Contractor will be required to prepare and submit, with the final report, a summary (not to exceed 200 words) of salient results achieved during the performance of the contract. This report will be required on or before the completion date of the contract.

b. Other Reports/Deliverables: See Attachment 4.

SECTION D - PACKAGING, MARKING AND SHIPPING

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

SECTION E - INSPECTION AND ACCEPTANCE

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

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

c. Inspection and acceptance will be performed at, DAIDS, NIAID, NIH, DHHS, 6610 Rockledge Drive, Bethesda, MD, 20892.

Acceptance may be presumed unless otherwise indicated in writing by the Contracting Officer or the duly authorized representative within 30 days of receipt.

d. This contract incorporates the following clause by reference, with the same force and effect as if it were given in full text. Upon request, the Contracting Officer will make its full text available.

FAR Clause **52.246-5, Inspection of Services - Cost-Reimbursement** (April 1984).

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

SECTION F - DELIVERIES OR PERFORMANCE

ARTICLE F.1. DELIVERIES

a. Satisfactory performance of this contract shall be deemed to occur upon performance of the work described in Article C.1. and upon delivery and acceptance by the Contracting Officer, or the duly authorized representative, of the services specified in the Delivery Schedule which are described in SECTION C of this contract.

b. Deliveries required by the contractor shall be made f.o.b. destination as set forth in FAR Clause 52.247-35, F.o.b. Destination, Within Consignees Premises (April 1984) [and any specifications stated in SECTION D, PACKAGING AND MARKING AND SHIPPING, of this contract] to the address/addressee listed below:

DELIVERY POINT:

National Institutes of Health
National Institute of Allergy and Infectious Diseases
Building 6700-B, Room 3214

Rockledge Drive
BETHESDA MD 20892- 7612

c. Unless otherwise specified, deliveries shall be made to the Delivery Point specified above Mondays through Fridays (excluding Federal Holidays) between the hours of 8:30 a.m. and 5:30 p.m. EST only. Supplies or services scheduled for delivery on a Federal holiday shall be made the following day.

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

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

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1) CLAUSE:

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

SECTION G - CONTRACT ADMINISTRATION DATA

ARTICLE G.1. PROJECT OFFICER

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

[To be specified prior to award]

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

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

The Government may unilaterally change its Project Officer designation.

ARTICLE G.2. KEY PERSONNEL

Pursuant to the Key Personnel clause incorporated in this contract, the following individual(s) is/are considered to be essential to the work being performed hereunder:

NAME TITLE

[To be specified prior to award]]

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

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

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

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

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

Contract No. (This is the 17 digit number that appears in Block 2 of the SF-26, i.e. HHSN2662007xxxxxC.)

ADB Contract No. (This is the 10 digit number that appears in the upper left hand corner of the SF-26, i.e. N01-AI-7xxxx.)

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

Contracting Officer
Office of Acquisitions, DEA
National Institute of Allergy and Infectious Diseases, NIH, DHHS
Room 3214, MSC 7612
6700B Rockledge Drive
BETHESDA MD 20892-7612

(2) Inquiries regarding payment of invoices should be directed to the designated billing office, 1-866-410-5787 and use ext. 27149 to have FedVRS call me and my regular phone number is (301) 496-2509.

ARTICLE G.4. INDIRECT COST RATES

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

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

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

ARTICLE G.5. GOVERNMENT PROPERTY

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

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

ARTICLE G.6. POST AWARD EVALUATION OF CONTRACTOR PERFORMANCE

a. Contractor Performance Evaluations

Interim and final evaluations of contractor performance will be prepared on this contract in accordance with FAR 42.15. The final performance evaluation will be prepared at the time of completion of work. In addition to the final evaluation, interim evaluations will be prepared annually to coincide with the anniversary date of the

contract.

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

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

b. Electronic Access to Contractor Performance Evaluations

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

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

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

SECTION H - SPECIAL CONTRACT REQUIREMENTS

ARTICLE H.1. HUMAN SUBJECTS

It is hereby understood and agreed that research involving human subjects shall not be conducted under this contract, and that no material developed, modified, or delivered by or to the Government under this contract, or any subsequent modification of such material, will be used by the Contractor or made available by the Contractor for use by anyone other than the Government, for experimental or therapeutic use involving humans without the prior written approval of the Contracting Officer.

ARTICLE H.2. CONTINUED BAN ON FUNDING OF HUMAN EMBRYO RESEARCH

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

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

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

[Applicable information to be included at award]

ARTICLE H.3. NEEDLE EXCHANGE

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

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

[Applicable information to be included at award]

ARTICLE H.4. ANIMAL WELFARE

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

ARTICLE H.5. INTRODUCTION OF RODENTS AND RODENT PRODUCTS

No rodent or rodent product shall be delivered into the NIH, NIAID environment (NIH) directly, or through collaborative research or holding facilities under contract to NCI except by permit. Direct shipments to NIH from a Division of Veterinary Resources (DVR), Office of Research Services (ORS) approved source will be considered exempt. Non-exempt sources must be approved by permit issued through the DVR, ORS. The permit must be obtained by the Contractor prior to the shipment to NIH of the rodents and/or rodent products. The Contractor must be sure that this permit exists and is current before transferring rodents or rodent products into the NIH, NIAID environment. Refusal or negligence to do so will be considered a material breach of contract and may be treated as any other such material breach. Applications for permits should be submitted by facsimile not less than 30 days prior (60 days in situations where quarantine is likely) to shipping date to: NIH Division of Veterinary Resources (DVR), Office of Research Services (ORS), Building 14G, Service Rd. South, Room 102, BETHESDA MD 20892-5210, (301)496-2527, FAX: (301) 402-0352.

ARTICLE H.6. PROTECTION OF PERSONNEL WHO WORK WITH NONHUMAN PRIMATES

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

ARTICLE H.7. SUBCONTRACTING PROVISIONS

a. Small Business Subcontracting Plan

(1) The Small Business Subcontracting Plan, dated [to be completed upon award] is attached hereto and made a part of this contract.

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

b. Subcontracting Reports

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

(1) Individual Subcontract Reports (ISR)

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

April 30th
October 30th

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

For both the Individual and Summary Subcontract Reports, the Contract Specialist shall be included as a contact for notification purposes at the following e-mail address:

JLaVine@niaid.nih.gov
Joshua LaVine, Contract Specialist, OA, NIAID, DEA, DHHS

ARTICLE H.8. SALARY RATE LIMITATION LEGISLATION PROVISIONS

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

b.

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

[Applicable information to be included at award]

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

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

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

ARTICLE H.9. INFORMATION SECURITY

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

a. Information Type

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

[ ] Administrative, Management and Support Information:

[X] Mission Based Information:

b. Security Categories and Levels

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

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

c. Position Sensitivity Designations

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

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

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

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

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

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

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

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

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

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

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

d. Systems Security Plan

The contractor shall protect Federal automated information systems that are developed or accessed by the contractor. System security shall be accomplished in accordance with the contractor=s System Security Plan dated [to be inserted at award]. The plan must:

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

--OR--

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

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

(3) Include an acknowledgment of its understanding of the security requirements.

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

e. Rules of Behavior

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

f. Information Security Training

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

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

Contractor staff shall complete the following additional training prior to performing any work under this contract:
[Additional courses will be listed here in the resultant contract, if applicable.]

g. Personnel Security Responsibilities

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

h. Commitment to Protect Departmental Information Systems and Data

(1) Contractor Agreement

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

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

(2) Contractor-Employee Non-Disclosure Agreements

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

i. References

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

ARTICLE H.10. ENERGY STAR REQUIREMENTS

Executive Order 13123, AGreening the Government Through Efficient Energy Management@ and FAR 23.203 require that when Federal Agencies acquire energy using products, they select, where life-cycle cost-effective, and available, ENERGY STAR7 or other energy efficient products.

Unless the Contracting Officer determines otherwise, all energy-using products acquired under this contract must be either an ENERGY STAR7 or other energy efficient product designated by the Department of Energy=s Federal Energy Management Program (FEMP).

For more information about ENERGY STAR7 see http://www.energystar.gov/
For more information about FEMP see http://www.eere.energy.gov/

ARTICLE H.11. PUBLICATION AND PUBLICITY

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

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

ARTICLE H.12. PRESS RELEASES

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

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

[Applicable information to be included at award]

ARTICLE H.13. REPORTING MATTERS INVOLVING FRAUD, WASTE AND ABUSE

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

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

ARTICLE H.14. YEAR 2000 COMPLIANCE ITEMS

In accordance with FAR 39.106, Information Technology acquired under this contract must be Year 2000 compliant as set forth in the following clause(s):

1. Service Involving the Use of Information Technology

YEAR 2000 COMPLIANCE --SERVICE INVOLVING THE USE OF INFORMATION TECHNOLOGY

The Contractor agrees that each item of hardware, software, and firmware used under this contract shall be able to accurately process date data (including, but not limited to, calculating, comparing and sequencing) from, into and between the twentieth and twenty-first centuries and the Year 1999 and the Year 2000 and leap year calculations.

YEAR 2000 COMPLIANT ITEMS: TBD

(End of Clause)

2. Noncommercial Supply Items Warranty

YEAR 2000 WARRANTY--NONCOMMERCIAL SUPPLY ITEMS

The contractor warrants that each noncommercial item of hardware, software, and firmware delivered or developed under this contract and listed below shall be able to accurately process date data (including, but not limited to, calculating, comparing and sequencing) from, into and between the twentieth and twenty-first centuries and the Year 1999 and the Year 2000 and leap year calculations, when used in accordance with the item documentation provided by the contractor, provided that all listed or unlisted items (e.g., hardware, software and firmware) used in combination with such listed item properly exchange date data with it. If the contract requires that specific listed items must perform as a system in accordance with the foregoing warranty, then that warranty shall apply to those listed items as a system. The duration of this warranty and the remedies available to the Government for breach of this warranty shall be as defined in, and subject to, the terms and limitations of any general warranty provisions of this contract provided that notwithstanding any provision to the contrary in such warranty provision(s), or in the absence of any such warranty provision(s), the remedies available to the Government under this warranty shall include repair or replacement of any listed item whose noncompliance is discovered and made known to the contractor in writing within ninety (90) days after acceptance. Nothing in this warranty shall be construed to limit any rights or remedies the Government may otherwise have under this contract with respect to defects other than Year 2000 performance.

YEAR 2000 COMPLIANT ITEMS: TBD
(End of Clause)

3. Commercial Supply Products Warranty

YEAR 2000 WARRANTY--COMMERCIAL SUPPLY ITEMS

The contractor warrants that each hardware, software and firmware product delivered under this contract and listed below shall be able to accurately process date data (including, but not limited to, calculating, comparing, and sequencing) from, into, and between the twentieth and twenty-first centuries and the Year 1999 and the Year 2000 and leap year calculations, when used in accordance with the product documentation provided by the contractor, provided that all listed or unlisted products (e.g., hardware, software, firmware) used in combination with such listed product properly exchange date data with it. If the contract requires that specific listed products must perform as a system in accordance with the foregoing warranty, then that warranty shall apply to those listed products as a system. The duration of this warranty and the remedies available to the Government for breach of this warranty shall be as defined in, and subject to, the terms and limitations of the contractor's standard commercial warranty or warranties contained in this contract, provided that notwithstanding any provision to the contrary in such commercial warranty or warranties, the remedies available to the Government under this warranty shall include repair or replacement of any listed product whose non-compliance is discovered and made known to the contractor in writing within ninety (90) days after acceptance. Nothing in this warranty shall be construed to limit any rights or remedies the Government may otherwise have under this contract with respect to defects other than Year 2000 performance.

YEAR 2000 COMPLIANT ITEMS: TBD
(End of Clause)

ARTICLE H.15. ANTI -LOBBYING

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

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

Congress or any State legislature.

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

[Applicable information to be included at award]

ARTICLE H.16. INTELLECTUAL PROPERTY OPTION TO COLLABORATOR

NIAID may collaborate with an outside investigator who has proprietary rights to compounds which may be assigned under this contract. This collaborator will be identified by the Project Officer (PO) at the time of assignment and in this case, the following option regarding Intellectual Property Rights will be applicable.

Contractor agrees to promptly notify the NIAID and "Collaborator" in writing of any inventions, discoveries or innovations made by the contractor's principal investigator or any other employees or agents of the contractor, whether patentable or not, which are conceived and/or first actually reduced to practice in the performance of this study using Collaborator's Study Agent (hereinafter "Contractor Inventions").

Contractor agrees to grant to Collaborator: (1) a paid-up nonexclusive, nontransferable, royalty-free, world-wide license to all Contractor Inventions for research purposes only; and (2) a time-limited first option to negotiate an exclusive world-wide royalty-bearing license for all commercial purposes, including the right to grant sub-licenses, to all Contractor Inventions on terms to be negotiated in good faith by Collaborator and Contractor. Collaborator shall notify Contractor, in writing, of its interest in obtaining an exclusive license to any Contractor Invention within six (6) months of Collaborator's receipt of notice of such Contractor Invention(s). In the event that Collaborator fails to so notify Contractor or elects not to obtain an exclusive license, then Collaborator's option shall expire with respect to that Contractor Invention, and Contractor will be free to dispose of its interests in such Contractor Invention in accordance with its own policies. If Contractor and Collaborator fail to reach agreement within ninety (90) days, (or such additional period as Collaborator and Contractor may agree) on the terms for an exclusive license for a particular Contractor Invention, then for a period of six (6) months thereafter, Contractor shall not offer to license the Contractor Invention to any third party on materially better terms than those last offered to Collaborator without first offering such terms to Collaborator, in which case Collaborator shall have a period of thirty (30) days in which to accept or reject the offer.

Contractor agrees that notwithstanding anything herein to the contrary, any inventions, discoveries or innovations, whether patentable or not, which are not Subject Inventions as defined in 35 U.S.C. 201(e),* arising out of any unauthorized use of the Collaborator's Study Agent shall be the property of the Collaborator (hereinafter "Collaborator Inventions"). Contractor will promptly notify the Collaborator in writing of any such Collaborator Inventions and, at Collaborator's request and expense, Contractor will cause to be assigned to Collaborator all right, title and interest in an to any such Collaborator Inventions and provide Collaborator with reasonable assistance to obtain patents (including causing the execution of any invention assignment or other documents). Contractor may also be conducting other more basic research using Study Agent under the authority of a separate Material Transfer Agreement (MTA), or other such agreement with the Collaborator. Inventions arising thereunder shall be subject to the terms of the MTA, and not to this clause.

*35 U.S.C. (e): The term "subject invention" means any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement: Provided, that in the case of a variety of plant, the date of determination (as defined in section 41(d)(FOOTNOTE 1) of the Plant Variety Protection Act (7 U.S.C. 2401(d))) must also occur during the period of contract performance.

Protection of Proprietary Data

Data generated using an investigational agent proprietary to a Collaborator will be kept confidential and shared only with the NIAID and the Collaborator. The Contractor retains the right to publish research results subject to the terms of this contract.

ARTICLE H.17. HOTEL AND MOTEL FIRE SAFETY ACT OF 1990 (P.L. 101-391)

Pursuant to Public Law 101-391, no Federal funds may be used to sponsor or fund in whole or in part a meeting, convention, conference or training seminar that is conducted in, or that otherwise uses the rooms, facilities, or services

of a place of public accommodation that do not meet the requirements of the fire prevention and control guidelines as described in the Public Law. This restriction applies to public accommodations both foreign and domestic.

Public accommodations that meet the requirements can be accessed at: http://www.usfa.fema.gov/hotel/index.htm

ARTICLE H.18. NIH POLICY ON ENHANCING PUBLIC ACCESS TO ARCHIVED PUBLICATIONS RESULTING FROM NIH-FUNDED RESEARCH

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

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

PART II - CONTRACT CLAUSES

SECTION I - CONTRACT CLAUSES

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

General Clauses for a Cost-Reimbursement Research and Development Contract
General Clauses for a Cost-Reimbursement Contract with Non-Profit Organizations Other than Educational Institutions

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

ARTICLE I.2. AUTHORIZED SUBSTITUTIONS OF CLAUSES

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

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

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

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

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

ARTICLE I.3. ADDITIONAL CONTRACT CLAUSES

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

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

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

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

"(c) Waiver of evaluation preference.....

