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

RFP-NIH-NIAID-DAIT-05-37
MEDICAL COUNTERMEASURES AGAINST RADIOLOGICAL THREATS: PRODUCT DEVELOPMENT SUPPORT SERVICES

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

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

3. **Issue Date:**	4. **Due Date:** June 10, 2005 **Time:** 4:00 PM, EST	5. **Small Bus. Set-Aside:** [ ]Yes [X] No **8(a) Set-Aside:** [ ]Yes [X] No **NAICS #:** 541710 (See Part IV, Section L.)
April 27, 2005		

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 Limitations: 150 pages

9. **Issued By:**	10. [X] **NIAID reserves the right to make awards without discussion.**	
Carl A. Newman Contracting Officer, PRCB Contract Management Program, DEA NIH, NIAID 6700-B Rockledge Drive Room 3214, MSC 7612 Bethesda, MD 20892-7612	11. **Options:** **[X] No** **[ ] Yes** (See Part IV, Section L.)	12. **Period of Performance:** September 30, 2005 to September 29, 2010

13. **Primary Point of Contact:**	14. **Secondary Point of Contact:**	15. **Protest Officer:**
Name : **Carl Newman** **Phone:** 301-496-8371 **Fax:** 301-402-0972 **E-Mail:** cnewman@niaid.nih.gov	**Name:** Paul McFarlane **Phone:** 301-496-0349 **Fax:** 301-402-0972 **E-Mail:** pmcfarlane@niaid.nih.gov	Program Director, CMP Address (see Block 9.)

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

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

18. **DELIVERY ADDRESS INFORMATION**

19. **Hand Delivery or Overnight Service:**	20. **U.S. Postal Service or an Express Delivery Service**
Carl A. Newman Contract Management Program, DEA NIAID, NIH 6700-B Rockledge Drive, Room 3214 Bethesda, MD 20817	Carl A. Newman Contract Management Program, DEA NIAID, NIH 6700-B Rockledge Drive, Room 3214, MSC 7612 Bethesda, MD 20892-7612

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

Updated thru FAC 2001-27 (3/28/2005)

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BACKGROUND

World events over the past decade have highlighted the growing threat of terrorism and its many forms, including the 1995 Oklahoma City bombing, the 1995 Tokyo sarin gas attack, the terrorist attacks in the U.S. on September 11, 2001, and the deliberate spread of anthrax and ricin through the U.S. postal service and Congressional office buildings in recent years. These incidents provide insight into the range of approaches used by terrorists, including the potential to use chemical, biological, and radiological/nuclear weapons. Threats may include the use of nuclear weapons or devices, attacks on nuclear power plants or reactors, detonation of radiological dispersal devices (RDDs) or "dirty bombs," which combine radioactive material with conventional explosives) or the placement of radiation sources in public locations or in food or water.

The effects of radiation on the body may appear within minutes or develop many years after exposure. Radiation injury is directly proportional to the dose absorbed by the body. Depending on the dose of whole-body exposure to external radiation, the effects can range from an increased risk of cancer years after exposure to more acute effects, including transient nausea and vomiting; hematopoietic and gastrointestinal injury, leading to immunosuppression and infection; metabolic abnormalities; and hemorrhage and anemia. At high exposure levels, damage to the cardiovascular and central nervous systems may lead to early mortality.

Introduction

Recent meetings convened by the White House Office of Science and Technology Policy, Homeland Security Council and Radiological/Nuclear Threat Countermeasures Working Group, and the National Institutes of Health (NIH) identified serious deficiencies in the available medical countermeasures to radiological and nuclear threats. Few medical countermeasures currently exist, and there is no dedicated program within a Federal research agency to address this problem. The Department of Health and Human Services (DHHS) has assigned the NIH the responsibility to identify, characterize, and develop new medical countermeasures against radiological or nuclear attacks. A robust research and development program in this area will begin to yield new diagnostic tools, radio-protectors and mitigators and therapeutic agents to facilitate an effective response against radiological injury. On October 14, 2004, the NIH convened an expert panel to review the “NIH Strategic Plan and Research Agenda for Medical Countermeasures against Radiological and Nuclear Threats.” This strategic plan and research agenda outline a flexible, collaborative, and comprehensive NIH research and product development program focused on medical therapies and diagnostics to counter radiation injury. On behalf of the NIH, the National Institute of Allergy and Infectious Diseases (NIAID) is charged with implementing this research agenda.

The “Medical Countermeasures Against Radiological Threats: Product Development Support Services” contractor will provide: a variety of assays to screen for and confirm compound activity, safety pharmacology, and toxicology; use animal models of radiation injury, protection, therapy, or recovery to provide mechanistic, safety, and animal efficacy data to support U.S. Food and Drug Administration (FDA) approval for human use when it is not ethical to perform human efficacy studies; conduct human safety studies; and formulate and manufacture products under current Good Manufacturing Practices (cGMP).

It is anticipated that products that prove efficacious and can be delivered effectively will be deposited in the Strategic National Stockpile (SNS). The SNS is a national repository of antibiotics, antitoxins, chemical antidotes and other lifesaving pharmaceuticals and medical materials. There is an immediate need to move promising medical countermeasures through development and licensure, and into the SNS, which, currently, includes a limited number of medications for use following radiation exposure.

Few radiation medical countermeasures have been developed to date. Therefore, the requirements for investigational new drug application (IND), new drug application (NDA), and/or biologics license application (BLA) submissions and licensure are uncertain and will have to be determined for each product candidate. Of particular note is that it is unlikely that efficacy testing for these products will be done in humans. Therefore, the FDA will rely on information generated from animal efficacy studies done in accordance with Good Laboratory Practices (GLP) regulations to demonstrate efficacy, as described in the Code of Federal Regulations (CFR) Title 21, Parts 314 and 601 "New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs when Human Efficacy Studies Are Not Ethical or Feasible." The final rule is available at: http://www.fda.gov/cber/rules/humeffic.pdf. The Contractor will need to maintain awareness of the evolving regulatory requirements for animal research and with the FDA regulatory guidelines for animal studies in support of licensure. Products and compounds submitted for evaluation will include prophylactic agents or radioprotectors that must be given before radiation exposure, radiation mitigators that reduce the potential severity of injury, and radiation therapeutics that are given after overt symptoms develop.

This contractor will not identify or conduct basic research on new medical countermeasures. The NIAID anticipates that products selected by the government for screening, testing, and development will come from industry, academia, and government agencies. The NIAID currently has two solicitations targeted at the development of radiation medical countermeasures. One is a grant under the Request for Applications (RFA) for "Centers for Medical Countermeasures against Radiation" (RFA AI-04-045). Its primary goal is to develop new medical products to protect against, mitigate the effects of, and treat the short and long-term consequences of radiation exposure due to terrorist attack. The other is a grant under the RFA for "Protecting the Immune System against Radiation: BioShield Accelerated Product Development" (NOT AI-04-044). Its primary goal is to support research projects to accelerate the development of medical products for immune reconstitution to counter injury from radiological or nuclear terrorist attacks. In contrast, this "Medical Countermeasures Against Radiological Threats: Product Development Support Services" contract will complement the grant programs by providing the expertise, capabilities, facilities, and the full range of product development support services to obtain FDA licensure.

The work to be performed under this contract will be initiated by the NIAID Contracts Office through a mechanism called "work assignments." The Government is planning to make one award to a single contractor that will carry out the efforts described in the Statement of Work.

STATEMENT OF WORK

The Contractor shall independently, and not as an agent of the Government furnish all the necessary services, qualified personnel, materials, equipment, and facilities, not otherwise provided by the Government under the terms of this contract directly as needed to perform the work set forth below. The Contractor will provide the required product development support services including the following: preclinical screening and efficacy and pharmacology studies; nonclinical safety evaluations; formulation, stability testing and current Good Manufacturing Practice (cGMP) production of candidate drugs; clinical safety and Good Laboratory Practice (GLP) animal efficacy studies; and all documentation for submissions to the U.S. Food and Drug Administration (FDA) for approval and/or licensure of medical countermeasures against radiation injury in humans. It is anticipated that products will enter the evaluation and development pathway at various stages from proof-of-principle to label claim extension. The number of products to be evaluated at each stage is not known.

Except for the initial screening of compounds or when otherwise indicated by the NIAID Project Officer (PO), studies will be performed in accordance with GLP regulations (21 CFR 58), cGMP regulations or Good Clinical Practices (GCP) regulations.

The areas of work to be performed are (A-F):

A. Project Management, Data Management and Statistical Analysis and Administrative Support
B. Development and Performance of Animal Models For Screening and Efficacy Testing Including GLP Animal Efficacy Under The FDA Animal Rule
C. Chemistry, Manufacturing and Controls (CMC) Support Services
D. Nonclinical Safety Studies for Investigational New Drug Application (IND)/New Drug Application (NDA/Biologics License Application (BLA) Submissions
E. Phase I Clinical Safety and Pharmacology Testing
F. Transition Plan

A. PROJECT MANAGEMENT, DATA MANAGEMENT AND STATISTICAL ANALYSIS, AND ADMINISTRATIVE SUPPORT

The Contractor shall provide all support and support services needed for this scope of work from animal model development, screening, preclinical and nonclinical testing, formulation development, stability studies, cGMP production, human clinical safety studies/GLP animal efficacy studies to preparation and submission of IND/NDA/BLA documents for licensure of candidate radiological medical countermeasure drugs or diagnostics.