[ ] Offeror elects to waive the evaluation preference."

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

(3) FAR Clause **52.223-3, Hazardous Material Identification and Material Safety Data** (January 1997), with **Alternate I** (July 1995).

(4) FAR Clause **52.223-12, Refrigeration Equipment and Air Conditioners** (May 1995).

(5) FAR Clause **52.227-14, Rights in Data – General, with Alternate V** (June 1987)

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

(7) FAR Clause **52.230-2, Cost Accounting Standards** (April 1998).

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

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

(10) FAR Clause **52.245-19, Government Property Furnished "As Is"** (April 1984).

(11) FAR Clause **52.246-23, Limitation of Liability** (February 1997).

AND/OR

(12) FAR Clause **52.246-24, Limitation of Liability - High-Value Items** (February 1997).

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

(1) HHSAR Clause **352.223-70, Safety and Health** (January 2001). [This clause is provided in full text in Section J - Attachments.]

(2) HHSAR Clause **352.224-70, Confidentiality of Information** (April 1984 - including revisions mandated by the 1/3/2005 Federal Register notice which was effective March 2005).

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

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

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

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

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

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

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

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

Notice to Employees

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Severe forms of trafficking in persons means--

(1) Sex trafficking in which a commercial sex act is induced by force, fraud, or coercion, or in which the person induced to perform such act has not attained 18 years of age; or
(2) The recruitment, harboring, transportation, provision, or obtaining of a person for labor or services,

through the use of force, fraud, or coercion for the purpose of subjection to involuntary servitude, peonage, debt bondage, or slavery. Sex trafficking means the recruitment, harboring, transportation, provision, or obtaining of a person for the purpose of a commercial sex act.

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

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

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

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

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

(A) All host country Government laws and regulations relating to severe forms of trafficking in persons, procurement of commercial sex acts, and use of forced labor; and
(B) All United States laws and regulations on severe forms of trafficking in persons, procurement of commercial sex acts, and use of forced labor which may apply to its employees' conduct in the host nation, including those laws for which jurisdiction is established by the Military Extraterritorial Jurisdiction Act of 2000 (18 U.S.C. 3261-3267), and 18 U.S.C 3271, Trafficking in Persons Offenses Committed by Persons Employed by or Accompanying the Federal Government Outside the United States;

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

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

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

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

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

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

(6) Suspension or debarment.

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

PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

SECTION J - LIST OF ATTACHMENTS

The following documents are incorporated into this RFP:
SOLICITATION ATTACHMENTS:

Attachment No.	Title	Location
Attachment 1:	Packaging and Delivery of Proposal	Linked to the Attachment Title
Attachment 2:	Proposal Intent Response Sheet	Linked to the Attachment Title
Attachment 3:	Statement of Work	Linked to the Attachment Title
Attachment 4	Reporting Requirements and Deliverables	Linked to the Attachment Title
Attachment 5	Appendix A - Additional Technical Proposal Instructions	Linked to the Attachment Title
Attachment 6	Appendix B - Additional Business Proposal Instructions	Linked to the Attachment Title
Attachment 7	Appendix C - Additional Business Proposal Instructions	Linked to the Attachment Title
Attachment 8	Appendix D - Additional Business Proposal Instructions	Linked to the Attachment Title
Attachment 9	Appendix E - Additional Business Proposal Instructions	Linked to the Attachment Title

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

Attachment No.	Title	Location
Attachment 10	Reserved.	
Attachment 11	Reserved.	
Attachment 12:	Technical Proposal Cost Summary	http://www.niaid.nih.gov/contract/forms/form5.rtf
Attachment 13:	Summary of Related Activities	http://www.niaid.nih.gov/contract/forms/form6.rtf
Attachment 14:	Government Notice for Handling Proposals	http://www.niaid.nih.gov/contract/forms/form7.pdf
Attachment 15:	Reserved.	
Attachment 16:	Project Objectives, NIH 1688-1	http://rcb.cancer.gov/rcb-internet/forms/nih1688-1.pdf

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

Attachment No.	Title	Location
Attachment 17:	Proposal Summary and Data Record,	http://www.niaid.nih.gov/contract/forms.htm

	NIH-2043	
Attachment 18:	Small Business Subcontracting Plan	http://rcb.cancer.gov/rcb-internet/forms/sb-subplan-nci.pdf
Attachment 19:	Breakdown of Proposed Estimated Costs (plus Fee) with Excel Spreadsheet	http://oamp.od.nih.gov/contracts/BUSCOST.HTM http://oamp.od.nih.gov/Division/DFAS/spshexcl.xls
Attachment 20:	Offeror 's Points of Contact	http://www.niaid.nih.gov/contract/forms.htm
Attachment 21:	Reserved.	
Attachment 22:	Reserved.	
Attachment 23:	Disclosure of Lobbying Activities, OMB Form SF-LLL	http://rcb.cancer.gov/rcb-internet/forms/sflllin.pdf

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

Attachment No.	Title	Location
Attachment 24:	Reserved.	
Attachment 25:	Monthly Summary Sheet of Sales	http://rcb.cancer.gov/rcb-internet/forms/monsales.pdf
Attachment 26:	Reserved.	
Attachment 27:	Reserved.	
Attachment 28:	Invoice/Financing Request and Contract Financial Reporting Instructions--Cost Reimbursement, NIH(RC)-4	http://rcb.cancer.gov/rcb-internet/forms/rc4.pdf
Attachment 29:	Reserved.	
Attachment 30	Reserved.	
Attachment 31	Reserved.	
Attachment 32:	Safety and Health, HHSAR Clause 352.223-70	http://www.niaid.nih.gov/contract/forms/form10.pdf
Attachment 33:	Procurement of Certain Equipment, NIH(RC)-7	http://www.niaid.nih.gov/contract/forms/NIH-RC-7.pdf
Attachment 34	Reserved.	
Attachment 35	Reserved.	
Attachment 36:	Government Property Schedule	Linked to the Attachment Title
Attachment 37	Reserved.	
Attachment 38:	Commitment To Protect Non-Public Information Contractor Agreement	http://irm.cit.nih.gov/security/Nondisclosure.pdf
Attachment 39:	Roster of Employees Requiring Suitability Investigations	http://ais.nci.nih.gov/forms/Suitability-roster.xls
Attachment 40:	Employee Separation Checklist	http://rcb.cancer.gov/rcb-internet/forms/Emp-sep-checklist.pdf

PART IV - REPRESENTATIONS AND INSTRUCTIONS

SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFEROR S

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

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

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

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

SECTION L - INSTRUCTIONS, CONDITIONS AND NOTICES TO OFFEROR S

1. GENERAL INFORMATION

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(End of Provision)

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 Offeror s 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.

b. **NAICS CODE AND SIZE STANDARD**

Note: The following information is to be used by the Offeror in preparing its Representations and Certifications

(See Section K of this RFP), specifically in completing the provision entitled, SMALL BUSINESS PROGRAM REPRESENTATION, FAR Clause 52.219-1.

(1) The North American Industry Classification System (NAICS) code for this acquisition is 541720. .

(2) The small business size standard is $6,500,000.

THIS REQUIREMENT IS NOT SET-ASIDE FOR SMALL BUSINESS. However, the Federal Acquisition Regulation (FAR) requires in EVERY solicitation, (except for foreign acquisitions) the inclusion of the North American Industry Classification (NAICS) Code and corresponding size standard which best describes the nature of the requirement in the solicitation.

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

It is anticipated that One Award will be made from this solicitation and that the award will be made on/about July 29, 2007.

It is anticipated that the award from this solicitation will be a multiple-year cost reimbursement type contract completion with a term of 7 years, and that incremental funding will be used [see Section L.2.c. Business Proposal Instructions].

d. **ESTIMATE OF EFFORT**

It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the effort to be approximately 8.2 Full Time Equivalent (FTEs) per year. This information is furnished for the Offeror 's information only and is not to be considered restrictive for proposal purposes.

e. **COMMITMENT OF PUBLIC FUNDS**

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

f. **COMMUNICATIONS PRIOR TO CONTRACT AWARD**

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

g. **RELEASE OF INFORMATION**

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

h. **COMPARATIVE IMPORTANCE OF PROPOSALS**

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

i. **PREPARATION COSTS**

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

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

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

Contracting Officer
Office of Acquisitions
National Institute of Allergy and Infectious Diseases
Room 3214
6700B Rockledge Drive MSC 7612
BETHESDA MD 20892-

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

(End of Provision)

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

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

(End of provision)

2. INSTRUCTIONS TO OFFEROR S

a. GENERAL INSTRUCTIONS

INTRODUCTION

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

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

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

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

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

I. COVER PAGE

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

II. TECHNICAL PROPOSAL

It is recommended that the technical proposal consist of a cover page, a table of contents, and the information requested in the Technical Proposal Instructions and as specified in SECTION J, List of Attachments.

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.

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

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

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

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

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

(5) **Alternate Proposals**

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

(6) **Evaluation of Proposals**

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

(7) **Potential Award Without Discussions**

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

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

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

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

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

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

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

(9) **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.

(10) **Selection of Offeror s**

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

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

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

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

(1) Communications will be held with Offeror s 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 Offeror s whose exclusion from, or inclusion in, the competitive range is uncertain.

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

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

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

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

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

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

EACH INSTITUTION MUST:

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

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

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

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

(e) Maintain records, identifiable to each award, of all financial disclosures and all actions taken by the institution with respect to each conflicting interest for: (1) in the case of grants, at least three years from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 CFR Part 74.53(b) and (2) in the case of contracts, 3 years after final payment or, where applicable, for the other time period specified in 48 CFR Part 4 Subpart 4.7, Contract Records Retention.

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

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

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

2) prior to the Institution's expenditure of any funds under the award, the Institution will report to the awarding component the existence of a conflicting interest (but not the nature of the interest or other details) found by the Institution and assure that the interest has been managed, reduced or eliminated in accord with the regulations; and for any interest that the Institution identifies as

conflicting subsequent to the expenditure of funds after award, the report will be made and the conflicting interest managed, reduced, or eliminated, at least on a temporary basis within sixty days of that identification;

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

4) the Institution will otherwise comply with the regulations.

Institutional Management of Conflicting Interests

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

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

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

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

(12) **Past Performance Information**

a) Offeror s shall submit the following information as part of its business proposal.

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

Include the following information for each contract or subcontract:

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

The Offeror shall submit comparable information on all subcontractors that the Offeror proposes to perform a major subcontract under this effort. For the purpose of this solicitation, a “major subcontract” is defined as a subcontract that exceeds $500,000.

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

b) Each Offeror will be evaluated on its performance under existing and prior contracts for similar products or services. The Government is not required to contact all references provided by the Offeror . Also, references other than those identified by the Offeror may be contacted by the Government to obtain additional information that will be used in the evaluation of the Offeror 's past performance.

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

This Solicitation incorporates one or more solicitation provisions by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. The Offeror is cautioned that the listed provisions may include blocks that must be completed by the Offeror and submitted with its quotation or offer. In lieu of submitting the full text provisions, the Offeror may identify the provision by paragraph identifier and provide the appropriate information with its quotation or offer. Also, the full text of a solicitation provision may be accessed electronically at this address: http://www.arnet.gov/far/.

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1):

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

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

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

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

b. TECHNICAL PROPOSAL INSTRUCTIONS

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

(1) **Technical Discussions**

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

a) **Project Objectives, NIH-1688-1**

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

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

The information required under the ASummary of Objectives@ portion of the form MUST meet the requirements set forth in the section of the form entitled, **AINSTRUCTIONS:@**

b) **Statement of Work**

(1) Objectives

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

(2) Approach

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

(3) Methods

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

(4) Schedule

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

c) **Personnel**

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

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

(1) Principal Investigator/Project Director

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

(2) Other Investigators

List all other investigators/professional personnel who will be participating in the project.

Discuss the qualifications, experience, and accomplishments. State the estimated time each will spend on the project, proposed duties on the project, and the areas or phases for which each will be responsible.

(3) Additional Personnel

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

-The specific items or expertise they will provide.

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

-Willingness to act as a consultant.

-How rights to publications and patents will be handled.

(4) Resumes

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

(2) **Technical Evaluation**

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

(3) **Additional Technical Proposal Information**

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

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

(4) **Other Considerations**

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(6) **Sharing Research Data**

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

The NIH endorses the sharing of final research data to expedite the translation of research results into

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

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

(7) **Sharing of Model Organisms for Biomedical Research**

The NIH Research Tools Policy, also referred to as Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, December 1999, supports the concept of timely sharing and distribution of research resources. In accordance with NIH Guide Notice NOT-OD-04-042, dated May 7, 2004, and the September 10, 2004 extension of this policy NOT-OD-04-066, the NIH provides further sharing guidance with particular attention on model organisms for biomedical research. Such organisms include, but are not limited to: mammalian models such as the mouse and rat, and non-mammalian models, such as budding yeast, social amoebae, round worm, fruit fly, zebra fish, and frog. Research resources to be shared include genetically modified or mutant organisms, sperm, embryos, protocols for genetic and phenotypic screens, mutagenesis protocols, and genetic and phenotypic data for all mutant strains.

Offeror s must include in their technical proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding so that other researchers can benefit from these resources, OR provide appropriate reasons why such sharing is restricted or not possible. A reasonable time frame for periodic disposition of material and associated data must be specified in the proposal. In addition, the plan must address if, or how, Offeror s will exercise their intellectual property rights while making model organisms and research resources available to the broader scientific community. At a minimum, the plan should address the following:

- Will material transfers be made with no more restrictive terms than in a Simple Letter Agreement (SLA) (http://ott.od.nih.gov/NewPages/Rtguide_final.htm)for the transfer of materials or the Uniform Biological Material Transfer Agreement (UBMTA) (http://ott/od/nh/gov/NewPages/UMTA.pdf)?

- How will inappropriate Areach-through@ requirements (as discussed in the NIH Research Tools Policy) on materials transferred be discussed?

- How will technologies remain widely available and accessible to the research community, for example, if any intellectual property rights arise for which a patent application may be filed?

Offeror s may request funds in their cost proposal to defray reasonable costs associated with sharing materials or data or transfer of model organisms and associated data to appropriate repositories.

(9) **Information Security is applicable to this solicitation and the following information is provided to assist in proposal preparation.**

IMPORTANT NOTE TO OFFEROR S: The following information shall be addressed in a separate section of the Technical Proposal entitled, AInformation Security.@

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

(a) Information Type

[ ] Administrative, Management and Support Information:

[X] Mission Based Information:

(b) Security Categories and Levels

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

(c) Position Sensitivity Designations

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

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

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

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

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

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

(d) Systems Security Plan

The Offeror =s proposal must:

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

-OR-

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

(i) Security Awareness Training
(ii) Logical Access Control
-Network (ex: firewall)
-System (ex: network OS, tcp wrappers, SSH)
-Application (ex: S-LDAP, SSL)

-Remote Access (ex: VPN)
-Monitoring and support (ex: IDS, pager, NOC)

(iii) Protection against data loss
-OS security (ex: patch management, configuration)
-Application security (ex: patch management)
-Database security
-Back-up and recovery
-Fault tolerance, high availability

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

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

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

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

(e) Information Systems Security Training

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

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

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

(f) References

DHHS Information Security Program Policy: http://www.hhs.gov/ohr/manual/pssh.pdf
DHHS Personnel Security/Suitability Handbook: http://www.hhs.gov/ohr/manual/pssh.pdf
NIST Special Publication 800-16, Information Technology Security Training Requirements: http://csrc.nist.gov/publications/nistpubs/800-16/800-16.pdf
Appendix A-D: http://csrc.nist.gov/publications/nistpubs/800-16/AppendixA-D.pdf
NIST SP 800-18, Guide for Developing Security Plans for Information Technology Systems: http://csrc.nist.gov/publications/nistpubs/index.html
NIST SP 800-60, Guide for Mapping Types of Information and Information Systems to Security Categories, Volume I: http://csrc.nist.gov/publications/nistpubs/800-60/SP800-60V1-final.pdf
NIST SP 800-60, Guide for Mapping Types of Information and Information Systems to Security Categories, Volume II: http://csrc.nist.gov/publications/nistpubs/800-60/SP800-60V2-final.pdf
NIST SP 800-64, Security Considerations in the Information System Development Life Cycle: http://csrc.nist.gov/publications/nistpubs/800-64/NIST-SP800-64.pdf
NIH Computer Security Awareness Training Course: http://irtsectraining.nih.gov/
Roster of Employees Requiring Suitability Investigations: http://ais.nci.nih.gov/forms/Suitability-roster.xls
NCI Information Technology Security Policies, Background Investigation Process: http://ais.nci.nih.gov/
NIH Systems Security Plan Template (detailed): http://irm.cit.nih.gov/security/secplantemp.doc

NIH Information Technology General Rules of Behavior: http://irm.cit.nih.gov/security/nihitrob.html
Commitment To Protect Non-Public Information - Contractor Agreement:
http://irm.cit.nih.gov/security/Nondisclosure.pdf

c. BUSINESS PROPOSAL INSTRUCTIONS

(1) Basic Cost/Price Information

The business proposal must contain sufficient information to allow the Government to perform a basic analysis of the proposed cost or price of the work. This information shall include the amounts of the basic elements of the proposed cost or price. These elements will include, as applicable, direct labor, fringe benefits, travel, materials, subcontracts, purchased parts, shipping, indirect costs and rate, fee, and profit.

(2) Proposal Cover Sheet

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

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

This cover sheet information is for use by Offeror s to submit information to the Government when cost or pricing data are not required but information to help establish price reasonableness or cost realism is necessary. Such information is not considered cost or pricing data, and shall not be certified in accordance with FAR 15.406-2.

(3) Information Other than Cost or Pricing Data

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

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

The information may be submitted in the Offeror's own format.

b) The information submitted shall be at the level of detail described below.

1. Direct Labor

Provide a time-phased (e.g., monthly, quarterly, etc.) breakdown of labor hours, rates, and cost by appropriate category. Key personnel will be separately estimated as above and identified. Give the basis for the estimates in each case.

2. Materials

Provide a consolidated price summary of individual material quantities included in the various tasks, orders, or contract line items being proposed and the basis for pricing (vendor quotes,

invoice prices, etc.).

3. **Subcontracted Items**

Include parts, components, assemblies, and services that are to be produced or performed by others in accordance with Offeror's design, specifications, or direction and that are applicable only to the prime contract. For each subcontract over $550,000, the support should provide a listing by source, item, quantity, price, type of subcontract, degree of competition, and basis for establishing source and reasonableness of price, as well as the results of review and evaluation of subcontract proposals when required by FAR 15.404-3.

4. **Raw Materials**

Consists of material in a form or state that requires further processing. Provide priced quantities of items required for the proposal.

5. **Purchased Parts**

Includes material items not covered above. Provide priced quantities of items required for the proposal.

6. **Fringe Benefits**

Show fringe benefits as a separate line item. Include the rate(s) and/or method of calculating fringe benefits. Provide a copy of your fringe benefit rate or institutional guidelines.

7. **Indirect Costs**

Indicate how Offeror has computed and applied Offeror 's indirect costs, including cost breakdowns, and provide a basis for evaluating the reasonableness of proposed rates. Indicate the rates used and provide an appropriate explanation. Where a rate agreement exists, provide a copy.

8. **Special Equipment**

If direct charge, list any equipment proposed including description, price, quantity, total price, purchase or lease, and the basis for pricing.

9. **Travel**

Provide the cost of travel including destination, duration, purpose, per diem, transportation, and the basis for pricing.

10. **Other Costs**

List all other costs not otherwise included in the categories described above (e.g., computer services, consultant services) and provide basis for pricing.

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

(a) Exceptions from cost or pricing data.

(1) In lieu of submitting cost or pricing data, Offeror s may submit a written request for exception by submitting the information described in the following subparagraphs. The Contracting Officer may require additional supporting information, but only to the extent necessary to determine whether an exception should be granted, and whether the price is fair and reasonable.
(i) Identification of the law or regulation establishing the price offered. If the price is

controlled under law by periodic rulings, reviews, or similar actions of a governmental body, attach a copy of the controlling document, unless it was previously submitted to the contracting office.

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

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

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

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

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

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

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

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

(End of provision)

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

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

This does not preclude the Offeror from absorbing that portion of an employee's annual salary (plus the dollar amount for fringe benefits and associated indirect costs) that exceeds a rate of the Executive Schedule, Level I*. The salary rate limitation set by P.L. 109-149 applies only to Fiscal Year 2006 funds,

however, salary rate ceilings for subsequent years may be included in future DHHS appropriation acts. Multi-year contracts awarded pursuant to this solicitation may be subject to unilateral modifications by the Government if an individual's annual salary exceeds any salary rate ceiling established in future appropriations acts. The Executive Schedule, Level I* annual salary rate limit also applies to individuals proposed under subcontracts; however it does not apply to consultants. P.L. 109-149 states in pertinent part:

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

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

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

(6) **HUBZone Small Business Concerns**

Small Business Offeror s 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.

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

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

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

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

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

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

Offeror s shall include with their offers, SDB targets, expressed as dollars and percentages of total contract value, in each of the applicable, authorized NAICS Subsector(s). The applicable authorized NAICS Subsector(s) for this project is (are) identified elsewhere in this RFP. A total target for SDB participation by the prime contractor, that includes any joint ventures and team members, shall be provided as well as a total target for SDB participation by subcontractors. In addition, Offeror s 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. Offeror s should note that addressing the extent of small disadvantaged business participation **is not in any way intended to be a substitute** for submission of the subcontracting plan, if it is required by this solicitation. An example of the type of information that might be given (in addition to the narrative describing the plan for meeting the targets) follows:

EXAMPLE

Targets for SDB Participation - NAICS Subsector 223

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

*Note: FAR Subpart 9.6 defines AContractor 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.

(8) **Qualifications of the Offeror**

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

a) **General Experience**

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

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

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

c) **Performance History**

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

d) **Pertinent Contracts**

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

e) **Pertinent Grants**

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

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

(9) **Other Administrative Data**

Property

(1) 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:

(a) 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.

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

(2) 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.

(3) The management and control of any Government property shall be in accordance with DHHS Publication (OS) 686 entitled, "Contractor's 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.

(1) The solicitation number (or other procurement identification number).
(2) The Offeror’s name and remittance address, as stated in the offer.

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

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, (June 2003)

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

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

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

(End of Provision)

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

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

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

(10) **Subcontractors**

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

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

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

c) The amount of time and facilities available to this project.

d) Information on its cognizant field audit offices.

e) How rights to publications and patents are to be handled.

f) A complete cost proposal in the same format as the Offeror 's cost proposal.

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

(11) **Offeror 's Annual Financial Report**

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

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

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

(13) **Travel Costs/Travel Policy**

a) **Travel Costs - Commercial**

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

b) **Travel Policy**

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

written travel policy, the Offeror shall so state.

SECTION M - EVALUATION FACTORS FOR AWARD

TECHNICAL EVALUATION CRITERIA
SAFETY EVALUATION OF ANTI-INFECTIVE AGENTS
NIH-NIAID-DAIDS-07-24

A. GENERAL

Selection of an Offeror for contract award will be based on an evaluation of proposals against four factors. The factors, in order of importance, are: technical, cost/price, past performance, and Small Disadvantaged Business (SDB) participation. Although technical factors are of paramount consideration in the award of the contract, cost/price, past performance and SDB participation are also important to the overall contract award decision. All evaluation factors other than cost/price, when combined, are significantly more important than cost or price. The trade-off process described in FAR 15.101-1 may be employed. This process permits tradeoffs among cost/price and non-cost factors and allows the Government to consider award to other than the lowest priced or highest technically rated Offerer. In any event the Government reserves the right to make an award to that Offeror whose proposal provides the best overall value to the Government.

The Technical Proposal will receive paramount consideration in the selection of the Contractor for this acquisition, and should, therefore, be as complete and specific as possible. The Technical Proposal should address each specific element of the Statement of Work. The technical merits of each proposal will be carefully evaluated in terms of the scientific requirements in the Statement of Work as reflected in the detailed criteria listed below. The evaluation will be based upon the demonstrated capabilities of the prospective contractors in relation to the needs of the project as set forth in this RFP. Failure to provide the information required to evaluate the proposal may result in rejection of the proposal without further consideration.

In the event that the technical evaluation panel finds that two or more Offerors are approximately equal in technical ability, then the estimated cost of performance may become paramount. While high competence is sought, CAPABILITIES THAT EXCEED THOSE NEEDED FOR SUCCESSFUL PERFORMANCE OF THE CONTRACT STATEMENT OF WORK ARE NOT REQUESTED. In any event, the Government reserves the right to make an award to the best advantage of the Government, cost and other factors considered, or to make no award.

Listed on the following pages are the Mandatory Qualification and Technical Evaluation Criteria. Mandatory Qualification Criteria establish which proposals will be considered for further review. Technical Evaluation criteria are used by the Technical Evaluation Committee to evaluate the technical merit of the proposals. Offerors must submit information sufficient to evaluate their proposals based on these criteria and must document the feasibility of successful implementation of the Statement of Work requirements of this RFP. The criteria are listed below with weights assigned for evaluation purposes. PROPOSALS WILL BE JUDGED SOLELY ON THE WRITTEN MATERIAL PROVIDED BY THE OFFERORS.

B. MANDATORY QUALIFICATION CRITERION

The Mandatory Qualification Criteria must be met at the time of the original proposal submission. The Offeror must demonstrate experience in conducting preclinical safety studies in compliance with the Good Laboratory Practice Regulations (GLP) as published in 21 CFR Part 58 (Good Laboratory Practice for Nonclinical Laboratory Studies). A copy of the three (3) most recent FDA GLP inspection reports and the Organization's responses shall be provided. In addition, the Offeror shall provide copies of the title and signature pages from six (6) examples of reports of studies conducted in compliance with 21 CFR Part 58, including the signature of the Quality Assurance Officer. The Offeror shall provide documentation of the ability of the Offeror to routinely conduct multiple concomitant safety assessment studies in compliance with GLPs. This may be copies of the Master Study Schedule or other scheduling vehicle. Finally, the Offeror shall provide a list of SOP titles that are used in conducting GLP studies, and shall document the GLP training received by the Offeror's regulatory and scientific staff. Failure to provide all the required documentation for the Mandatory Qualification Criteria will result in rejection of the proposal without further consideration. The documentation of the Mandatory Qualification Criteria will be reviewed by the Project Officer prior to the general technical review of the Technical Proposal.

C. TECHNICAL EVALUATION CRITERIA

CRITERION — WEIGHT

1. Technical Approach and Awareness of the Problem — 65 points

   a. Comprehensiveness of the approach and scientific soundness of the methodology used by the Offeror and any proposed subcontractor in conducting and evaluating *in vivo* toxicology and pharmacokinetic studies with chemical and biological therapies; and *in vitro* drug metabolism. (25 points)

   b. Comprehensiveness of the approach and scientific soundness of the methodology proposed by the Offeror and any proposed subcontractor to evaluate specialized target organ toxicity and experience in conducting those tests on a routine basis using anti-infective therapies; experience with innovative evaluations such as toxic genomics. (20 points)

   c. Comprehensiveness of the approach and scientific soundness of analytical and formulation chemistry techniques and procedures proposed by the Offeror and any potential subcontractor; innovativeness and practicality in solving problems previously encountered in GLP toxicology studies on anti-infective. (20 points)

2. Personnel — 20 points

   a. Documented availability of a highly qualified Principal Investigator with strong scientific credentials in general systemic toxicology (e.g. D.A.B.T.), and with a wide range of experience in managing an inter-disciplinary team of scientists in the conduct of preclinical systemic toxicology studies, special target organ toxicity studies, pharmacokinetic and pathology investigations on chemical and biological anti-infective therapies. (10 points)

   b. Documented availability, experience, and qualifications of professional staff in pathology, pharmacokinetics, analytical and formulation chemistries; documented experience of the proposed staff in performing team-oriented studies of a similar nature to those requested under the Statement of Work, including work with biological therapies; time commitment of the non-technical support staff. Includes qualifications, training, availability, and experience of proposed subcontractor personnel. (10 points)

3. Facilities and Organizational Experience: — 15 points

   Evidence of organizational experience in supporting the conduct of studies similar to those required by the RFP, including a workable administrative structure, an experienced Quality Control unit, availability of necessary on-site laboratory space, analytical equipment, accredited animal quarters, computer resources and a health and safety plan; a demonstrated capability and willingness of the organizational structure to be flexible and responsive in meeting the testing and reporting requirements of previous contracts in a timely fashion. Includes availability and adequacy of facilities and organizational experience of any proposed subcontractor. (15 points)

TOTAL POSSIBLE POINTS: 100

SOLICITATION ATTACHMENTS INCLUDED WITH THE RFP

The following pages include Attachments applicable to this RFP as specified in SECTION J - List of Attachments

PACKAGING AND DELIVERY OF THE PROPOSAL

PAPER SUBMISSION: The paper copy is the official copy for recording timely receipt of proposals.

SUBMISSION OF PROPOSALS BY FACSIMILE IS NOT ACCEPTABLE.

A. EXTERNAL PACKAGE MARKING:

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

NIH-NIAID-DAIDS-07-24
TO BE OPENED BY AUTHORIZED "GOVERNMENT PERSONNEL ONLY"

B. PAPER COPIES and CD-Rom to:

If Hand Delivery or Express Service	**If using U.S. Postal Service**
Joshua J. LaVine Contract Specialist Office of Acquisitions, DEA, NIAID, NIH 6700-B Rockledge Drive, Room 3214 Bethesda, Maryland 20817	Joshua J. LaVine Contract Specialist Office of Acquisitions, DEA, NIAID, NIH 6700-B Rockledge Drive, Room 3214, MSC 7612 Bethesda, Maryland 20892-7612

NOTE: All material sent to this office by Federal Express should be sent to the Hand Carried Address.

NOTE: The U.S. Postal Service's "Express Mail" does not deliver to the hand delivered 20817 zip code address. Any package sent to this address via this service will be held at a local post office for pick-up. THE GOVERNMENT IS NOT RESPONSIBLE FOR PICKING UP ANY MAIL AT A LOCAL POST OFFICE. If a proposal is not received at the place, date, and time specified herein, it will be considered a "late proposal," in accordance **with HHSAR 352.215-70, Late Proposals and Revisions** (NOV 1986).

C. NUMBER OF COPIES:

TECHNICAL PROPOSAL PAGE LIMITS (see table below).

PAGES THAT ARE 2-SIDED WILL COUNT AS 2 PAGES.

TOTAL PAGE COUNT DOES NOT INCLUDE: 1 Cover and 1 Back Page; 1 Table of Contents; Section Dividers that do not contain information other than title of Section.

PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE PROPOSAL AND WILL NOT BE PROVIDED TO THE REVIEWERS TO BE READ OR EVALUATED.