The Contractor shall:

1. Receive work assignments that have been developed by the NIAID PO and approved by the NIAID Contracting Officer (CO). The Contractor is required to have professional staff with appropriate scientific training and experience to analyze, compile, and prepare reports in formats for regulatory submissions.

2. Provide a Principal Investigator (PI) for overall project management and communication with the NIAID PO. The PI shall maintain an electronic system for project management that tracks and monitors project status. All data, samples, and information developed will be retained and stored according to the

applicable regulatory requirements. In addition, the PI shall provide reports or summaries of data in appropriate formats for FDA submission or as described by the NIAID PO. The PI shall provide specific project/task manager(s) to coordinate and integrate all preclinical developmental, nonclinical safety and efficacy, cGMP production, human clinical safety study, data management, and regulatory submission activities conducted under this contract for any assigned product. Provide a research and administrative team and facilities that include all expertise and capabilities needed for the efficient completion of specific tasks. The team (the Contractor and/or subcontractors) should have previous expertise and a proven track record in the field of radiation biology research.

3. Provide a plan to the NIAID PO that describes how each work assignment [e.g., project management, candidate product development strategy and plan (including preclinical, nonclinical and clinical studies to obtain FDA licensure), screening, safety toxicology, process development and production, safety, regulatory documentation, and information and data management] will be completed that includes key development objectives and milestones, proposed budgets, proposed time schedules for achieving task objectives and milestones, and a QA/QC plan. The NIAID PO will review this plan and approve start of work or request modifications for further review.

4. Identify appropriate resources for the services required for any assigned activity. If services or work will be subcontracted, prepare statements of work for subcontractors and submit them for approval to the NIAID PO.

a. Establish a process for identification/solicitation/review/selection of future subcontractors beyond those consented to at contract award should the need for additional subcontractors arise. This includes the criteria to be used in the review, selection of reviewers, the process for review, timelines and any other relevant factors to be used to ensure appropriate resources are available when needed;

b. Upon identification of appropriate sources and consent of the NIAID CO, issue agreements to initiate work; and

c. Oversee and monitor subcontractors' work. Additionally, ensure personnel, equipment and facilities are compliant with appropriate regulatory requirements.

5. The Contractor shall provide data management capabilities and equipment to submit, compile, store, analyze, track and retrieve all materials, information and documents in a secure environment as specified by the Code of Federal Regulation (CFR) Title 21. The database and management system shall also interface with project management activities and other product development activities, so that secure electronic communications, including email, word processing and data files, can be accomplished between the Contractor, NIAID staff, subcontractors, consultants, grantees and suppliers.

6. Abide by terms of the Confidentiality Agreements with product sponsors signed by the NIAID. The Contractor shall maintain the confidentiality of proprietary data and information provided to them during contract performance. Copies of Confidentiality Agreements will be provided to the Contractor prior to or simultaneous with the delivery of the therapeutic compounds covered by the agreements. Develop and implement Standard Operating Procedures (SOPs) to safeguard proprietary and confidential information and data. Access to these files should be restricted to the NIAID PO, the Contractor's PI, and involved staff.

7. Ensure that appropriate documents are negotiated and signed (i.e. Material Transfer Agreements or Clinical Trial Agreements) covering liability associated with the use of manufacturer's products during product development and clinical trial testing.

8. Meet to collaborate with the NIAID PO and other Government staff or involved scientists, as designated by the NIAID PO.

a. The PI, key personnel and/or project managers shall communicate informally via email and telephone as agreed upon with the NIAID PO and meet with the NIAID PO at least quarterly or as needed, in order to provide oral, electronic (email) or written presentations with updates on the status of each assigned activity.

b. Organize, coordinate, and record minutes for all meetings including any ad hoc advisory or other technical advisory groups to the Contract, and meeting with the FDA or other regulatory agencies.

9. Develop and maintain efficient, effective procedures for documentation of receipt of compound/test article shipments from the Contractor or the NIAID PO. Provide for a computerized inventory of compound/test article identifiers, amounts available, and storage locations.

10. Provide experimental study design and protocols as required.

11. Organize, maintain, and transfer information on protocols and test results, as well as provide reports of these to the NIAID PO. Establish electronic message and document transfer capability with the NIAID PO.

12. Provide regulatory, statistical, clinical coordination and GCP compliance support.

a. Provide technical and administrative assistance in the preparation, assembly, submission and maintenance of 510(k), PMAs, INDs, NDAs, and BLAs. Assistance includes writing and editing documents for subsequent submission to the appropriate regulatory authorities, NIAID, and sponsor-companies.

b. Assist the NIAID PO in the preparation and submission of responses to correspondence from regulatory authorities relating to INDs, NDAs and BLAs, interim and annual reports, Investigator Brochures, etc.

c. Maintain electronic and hard copy files of all documents related to correspondence and submissions to regulatory authorities. Provide adequate storage space and store all hard copy files in binders in locked, fire-protected storage, in an orderly manner easily accessible to the NIAID PO and appropriate Contractor staff.

d. Provide regulatory advice, expertise and review for compliance with appropriate regulatory requirements and regulations. Assist the NIAID PO in ensuring compliance with GLP, cGMP, and GCP related to chemistry, manufacturing, controls; preclinical and nonclinical development; GLP animal efficacy studies; and human clinical safety studies.

13. Upon request of the NIAID PO, the Contractor will establish and support a data coordinating and statistical center for Phase I human safety and animal efficacy studies conducted by third party entities, such as NIH funded grantees, commercial organizations and suppliers. This work will include the following activities.

a. Establish and revise as necessary, SOPs to conduct clinical site monitoring for Phase I human safety trials. SOP's will be reviewed and approved by the PO.

b. Provide fully trained clinical site monitors with documented evidence of education and training to monitor Phase I trials.

c. Provide a monitoring plan for review and approval by NIAID PO that includes frequency of monitoring visits and a list of documents that will be monitored at each site visit including site initiation and close-out visits.

d. Provide NIAID PO with comprehensive monitoring reports for each site visit that includes but is not limited to the following: enrollment, missing documentation, adherence to GCP, protocol violations, reports of adverse and serious adverse events, adequacy of source documents, case report form accuracy, regulatory compliance, and drug accountability.

e. Design and develop study case report forms in collaboration with the clinical sites and NIAID. Provide MedDRA coding for adverse events and file appropriate documentation.

f. Establish and administer efficient, reliable and responsive systems for the collection, management, quality assurance and reporting of study data. Develop, implement, and maintain security requirements, to include:

(1) An Automated Information System (AIS) Security Profile, which at a minimum shall include: the System's Security Plan (SSP); the Risk Analysis (RA); the Continuity of Operations Plan (COOP; also known as the Contingency Plan);

(2) A log or record of the results from testing the COOP, existing plans and progress reports for implementing additional security safeguards and controls; and the system access authorization list. The profile shall be kept-up-to-date for review and potential inspection upon demand by NIH/DHHS authorized agents. Upon request, copies of specified profile documents shall be presented to NIH/DHHS for its own system's security reporting purposes. At a minimum, the COOP shall cover emergency operations, backup operations, and recovery plans to assure continuous operations of the system's facility;

(3) The preparation and submission, for NIAID PO approval, of a RA following the guidance given in part 6, Chapter VI of the HHS IRM Manual. The RA is to be maintained and updated every three years, or in advance of implementing major system modifications or enhancements;

(4) The preparation and submission of an annual SSP, following the instruction in OMB Bulletin 90-08;

(5) Provision of a plan and SOP which will be reviewed and approved by the PO for compliance with the Privacy Act.

g. In collaboration with NIAID and external entities, identified by the NIAID PO, establish and implement a safety reporting system and if necessary provisions for a licensed medical doctor to serve as a medical monitor.

h. As requested by the NIAID PO, design and conduct interim and final statistical analyses of study data, develop recommendations for modifications in the design with respect to statistical parameters such as sample size, prepare interim reports on accrual, retention, compliance, and provide statistical support for the activities of a independent Data and Safety Monitoring Boards (DSMB).

i. Contractor shall support, utilize and maintain data management tools, including data documentation and data dictionaries, data entry software, editing programs to allow reading and analysis of the data, and hard copies of the original data collected from study participants from all studies supported by the Contractor.

14. Contractor shall comply with all applicable health and safety regulations while conducting the work set forth herein. Provide safe facilities and the resources to conduct work in accordance with all applicable state, local and federal licensing requirements for working with potentially hazardous materials, including radionuclides. Ensure adherence to all requirements for storage of hazardous and radioactive materials.

a. Implement procedures to store and dispose of hazardous materials, including radioactive waste;

b. Provide facilities and equipment to receive, store, and manipulate radioactive materials; systems to track stocks of radionuclides, access to those stocks, their use, and disposal; and

c. Provide protective garments, equipment, and sufficient monitoring to assure safe handling of potentially hazardous materials.