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

Document	Number of Copies	Page Limits
Technical Proposal	PAPER One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES ELECTRONIC FILES ON CD Sixteen (16) Compact Disks containing an electronic copy of the Technical Proposal in a Portable Document Format (PDF) [NOTE: 1 file on each disk.]	Limited to not-to-exceed 200 pages including all appendices.
Technical Proposal Appendices Any materials not available electronically (i.e. SOPs, Pertinent Manuals, Non-scannable Figures or Data, and Letters of Collaboration/Intent also count in the page limit).	PAPER One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES ELECTRONIC FILES ON CD Sixteen (16) Compact Disks containing an electronic copy of the Appendices in a Portable Document Format (PDF) [NOTE: 1 file on each disk.] If any Appendices are not available electronically, 16 hard copies of each page must be provided.	[NOTE: Included in the 200 total page count.]
Business Proposal	PAPER One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES ELECTRONIC FILES ON CD One (1) Compact Disk containing an electronic copy of the Business Proposal in a Portable Document Form (PDF).	N/A
Breakdown of Proposed Estimated Cost	This Attachment should be submitted also as a separate Excel file on the Business Proposal Compact Disk.	N/A

PROPOSAL INTENT RESPONSE SHEET

NIH-NIAID-DAIDS-07-24
Safety Evaluation of Anti-infective Agents

Please review the attached Broad Agency Announcement. Furnish the information requested below and return this page by September 18, 2006. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

[ ] DO INTEND TO SUBMIT A PROPOSAL
[ ] DO NOT INTEND TO SUBMIT A PROPOSAL FOR THE FOLLOWING REASONS:

Company/Institution Name (print): _____
Address (print): _____
_____
_____
_____

Project Director's Name (print): _____
Title (print): _____
Signature/Date: _____
Telephone Number and E-mail Address (print clearly):
_____
_____

***Name of individual to whom electronic proposal instructions should be sent:**

Name: _____
Title: _____
E-Mail Address: _____
Telephone Number: _____

Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):
_____
_____
_____
_____
(Continue list on a separate page if necessary)

Names of Professional Staff To Be Proposed (print):
_____
_____
_____
_____
(Continue list on a separate page if necessary)

RETURN VIA FAX OR E-MAIL TO:

Office of Acquisitions, NIAID, NIH, DHHS
Room 3214
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn: Joshua J. LaVine
NIH-NIAID-DAIDS-07-24
FAX# (301) 480-4675
Email: JLaVine@niaid.nih.gov

STATEMENT OF WORK
SAFETY EVALUATION OF ANTI-INFECTIVE AGENTS
NIH-NIAID-DAIDS-07-24

OVERALL OBJECTIVE AND SCOPE

The Division of AIDS, National Institute of Allergy and Infectious Diseases (NIAID), maintains a portfolio of drug development contracts to assist academic investigators and small pharmaceutical firms by providing the preclinical resources necessary to support submission of an Investigational New Drug (IND) application to the Food and Drug Administration (FDA). The objective of this contract is to support the NIAID in its mission to develop safe and effective therapies for the treatment of infectious diseases caused by Human Immunodeficiency Virus (HIV), Mycobacterium tuberculosis, Plasmodium sp., opportunistic pathogens that infect AIDS patients, and others. The NIAID requires a Safety Evaluation Contract to assess the health and safety potential of new therapies under development by, or with the support of, the Division of AIDS, NIAID. The scope of this effort is to evaluate the toxicity and pharmacokinetics of potential chemical and biological therapies for AIDS and other infectious diseases in various laboratory animal species.

TECHNICAL REQUIREMENTS

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

All projects will be assigned to the Contractor in writing by the Project Officer. The Contractor shall not initiate or conduct studies using contract funds without prior approval by the Project Officer. The chemicals submitted to the Contractor for toxicity and/or pharmacokinetic assessment will mainly be small organic molecules or biologic molecules, and all will be provided to the Contractor by the NIAID.

The major tasks to be carried out by this contract are:

1. Initial Transition
2. Project Planning and Initiation
3. Preclinical Evaluation of Candidate Drugs
4. Development of New Toxicology Models
5. Evaluation of Data
6. Project Management
7. Final Transition

The above tasks include the following detailed requirements:

Task 1. INITIAL TRANSITION

In the event of transition to a new Contractor, the Contractor shall ensure an orderly transition of activities from the predecessor contractor, as follows:

Upon award of the new contract the Project Officer will provide the new Principal Investigator (of the successor Contractor) with a copy of the Final Transition Plan of the outgoing contractor. Within 15 days of contract award the new Contractor shall provide to the Project Officer an Initial Transition Plan and timetable for the receipt, storage, and study (as necessary) of all of the items included in the outgoing contractor's Final Transition Plan. This may include equipment, archived study materials, histologic slides and/or paraffin blocks and all other study materials. Upon approval by the Project Officer, the new Contractor shall implement the initial transition plan within 30 days of award of the contract.

Task 2. PROJECT PLANNING AND INITIATION

Studies will be assigned to the Contractor in writing by the Project Officer and will outline the background and basic needs of the proposed study. The Contractor shall not initiate or conduct studies using contract funds without prior approval by the Project Officer. Within 14 calendar days of receipt of a study assignment, the Contractor shall provide a written Protocol to the Project Officer for approval. The Protocol (based on sample SOP protocols for evaluating toxicology and pharmacokinetics provided in Appendix E), describing the approach to the assignment, may be in outline form, but shall be of sufficient detail such that the rationale for each step is clear and the methods to accomplish the task are provided in sufficient detail to permit

evaluation of progress. Resources necessary to accomplish the request shall be specified, and a timeline for accomplishing the assignment shall be provided. The Project Officer will respond within 14 calendar days of receipt of the Protocol with comments which shall be incorporated prior to commencing work. Project initiation shall proceed only upon approval of the Protocol by the Project Officer via e-mail.

Task 3. PRECLINICAL EVALUATION OF CANDIDATE DRUGS

Using the Standard Operating Procedures provided in Appendix D, the Contractor shall conduct preclinical toxicity evaluations on experimental anti-infective therapies, using Protocols (Appendix E) approved by the Project Officer in consultation with the Principal Investigator. Experimental therapies will be provided by NIAID. The toxicity evaluations to be performed by the Contractor shall be:

a. determine in rodents the maximally tolerated dose (MTD);
b. using Good Laboratory Practices, determine in rodents the acute and subchronic systemic toxicity, and establish relevant pharmacokinetic parameters in these species;
c. using Good Laboratory Practices, determine the in vitro genetic toxicity of experimental therapies;
d. using Good Laboratory Practices, determine in a non-rodent large animal (e.g. dog or non-human primate) the acute and subchronic systemic toxicity of experimental therapies, and establish relevant pharmacokinetic parameters in this species;
e. determine the pharmacokinetics of potential therapies in rodents and nonrodents, including non-human primates;
f. determine in rodents the toxicity of experimental therapies to specialized target organs such as the central nervous system or the immune system;
g. using Good Laboratory Practices determine the local toxicity of experimental therapies to specialized target tissue (e.g. vagina, etc.); and
h. conduct in vitro studies to evaluate the potential of experimental therapies to undergo metabolism in test animals and humans.

Task 4. DEVELOPMENT OF NEW TOXICOLOGY MODELS

Maintain awareness of evolving regulatory requirements for preclinical toxicologic evaluations for chemicals and biologics, develop new models or test systems as required to meet new needs, and maintain a state-of-the-art preclinical toxicity testing program.

Task 5. EVALUATION OF DATA

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. The Offeror should ensure that experimental design and data evaluation are assessed by individuals trained in biostatistical analysis.

Task 6. PROJECT MANAGEMENT

a. Overall Management

Provide a technical and administrative infrastructure to ensure the efficient planning, initiation, implementation, and management of all projects carried out under this contract. This infrastructure shall include a Principal Investigator or Program Manager with responsibility for overall project management and communications, tracking, monitoring, and reporting on project status and progress. The infrastructure shall also include an independent Quality Assurance unit to oversee institutional compliance with GLP regulations.

b. Confidentiality of Data

Maintain confidentiality of data in accordance with the Intellectual Property Clause incorporated into the contract (See Appendix C). Abstracts or manuscripts based on data generated under this contract shall not be submitted for publication or presentation until written concurrence has been received from the Project Officer. The Project Officer will respond within 14 days of receipt of the draft document.

c. Safety Issues

i. Conduct work in accordance with the Safety and Health Clause (HHSAR Clause 352.223-70 (1/01)) incorporated into the contract, the Contractor's Safety and Health Plan, and all applicable Federal, state, and local guidelines and regulations, including Recommendations for the Safe Handling of Cytotoxic Drugs, NIH Publication No. 92-2621 (http://www.nih.gov/od/ors/ds/pubs/cyto/) and the NIH Guidelines for the Laboratory Use of Chemical Carcinogens, NIH

Publication No. 81-2385 (http://grants2.nih.gov/grants/guide/notice-files/not92-070.html).

ii. Provide training, protective garments, equipment, and monitoring to assure safe handling of potentially hazardous materials for all personnel involved in any activities provided under the contract.

d. Communications with the Project Officer

i. Establish a means of electronic communication with the Project Officer sufficient to support exchange of e-mail and the submission of data files and reports if requested.

ii. Provide updates of project status via telephone or e-mail when requested by the Project Officer, or minimally no less than once per month, and more frequently during study initiation and during the in-life portion of the study.

iii. Submit Protocols, Quarterly Progress Reports, Protocol Reports, Annual Progress Reports, and the Final Report in accordance with the required contents and due dates stated in the Reporting Requirements and Deliverables section of the contract.

iv. Meet with the Project Officer at least once each calendar year. Meetings will be held in a location and on a date designated by the Project Officer after consultation with the Principal Investigator. Meetings minimally shall last a half day and shall be attended by the Principal Investigator, contract staff, the Project Officer and/or other staff. If this meeting is an on-site visit at the Contractor's facility, plan (with the input of the Project Officer), conduct and summarize the results of the site visit in writing for inclusion in the Quarterly Progress Report.

Task 7. FINAL TRANSITION

Ensure an orderly transition of contract-related materials to a successor contractor or to the Government. By the end of the third quarter of the final year of this contract, provide a transition plan and prepare to implement an orderly transition of data, tissues, slides, reagents, therapies, and equipment to a successor contractor or to the Government, subject to Project Officer approval. Include an estimate of cost for shipping materials to a successor contractor or to the Government. If requested by the Contract Officer, deliver either to the Government or to a successor contractor by the completion date of the contract the following items: original data, reagents, stored specimens (e.g. slides, tissues, paraffin blocks, etc.) and any necessary information related thereto, and Government-furnished equipment and property.

REPORTING REQUIREMENTS AND DELIVERABLES
SAFETY EVALUATION OF ANTI-INFECTIVE AGENTS
NIH-NIAID-DAIDS-07-24

A. TECHNICAL REPORTS

In addition to those reports required by the other terms of this contract, the Contractor shall prepare and submit the following reports in the manner stated below.

Quarterly Progress Report
Brief Quarterly Progress Reports summarizing the status of all work in progress shall be provided to the Project Officer every three months beginning 90 days after the award date of the contract. Quarterly Progress Reports (ten page maximum) shall detail the status of all studies, preliminary results of studies in progress, problems encountered and proposed means of resolution, anticipated dates for completion of the study and submission of the draft Protocol Report. Quarterly Progress Reports shall include a cumulative listing of Protocol Reports submitted in draft or final form since the award of the contract, and a cumulative list of all therapies studied under the contract. Quarterly Progress Reports shall be due to the NIAID 14 calendar days after the conclusion of the reporting period. Separate Quarterly Progress Reports are not required for the period when an Annual Progress Report or the Final Report is due.

Annual Progress Report
The Contractor shall submit an Annual Progress Report that provides a summary of the work accomplished during the previous twelve months. Annual Progress Reports shall be submitted within 15 days of the anniversary date of the contract. A separate Annual Progress Report shall not be required for the period when the Final Report is due. The Annual Progress Report shall follow the format described below for Protocol Reports, and shall include a tabular, cumulative listing of all therapies studied since the contract began, and the studies that were conducted on each therapy. The Annual Progress Report may be compiled as a collection of abbreviated Protocol Reports (title page, appropriate summary and conclusion sections). The Annual Progress Report shall provide a summary of work accomplished during the previous twelve months, with a more detailed presentation of work completed within the previous three months. An Annual Progress Report shall not be due when the Final Report is due.

Draft Final Report
A Draft Final Report shall be submitted to the Project Officer 30 days prior to the completion date of the contract. The Project Officer will review the Draft Final Report and provide the Contractor with written comments within 15 days of receipt. These comments shall be used by the Contractor in preparing the Final Report.

Final Report
A Final Report shall be submitted by the completion date of the contract and shall include the entire contract period of performance. This report shall consist of the work performed and results obtained for the entire contract period of performance. The Final Report shall be in sufficient detail to describe comprehensively the studies conducted and the results achieved. The Final Report shall be submitted on or before the last day of the contract performance period.

Summary of Salient Results – (Form 1688-1)
The Contractor shall submit, with the Final Report, a summary of salient results achieved during the performance of the contract.

B. TECHNICAL REPORTS DELIVERY SCHEDULE

Item	Type of Report	Initial Report Due	Recipients & Number of Copies	Subsequent Reports Due
1.	Quarterly Progress Report	3 Months after Effective Date of Contract (EDOC)	1 -- PO 1 -- CO	Quarterly; due on or before 15 days following the end of each 3 month period beginning with the start of the contract. Quarterly report not due when Annual Progress Reports or Final Report due.
2.	Annual Progress Report	Anniversary Date of Contract	2 -- PO 1 -- CO	Annually; due within 15 days after the anniversary date. Annual Progress Report not due when Final Report due.

3.	Draft Final Report	30 Days prior to expiration date of contract.	1 – PO 1 -- CO	
4.	Final Report	By expiration date of the contract.	2 -- PO 1 -- CO	
5.	Form 1688-1	At expiration date of the contract.	1 -- PO 1 -- CO	N/A

C. OTHER REPORTS/DELIVERABLES

Invention Report Requirement
Invention Reports are to be submitted as necessary to the Project Officer if patents are filed by the Contractor as a result of intellectual property which may derive from studies assigned throughout the course of the contract award. Patent Rights (FAR 52.227-11 or 52.227-13) will be included in the contract.

Study Protocols
Within 14 days of receipt of a study assignment the Contractor shall provide to the Project Officer a written Study Protocol for approval. The Study Protocol template can be selected from those provided in Appendix E of this RFC and modified as needed to meet the needs of the specific study. More information on the content of Study Protocols is provided in Task 2 of the Statement of Work.

Protocol Reports
The data and results from each protocol in which a particular therapy is studied shall be submitted to the Project Officer within ninety (90) days after the final sampling point of the protocol. The Protocol Report shall accurately and completely describe study design; procedures and findings; present an analysis and summary of the data followed by conclusions derived from the analysis; and shall be in a format suitable for submission to the FDA as a component of an IND application. The Protocol Report must include the protocol followed; all raw and summarized data including data from interim sacrifice or sampling points; drug level evaluations; and pharmacokinetic parameters.

The Protocol Report shall also include, minimally:

1. a cover page to include title, contract number, authors, laboratory address, dates of initiation and completion, and sponsor;

2. a comprehensive summary of the study to be placed after the cover page;

3. the signature of the Study Director;

4. a table of contents;

5. for studies conducted in compliance with Good Laboratory Practices, a statement prepared and signed by the director of the Quality Assurance Unit attesting to the fact that the study was conducted in full compliance with 21 CFR Part 58, and which refers to all phases of the study, including location of raw data records, reports and samples;

6. statistical evaluation of differences between (or among) treatment and control groups;

7. data from each individual animal in each study (provided as an Appendix), as well as a tabular summary of data for each treatment group, compared with a tabular presentation of ranges of historical control values presented in the context of individual control animals from the study; and

8. an evaluation of the meaning and significance of the data, particularly as it relates to potential effects of the experimental therapy in humans.

Initial Transition Plan
Within 15 days of contract award the Contractor shall provide an Initial Transition Plan and timetable for the receipt storage and study (as necessary) of all of the items potentially being transferred from the out-going Contractor. This may include

equipment, test agents, archived samples from completed studies, etc.

Final Transition Plan
Ninety days before the expiration date of the contract, the Contractor shall provide a Final Transition Plan to the Project Officer for the orderly transition of contract-related materials to a successor contractor or to the Government. Materials may include equipment, tissues, slides, reagents, therapies and data not already transferred to the Government. The Final Transition plan shall include an estimated cost of shipping materials to a successor contractor or to the Government.

D. OTHER REPORTS DELIVERY SCHEDULE

Item	Type of Report	Initial Report Due	Recipients & Number of Copies	Subsequent Reports Due
1.	Protocol Report	90 days after completion of a study	2 - PO 1 - CO	As required
2.	Invention Report	As required	1 - PO 1 - CO	As required
3.	Initial Transition Plan	Within 15 days of contract award	1 - PO 1 - CO	N/A
4.	Final Transition Plan	90 days before contract expiration	1 - PO 1 - CO	N/A
5.	Study Protocols	Within 14 days of Study assignment	1 - PO	As required

E. DELIVERABLES

The items specified below will be required to be delivered F.O.B., destination as set forth in FAR 52.247-35, F.O.B. DESTINATION, WITHIN CONSIGNEES PREMISES (APRIL 1984), and in accordance with and by the date(s) specified below.

Upon completion of this contract, all archived specimens, tissues, fluids, and other materials collected and/or analyzed under this contract shall be delivered to the Government and/or subsequent contractors. Any experimental data not previously delivered to the Project Officer shall be provided.

Item	Type of Deliverable	SOW Reference	Due	Recipient	Subsequent Deliverables Due
1.	Archived samples and/or specimens from GLP studies	SOW Task 3	At contract expiration	To be specified 90 days prior to contract expiration	N/A
2.	Data not previously delivered	SOW Task 3	At contract expiration	To be specified 90 days prior to contract expiration	N/A

F. COPIES OF REPORTS SHALL BE SENT TO THE FOLLOWING ADDRESSES:

Address: Project Officer
Drug Development and Clinical Sciences Branch
Division of AIDS/NIAID/NIH

6700B Rockledge Dr., Room 5151
Bethesda, MD 20892 (20817 for overnight deliveries)

Contract Officer
Office of Acquisitions
Division of Extramural Affairs/NIAID/NIH
6700B Rockledge Dr., Room 3149
Bethesda, MD 20892 (20817 for overnight deliveries)

SAFETY EVALUATION OF ANTI-INFECTIVE AGENTS
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APPENDIX A - ADDITIONAL TECHNICAL PROPOSAL INSTRUCTIONS
FORMAT FOR TECHNICAL PROPOSAL – TABLE OF CONTENTS

It is strongly recommended that Offerors use the following template as the Table of Contents for the technical proposal. All information presented in the Technical Proposal should be presented in the order specified below.

The following additional Technical Proposal instructions reflect the requirements of the RFP and are meant to provide additional instructions as well as a uniform format for Technical Proposals. The information requested in these instructions should be used as a guide for formatting and preparing the proposal. Offerors should follow the instructions in Section L of the solicitation, and include the information requested in this appendix.

Offerors are advised to give careful consideration to the Statement of Work, all reference material, appendices and attachments, the Technical Evaluation Criteria, and, the RFP as a whole, in the development of your proposal.

Offerors who propose subcontracts to perform portions of the Statement of Work should clearly identify the specific tasks for which they plan to utilize subcontractors, as well as the method and level of integration between the prime and subcontractor(s), and the expected advantages of such an approach.

Offerors are reminded that the total page limitation for the technical proposal is 200 pages.

TECHNICAL PROPOSAL – TABLE OF CONTENTS

SECTION 1

I. PROPOSAL TITLE PAGE. Include RFP title and number, name of organization, DUNS number, proposal part, and identify if the proposal is an original or copy.
II. PROJECT OBJECTIVES, NIH FORM 1688
III. GOVERNMENT NOTICE FOR HANDLING PROPOSALS
IV. TABLE OF CONTENTS
V. PROPOSAL SUMMARY AND DATA RECORD (NIH-2043)
VI. MANDATORY QUALIFICATION CRITERIA

SECTION 2

MANDATORY QUALIFICATION CRITERIA

Section M of this solicitation includes Mandatory Qualification Criteria. **The Mandatory Qualification Criteria must be met at the time of the original proposal submission.** Information to support compliance must be provided for the prime Contractor and any proposed subcontractor. All Offerors must provide the requested supporting documentation. If you fail to meet these criteria at the time of submission of the original proposal, your proposal will not be considered further for award. Include all information relevant to the Mandatory Qualification Criteria in this clearly marked section of your Technical Proposal, including copies of all materials necessary to demonstrate that you have met the Mandatory Technical Qualification Criteria. Offerors must demonstrate experience in conducting preclinical safety studies in compliance with the Good Laboratory Practice Regulations (GLP) as published in 21 CFR Part 58 (Good Laboratory Practice for Nonclinical Laboratory Studies). A copy of the most recent FDA GLP inspection report and the Organization's response shall be provided. In addition the Offeror shall provide copies of the title and signature pages from six (6) examples of recent reports of studies conducted in compliance with 21 CFR Part 58, including the signature of the Quality Assurance Officer. The Offeror shall provide documentation of the ability

of the Offeror to routinely conduct multiple concomitant safety assessment studies in compliance with GLPs. This may be copies of the Master Study Schedule or other scheduling vehicle. Finally, the Offeror shall provide a list of SOP titles that are used in conducting GLP studies, and shall document the GLP training received by the Offeror 's regulatory and scientific staff.

SECTION 3
TECHNICAL PLAN

The scope of this effort is to evaluate the toxicity and pharmacokinetics of potential chemical and biological therapies for AIDS and other infectious diseases in various laboratory animal species. The Government will provide therapeutic agents to be studied. The Offeror should demonstrate experience developing or adapting analytical methods and formulations for experimental therapeutics.

Technical Proposals shall describe specifically how the Offeror shall fulfill each of the items of the SOW. In addition, Technical Proposals shall include procedures for initiation of contract studies in a timely manner and shall describe how studies in general are prioritized within the organization and the level of priority this contract shall receive. The Technical Proposal shall document prior success in the timely completion of studies such as those requested in the SOW.

Project Planning and Initiation (SOW Task 2)

Although model protocols are provided in Appendix E, the Offeror should provide examples of protocols used previously in studying the acute toxicity, subchronic toxicity, and pharmacokinetic of anti-infective agents, with timelines to show initial assignment, first and final drafts of the protocols, first and last treatment dates, final sacrifice date, and date of submission of the protocol report.

Preclinical Evaluation of Candidate Drugs (SOW Task 3)

Although every effort will be made by the NIAID to provide analytical methods for the detection of experimental therapeutics for use in these studies there may be instances where this information will not be available. In those cases it is expected that the Contractor shall have the ability to develop these techniques or modify existing literature techniques using their own internal chemistry support resources and to formulate experimental therapies for administration to laboratory animals. This capability also will be required as specified in SOPs #5, and #7., found in Appendix D. Thus the Offeror should fully describe its chemistry and formulation support capability in the Technical Proposal in sufficient detail to permit evaluation of this aspect of its capabilities and experience. Include an example of when the Offeror developed a bioanalytic method and an oral formulation for both a New Chemical Entity and a Biologic for use in a subchronic toxicity study of an anti-infective conducted in compliance with GLPs.

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 or proteins also will be studied. The Offeror should document experience evaluating both conventional organic chemical molecules and biological therapies (e.g. nucleic acid plasmids or proteins). Although the Government cannot anticipate the number or type of biological therapies that might be evaluated during the course of the award, the Offeror shall demonstrate experience conducting and evaluating GLP toxicology and pharmacokinetic studies using both conventional organic chemical molecules and biologic therapeutics.

Task 3b, 3c, and 3d

Although some flexibility may be allowed in the development of protocols for the assessments specified under Item #3b, 3c and 3d, the data generated in these studies will be provided to the FDA as part of a packet of information requesting permission to administer the therapy to humans, and thus the general requirements for these tests are largely dictated by that agency. Sample protocols previously used for this kind of testing are indicative of the kind of protocols that may be required, and are provided in Appendix E. The Offeror should provide copies of protocols previously used that generate results similar to those to be expected by using acute and subchronic protocols presented in Appendix E.

Task 3f and 3h

The FDA has not published specific protocols to be used for determining specialized target organ toxicity 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 studies of vaginal irritation, CNS

toxicity, immunotoxicity, and *in vitro* metabolic potential, 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.

Development of New Toxicology Models (SOW Task 4)

Demonstrate experience and expertise in developing cutting edge state-of-the-art toxicity protocols (e.g. toxicogenomics or similar) and in conducting studies on anti-infective drugs using these methods.

Project Management (SOW Task 6)

Task 6a, Overall Management
The Offeror shall describe an administrative framework showing clear lines of authority and a detailed work plan showing proposed time schedules for achieving contract objectives and maintaining quality control over the implementation and operation of the contract, and any subcontracts. Documentation should include all previous and current projects of a similar nature, including the contract number or grant number, the sponsoring agency, the Project Officer, and a brief description of the project. In the event that it is necessary for the Offeror to propose to subcontract a portion of the work, the Offeror should propose specific subcontractor(s) as necessary to complete the required work. Letters of intent to provide this service should be provided by the potential subcontractor(s). A narrative of the subcontractor's qualifications and detailed cost estimate should be submitted with the proposal. In addition, the Offeror should submit documentation of previous experience working with the subcontractor, and the subcontractor's ability to do work in compliance with GLPs if necessary for the work to be performed, and should clearly identify in the Offeror 's proposal the level of effort and all costs associated with the subcontract(s). Similar technical information should be provided as part of the Technical Proposal as that required from the prime Contractor; i.e., technical approach, methods, experience, personnel qualifications, facilities, resources, timeliness, etc.

Offerors shall provide a project organizational chart to include the Quality Assurance Unit. The method of prioritizing work assignments shall be described and the priority given to this contract by the Offeror should be presented and justified. Experience in preparing and following toxicology protocols and SOPs shall be provided and success in adhering to time lines shall be documented. Provide a history of regulatory inspections and responses, including copies of inspection reports. If no regulatory inspection reports were issued, provide the date of the inspection and state the reason no reports were issued.

Task 6b. Confidentiality of Data
Describe the procedures that shall be employed to safeguard the confidentiality of information provided to the Offeror by third parties or the Government, as well as data generated during the performance of the contract.

Task 6c. Safety Issues
The Government considers all drugs and chemical substances as potentially hazardous; therefore, the handling and transport of all compounds under this contract shall be in accordance with all applicable local, state, and Federal regulations including health and safety standards. The Offeror and any proposed subcontractor shall possess and follow a Safety and Health Plan for compliance with all relevant Federal, state, and local guidelines and regulations regarding exposure to potentially hazardous drugs and chemicals. The Offeror shall provide a copy of its Health and Safety Plan which shall include discussions of such topics as training and monitoring of personnel, the use of protective garments and equipment by personnel, and protocols for dealing with chemical spills and accidents.

Task 6d. Communication with the Project Officer
Describe the computer hardware and software used in your facility. Describe your experience hosting site visits from Government Project Officers and provide the agendas and summaries from the last three of these meetings. Discuss your prior experience in communicating via either email or telephone with your previous Project Officers, including frequency, agenda items and the staff person who initiated the communication and selected agenda items.

SECTION 4

ORGANIZATIONAL MANAGEMENT

The Technical Proposal shall include all information relevant to organizational and individual experience and management necessary for successful completion of the SOW. Proposals shall include a Staffing Plan for the conduct of the Statement of Work, including role descriptions and level of effort of key scientific, technical, and administrative personnel, and appropriate lines of authority and responsibility. Describe in detail the responsibilities and level of effort of all proposed professional personnel, including any proposed subcontractor personnel, who will be assigned to the contract.

SECTION 5

PERSONNEL

Describe the experience and qualifications of all scientific, technical and regulatory personnel, including key personnel of any proposed subcontractor. Describe qualifications and relevant training (limit CVs to 2-3 pages), previous experience doing similar complex projects, availability for the proposed project and summary of related activities. Present the full qualifications of the Principal Investigator or Project Manager, including a description of experience conducting multiple simultaneous complex projects such as those required in this RFP and experience/history working with the team proposed for this RFP. Provide a description of the experience of non-technical support personnel and the time each will be committed to this project, as well as their time commitment to other projects. Include similar information for key support personnel of any proposed subcontractor.

SECTION 6

FACILITIES AND RESOURCES

The Technical Proposal shall document availability and adequacy of facilities, equipment, space and other resources necessary to carry out the Statement of Work, including identification and description of support resources (including chemistry and formulation resources, clinical pathology resources, pathology and histopathology resources) which will be required to effectively complete the SOW**.** Provide a floor plan and describe in detail the proposed work flow and group/individual interactions. Include similar documentation for availability and adequacy of facilities and resources of any proposed subcontractor.

SECTION 7

TABLE OF CONTENTS FOR DOCUMENTATION REQUIRED UNDER SECTION L OF THE SOLICITATION

Section L of the RFP provides minimum documentation requirements for the following items. The required information described in Section L should be assembled together, in the following clearly marked sections of the technical proposal. Refer to Section L of the RFP for specific requirements. Also read each section below, carefully. In some cases Offeror s may be asked to provide documentation that is in addition to the minimum requirements identified in Section L.

I) Animal Welfare
Section L of the RFP specifies the minimum documentation requirements for Animal Welfare compliance. All related documentation shall be included in the proposal in a clearly marked section. The Technical proposal should document all information necessary to evaluate animal welfare issues. Minimally this should include the relevant accreditation of the Offeror 's animal housing facility, the animal welfare assurance number, and a full discussion of the composition and function of the Institutional Animal Care and Use Committee.

II) IT Systems Security
Section L of the RFP specifies the minimum documentation requirements for IT Systems security. All related documentation should be included in the proposal in this clearly marked section. The Technical Proposal shall include a plan for IT Systems security as required by this RFP that meets the requirements of "HHS SECURE ONE" as defined in SOW Task 1.

III) Project Objectives, NIH 1688-1

The Technical Proposal shall include a completed NIH Form 1688-1.

SAFETY EVALUATION OF ANTI-INFECTIVE AGENTS
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APPENDIX B -- ADDITIONAL BUSINESS PROPOSAL INSTRUCTIONS AND UNIFORM COST ASSUMPTIONS

In addition to the format requirements for the business proposal that are contained in Section L of the solicitation, the information provided in this appendix is intended to provide uniform cost assumptions and business clarifications.

Offeror s are advised to give careful consideration to the Statement of Work, all reference material provided as appendices and attachments, and the Technical Evaluation Criteria, and, the RFP as a whole, in the development of your proposal. The information requested in these instructions should be used as a guide for the development and formatting of your Business Proposal. Offeror s should consider and include the information requested in this appendix, as well as any other information which will benefit the proposal.

BUSINESS PROPOSAL – TABLE OF CONTENTS

SECTION 1 – PROPOSAL COVERSHEET

SECTION 2 – COST OR PRICE SUPPORT
Section L of the RFP specifies the minimum documentation requirements for cost data and all cost related support. In addition to a standard seven (7) year annual cost proposal, the Offeror shall prepare a cost proposal per protocol that will be used. All related documentation shall be included in the proposal in a clearly marked section.

SECTION 3 – UNIFORM COST ASSUMPTIONS
1) Technical Cost Assumptions

Task 3a. For the purposes of preparing a cost estimate, assume MTD will be determined in nine (9) experimental therapies each year using the protocol presented in Appendix E-1.

Task 3b. For the purposes of preparing a cost estimate, assume acute and 28 day toxicity studies will be conducted in rats on three (3) experimental therapies each year using the protocol presented in Appendix E-3 and E-4.

Task 3c. For the purposes of preparing a cost estimate, assume *in vitro* genetic toxicity will be determined on five (5) experimental therapies each year using the protocol presented in Appendix E-7.

Task 3d. For the purposes of preparing a cost estimate, assume one acute and one 28 day toxicity study will be conducted in dogs each year using the protocol presented in Appendix E-5 and E-6.

Task 3e. For the purposes of preparing a cost estimate, assume that two pharmacokinetic studies will be conducted in non-human primates each year using the protocol presented in Appendix E-2.