15. Provide documentation to meet the following requirements as a part of the work assignments and ensure that the necessary registration, compliance and/or accreditation is maintained throughout the life of the contract:

a. Document permission to use irradiation facilities, including those with the capability to provide total body irradiation of large animals (non-human primates) and inhalation or ingestion of radionuclides as required by the Statement of Work, and fully document the capacity for testing the products as proposed. If transport of animals is required, provide documentation of transport procedures and GLP compliance.

b. Document the availability of appropriate storage space to maintain necessary test articles.

c. Document access to an Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC)-accredited (or equivalent) animal facility and the capacity (appropriate cage space, etc.) needed for testing the products as proposed.

d. Contractor is required to meet the animal demands of the statement of work, have readily available resources for animal purchases and implement the purchase of animals in a time effective, cost effective and appropriate manner.

16. Conduct work with animals in accordance with all federal requirements and the Animal Welfare Act and Public Health Service policy, including the implementation of an animal care and use program and animal use protocol approval process. For safety/toxicology and pharmacology testing and efficacy studies intended to support the clinical use of a test article in humans, the Contractor shall also:

a. Retain and store all records, drug candidate and biological samples, histopathology slides, etc. and make them available as indicated under GLP guidelines.

b. Comply with evolving regulatory requirements for nonclinical evaluations of chemicals or biologics, including efficacy, safety/toxicology and pharmacology studies in support of licensure, such as 21 CFR Parts 312, 314 and 601 and develop new test systems or models as required to meet new needs.

17. Support the preparation and submission of study protocols, statistical and analysis plans, data management and Investigator's Brochure, Investigational New Drug (IND), New Drug Application (NDA) or Amendment, or Biologic License Application (BLA) or Supplement to the Food and Drug Administration (FDA).

For all studies intended to support the licensure or clinical use of a test article in humans, the Contractor shall:

a. Prepare all materials, e.g. study protocols, data, data analyses (including statistical analyses), records, reports and other information required for FDA submission and provide to the NIAID PO or to a designated third party; and

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

18. Report progress in written form according to Reporting Requirements (refer to the "Deliverables and Reporting Requirements" in this RFP).

19. Collaborate and work with third party entities (e.g., grantees, companies, other federal government agencies and suppliers) as directed by the NIAID PO.

B. DEVELOPMENT AND PERFORMANCE OF ANIMAL MODELS FOR SCREENING AND EFFICACY TESTING INCLUDING GLP ANIMAL EFFICACY UNDER THE FDA ANIMAL RULE

The Contractor shall develop animal models to screen candidate drugs for radiological countermeasure efficacy and to evaluate lead candidates at various stages of development for efficacy. The objectives are to develop and use models as standards that can provide quantifiable and comparable data to 1) screen drug candidates for initial activity and 2) further evaluate the efficacy of selected drug candidates for the development of comparative, mechanistic and pharmacological information. These efficacy studies will include pivotal animal studies to supplant human clinical efficacy when human clinical studies are not ethical or feasible as specified by the FDA Animal Rule. The animal models must include the ability to evaluate multiple doses of candidate drugs, multiple radiation exposure levels, and routes of administration. In addition, the Contractor must conduct independent, third-party tests to confirm indication claims for compounds in development. The Contractor must have instrumentation and equipment necessary to perform tasks outlined in the statement of work.

The Contractor shall:

1. Develop animal models(s) of human radiation exposure injury that can be used to as standards to evaluate the activity and/or efficacy of test compounds to reduce radiation-induced damage to the hematopoietic system, the gastrointestinal system, the lungs, and DNA (mutagenesis). Evaluation capabilities of the animal model shall include the following:

    a. Quantitative assessments, which detect differences, with at least a minimal level of statistical confidence (ie., 95% Confidence), between treatment groups of animals, with specific indicators including survival and selected indicators of radiation-induced morbidity.

    b. Evaluation of mechanistic, molecular, physicochemical, biological, and immunological parameters in animal models to support development of radiation/nuclear countermeasures and dose detection methods.

    c. Performance of bioassays in order to quantify radiation exposure (biodosimetry).

    d. Appropriate observations and measures of general toxicity including body weight, food consumption, body temperature, behavior, and other indicators of general health as appropriate.

2. Develop animal model(s) of human radiation exposure injury that can be used as standards to evaluate efficacy of test compounds that decorporate internal radiation sources from ingested, inhaled, or absorbed radionuclides.

3. Perform efficacy evaluation and comparison studies on candidate compounds as specified in work assignments to permit further product development including the assessment and optimization of: drug candidate formulations, route of administration, effective dose levels, and timing of administration.

4. Develop GLP animal models of human radiation exposure injury that can be used as standards to obtain data sufficient to demonstrate efficacy of radiological/nuclear medical countermeasure drug candidates when human efficacy studies are not feasible or not ethical to obtain.

5. Perform GLP animal studies as specified in work assignments to obtain data sufficient to demonstrate efficacy of radiological/nuclear medical countermeasure candidate products when human efficacy studies are not feasible or not ethical to obtain.

6. Comply with of the evolving regulatory environment regarding requirements for animal research and the FDA regulatory guideline for animal studies in support of licensure, such as the 21 CFR Parts 314 and 601 “New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs when Human Efficacy Studies Are Not Ethical or Feasible.”

7. Provide all facilities including irradiation facilities, staff and equipment to conduct the work in compliance with appropriate quality assurance, health and safety, animal care and regulatory requirements.

8. Collect and prepare blood, cell, and tissue samples for necropsy and analysis.

9. Retain and store all records, drug candidate materials, biological samples, histopathology slides, etc. and make them available as indicated under GLP guidelines, or as requested by the Project Officer.

10. Provide a final report for each study to the NIAID PO.

11. Provide all data, information, records and reports required for writing and submission of an Investigational New Drug Application (IND)/New Drug Application (NDA) or Biologics License Application (BLA).

C. CHEMISTRY, MANUFACTURING AND CONTROL TESTING (CMC) SUPPORT SERVICES

The third activity under this contract is the formulation development, production development, stability testing and current Good Manufacturing Practice (cGMP) manufacture of drug candidates as well as the cGMP manufacture of drug products when directed by the NIAID PO. It is anticipated that most of the drug candidates and products will be manufactured by and made available from biotechnology and pharmaceutical companies. The intent is to provide these services when needed and when requested by the NIAID PO. This activity could include the development and validation of all analytical methods and manufacture of drug candidates for the production of lots suitable for IND-enabling safety and activity studies, stability studies, GLP animal efficacy studies, and clinical studies. The candidates may be new small molecule or biological entities.

The Contractor shall develop test candidate products as required and requested by the NIAID PO to support clinical use in humans of a therapeutic product.

When requested by the NIAID PO, the Contractor shall:

1. Develop and quantify validated analytical methods in support of GLP safety and pharmacokinetic studies and in support of clinical studies, to include:

a. Validated analytical methods for assessing concentration, identity, integrity, protective efficacy, purity, potency, sterility, stability, and contamination for testing bulk active ingredients and formulated products.

b. Validated analytical methods for assessing concentrations of test article or active metabolite in biological fluids, such as blood, for testing of pharmacokinetics.

2. Develop validated analytical methods to support stability studies, in-process Quality Assurance (QA)/Quality Control (QC), and product release to include:

a. Validated analytical methods for assessing concentration, identity, integrity, protective efficacy, purity, potency, sterility, stability, and contamination for testing bulk active ingredients, excipients and formulated products.

3. Perform stability studies in compliance with cGMP to support regulatory submissions.

4. Provide the infrastructure, resource and facilities for the development of cGMP compliant manufacturing processes and procedures, and for the cGMP manufacture of bulk products and formulated products (small molecules and biologics) including sterilization, packaging, labeling, storage and distribution that meet FDA-required GLP and cGMP standards. The activities include:

a. development of lab scale, pilot scale, and production scale manufacturing plans and activities for drug candidates and products;

b. production of batches and lots of candidate drugs and products for the conduct of GLP safety studies, stability studies, GLP animal efficacy studies, and clinical safety studies;

c. performance of necessary tests on each batch for the assessments of concentration, identity, integrity, protective efficacy, purity, potency, and contamination for cGMP bulk drug substance and drug product characterization tests required for release for clinical use and periodic assessment of post-production product stability;

d. oversight and audit of facilities and studies to ensure personnel, equipment and facilities are compliant with appropriate regulatory requirements; and

e. compilation of information, preparation of reports and preparation of materials for regulatory submissions.

D. NONCLINICAL SAFETY STUDIES FOR IND/NDA/BLA SUBMISSIONS

The fourth activity under this contract is the pharmacological and GLP toxicology testing of drug candidate and products for safety in small and large animals. This activity includes all such tests that are required to support clinical use in humans; testing must be sufficient to meet requirements for IND/NDA/BLA filing and performed under GLP requirements (21 CFR 58).

The Contractor shall test candidate products for safety/toxicity and perform pharmacology studies as required to support clinical use in humans of a therapeutic product.