Task 3f. Because the FDA has not established protocols for specialized target organ toxicity studies, these studies shall not be included in the cost proposal.

Task 3g. For the purposes of preparing a cost estimate, assume that two chemicals will be studied each year for their irritation potential to vaginal mucosa using the standard rabbit vaginal irritation model described by Eckstein *et al* as published in J. Reprod. Fertil. 20:85 (1969).

Task 3h. For the purposes of preparing a cost estimate, assume that three (3) chemicals will be evaluated for their *in vitro* biotransformation potential in rat liver preparations using the protocol presented in your Technical Proposal, Task 3h of the Statement of Work.

2) Travel
Offeror s shall include a uniform assumption of one trip to Bethesda, MD per year, for one day, for one person.

3) Equipment (GFE)
Government furnished equipment that will be transferred to the successful Offeror includes: (a) Model 1205 Betaplate (Wallac, Inc.) purchased new in l994; (b) Harvester 96 (Tomtec, Inc.) purchased new in l994; (c) Ultra-Low upright Freezer (Revco, Inc.), purchased new in 2005.

4) Estimated Level of Effort
The estimated level of effort for this RFP assumes an overall staffing requirement of approximately 8.2 full time equivalents (FTEs) per year. This information is furnished to Offeror s for information purposes only and is not to be considered restrictive for proposal purposes.

SECTION 4 - TABLE OF CONTENTS FOR DOCUMENTATION REQUIRED UNDER SECTION L OF THE SOLICITATION

I) Small Business Subcontracting Plan
Section L of the RFP specifies the minimum documentation requirements for completing a subcontracting plan. This plan shall be turned in with the original proposal. All related documentation shall be included in the proposal in a clearly marked section.

II) Extent of Small Disadvantaged Business Participation
Section L of the RFP specifies the minimum documentation requirements for small disadvantaged business utilization. This information shall be provided with the original proposal. All related documentation shall be included in the proposal in a clearly marked section.

III) Past Performance Data, including references
Section L of the RFP specifies the minimum documentation requirements for providing past performance information. This information shall be provided with the original proposal. All related documentation shall be included in the proposal in a clearly marked section.

APPENDIX C
INTELLECTUAL PROPERTY OPTION
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The Intellectual Property Option will be offered to NIAID's Third Party Providers of Proprietary Material *and* provides protection of resultant proprietary data. This Article must be included in any subcontract for evaluation of material. The Subcontractor shall then have all the obligations of the Contractor.

The goal of this contract is to promote the development of critical biological information by evaluating various materials for anti-microbial activity. For the purposes of this agreement, "material" includes compositions of matter, and associated information such as methods of making or using the compositions. It is expected that the great majority of materials will be proprietary to third parties. It is clear from the NIAID's experience that third party providers ("Provider") will not provide their proprietary material ("Material") without assurance that the intellectual property rights associated with their Materials will be protected. Accordingly, to encourage Providers to provide their Materials for evaluation under this contract the Contractor agrees to this Intellectual Property Option to the Provider, which requires the Contractor and its subcontractors to provide a research use license and a commercialization license option to Subject Inventions made under the contract to the Providers as follows:

The Contractor agrees to promptly notify the NIAID and the Provider in writing of any Subject Inventions of the Contractor, its principal investigator and/or any other employees or agents of the Contractor, whether patentable or not, which are conceived and/or first actually reduced to practice in the performance of work under this contract using a Provider's Material (hereinafter "Contractor Invention"). The notice shall inform the Provider(s) of its right to the option set forth herein. This may be accomplished by attaching a copy of this Intellectual Property Option to the notice.

(1) Single Provider

With respect to Contractor Inventions resulting from the use of Material provided by one Provider, the Contractor agrees to grant to the Provider: (i) a paid-up nonexclusive, nontransferable, royalty-free, world-wide license to all Contractor Inventions for research purposes only; and (ii) a time-limited first option to negotiate an exclusive, world-wide royalty-bearing license for all commercial purposes, including the right to grant sub-licenses, to any Contractor Invention on terms to be negotiated in good faith by the Provider and the Contractor, subject to the following conditions:

The Contractor will allow the Provider three (3) months from the date the Contractor sends written notice to the Provider of the existence of a Contractor Invention (or such additional period as the Provider and the Contractor may agree) to notify the Contractor in writing, whether or not it wants to obtain an exclusive license to the Contractor Invention. If the Provider fails to notify the Contractor in a timely fashion then the Contractor's obligation to offer the Provider a license option with respect to that Contractor Invention will expire, and the Contractor will be free to dispose of its interests in such Contractor Invention in accordance with the Contractor's policies. If the Contractor and the Provider fail to reach agreement within ninety (90) days, (or such additional period as the Provider and the Contractor may agree) on the terms for an exclusive license for a particular Contractor Invention, then for a period of six (6) months thereafter the Contractor will not offer to license that Contractor Invention to any third party on materially better terms than those last offered to the Provider without first offering such terms to the Provider, in which case the Contractor will offer the Provider a period of thirty (30) days in which the Provider can accept or reject the offer.

(2) Multiple Providers

With respect to a Contractor Invention resulting from the use of Materials provided by multiple Providers, but which is an improvement only to a Material of a specific Provider, the Contractor agrees to grant to that Provider the rights described above in (1).

With respect to any Contractor Inventions resulting from the use of Material from multiple Providers, but that are not improvements to or specific to a single Material, the Contractor agrees to grant to each

Provider who provided Material: (i) a paid-up nonexclusive, nontransferable, royalty-free, world-wide license to all Contractor Inventions for research purposes only; and (ii) a time-limited first option to negotiate a co-exclusive, world-wide royalty-bearing license for all commercial purposes, including the right to grant sub-licenses, to all such Contractor Inventions on terms to be negotiated in good faith by each Provider and the Contractor, subject to the following conditions:

The Contractor will allow each Provider three (3) months from the time the Provider is sent written notice by the Contractor of the existence of a Contractor Invention (or such additional period as each Provider and the Contractor may agree) to notify the Contractor, in writing, whether or not the Provider wants to obtain a co-exclusive license to the Contractor Invention. If a Provider fails to notify the Contractor in a timely fashion then Contractor's obligation to offer that Provider a license option with respect to that Contractor Invention will expire and the Contractor will continue to offer an option to a co-exclusive license to the other Providers as set forth herein. If there is a single other Provider, it shall be offered an option to an exclusive license as though it were a single Provider. If no Provider notifies the Contractor in a timely fashion the Contractor will be free to dispose of its interests in such Contractor Invention in accordance with the Contractor's policies.

Provider Inventions

The Contractor agrees that notwithstanding anything herein to the contrary, any invention or discovery, whether patentable or not, which is not a Subject Invention as defined in 35 USC 201(e)[1] but arises out of an intentional and unauthorized use or modification of the Provider's Material by the Contractor and/or any other employees or agents of the Contractor, will be the property of the Provider (hereinafter "Provider Invention"). The Contractor will promptly notify the Provider in writing of any such Provider Inventions and, at the Provider's request and expense, the Contractor will cause to be assigned to the Provider all right, title and interest in and to any such Provider Inventions and give the Provider any assistance reasonably necessary to obtain patents (including causing the execution of any invention assignment or other documents). The NIAID recognizes that the Contractor may also be conducting other research using the Provider's Material under the authority of a separate agreement with the Provider during the term of this contract; any invention arising under such separate agreement will not be subject to the terms of this provision entitled, "Provider Inventions."

Protection of Proprietary Data

All Materials, data and other information supplied by the Provider or the Project Officer shall be assumed to be confidential unless specifically identified as not confidential in writing by the Project Officer. The Contractor agrees that its principal investigator and/or any other employees or agents of the Contractor will provide the data generated under this contract exclusively to the NIAID or if directed by the NIAID, to the Provider and the FDA or other appropriate Federal agency. The Contractor understands that the NIAID must negotiate individual agreements with the various Providers to obtain Materials and that the terms of the agreements may vary. The NIAID intends that these agreements will provide for the Contractor's right to publish results generated by the Contractor under this contract after a reasonable period of time to allow the Provider to file patent applications and to protect its proprietary information. The Contractor agrees to enter into confidentiality agreements with Providers when required by the Providers as a condition for the Contractor to receive Materials. Such agreements shall reference this contract by contract number and shall be consistent with any agreement the NIAID has entered into with the Provider to obtain Materials. In the event the Contractor reasonably objects to the terms of the confidentiality agreement, the Contractor shall promptly bring such objection to the attention of the Contracting Officer for an appropriate resolution.

[1]35 USC 201(e): The term "subject invention" means any invention of the Contractor conceived or first actually reduced to practice in the performance of work under a funding agreement: Provided, That in the case of a variety of plant, the date of determination (as defined in section 41(d) of the Plant Variety Protection Act (7 U.S.C. 2401(d)) must also occur during the period of contract performance.

APPENDIX D
MINIMAL STANDARD OPERATING PROCEDURES
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All studies to be conducted under this contract will adhere to the following minimal standard operating procedures:

1. **Type of Studies**: Studies performed under this contract are nonclinical laboratory studies and may require compliance with FDA Good Laboratory Practice Regulations. Data from some studies therefore will be included in a report to be submitted to the FDA, and the studies must include appropriate quality assurance documentation.

2. Standard Operating Procedures: All operations pertaining to these studies, unless specifically defined in the protocol, will be performed according to Standard Operating Procedures (SOP) maintained by the Quality Assurance Unit of the contract laboratory and any deviations must be documented by the Study Director. The titles of these SOPs must be provided as a part of the Proposal, and all SOPs must be made available to the review panel if requested.

3. Records: Data will be verified by the laboratory's Quality Assurance Unit and stored in accordance with the Good Laboratory Practice Regulations. As part of the proposal the Offeror should provide in detail the organization and functioning of the Quality Assurance Unit.

4. **Chemical Verification**: Compound identity, strength, stability and purity as well as documentation of methods for detection in biological fluids, if known, will be provided for each compound by the Project Officer. Confirmation of identity and purity will be the responsibility of the Contractor upon receipt of each shipment of each therapy and before any testing commences. Sufficient quantity of drug should be reserved for archiving from each lot and each shipment used.

5. **Formulation, Stability and Storage:** Information on formulation, stability, and storage conditions, if known, will be provided at time of request for testing. It is anticipated that all bulk drug shipments will be stored at 4^{o} C, and dosing solutions will be made fresh daily.

6. **Plasma Compatibility and Hemolytic Potential:** Upon receipt of each new drug, the Contractor shall determine the hemolytic potential and plasma compatibility of each drug, unless available from the literature, using blood and plasma from rats, dogs, and humans (human blood should be obtained by purchase from a blood bank). Standard methods (to be specified in the Proposal) may be used to evaluate these effects. No further testing will be started without the approval of the Project Officer after review of the results.

7. **Drug Concentration Analysis**: Drug concentration analyses will be performed on each newly-formulated dosing solution prior to administration. The dose solution must be within $\pm$10% of the theoretical concentration and results of these analyses will be provided in the Protocol Reports. An adequate quantity of each dosing mixture will be retained for possible repeat analysis until the acceptance of the protocol report of this compound.

8. **Animal Care and Housing:** Animal quarters of the Offeror will be accredited by a suitable national accrediting organization (e.g. American Association of Laboratory Animal Sciences). General procedures for animal care and housing will be in accordance with DHHS Publication No. (NIH) 85-23 (Revised, 1985) and Public Law 91-579 (U.S. Dept. of Agriculture Animal Welfare Act). Rats are to be housed (no more than 3 per cage) by dose and separated by sex. Appropriate caging and bedding (not cedar or pine chips) will be used. No contaminants may be present in the bedding which could interfere with the results of the study. Dogs will be housed no more than two per run as specified in the guidelines and shall be separated by gender.

9. Diet and Water Supply: The rodent diet is to be certified, commercial, dry rodent chow provided ad libitum. The water source will be the public supply given ad libitum. No contaminants may be present in the chow or water which could interfere with the results of the study. For dogs and monkeys, a certified, commercial dry chow or meal with the following minimum composition will be used:

- Approximately 10% moisture

- At least 20% crude protein
- Approximately 5% fat
- Nutritionally adequate amounts of minerals
- Both water soluble and fat soluble vitamins

Dogs and monkeys will be exposed to their daily ration for a total period of 1-2 hours per day. The quantity of the daily ration will be sufficient to meet nutritional requirements. The water source will be the public supply given ad libitum. No contaminants will be present in the feed or water which could affect the results of the study.

10. Animal Identification: All animals will be uniquely identified by tatoo (dogs and monkeys) or ear tag (rats). Positive identification will be required at least after every cage change, blood sampling and dosing.

11. **Quarantine:** All rats are to be quarantined for a minimum of seven days prior to baseline measurements. No prophylactic or therapeutic treatment will be administered during the quarantine period. Only healthy rats will be placed on study. After receipt, dogs and monkeys will be held in quarantine for a minimum of 14 days after receipt by the animal facility and prior to baseline measurements. A complete physical examination including a fecal examination for internal parasites, clinical pathology, body weight and rectal temperature will be performed on dogs and monkeys within seven days of receipt. All data will be recorded. If the physical examination indicates the presence of internal parasites, animals will be administered a vermifuge recommended by the staff Veterinarian and approved by the Project Officer. Only positive animals will be treated for parasites. If treatment is necessary, a minimum of 28 days after the conclusion of therapy will elapse prior to initial dosing. All animals selected for study will be in good physical condition. Dogs or monkeys maintained as part of an on-site animal colony will undergo a complete physical exam (including clinical chemistry and hematology analysis) prior to use on any protocol. Results will be recorded and only completely healthy animals will be used.

12. **Randomization**: In order to obtain groups that are comparable by weight, animals will be randomized to treatment groups using a computer-based body weight stratification procedure to be provided by the Contractor. Individual body weights for randomization will be determined on Day -3.

13. **Dosing Calculations:** Validation of drug identity and all calculations for amount of drug given will be checked by a second individual who will initial and date the verification. Dosing will be on a standard volume per unit of body weight.

14. Pathology: Sections of paraffin-embedded tissues will be cut approximately five microns thick and stained with hematoxylin and eosin. Tissues will be examined microscopically by a veterinary pathologist. Records of gross findings for a specimen from postmortem observations shall be available to the pathologist when examining that specimen histopathologically.

Moribund animals should be terminated out of sequence. Authorization to terminate moribund animals will be made by the Study Director or other qualified individual after examination of the animals. Termination of moribund animals will follow the same procedure as for scheduled necropsies, with complete histopathology and clinical pathology performed. Animals found dead will have a complete necropsy, unless severely autolyzed. Animals found dead outside of normal working hours will be necropsied as soon as possible, with the carcass refrigerated (not frozen) in the interim period (not to exceed 24 hours). Body and organ weights will be taken and a complete necropsy will be performed unless tissues are extensively autolyzed.

All animals will have final body weights taken and have blood drawn for clinical pathology determinations prior to termination. A complete necropsy and all antemortem observations will be recorded for each animal and commented on or confirmed at necropsy. Animals that are clinically normal will be so indicated. A pathologist will be available during the necropsy to examine any unusual findings.

All lesions should be categorized either as drug-related or nondrug-related. Each lesion should be listed and coded by the most specific topographic and morphologic diagnoses, severity, and distribution using Systemized Nomenclature of Medicine (SNOMED) codes.

APPENDIX E
EXAMPLE STANDARD STUDY TEMPLATES
NIH-NIAID-DAIDS-07-24

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E-1 MAXIMALLY TOLERATED DOSE IN RATS

A. **Objective**: To provide estimates of maximally tolerated doses following intravenous and oral administration to rats.

B. Test Animals: Young (8-12 weeks) adult male outbred (e.g. Sprague Dawley) rats will be used in these studies.

C. **Experimental Design:**

1. **Dosage Groups:** After randomization, the moving averages method of Dixon (J. Amer. Statis. Assoc, 26:967), or another suitable method, will be used to estimate the median lethal and threshold lethal doses of the experimental drug.