The Contractor shall when requested by the NIAID PO:

1. Develop a nonclinical strategy and plan, at the request of the NIAID PO, for each specific drug candidate or product as identified by the NIAID PO. The plan should provide the strategy and the pharmacologic and toxicologic protocols appropriate for IND/NDA/BLA submission.

2. All tests required to qualify a drug candidate product for human administration including the list below. Such testing must also include all tests required for an Investigational New Drug (IND) application. All studies must be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58) unless otherwise specified by the NIAID PO in writing.

a. Preclinical toxicity evaluations of drug candidates or other test articles in animals to include:

1) Determination of the maximally tolerated dose (MTD),
2) Determination of the acute and subchronic systemic toxicity,
3) Determination of relevant pharmacokinetic/toxicokinetic parameters,

4) Bioavailability studies, and
5) Absorption, distribution, metabolism and excretion (ADME) studies.

b. Nonclinical toxicity and safety pharmacology evaluations of drug candidates or other test articles in animals (rodents and non-rodents) to include:

1) acute systemic toxicity,
2) subchronic systemic toxicity,
3) repeat dose toxicity studies, and
4) establishment of relevant pharmacokinetic parameters.

c. Other preclinical toxicity/safety studies, using appropriate animal and *in vitro* assays to include:

1) Genetic toxicity of candidate drugs or test articles,
2) Carcinogenicity studies that may be appropriate under certain conditions, such as when compounds are expected to be administered for extended periods of time. Such studies shall be performed when necessary,
3) Reproductive toxicity studies: Reproductive toxicity studies must be performed prior to the use of these therapies in pregnant women. Such studies shall include fertility, general reproductive performance, teratology, and developmental toxicity,
4) Immunotoxicity studies to determine the toxicity of candidate drugs to the immune system, or other specialized target organ system,
5) Biotransformation assays: Assays, conducted *in vitro* to evaluate the potential of candidate drugs to undergo biotransformation in test animals and humans,
6) Additional pharmacologic assays: Assays and studies to determine additional pharmacologic parameters of candidate drugs such as the following: tissue distribution, mass balance, etc., and
7) All other safety and pharmacology assays and studies that may be required for a particular drug candidate.

3. In addition, the Contractor shall:

a. Evaluate the data resulting from the conduct of the above studies and draw relevant conclusions about pharmacokinetics, target organ(s) of toxicity, and likely human adverse reactions to the evaluated candidate drugs.
b. Provide all data, information, records and reports in formats ready for FDA submission in support of IND/NDA/BLA.
c. Retain and store all records, samples, histopathological slides, etc. and make them available as directed by the Project Officer and as indicated under GLP guidelines.
d. Comply with evolving regulatory requirements for preclinical and nonclinical toxicologic evaluations for chemicals or biologics, and develop new test systems or models as required to meet new needs.
e. Acquire, validate, and utilize assay/organism-specific standardized reagents and controls to the extent possible.
f. Participate as necessary in discussions with the FDA during pre-IND, IND, and pre-NDA/BLA meetings.

E: PHASE I CLINICAL SAFETY AND PHARMACOLOGY TESTING

The fifth activity under this contract is the testing of candidate products for safety in human subjects. This activity includes all such tests as are required to support an NDA or BLA or amendment to existing NDAs or BLAs and will be conducted according to GCP. Since clinical safety information will not be available from Phase II or Phase III clinical studies, it is anticipated that the Phase I Clinical Safety studies conducted would require 300 – 500 subjects.

It is anticipated that the Contractor will not hold the IND for any human trials to be conducted. The IND will be held by the organization that holds proprietary rights to the product or by the Division of Allergy, Immunology and Transplantation (DAIT), NIAID. The Contractor may be required to coordinate the Institutional Review Board (IRB) approvals and informed consent documentation. The Contractor may be requested to work directly with the FDA for Master file, IND, Premarket Notification [510(k)], Premarket Approval (PMA), NDA or BLA submissions.

The Contractor shall provide services to plan, initiate, conduct, audit and report on human clinical Phase I safety and pharmacokinetic studies on candidate drug products in normal human subjects in accordance with GCP guidelines. Perform all such tests as are required to support approval of a radiological medical countermeasure candidate drug.

The Contractor shall:

1. Develop and submit for review and approval to NIAID PO, a clinical development plan for the evaluation of the candidate drug products for the conduct of Phase I clinical trials for safety and pharmacokinetics.

2. Develop clinical protocols, identify, recruit and establish appropriate clinical sites, conduct and implement the clinical trial(s), establish and implement a clinical site monitoring plan, report and record adverse events and serious adverse events, develop and conduct statistical analyses and data management plans. Prepare all documents required for clinical studies such as, Investigator Brochures, Case Report Forms, subject informed consent forms, and any materials as requested by the NIAID PO for Institutional Review Board (IRB) submission/approvals.

3. The Contractor shall provide an interim clinical trial report that includes data summary, data analysis and interpretation and conclusions for the Phase I trials. These data may be used by the Government and/or the Contractor for consultations with the FDA concerning planning for subsequent product development and clinical trials.

4. When each Phase I clinical trial is completed, the Contractor shall provide a final report that captures all Phase I clinical trial follow-up. The report shall include data summary, analysis (total analysis as well as site-specific analysis if multiple sites are chosen) and interpretation as well as final conclusions and recommendations.

5. The Contractor shall participate in regular meetings to coordinate and direct the contract efforts as directed by the NIAID PO. Such meetings shall include meetings with the Contractor to discuss clinical protocol design and data management; meetings with the Contractor and other NIAID officials to discuss technical, regulatory and ethical aspects of the program. These meetings may include representatives of the developer of the test article, as determined by the NIAID PO.

F. TRANSITION PLAN

The Contractor shall:

1. Provide for an orderly transition at the end of the contract.

a. Submit a written transition plan to be reviewed and approved by the NIAID PO six months prior to the completion date of the contract to ensure an orderly transition of this project to a subsequent contractor or to the Government.

b. Transfer all electronic files in a format specified by the NIAID PO on/before the completion date of the contract.

c. Transfer all hard copy files in an organized manner as specified by the NIAID PO to a location specified by the NIAID PO on/before the completion date of the contract.

d. Maintain full operational capacity until the completion date of the contract.

e. Return all remaining stock of test compound to the NIAID Project Officer or to an organization designated by the NIAID Project Officer.

f. Submit all software, source codes and data to NIAID.

REFERENCES:

1. APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG
http://www.access.gpo.gov/nara/cfr/waisidx_04/21cfr314_04.html

2. INVESTIGATIONAL NEW DRUG APPLICATION
http://www.access.gpo.gov/nara/cfr/waisidx_04/21cfr312_04.html

3. APPLICATIONS FOR BIOLOGICAL LICENSE
http://www.access.gpo.gov/nara/cfr/waisidx_04/21cfr601_04.html

4. FDA ANIMAL RULE
http://www.fda.gov/cber/rules/humeffic.pdf

DELIVERABLES

The Contractor shall provide the following information to the NIAID Program Officer and Contracting Officer:

Reporting Requirements

a. Technical Progress Reports

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 are set forth in the **REPORTING REQUIREMENTS** Section of the specific RFP.

1) Quarterly Progress Report every 90 days that provides a summary of activities for the period and budgets/ expenditures to date and projected future work on work assignments due 15 calendar days after the close of the quarter.

2) Annual Report - in lieu of the fourth progress report (Due on contract anniversary).

3) Final Report will be submitted to the NIAID Project Officer and the Contract Officer (due 30 days after the close of the contract). The following components will be included in the final report:
   - Face page to include contract number, contract title, performance period covered, Contractor's name and address, telephone, telefax and E-mail address and submission date.
   - Introduction covering the purpose and scope of the contract effort including a summary of salient results. The Contractor shall submit a summary, not to exceed 200 words, of salient results achieved during performance of the contract.
   - Executive summary, to include fulfillment of production goals and of the specific aims set forth in the proposal.
   - A detailed description of the work performed. Full reporting of inventions (including name(s) of inventor(s), title(s) of invention(s) and date each invention was reported to NIH) first conceived or actually reduced to practice, as well as any copyrights produced, under the contract.

b. 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 expiration date of the contract.

c. Other Reports/Deliverables

1) Annual Report for Clinical Research (Due 45 days from the end of the annual performance period.
2) Final Study Reports to include protocol, results, and data analysis in a form for submission to the FDA in support of an IND and licensure (Due within 30 days of final study analysis or conclusion of experiment if no study analysis is being performed).

3) Candidate Product Development Strategy and Plan to include candidate product development strategy for preclinical, nonclinical and clinical studies to obtain FDA licensure
4) Copies of all raw data.
5) Copies of validation protocols, testing protocols, and validation reports

6) Copies of all regulatory documentation and associated correspondence required by FDA.
7) Written minutes for all meetings including any ad hoc advisory or other technical advisory groups to the Contract, and meetings with the FDA or other regulatory agencies.
8) Clinical site monitoring plan, site visit monitoring reports, and monitoring SOPs. Provide interim and final statistical analyses reports for Phase I human safety trials, data management plans, and adverse and serious adverse events listing reports. Provide all documents required for clinical studies such as, Investigator Brochures, Case Report Forms, subject informed consent forms, and materials for Institutional Review Board (IRB) submission.
9) SOPs to safeguard proprietary and confidential information and data.
10) Risk Analysis (RA), annual System Security Plan (SSP), and SOP for compliance with the Privacy Act.
11) Experimental study design and protocols
12) 510(k), PMAs, INDs, NDAs, and BLAs.
13) Responses to correspondence from regulatory authorities
14) Interim Statistical Analyses
15) Final Statistical Analyses
16) Statistical and Analysis Plans,
17) Data Management and Investigator's Brochure
18) Investigational New Drug (IND)
19) New Drug Application (NDA) or Amendment
20) Biologic License Application (BLA) or Supplement to the Food and Drug Administration(FDA)
21) Final Report for Each Study/Work Assignment
22) Records and Reports required for Writing and Submission of an Investigational New Drug Application (IND)/New Drug Application (NDA) or Biologics License Application (BLA)
23) Nonclinical Strategy and Plan
24) Clinical Development Plan for the Evaluation of the candidate drug products
25) Interim Clinical Trial Report that Includes Data Summary, Data Analysis and Interpretation and Conclusions for the Phase I Trials.
26) Source Code
27) Object Code
28) Special Reports or Analyses as required by the SOW
    a. Tables, Text, Graphs and Diagrams as needed in collaboration with investigators and NIAID staff for presentation at meetings or professional conferences and other special reports concerning study findings,
    b.Reports with custom formats summarizing data for monitoring study progress or product safety or for use by separate site monitoring Contractor, if requested by the Project Officer
    c. Protocol development materials, abstracts/protocol summaries for NIH clinical trials database and other databases specified by the Project Officer.
    d. Quality assurance/quality control plans, training materials used, developed or maintained under the contract as specified by the Project Officer.
    e. All data files, computer programs, computer software, computer manuals, and all written documentation of any programs as specified by the Project Officer.
29) Interim and final statistical analyses of study data as defined by the protocol,
30)At the completion of the Phase I safety trial, the Contractor shall deliver a cleaned and edited public use data set on media to be determined at the time of delivery, and copies of all data management tools, including data documentation and data dictionaries, data entry software and editing programs to allow reading and analysis of the data. The Contractor shall provide appropriate computer programs capable of: (1) reading and manipulation all data, and (2) creating SAS compatible databases. The Contractor shall also deliver an audit trail of all raw

data corrections, hard copies of the original data collected from study participants from all studies, and all logs and other records related to data collection, entry, editing, analysis and transfer.

31) Transition plan (as described in the Statement of Work) - six months prior to the completion date of the contract.

Note 1: For Other Deliverables, Items 3-30, due dates shall be 45 days from the end of the specific work assignment.

Note 2: The items set forth above are likely to become reports or deliverables under the contract. As the efforts will be detailed in individual work assignments, reports and deliverables will be specified herein.

Number of Copies: 3 (one electronic and two hardcopies)

Addresses/Distribution: Contracting Officer, NIAID, 6700-B Rockledge Drive, Bethesda, MD 20892 and Project Officer, NIAID 6610 Rockledge Drive, Bethesda, MD 20892

PART I - THE SCHEDULE

SECTIONS B - H -- UNIFORM CONTRACT FORMAT - GENERAL

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

http://rcb.cancer.gov/rcb-internet/wkf/sample-contract.htm

PART II – CONTRACT CLAUSES

SECTION I - CONTRACT CLAUSES

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

ARTICLE I.1. GENERAL CLAUSES

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

The following General Clause Listings 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

ARTICLE I.2. AUTHORIZED SUBSTITUTIONS OF CLAUSES

ITEM 3: FAR Clause **52.215-15**, **Pension Adjustments and asset Reversions** (OCTOBER 2004), FAR Clause 52.215-18, **Reversion or Adjustment of Plans for Post Retirement Benefits(PRB) other than Pensions** (OCTOBER 1997) and 52.215-19, **Notification of Ownership Changes** (OCTOBER 1997), are deleted in their entirety.

ITEM 4: **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.

No additional or supplemental Authorized Substitutions of Clauses are applicable to this solicitation. See **I.2 Authorized Substitutions of Clauses** of SECTION I at http://rcb.cancer.gov/rcb-internet/wkf/sectioni.pdf for the general listing of Authorized Substitutions of Clauses.

ARTICLE I.3. ADDITIONAL CONTRACT CLAUSES

ITEM 50: FAR Clause **52.219-9 Small Business Subcontracting Plan** Alt II (Oct 2001) is applicable to this solicitation.

ITEM 51: FAR Clause **52.227-16, Additional Data Requirements** (JUNE 1987), is applicable to this solicitation.

ITEM 52: FAR Clause **52.227-17, Rights in Data--Special Works** (JUNE 1987), is applicable to this solicitation.

ITEM 54: FAR Clause **52.227-19, Commercial Computer Software--Restricted Rights** (JUNE 1987), is applicable to this solicitation.

ITEM 59: FAR Clause **52.237-3, Continuity of Services** (JANUARY 1991), is applicable to this solicitation.

ITEM 63: FAR Clause **52.242-12, Report of Shipment (REPSHIP)** (JUNE 2003), is applicable to this solicitation.

No additional or supplemental Additional Contract Clauses are applicable to this solicitation. See **I.3 Additional Contract Clauses of** SECTION I at http://rcb.cancer.gov/rcb-internet/wkf/sectioni.pdf for the general listing of Additional Contract Clauses.

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

No additional or supplemental Additional FAR Contract Clauses Included in Full Text are applicable to this solicitation. See **I.4. Additional FAR Contract Clauses Included in Full Text** of SECTION I at http://rcb.cancer.gov/rcb-internet/wkf/sectioni.pdf for the general listing of Additional FAR Contract Clauses Included in Full Text.

PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

SECTION J - LIST OF ATTACHMENTS

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

PACKAGING AND DELIVERY OF PROPOSALS: **(http://www.niaid.nih.gov/contract/eproposal.htm#pack)**

HOW TO PREPARE AN ELECTRONIC PROPOSAL: **(http://www.niaid.nih.gov/contract/eproposal.htm#electronic)**

PROPOSAL INTENT RESPONSE SHEET SUBMIT ON/BEFORE: May 27, 2005 (Attached to this listing)

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

RFP FORMS AND ATTACHMENTS:

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

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

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

Technical Proposal

NIH 1688-1 (9/02), Project Objectives

Technical Proposal Cover Sheet - (required with original and final proposals)

Technical Proposal Cost Summary - (required with original and final proposals)

Summary of Related Activities - (required with original proposal)

Government Notice for Handling Proposals

Targeted/Planned Enrollment Table

Proposal Intent Response Sheet (required prior to proposal -- see RFP for submission date)

Information Technology Systems Security

Business Proposal

Proposal Summary and Data Record, NIH 2043 (cover sheet required with original and final proposals)

Breakdown of Proposed Estimated Costs (plus Fee) (required with original and final proposals)

Certificate of Current Cost and Pricing Data

Electronic Cost Proposal (required with original and final proposals)

Offeror's Points of Contact (required with original proposal)

Small Business Subcontracting Plan

TO BECOME CONTRACT ATTACHMENTS (INFORMATION ONLY):

Sample Contract Format for R&D, Cost-Reimbursement Contracts

Human and Animal Subject Protection -- DHHS Office for Human Research Protections (OHRP) (complete information)

Privacy Act System of Records (online guidelines)

NIH Women and Minority Policy

NIH Policy for the Inclusion of Children as Participants in Research Involving Human Subjects

Protection of Human Subjects Assurance, Identification, Certification, Declaration, OF310
(application for or certification to conduct human subject studies; submit with technical proposal)

Invoice Instructions -- Cost Reimbursement NIH(RC)-4
(format and instructions for contractor reimbursement via invoice)

Procurement of Certain Equipment, NIH (RC)-7

Research Patient Care Costs, NIH (RC)-11 (guidelines)

Subcontracting Form for Individual Contracts, SF 294 -- NIH Small Business Office (SBO)
(semi-annual report; submission required for large businesses)

Subcontracting Form for Individual Contracts, SF 295 -- NIH Small Business Office (SBO)
(annual report; submission to Small Business Administration required for large businesses)

Report of Government Owned, Contractor Held Property
(annual report; submitted each year of active contract)

Safety and Health Clause (if applicable to project)

Disclosure of Lobbying Activities, SF-LLL

Inclusion Enrollment Report
(Effective 10/22/01, this form replaces the "Annual Technical Progress Report Format for Each Study")

Contract Work Assignment

Commitment to Protect Non-Public Information Contractor Agreement

PART IV – REPRESENTATIONS AND INSTRUCTIONS

SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

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

1. REPRESENTATIONS AND CERTIFICATIONS

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

http://rcb.cancer.gov/rcb-internet/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 THE REPRESENTATIONS AND CERTIFICATIONS AS PART OF YOUR ORIGINAL BUSINESS PROPOSAL. ADDITIONALLY, REPRESENTATIONS AND CERTIFICATIONS MUST ALSO BE COMPLETED FOR ANY PROPOSED SUBCONTRACTORS.