2. **Route of Administration:** Test compound will be administered intravenously and orally to separate groups of animals.

3. Measurements: Rats will be observed hourly for the first 6 hours after dosing, and at 24 hours. Clinical signs of toxicity, such as lethargy, piloerection, tremors, fluid discharge, etc will be recorded, as well as lethality. Intent of these studies is NOT to arrive at a firm median lethal dose, but rather to arrive at an estimated lethal dose, that can be used as the upper limit of dosing schedules for pharmacokinetic, acute, and multiple dose toxicity studies. It is anticipated that no more than 10 animals per route will be required for these studies.

NOTE: These studies may be conducted under conditions that do not require adherence to GLP guidelines.

E-2 PHARMACOKINETIC STUDIES

A. Objective: To determine plasma elimination kinetics after single intravenous and oral administrations in several species.

B. **Test Animals:** Young adult male and female outbred rats (e.g. Sprague Dawley), and/or purebred beagle dogs and/or nonhuman primates (Macaca sp.)

C. Experimental Design:

1. Group Assignments: Two groups of animals composed of equal numbers of males and females will be dosed as follows:

Dose Group	Day 0	Day 7
I (low)	IV	PO
II (high)	IV	PO

Group sizes of dogs and monkeys will be one (l) animal of each gender per group. Group size for rats will be a minimum of 3 animals per sex per group. Rats will be grouped such that no more than two interim blood samples will be drawn from any single animal.

2. Route of Administration: The test compound will be given intravenously and orally to the same animals.

3. Dosing Procedure: Separate animals will receive different doses of test agent. The same animals will receive both a single intravenous injection on Day 0 followed by a single oral gavage administration on Day 7. Dose calculations will be based on the individual body weight on each treatment day.

4. Measurements:

a. Clinical Signs: Baseline body temperatures of dogs and monkeys will be taken on Day -3 and three (3) hours after dosing on both Day 0 and Day 7. All adverse clinical signs will be recorded throughout the course of the study.

b. Body Weight, Food and Water Consumptions: Body weights will be taken and recorded on the day of the study. Animals will be fasted overnight before treatment and for 6 hours following treatment. Body weights of dogs

and monkeys will be recorded on Study Days 0, 7, and 14 and 21. Food and water consumption measurements are not required.

c. Clinical Pathology: All dogs and monkeys will be fasted overnight and bled for clinical pathology once on Day -3 and again on Study Days 2, 6, 8, and 22. In no case will animals be bled from the intravenous treatment site.

d. Plasma Drug Level Determination: Blood samples will be obtained from animals at the following times after dosing on Day 0: 0, 2, 5, 10, 20, 30, 45, 60, 90, 120 minutes, and 4, 6, 8, 12, and 24 hours; and at the following times after dosing on Day 7: 0, 20, 40, 60, 90, 120 minutes, 4, 8, 12, 16, and 24 hours. If measurable drug levels are present at 24 hours, an additional blood sample will be drawn at 48 hours after dosing for determination of plasma drug concentration.

An aliquot of each sample will immediately be mixed with anticoagulant, centrifuged, and plasma removed and frozen until analyzed. Drug concentration will be determined by analytical procedures supplied by the Project Officer. Standard pharmacokinetic parameters (e.g. bioavailability, renal clearance, volume of distribution, half-life, etc.) will be determined.

e. Necropsy Procedure: Dogs and monkeys will be considered off study on Day 22, but will not be sacrificed. If all clinical chemistry determinations have returned to baseline, and drug levels are undetectable, by Study Day 22, then these animals may be used in other subsequent studies (e.g. acute or subchronic toxicity studies). Rats will be humanely sacrificed 24 hours after the final blood sample taken after the Day 7 administration.

E-3 ACUTE TOXICITY IN RATS

A. Objective: To determine the maximally tolerated dose, potential reversibility of lesions, and relative toxicity of single or multiple administrations.

B. Test Animals: Outbred young (8-12 week) adult rats (e.g. Sprague-Dawley) of both genders will be used.

C. Experimental design:

1. Single Administration:

a. Group Assignments: After randomization, 12 rats of each gender will be divided among three treatment groups and one vehicle control (VCTL) group (three rats/sex/group). Animals will be humanely sacrificed and necropsied 24 hours after drug administration.

b. Route of Administration: The test compound will be given intravenously and by oral gavage to separate groups of animals. The day of drug administration will be designated Study Day 0. Rats in the vehicle control group will receive a volume equivalent to the greatest volume given to drug-treated animals on a ml/kg basis and on the same schedule as the treatment groups.

c. Measurements:

Clinical Signs: Observe the rats hourly for the first 6 hours after dosing and then as often as clinical signs warrant. Rat identification numbers, dose volumes, drug formulations, vehicle, clinical effects, time of death, and other pertinent information will be recorded.

Body Weight: Individually weigh all rats on the day of treatment and terminally prior to sacrifice (Day 1).

Clinical Pathology: Blood should be drawn from each rat by cardiac puncture for clinical pathology determinations rior to scheduled (Day 1) or moribund sacrifice. The following parameters will be determined on each blood sample:

Hematology
erythrocyte count (RBC) - 10^6/mm3
hemoglobin (HGB) - g/dL
hematocrit (HCT) - %
mean corpuscular volume (MCV) - u^3

mean corpuscular hemoglobin (MCH) - uug
mean corpuscular hemoglobin concentration (MCHC) - %
platelet count (Plate) - $10^3/mm^3$
reticulocyte count (RETIC) - % RBC
total leukocyte count (WBC) - $10^3/mm^3$
differential leukocyte count - %
nucleated red blood cell count (nRBC) - nRBC/100 WBC

Clinical Chemistry
blood urea nitrogen (BUN) - mg/dL
serum aspartate transaminase (AST) - I.U./L
serum alanine transaminase (ALT) - I.U./L
alkaline phosphatase (Alk. Phos.) - I.U./L
serum glucose (BS) - mg/dL
creatinine (CREAT) - mg/dL

Plasma Drug Level Determination: Blood samples will be drawn from each rat at a time after the last dose that eflects maximal plasma drug levels as determined in the pharmacokinetic studies. Each sample will be mixed with anticoagulant, centrifuged, and the plasma removed and frozen until analyzed. A blood sample for plasma drug level determination will be obtained when possible prior to sacrifice of moribund rats. Analytical procedures will be supplied by the Project Officer.

d. **Necropsy Procedure:** The tissues listed below will be examined, sampled and fixed in cold, buffered, isotonic 10% formaldehyde.

Colon
Heart
Ileum
Kidney
Liver
Lungs
Lymph node (mesenteric)
Spleen
Stomach (fundic area)
Thymus

In addition, sections of any tissues with gross lesions will be preserved in fixative. Only the fixed tissues from the control group, and highest dose group with minimal lethality will be embedded, blocked, sectioned and evaluated. The decision to examine tissues from the other dose groups will be made by the Study Director and Project Officer based on available information.

2. Multiple Administrations:

a. Group Assignments: After randomization, 24 rats of each gender will be divided among three treatment groups and one vehicle control (VCTL) group (six rats/sex/group).

b. Route of Administration: The test compound will be given either intraperitoneally or by oral gavage beginning on Study Day 0.

c. Dosing Procedure: Each rat will receive compound or vehicle once daily, or up to every eight hours depending on pharmacokinetic profile, for seven consecutive days beginning on study Day 0. Doses will be based upon each animal's individual body weight taken on the day of treatment. Rats in the vehicle control group will receive a volume equivalent to the greatest volume given to drug-treated animals on a ml/kg basis and on the same schedule as the treatment groups.

d. Measurements:

Clinical Signs: Observe the rats daily until Study Day 21, or more often as clinical effects warrant. Rat

identification numbers, dose volumes, drug formulations, vehicle, clinical effects, day of death, individual body weights as specified below and other pertinent information will be recorded.

Body Weight: Individually weigh all surviving rats on Study Days -3, 0, 1, 2, 4, 7, 10, 14, and terminally prior to sacrifice (Day 21). The rats should be weighed at approximately the same time each day.

Clinical Pathology: Blood should be drawn from each surviving rat for clinical pathology determinations on Days -3, 8, 14, and terminally prior to sacrifice (Day 21) and prior to moribund sacrifice. Blood will be taken from the retro-orbital sinus, except prior to sacrifice when cardiac puncture may be used. The same parameters as specified under the single dose study will be determined on each blood sample.

Plasma Drug Level Determination: Blood samples will be drawn from each rat at a time after the last dose that reflects maximal plasma drug levels as determined in the pharmacokinetic studies. The sample will be mixed with anticoagulant, centrifuged, and the plasma frozen until analyzed. A blood sample for plasma drug level determination will be obtained prior to sacrifice of moribund rats. Analytical procedures will be supplied by the Project Officer.

e. Necropsy Procedure: Half of the surviving rats in each group will be sacrificed on Day 7 and the other half on Day 21. The same tissues listed for the single dose study will be examined, sampled and fixed in cold, buffered, isotonic 10% formaldehyde. The rat identification will be retained with tissues taken during necropsy. In addition, sections of any tissues with gross lesions will be taken and preserved in fixative. Only the fixed tissues from the highest dose group with minimal lethality will be embedded and put into blocks. The decision to examine tissues from the other dose groups will be made by the Study Director and Project Officer based on available information.

E-4 28-DAY TOXICITY IN RATS

A. Objective: To determine target organ toxicity and its reversibility and to assess the safety of the dose producing an efficacious drug concentration in plasma of rats treated for 28 consecutive days.

B. Test Animals: Young (8-12 week) adult male and female outbred (e.g. Sprague-Dawley) rats will be used.

C. Experimental Design:

1. Group Assignments: After randomization, 48 rats of each sex (12 rats per sex/dose) will be assigned to three dose groups and a vehicle control group (VCTL).

GROUP	(MG/KG/DOSE)	# OF ANIMALS[a] STUDY START	# OF ANIMALS SACRIFICED[a] DAY 15	DAY 29	DAY 57
I (VCTL)	0	24	8	8	8
II	TBD	24	8	8	8
III	TBD	24	8	8	8
IV	TBD	24	8	8	8

[a] Equal numbers of males and females.

2. Route of Administration: The test compound will be given orally by gavage.

3. Dosing Procedure: Starting on Day 0, each rat will receive either vehicle or drug orally by gavage once, or up to once every eight hours, daily for 28 days. The amount of drug administered to each rat will be based on its most recent weight. The vehicle control group will receive vehicle on the same schedule as the drug treated animals.

4. Measurements:

a. Clinical Signs: The rats will be observed daily until Study Day 56. Rat identification numbers, dose volumes, drug formulations, vehicle, clinical effects, day(s) of death, individual body weights as specified below and other pertinent information will be recorded.

b. Body Weight: All surviving rats will be individually weighed on Study Days -3, 0, 4, 7, 11, 14, 21, 28, 35, 42, 49, and 56 (prior to sacrifice).

c. Clinical Pathology: Blood for clinical chemistry determinations will be drawn from each rat on Days -3, 7, 14, 21, 28, 35, 42 and prior to termination. Blood will be taken from the retro-orbital sinus, except prior to sacrifice when cardiac puncture may be used. The following parameters will be determined on each blood sample:

Hematology
erythrocyte count (RBC) - 10^6/mm3
hemoglobin (HGB) - g/dL
hematocrit (HCT) - %
mean corpuscular volume (MCV) - u^3
mean corpuscular hemoglobin (MCH) - uug
mean corpuscular hemoglobin concentration (MCHC) - %
platelet count (Plate) - $10^3/mm^3$
reticulocyte count (RETIC) - % RBC
total leukocyte count (WBC) - $10^3/mm^3$
differential leukocyte count - %
nucleated red blood cell count (nRBC) - nRBC/100 WBC

Clinical Chemistry
alanine transaminase (ALT) - IU/L
albumin (ALB) - g/dL
alkaline phosphatase (ALP) - IU/L
aspartate transaminase (AST) - IU/L
albumin/globulin ration (A/G)
blood urea nitrogen (BUN) - mg/dL
calcium (CAL) - mg/dL
chloride (CHL) - mEq/L
creatinine (CREAT) - mg/dL
creatine phosphokinase (CPK) - mg/dL
globulin (GLO) - g/dL
glucose (GLU) - mg/dL
phosphorus (PHO) - mg/dL
potassium (POT) - mEq/L
protein, total (TPR) - mg/dL
prothrombin time (PT) - sec
sodium (SOD) - mEq/L

d. Plasma Drug Level Determination: Blood samples for plasma drug level determination will be obtained from three randomly-selected rats of each gender from each dosage group prior to sacrifice on Days 14 and 28. Blood will be drawn at a time after dosing that is anticipated from pharmacokinetic studies to represent peak plasma levels of the drug. Sample will immediately be mixed with anticoagulant, centrifuged, and the plasma frozen until analyzed. A blood sample for plasma drug level determination will be obtained prior to sacrifice of moribund rats. Analytical procedures will be supplied by the Project Officer.

e. Necropsy Procedure: Four male and four female rats from each group will be sacrificed on Study Days 14, 28, and 56. All rats will have body weights measured, and blood will be drawn for clinical pathology determinations prior to termination. A complete necropsy and all ante mortem observations will be recorded for each rat and commented on or confirmed at necropsy. Rats which are clinically normal will be so indicated. A pathologist will be available throughout the necropsy procedure to examine any unusual findings. The tissues listed below will be examined, sampled and fixed in cold, buffered, isotonic 10% formaldehyde. The rat identification will be retained with tissues upon histologic processing.

Adrenals (both)
Bone marrow (femur) - two samples
Brain
Colon
Duodenum

Eye and attached optic nerve and optic disc
Gonads: Testes/ovaries (both)
Heart
Ileum
Jejunum
Kidneys (both)
Liver
Lungs (infuse with formalin)
Lymph node, mesenteric
Mammary gland
Pancreas
Pituitary gland
Salivary gland
Sciatic nerve
Skin
Spinal cord (thoracolumbar segment. If neurological signs are present, the whole cord should be taken.)
Spleen
Stomach (fundic area)
Thymus
Thyroid and Parathyroid glands
Urinary bladder
Uterus

In addition, sections of any tissues with gross lesions will be taken and preserved in fixative. All fixed tissues from vehicle control and highest dose groups will be embedded into blocks, sectioned, stained with hematoxylin and eosin and evaluated by a pathologist. Only for those tissues judged to be abnormal in the high dose group, will fixed tissue from the lower two groups also be imbedded and evaluated.

f. Micronucleus Evaluation. Cells are flushed from one femur into fetal bovine serum. Cells are concentrated, and spread on ethanol-cleaned microscope slides, air-dried, and fixed for five minutes in absolute methanol. Three slides will be prepared and evaluated from every animal necropsied on day 8. Slides are stained with acridine orange and evaluated using epifluorescence microscopy at 630X or 1000X. Two hundred RBC are scored to determine the ratio of polychromatic erythrocytes (PCE) to RBC, and approximately 2000 PCEs are evaluated to determine the proportion with micronuclei. The normal test for equality of binomial proportions is used to determine if treatment groups are elevated above control, and Cochran-Armitage test is used to determine if a significant dose-response is present.

E-5 ACUTE TOXICITY STUDY IN BEAGLE DOGS

A. Objective: To determine target organ toxicity and its reversibility at steady state plasma levels in dogs receiving multiple or continual administration.

B. Test Animals: Male and female purebred beagles (6-9 months of age;7-14 kg) will be used.

C. Experimental Design:

1. Group Assignments: Two dogs of each sex will be assigned to each of two dose groups and one vehicle control group (Group I) as shown below. Separate groups will be used for each route of administration.

		# OF ANIMALS[a]	# OF ANIMALS SACRIFICED[a]	
GROUP	(MG/KG)	STUDY START	DAY 5	DAY 19
I (VCTL)	0	4	2	2
II	TBD	4	2	2
III	TBD	4	2	2

[a] Equal numbers of males and females.