SECTION L - INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS

The following information is specific to this solicitation and is provided to supplement and/or complete the associated ITEMS presented at the SECTION L website at http://rcb.cancer.gov/rcb-internet/wkf/sectionl.pdf

I. GENERAL INFORMATION

ITEM 2: **Alternate I, of FAR Clause 52.215-1, INSTRUCTIONS TO OFFERORS-COMPETITIVE ACQUISTION,** is applicable to this solicitation.

ITEM 9: **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 NAICS Code is 541710.
(2) The small business size standard is 500.

ITEM 10: **THIS REQUIREMENT IS NOT SET ASIDE FOR SMALL BUSINESS,** is applicable to this solicitation.

ITEM 11: **TYPE OF CONTRACT AND NUMBER OF AWARD(S)**

It is anticipated that one award will be made from this solicitation and that the award will be made on/about September 30, 2005.

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

ITEM 16: **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 is specified in SECTION M of this solicitation. However, the Government reserves the right to make an award to the best advantage of the Government, cost and other factors considered.

II. GENERAL INSTRUCTIONS

ITEM 23: **Potential Award Without Discussions,** is applicable to this solicitation.

ITEM 26: **Care of Live Vertebrate Animals,** is applicable to this solicitation.

ITEM 27: **Possession, Use and Transfer of Select Biological Agents or Toxins,** is applicable to this solicitation.

ITEM 29: **Sharing Research Data,** is applicable to this solicitation

ITEM 31: **Specific Copyright Provisions Applicable to Software Development and/or Enhancements**

Under the provisions of the Rights in Data General clause (52.227-14), contractors must seek permission to establish a copyright for software and associated data generated under a contract. As a general rule, permission is normally granted provided, a paid-up, world-wide, irrevocable, nonexclusive license to the government is provided. This is to advise offerors that for this project, the government intends to assert additional copyright permissions under this contract.

The scope of the Government's interest in the copyright will be determined during negotiations.

ITEM 33: **Small Business Subcontracting Plan,** is applicable to this solicitation and the following information is provided to supplement this item to assist in proposal preparation:

The anticipated minimum subcontracting goals for this RFP are as follows:

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

ITEM 35: **Extent of Small Disadvantaged Business Participation,** is applicable to this solicitation.

ITEM 36: **Salary Rate Limitation in Fiscal Year 2005,** is applicable to this solicitation.

ITEM 39: **Past Performance Information** is applicable to this solicitation and the following information is provided to supplement this item to assist in proposal preparation:

Past Performance information shall be submitted as part of the business proposal.

A list of the last three contracts completed during the past three years and the last contracts awarded currently in process that are similar in nature to the solicitation workscope.

ITEM 48: **Prohibition on Contractor Involvement with Terrorist Activities**, is applicable to this solicitation.

ITEM 49: **Solicitation Provisions Incorporated by Reference:** The following provisions are applicable to this solicitation.

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

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

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

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

III. TECHNICAL PROPOSAL INSTRUCTIONS

ITEM 51: **Project Objectives, NIH-1688-1, is** applicable to this solicitation.

IV. BUSINESS PROPOSAL INSTRUCTIONS

ITEM 56: **Proposal Cover Sheet,** is applicable to this solicitation.

ITEM 60: **Requirements for Cost or Pricing Data or Information Other than Cost and Pricing Data [FAR Clause 52.215-20 (October 1997)],** is applicable to this solicitation.

ITEM 65: **Incremental Funding,** is applicable to this solicitation.

ITEM 67: **Certification of Visa's for Non-U.S. Citizens,** is applicable to this solicitation.

SECTION M - EVALUATION FACTORS FOR AWARD

1. GENERAL

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

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

2. HUMAN SUBJECT EVALUATION

This research project involves human subjects. NIH Policy requires:

(a) **Protection of Human Subjects from Research Risks**

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

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

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

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

(b) **Data and Safety Monitoring**

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

As a part of the evaluation for proposals, the reviewers will consider the acceptability of the proposed data and safety monitoring plan with respect to the potential risks to human participants, complexity of study design, and

methods for data analysis. Based on the evaluation of the response to this criterion, this section of the proposal may be rated "unacceptable" (i.e., concerns are identified as to the adequacy of the monitoring plan or no discussion can be found regarding the proposed monitoring plans) or "acceptable." If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

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

(c) **Women and Minorities**

Women and members of minority groups and their subpopulations must be included in the study population of research involving human subjects, unless a clear and compelling rationale and justification are provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. In addition, for NIH-Defined Phase III clinical trials, all proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to detect significant differences in intervention effect (see NIH Guide http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm, Definitions - Significant Difference) by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable, unless the Government has specified that this solicitation involves a sex/gender specific study or a single or limited number of minority population groups. The proposal also must include one of the following plans:

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

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

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

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

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

- whether the plan proposed includes minorities and both genders in adequate representation
- how the offeror addresses the inclusion of women and members of minority groups and their subpopulations in the development of a proposal that is appropriate to the scientific objectives of the solicitation
- the description of the proposed study populations in terms of sex/gender and racial/ethnic groups and the rationale for selection of such subjects
- if exclusion is proposed, that the rationale is appropriate with respect to the health of the subjects and/or to the purpose of the research.
- In addition, for gender exclusion, the reviewers will examine the rationale to determine if it is because:
  - the purpose of the research constrains the offeror's selection of study participants by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; very small numbers of subjects are involved; or
  - overriding factors dictate selection of subjects); or
  - gender representation of specimens or existing datasets cannot be accurately determined, and this does not compromise the scientific objectives of the research.
- For minority group exclusion, the reviewers will examine the rationale to determine if those minority groups are excluded because:
  - inclusion of those groups would be inappropriate with respect to their health,;or
  - inclusion of those groups would be inappropriate with respect to the purpose of the research.

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

If you determine that inclusion of women and minority populations is not feasible, you must submit a detailed rationale and justification for exclusion of one or both groups from the study population with the technical proposal. The Government will review the rationale to determine if it is appropriate with respect to the health of the subjects and/or the purpose of the research

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

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

(d) **Children**

Children (i.e. individuals under the age of 21) must be included in all human subject research unless there are clear and compelling reasons not to include them.
Your proposal must include a description of plans for including children. If you plan to exclude children from the required research, your proposal must present an acceptable justification for the exclusion. If you determine that exclusion of a specific age range of child is appropriate, your proposal must also address the rationale for such exclusion. Also, the plan must include a description of the expertise of the investigative team for dealing with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose/objective of the solicitation. Also, see Section L of the solicitation for further specific requirements on inclusion of children.

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

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

3. EVALUATION OF DATA SHARING PLAN

The offeror's plan for the sharing of final research data shall be assessed for appropriateness and adequacy. If your proposal does not include a plan or if the plan in your proposal is considered "unacceptable," and the Government includes your proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), you will be afforded the opportunity to further discuss, clarify or modify your data sharing plan during discussions and in your Final Proposal Revision (FPR). If your data sharing plan is still considered "unacceptable" by the Government after discussions, your proposal may not be considered further for award.

4. EVALUATION OF PLAN FOR SHARING MODEL ORGANISMS FOR BIOMEDICAL RESEARCH

The offeror's proposal must address the plans for sharing model organisms, OR state appropriate reasons why such sharing is restricted or not possible. Offerors must also address as part of the sharing plan if, or how, they will exercise their intellectual property rights while making model organisms and research resources available to the broader scientific community. The discussion areas regarding intellectual property outlined in Section L should be addressed.

If your proposal does not include a plan, appropriate reasons for restricting sharing, or, if the plan in your proposal is considered "unacceptable," and the Government includes your proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), you will be afforded the opportunity to further discuss, clarify or modify your plan for sharing model organisms during discussions and in your Final Proposal Revision (FPR). If your plan for sharing model organisms is still considered "unacceptable," or your justification for restricting sharing is still considered inappropriate by the Government after discussions, your proposal may not be considered further for award.

5. TECHNICAL EVALUATION CRITERIA

The technical evaluation committee will use these evaluation criteria when reviewing the technical proposals. Proposals will be judged solely on the written material provided by the Offeror. The criteria below are listed in the order of relative importance with weights assigned for evaluation purposes.

I. Scientific and Technical Approach to Statement of Work **Points: 45**

Comprehensiveness of the approach and scientific soundness of the methodology used to support the statement of work in animal model development and performance of candidate medical countermeasure screening; a range of Chemistry, Manufacturing and Controls (CMC) support services; nonclinical safety study evaluation of candidate medical countermeasures; conduct of Phase I Clinical safety and pharmacology testing; and the licensure of a radioprotectant, mitigator, therapeutic, or biodosimetry product with the FDA under the Animal Efficacy Rule. This includes the detailed description of the capabilities of the contractor including subcontractors and consultants to perform the range of tasks in the Statement of Work and in the following areas:

A) candidate product development strategy and plan, addressing toxicology, pharmacology (including absorption, distribution, metabolism, excretion), formulation, candidate medical countermeasure production to support testing and Phase I clinical studies (to include manufacture, storage, lot release and distribution under cGMP), and stability, bioavailability.

B) GLP nonclinical safety, pivotal nonclinical efficacy studies in non-human primates and clinical Phase I human safety and pharmacology studies.

C) project management controls to keep multidisciplinary and multiple project tasks on time and on budget, quality control measures, monitoring and tracking (GLP, cGMP, GCP), methods and resources to be used and the discussion of problems likely to occur with plans for addressing them.

D) document experience with FDA submissions including 510(k), PMAs, INDs, NDAs and BLAs.

E) Establishment of a data coordinating and statistical center.

II. Experience and Qualifications of Contractor's Management and Scientific Staff
Points: 30

A) Documented availability, leadership, expertise, relevant experience and proficiency of the Principal Investigator in directing work assignment type contracts or similar technical projects, managing subcontractors, developing drug products, developing protocols, conducting research and development in support of FDA submissions, and conducting human Phase I clinical trials. Outline of an administrative framework indicating clear lines of authority and responsibility for the project's management. Documented relevant experience of the Contractor in organizing, managing, and monitoring the work flow and task completion of the Contractor and its subcontractors. Completeness and adequacy of the proposed plan to ensure an orderly transition of deliverables (product, reagents, documents, data, etc.) at contract completion.

B) Adequacy of a plan for assessing, adding, monitoring and deleting subcontractors and/or consultants, and procedures for monitoring regulatory compliance of subcontractors and consultants to ensure they meet GLP, cGMP and GCP requirements to accomplish work. Adequacy of data sharing, animal model sharing, and human subjects protection procedures.

C) Adequacy and documented availability, experience, and capabilities of proposed professional staff, subcontractors and other professional and technical staff in providing pharmaceutical and diagnostic product development services for FDA submissions and clinical site monitoring, data coordinating and statistical analyses for clinical trials. Show qualifications, previous expertise and proven track record of the Contractor and subcontractors in the field of radiation biology research.

D) Ability of contractor to add staff, evaluate priorities, and manage simultaneous working groups and projects.

III. Facilities, Resources and Information Technology Support **Points: 25**

A) Adequacy and availability of appropriate laboratories, radiation exposure (including animal transport, when necessary), manufacturing and animal care facilities (including GLP/cGMP compliance and AAALAC accreditation), equipment, and resources necessary to safely and efficiently accomplish the Statement of Work.

B) Organizational experience of the Contractor to design and develop, establish, use, support and maintain a computer-based information technology and data management system with appropriate equipment for the storage, retrieval and analysis of all technical and clinical data related to the contract.

1) Adequacy and appropriateness of Contractor's data management capabilities and equipment to store, collate, analyze and retrieve data in a secure environment as specified in CFR Title 21, including a database design schema and data flow diagram.

2) Capability of the Contractor's proposed computer based information and data management system to interface with project management activities and other product development activities, so that secure electronic communications, including email, word processing and data files, can be accomplished between the Contractor, DAIT staff, subcontractors and consultants.

3) Adequacy of the Contractor's Security Model and plans to ensure the secure storage, transmission and verification of data that addresses areas of privacy and confidentiality.

4) Acceptability and completeness of the Contractor's plan to furnish hardware, software and the use of off-the-shelf products to develop a database that can be used to submit, compile and retrieve information and data generated in the product(s) development.

5) Adequacy of the Contractor's draft plan for a final database designed to establish and maintain a tracking system for data, specimens, reagents and products produced and released and human safety data. Also, adequacy of the Contractor's capability to analyze data in a format compatible with NIAID systems support and software.

Total: 100 Points

6. EVALUATION OF PAST PERFORMANCE

An evaluation of an Offeror's past performance information will be conducted subsequent to the technical evaluation. However, this evaluation will not be conducted on any Offeror whose proposal would not be selected for award based on the results of the evaluation of factors other than past performance.

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

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

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

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

The Government will consider the currency and relevance of the information, source of the information, context of the data, and general trends in the Offeror's performance. This evaluation factor will not be scored.

7. EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION

SDB participation will not be scored, but the Government's conclusions about overall commitment and realism of the offeror's SDB Participation targets will be used in determining the relative merits of the offeror's proposal and in selecting the offeror whose proposal is considered to offer the best value to the Government.

The extent of the offeror's Small Disadvantaged Business Participation Targets will be evaluated before determination of the competitive range. Evaluation of SDB participation will be assessed based on consideration of the information presented in the offeror's proposal. The Government is seeking to determine whether the offeror has demonstrated a commitment to use SDB concerns for the work that it intends to perform.

Offers will be evaluated on the following sub-factors:

a. Extent to which SDB concerns are specifically identified
b. Extent of commitment to use SDB concerns
c. Complexity and variety of the work SDB concerns are to perform
d. Realism of the proposal
e. Past performance of offerors in complying with subcontracting plan goals for SDB concerns and monetary targets for SDB participation
f. Extent of participation of SDB concerns in terms of the value of the total acquisition.

APPENDIX A
ADDITIONAL TECHNICAL PROPOSAL INSTRUCTIONS, SPECIAL CLAUSES, AND WORK ASSIGNMENTS

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, INCLUDE THE INFORMATION REQUESTED IN THIS APPENDIX, AS WELL AS *ANY OTHER* INFORMATION WHICH WILL BENEFIT THE PROPOSAL AND ASSIST IN THE EVALUATION OF THE OFFER.

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 ARE REMINDED THAT THE TOTAL PAGE LIMITATION FOR THE ENTIRE TECHNICAL PROPOSAL PACKAGE IS 150 PAGES. PLEASE REFER TO THE FOLLOWING LINK FOR SPECIFIC PROPOSAL PREPARATION INSTRUCTIONS WITH REGARD TO PAGE LIMITATIONS: www.niaid.nih.gov/contract/eproposal.htm#electronic

ADDITIONAL TECHNICAL PROPOSAL INSTRUCTIONS

1. REFERENCE THE STATEMENT OF WORK (GENERAL)

- It is anticipated that products will enter the evaluation and development pathway at various stages from proof-of-principle to label claim extension. The number of products to be evaluated at each stage is not known and the actual number of Phase I clinical safety and pharmacokinetic studies to be performed are unknown. (See Appendix B for uniform assumptions for proposal purposes.)

2. REFERENCE SECTION A OF THE STATEMENT OF WORK

- Describe in detail the responsibilities and level of effort for the Principal Investigator and Key Technical staff who will be assigned to the contract, and an administrative framework indicating clear lines of authority and responsibility for the personnel. Documentation shall be provided on the qualifications, knowledge, experience, education, competence, availability, and decision-making authority of the Principal Investigator and Key Technical Staff.

- Describe how the Offeror will identify, qualify, and select subcontractors and consultants.

- The Offeror should describe the data plan for the database management system that will be used for all studies and include a description of the data entry and validation, documentation of data corrections, routine maintenance and backup, data reporting and exporting system, access control, and disaster recovery.

3. REFERENCE SECTION B OF THE STATEMENT OF WORK

- Describe where and how animals will be exposed to radionuclides, how test articles will be administered, and how efficacy and general toxicity will be evaluated.

- Describe how animals and non-human primates will be obtained, housed, irradiated, transported to and from irradiation facilities if required, and provided with supportive care (if required) during the conduct of the studies.

- **The proposal should document any experience in preclinical evaluation of radiological medical countermeasure efficacy.**

4. REFERENCE SECTION D OF THE STATEMENT OF WORK

- The proposal should document any experience in nonclinical safety testing. The nonclinical part of the candidate product development strategy and plan shall outline in detail the tests and procedures to be used to qualify each type of product for human administration and provide an appropriate model for determining safety in small animals and in non-human primates.

5. REFERENCE SECTION E OF THE STATEMENT OF WORK

- The Offeror shall provide evidence of its previous experience with submission to Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER) and Center for Device and Radiological Health (CDRH). The proposal shall demonstrate their capability to obtain, store, collate, and arrange data and information in regulatory formats and to keep all information confidential and secure.

6. PROTECTION OF PROPRIETARY DATA

Information and data provided to or generated by the Contractor under this contract shall be treated confidentially and protected by an Advance Understanding to be included in the resulting contract and worded as follows:

"Because there is a likelihood that the Contractor will be utilizing and evaluating materials developed at private expense and subsequently provided to the Government by a third party Supplier, it is essential to include provisions that will protect the proprietary rights of the Supplier.

All information provided by the Supplier or Project Officer should be assumed to be confidential unless specifically identified as non-confidential in writing by the Project Officer. Confidential information may not be revealed without written permission. All materials supplied to the Contractor and all test results similarly are to be considered confidential. All materials supplied to the Contractor shall be utilized solely for contract-related research purposes and no unauthorized use or distribution of these materials will be permitted.