2. Route of Administration: The test article will be given by oral gavage and by continuous intravenous infusion to separate

groups of animals.

3. Dosing Procedure: The test article will be administered beginning on Study Day 0 to Groups II and III orally by gavage for five consecutive days, and to separate groups of animals as a 120-hour continuous intravenous infusion. Vehicle control animals (Group I) will receive the same treatment as Groups II and III but without drug added. Dose calculation will be based on the individual body weight on each treatment day.

4. Measurements:

a. Clinical Signs: Baseline body temperatures will be taken on Days -10 and -3, immediately before treatment commences on Day 0, and at 4, 12, 24, 48, 72, 96, 120 and 144 hours after the start of the infusion for dogs being treated by that route. Body temperatures will also be recorded on Study Day 7, 14, and 19. Animals will be observed for adverse clinical effects every 6-8 hours during the infusion and at least once daily thereafter or as clinical signs warrant. All adverse effects will be recorded.

b. Body Weight, Food and Water Consumptions: Body weights of all dogs treated by both routes will be recorded on Days -10, -3, 0, 1, 2, 3, 4, 5, 7, 14, and 19. Food intake will be measured and water intake estimated on Days -10 and -3. Food consumption will be recorded daily for the first week and on one day each week thereafter. Water intake will be estimated daily for the first week and weekly thereafter.

c. Ophthalmology: Ocular examinations will be performed on all dogs once during the pretest period (Day -3) and on all dogs prior to necropsy.

d. Clinical Pathology: All dogs will be fasted overnight and a blood sample obtained for clinical pathology evaluation on Days -10, -3, 0, 1, 2, 3, 4, 5, 8, 12, and 19. In no case will dogs that had received the infusion be bled from the treatment site. A blood sample will be obtained prior to necropsy of each dog sacrificed in a moribund condition. The following parameters will be determined on each blood sample:

Hematology

erythrocyte count (RBC) - $10^6/mm^3$
hemoglobin (HGB) - g/dL
hematocrit (HCT) - %
mean corpuscular volume (MCV) - u^3
mean corpuscular hemoglobin (MCH) - uug
mean corpuscular hemoglobin concentration (MCHC) - %
platelet count (Plate) - $10^3/mm^3$
reticulocyte count (RETIC) - % RBC
total leukocyte count (WBC) - $10^3/mm^3$
differential leukocyte count - %
nucleated red blood cell count (nRBC) - nRBC/100 WBC

Clinical Chemistry

alanine transaminase (ALT) - I.U./L
albumin (ALB) - g/dL
albumin/globulin ratio
alkaline phosphatase (Alk. Phos.) - I.U./L
aspartate transaminase (AST) - I.U./L
blood urea nitrogen (BUN) - mg/dL
calcium (Ca) - meq/L
chloride (Cl) - meq/L
creatinine (CREAT) - mg/dL
creatine phosphokinase (CPK) - mg/dL
globulin (GLO) - mg/dL
glucose (BS) - mg/dL
potassium (K) - meq/L
prothrombin time (PT) - sec
sodium (Na) - meq/L
total protein (T PROTEIN) - g/dL

e. Plasma Drug Level Determination: Blood samples for determination of plasma drug levels will be obtained from each dog at the following times after the start of the infusion: 0, 1, 2, 4, 6, 8, 12, 24, 48, 72, 96, 120, 121, 122, 124, 128 and 144 hours. An aliquot of each sample (approximately 2 ml) will be mixed immediately with anticoagulant, plasma prepared and frozen until analyzed. A blood sample will be drawn for plasma drug analysis prior to the sacrifice of moribund dogs. The concentration of drug in each plasma sample will be determined using analytical procedures supplied by the Project Officer.

f. Necropsy Procedure: Two dogs (one male and one female) from each group will be humanely sacrificed on Study Day 5, 24 hours after the final gavage treatment, or termination of the infusion. The remaining animals will be humanely sacrificed on Study Day 19. Dogs will be fasted overnight prior to necropsy. Body weights and blood samples for clinical pathology will be taken on the day of necropsy. The tissues listed below will be examined, sampled and fixed in cold, buffered isotonic 10% formaldehyde.

Adrenal (both)
Bone marrow (section from sternum)
Brain
Cecum
Colon
Duodenum
Eye and attached optic nerve and optic disc
Heart
Ileum
Jejunum
Kidneys (both)
Liver (right medial lobe with section of gall bladder, and left lateral lobe. Record total liver weight.)
Lung (left apical and left diaphragmatic lobes. Infuse one lobe with formalin. Samples of both formalin-infused and non-infused lung should be collected.)
Lymph nodes (mesenteric)
Mammary gland
Ovaries (record combined weight)
Pancreas
Pituitary
Salivary gland
Sciatic nerve
Skin: (injection site - including vein)
Spinal cord: (thoracolumbar segment)
Spleen
Stomach (fundic area)
Testes (epididymides attached)
Thymus
Thyroid and Parathyroids
Tonsil (palatine)
Urinary Bladder
Uterus

In addition, sections of any tissues with gross lesions will be taken and preserved in fixative. The identification mark from the dog will be preserved in fixative. A sample of all fixed tissues from control and high dose groups will be embedded, blocked, sectioned, and stained with hematoxylin and eosin for histological evaluation. Embedding of additional tissues will be dependent upon evaluation of these tissues and will be specified by the Study Director after consulting with the Project Officer.

E-6 28-DAY TOXICITY IN BEAGLE DOGS OR NON-HUMAN PRIMATES

A. Objective: To determine target organ toxicity and its reversibility and to assess the safety of the dose producing an efficacious drug concentration in plasma of dogs or monkeys treated for 28 consecutive days.

B. Test Animals: Male and female purebred beagle dogs (6-9 months of age; 7-14 kg) or adult male and female *Macaca sp*. will be used.

C. Experimental Design:

1. Group Assignments: Four animals of each sex will be randomly assigned to one of three different dose groups and two animals of each sex will be assigned to the vehicle control group, as shown below.

GROUP	(MG/KG/DOSE)	# OF ANIMALS STUDY START[a]	# OF ANIMALS SACRIFICED[a] DAY 28	DAY 56
I (VCTL)	0.0	4	2	2
II	TBD	8	4	4
III	TBD	8	4	4
IV	TBD	8	4	4

[a] Equal numbers of males and females.

2. Route of Administration: The test compound will be given orally in gelatin capsules beginning on Day 0.

3. Dosing Procedure: The test compound will be administered to Groups II, III and IV orally in capsules once daily, or no more frequently than every eight hours, for 28 consecutive days for a maximum theoretical total of 84 treatments. Animals in Group I (VCTL) will receive the same volume of encapsulated vehicle as the dogs in Group IV on the same treatment schedule. Dose calculations will be based on the most recent individual body weight.

4. Measurements:

a. Clinical Signs: Baseline body temperatures will be measured and recorded on Day -10, Day -3, three hours after dosing on Day 0 and twice a week during the dosing period, on Day 28 and weekly thereafter until Day 56 on the same day each week at approximately the same time each day, or as clinical signs warrant. Adverse clinical signs will be recorded as they occur throughout the 28-day dosing period. Animals will be observed after the administration of each dose for signs of toxicity and then at least once a day during the 28-day recovery period.

b. Body Weight, Food and Water Consumptions: Body weights will be recorded on Days -10 and -3, twice weekly during treatment, on Day 28 and weekly thereafter. Food consumptions will be measured and recorded on days -10 and -3, twice weekly during the dosing period, on Day 28 and weekly thereafter. Water intake will be estimated at the same time as food consumption is measured.

c. Ophthalmology: Ocular examinations will be performed on all animals once during the pretest period (Day -3), and on all animals prior to necropsy.

d. Clinical Pathology: All animals will be fasted overnight and blood drawn for clinical pathology on Days -10, -3, 2, 6, 13, 20, 27, and weekly thereafter until necropsy. Blood drawn on dosing days will be taken prior to treatment. A blood sample will be obtained prior to necropsy of each animal sacrificed in moribund condition. The following parameters will be determined in each blood sample:

Hematology
erythrocyte count (RBC) - $10^6/mm^3$
hemoglobin (HGB) - g/dL
hematocrit (HCT) - %
mean corpuscular volume (MCV) - u^3
mean corpuscular hemoglobin (MCH) - uug
mean corpuscular hemoglobin concentration (MCHC) - %
platelet count (Plate) - $10^3/mm^3$
reticulocyte count (RETIC) - % RBC
total leukocyte count (WBC) - $10^3/mm^3$
differential leukocyte count - %
nucleated red blood cell count (nRBC) - nRBC/100 WBC

Clinical Chemistry
alanine transaminase (ALT) - I.U./L

albumin (ALB) - mg/dL
albumin/globulin ratio
alkaline phosphatase (Alk. Phos.) - I.U./L
aspartate transaminase (AST) - I.U./L
blood urea nitrogen (BUN) - mg/dL
calcium (Ca) - meq/L
chloride (Cl) - meq/L
creatinine (CREAT) - mg/dL
globulin (GLO) - mg/dL
glucose (BS) - mg/dL
potassium (K) - meq/L
prothrombin time (PT) - sec
protein, total (T PROTEIN) - g/dL
sodium (Na) - meq/L

e. Plasma Drug Level Determination: Blood samples for determination of drug levels will be drawn from six animals (3 per sex) per dose group at 0 (immediately before dosing), 30, 60, 90, and 120 minutes, 3, 4, 6 and 8 hours after capsule administration on days 0, 6, 13, and 27. The same pair of animals should be used for plasma drug studies on each specified day. The sample (approximately 2 ml) will be mixed with anticoagulant, centrifuged, and the plasma removed and frozen until analyzed. A blood sample will be drawn for plasma drug analysis prior to the sacrifice of moribund animals during the dosing period. Plasma drug levels will be determined using analytical procedures supplied by the Project Officer.

f. Necropsy Procedure: Two male and two female animals from each drug treatment group and one male and one female animal from Group I(VCTL) will be humanely sacrificed on Day 28, 24 hours after the final dose. The remaining animals will be humanely sacrificed on study Day 56. All animals will be killed by ex-sanguination after administration of a barbiturate overdose. The most severely affected animals in each treatment group will be sacrificed on Study Day 28. The animals will be fasted overnight prior to necropsy. Body weights and clinical pathology samples will be taken on the day of necropsy. A complete necropsy and all antemortem observations will be recorded for each animal and commented on or confirmed at necropsy. The tissues listed below will be examined, sampled and fixed in cold, buffered isotonic 10% formaldehyde.

Adrenals (both)
Bone marrow (section from sternum)
Brain
Cecum
Colon
Duodenum (at level of common bile and pancreatic ducts)
Eyes (including optic nerve and optic disk)
Heart
Ileum
Jejunum
Kidneys (both)
Liver (right medial lobe with section of gall bladder and left lateral lobe. Record total liver weight.)
Lung (left apical and left diaphragmatic lobes. Infuse one lobe with formalin by gentle injection into the bronchus with a syringe [do not use a needle]. Samples of both formalin-infused and non-infused lung should be collected)
Lymph nodes (mesenteric)
Mammary gland (left cranial abdominal, from both sexes)
Ovaries (both)
Pancreas
Pituitary
Salivary gland
Sciatic nerve
Skin: Site 1. (nonfrictional surface - dorsal thorax)
Site 2. (frictional surface - elbow)
Spinal cord (thoracolumbar segment for routine sample, or entire spinal cord if

neurological signs indicate cord involvement)
Spleen
Stomach (fundic area)
Testes (epididymis attached)
Thymus
Thyroid and Parathyroids
Tonsil (palatine)
Urinary Bladder
Uterus (uterine horn)

In addition, sections of any tissues with gross lesions will be taken and preserved in fixative. The identification mark from the dog will be preserved in fixative. A sample of all fixed tissues from the vehicle control and high dose groups will be embedded into paraffin blocks, sectioned, stained with hematoxylin and eosin and evaluated by a pathologist. Additional fixed tissues will be routinely embedded and evaluated only for those tissues found abnormal in the high dose group.

E-7 IN VITRO GENETIC TOXICITY

E-7a Genetic Damage in Bacteria

A. **Objective:** The objective of this study is to evaluate the ability of the test article to induce genetic damage in the *Salmonella/E.coli* test system.

B. Test System: Tester strains of *Salmonella typhimuriam* to be used are: TA1535, TA1537, TA98 and TA100. In addition, the *E. coli* WP2(uvrA) strain also will be used. Equivalent testor strains that have been validated and accepted by FDA may be substituted for strains listed here.

C. Experimental Design:

1. Controls. Appropriate sterility and solvent controls for all solvents or carriers will be routinely used. In addition, separate positive controls will be run for each testor strain using chemicals with known mutagenic effect on the testor strain. Test agent will be tested in the presence and absence of a microsomal metabolic activation system. The presence of genetic markers and the plasmid should be regularly established.

2. Test article. Test article will be dissolved in an appropriate solvent and serially diluted until the appropriate test concentration is achieved.

3. Procedure. Plate incorporation assay essentially as described by Brusick *et al* (Mut. Res. 76:1690190; 1980) and Maron & Ames (Mut. Res. 113:173-215; l983) shall be used. A range finding test using a single indicator strain will be conducted over a range of at least 6 concentrations up to and including 5 milligrams per plate. Molten agar, indicator organisms, test article and metabolic activation enzymes will be combined and the mixture poured onto plates containing glucose agar. A minimum of 3 plates per test concentration will be incubated at 37^{o} C for 48 hours and revertant colonies counted.

D. Data evaluation: An experiment will be considered invalid when solvent and sterility controls are not within historical limits, when positive controls do not produce the expected positive response or when there are more than three cytotoxic, or less than three non-effective concentrations. In addition, results are invalid when testor strains are evaluated for the presence of genetic markers or plasmid and found to be anomalous. Appropriate statistical tests such as Levene's test, Dunnett's t test, and regression analysis for evaluation of dose-relatedness will be performed.

E-7b. Genetic Damage in Mammalian Cells

A. Objective: To evaluate 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.

B. Test System: L5178Y mouse lymphoma cells heterozygous at the tk locus will be used.

C. Controls: Cytogenetic analysis will be used to confirm that the banded karyotype of the cells is identical to that of the *tk*+/- cells from which they were derived. An aliquot of each frozen lot of cells will be tested for contamination by *Mycoplasma.* Each compound will be tested in the presence and absence of a microsomal metabolic activation system. Positive controls will

be used to verify the response of the *tk* cells to known mutagens acting at the *tk* locus.
D. Protocol: A cytotoxicity experiment will be conducted to determine the appropriate range of concentrations to be used in the mutagenesis experiment. A minimum range of concentrations of at least 1000-fold will be evaluated for cytotoxicity, up to and including five (5) milligrams per milliliter. For mutagenesis experiments, a minimum of 3 cultures will be evaluated per dose level for both active agent and controls. A minimum of 12 concentrations of test article shall be studied. For each compound studied a new source of cells will be thawed and expanded as a suspension culture.

An aliquot of cells will be incubated overnight with methotrexate in the presence of thymidine, hypoxanthine and glycine to eliminate cells lacking *tk* activity. Methotrexate will be removed and cells permit to continue in exponential growth for an additional 3-6 days before use. Cells will be exposed to test article for 48 hours in roller drums. Test article will be removed and cells resuspended in fresh medium and grown for an additional 2 days to permit expression and selection of the trifluorothymidine (TFT)-resistant cells. Viable resistant cells will be determined by seeding of serial dilutions of the cell cultures into growth medium supplemented with TFT. Cloning efficiency of known numbers of cells will be determined by counting resulting colonies after 10-12 days of incubation.

E. Data Evaluation: Minimally, the frequency of TFT resistant cells by agent concentration will be determined and the significance will be established from a 2-sided test of significance using the slope of the linear regression. The mean of the frequency of TFT resistant colonies will be compared to vehicle control. In addition, other relevant parameters (e.g. cell growth characteristics during exposure, cloning efficiency, colony size, etc.) may be determined.

GOVERNMENT PROPERTY- SCHEDULE