Any data generated under this contract must be submitted for the NIAID Project Officer review before submission for public presentation or publication. Contract support shall be acknowledged in all such publications. A 'publication' is defined as an issue of printed material or a document produced electronically and offered for public distribution or any communication or oral presentation of information. The Project Officer will review all submitted publications in a period of time not to exceed 90 calendar days from receipt, and will either agree to the publication/ disclosure, recommend changes or, as applicable, refer the document to the Supplier of the compound for their review. Information in any publication that is considered Confidential will be deleted by the Project Officer and/or the Supplier prior to approval.

7. PLANNED DEVIATIONS TO REQUIRED GENERAL CONTRACT CLAUSES FAR 52.227-11 AND FAR 52.227-14

The NIAID proposes to seek a deviation from FAR clause 52.227-11, Patent Rights-Retention by the Contractor (Short Form) (June 1989). Pursuant to a Determination of Exceptional Circumstances (DEC) as required by FAR 27.303, the NIAID proposes to modify this clause to restrict the contractor's rights to subject inventions arising under the contract. Subcontracts at all tiers awarded by the Contractor would need to comply with the deviated Patent Rights FAR clause if a DEC is implemented. Specifically, the Contractor and its Subcontractors at all tiers, would be required to assign to the Government or, if deemed appropriate by the NIAID and subject to certain rights reserved to the Government in the field of radiation/nuclear medical countermeasures, to a collaborating party designated by the Government, the entire right, title, and interest throughout the world to each subject invention, except to the extent that rights are retained by the Contractor under the Greater Rights Determination provision of the clause. The NIAID recognizes that inventions in areas outside of the radiation/nuclear medical countermeasure field may be of significant benefit to the U.S. Public Health objectives and therefore, the Contractor and Subcontractors would be encouraged to request greater rights to an identified invention outside the field of radiation/nuclear medical countermeasures. Further, the NIH would consider whether granting the requested rights would interfere with the rights of the Government or any collaborating party or might otherwise impede the ability of the Government or others to develop new candidates for radiation/nuclear medical countermeasures as well as potential enabling technologies that may result from data ensuing from evaluations performed under this contract useful for radiation/nuclear medical countermeasure discovery and development. Contractors and Subcontractors would also be encouraged to request greater rights where inventions relate to technology outside the NIAID's program and where the Contractor has negotiated with a supplier of a proprietary composition for the disposition of patent rights concerning a subject invention related to the composition for a field of use outside of radiation/nuclear medical countermeasures. Furthermore, the timing of data publication would need to be restricted to allow adequate time for patent applications to be filed on inventions arising from the

planned contract. The NIAID intends to accomplish this by a deviation from FAR clause 52.227-14, Rights in Data-General (June 1987). Specifically, although the NIAID encourages the publication of articles on research results, this clause would be narrowly modified to restrict the Contractor's right to use, release to others, reproduce, distribute, and publish data produced or used by the Contractor in the performance of this contract to allow adequate time for the filing of patent applications and to protect data that would be submitted as part of a regulatory filing. The NIAID would reserve the right to coordinate the timing of data publication so that appropriate domestic and international invention applications may be filed as appropriate. The deviated data rights FAR clause would apply to the Contractor and Subcontractors at all tiers. Potential Offerors are afforded an opportunity herewith to comment on the proposed use of these deviations and to identify what impact these deviations may have on their conduct of the work should they be awarded a contract. Comments should be provided, in writing, to the Point of Contact for this RFP. See the bottom of the front page of this RFP for this individual's name and contact information. Comments should be provided within 30 calendar days of the issue date of this RFP. Thereafter, the NIAID will consider this input and determine whether alternative courses of action may be appropriate.

8. WORK ASSIGNMENT PROCEDURES

In providing support under this contract, the Contractor shall initiate work only when so directed by a Work Assignment (Attachment provided in Section J.). Approval of a Work Assignment shall not constitute approval to exceed any item listed in the contract or general clauses of the contract. Work Assignment amounts shall not exceed the total amounts listed in the contract (time, dollars, effort, consultants, travel, etc.). The Project Officer with Contracting Officer approval, is authorized to initiate Work Assignments and to sign Work Assignments indicating satisfactory performance/delivery of the services/product required in each Work Assignment. The Contractor shall assure, prior to commencing work on any Work Assignment, that written approval of the Project Officer and the Contracting Officer has been obtained. A Work Assignment which does not contain both Contracting Officer and Project Officer approval signatures shall be considered invalid and costs incurred for such work shall be considered unallowable. The Contractor shall not exceed the estimated labor hours, estimated Work Assignment amount, or change the Work Assignment leader without prior written approval of the Project Officer and the Contracting Officer by modification of the Work Assignment. The day-to-day operational and administrative details of the Work Assignment system will be established by the Project Officer with input from the Contractor. The Work Assignment system will operate within the following general guidelines:

a.Work Assignment (W.A.) Information

(1) All work to be assigned under this contract shall relate directly to one or more of the task areas listed in the statement of work.

(2) Each W.A. shall be written for the conduct of a specific, finite task.

(3) Each new W.A. shall be numbered serially beginning with 01.

(4) Each W.A. shall be completed on the form entitled "NIAID/DAIT Contract Work Assignment" and listed as an Attachment in Section J of this contract.

(5) Upon award of the contract, an Administrative Work Assignment, as shown in SECTION J, Attachments, shall be issued on a yearly basis. This Work Assignment will cover the time and expenditures necessary for the administration of the contract.

b. Initiation of a W.A.

(l) The Project Officer will initiate Part I of the W.A.

(2) The Contractor shall complete Part II and obtain the appropriate signature. The Contractor shall forward the proposed W.A. to the Project Officer.

(3) Upon receipt of the proposed W.A. and after determining that the proposed W.A. is acceptable, the Project Officer will sign Part II to indicate recommendation for approval and forward to the Contracting Officer.

(4) Upon receipt, the Contracting Officer will review the proposed W.A.

(a) If approved, the Contracting Officer will sign Part II to indicate approval and will forward the W.A. to the Contractor with a copy to the Project Officer.

(b) If not approved, the Contracting Officer will notify the Project Officer, stating the reasons for disapproval.

(5) After receipt of the approved W.A., the Contractor shall begin work. The period of performance shall never precede the Contracting Officer Approval date.

c. Modification to a W.A.

(1) Each amendment to an existing work assignment shall contain the original W.A. number and shall designate a modification number. Modification numbers for each W.A. shall be serially numbered beginning with 01 (for example, Work Assignment 01, Modification No. 01).

(2) Each W.A. modification shall set forth in specific detail which portion(s) of the W.A. is to be modified. All Cost/Labor modifications shall be in the following format:

	Authorized to Date	This Modification	Revised Estimate
Labor Hours			
Cost Elements (List Each Element)			

d. Conclusion of a W.A.

(1) For each W.A. performed, the Contractor shall prepare PART III of the W.A. for submission to the Contracting Officer.

(2) This PART III submission shall include all actual information (cost, effort, and deliverables) relative to the W.A.

(3) PART III of the W.A. shall be submitted as soon as possible and not to exceed three months after the closing date of the W.A. For those Work Assignments which expire within three months prior to the contract expiration date, PART III of the Work Assignment shall be submitted on the final contract day.

(4) After verification that all work is complete and deliverables have been received and accepted, the Project Officer will sign Part III of the W.A. to indicate recommendation for approval and forward the W.A. to the Contracting Officer.

(5) After verification that the W.A. has been satisfactorily completed, the Contracting Officer will approve completion of the W.A. by signing Part III of the W.A. and forward to the Contractor.

CONTRACT WORK ASSIGNMENT (W.A.)

Contractor:_____ W.A. Title:
Contract No:
W.A. No:_____ Modification No.:_____ W.A. Originator:

Contracted Work Area:_____ Date Prepared:

==========

Part I. INITIATOR'S REQUEST

A. Period of Performance: From_____ to
B. Work Assignment Description

C. Work Assignment Leader

D. Deliverables

E. W.A. Response Due Date:

CONTRACT WORK ASSIGNMENT (W.A.)

Contractor:_____ Contract No:

W.A. No: _____Modification No: ____ Date Prepared:

==========

PART II. CONTRACTOR'S RESPONSE TO W.A. REQUEST

(The Contractor may attach additional sheets to this form to present requested data.)

A. Estimated Cost and Effort

1. Labor hours - list W.A. leader, specific individuals to be assigned, labor category, and estimated hours for each.
2. Labor costs - list by labor category and total.
3. Employee benefits.
4. Direct materials
5. Travel
6. Subcontracts
7. Other direct costs
8. Indirect costs
9. Total estimated costs for this Assignment

B. Detailed description of the approach to be used and of the deliverable(s). (Be specific.)

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APPROVAL TO PROCEED: The Contractor shall not exceed the estimated labor hours, estimated W.A. amount, or change the W.A. leader without the prior written approval of the Project Officer and the Contracting Officer.

==========

l. For the Contractor: _____ Date:
(Signature)
Typed name:

2. For the Government: _____ Date:
(Project Officer)

_____ Date:
(Contracting Officer)

CONTRACT WORK ASSIGNMENT (W.A.)

Contractor:_____ Contract No:

W.A. No:_____ Modification No: ____ Date Prepared:

==========

PART III. CONTRACTOR'S REPORT OF W.A. PERFORMANCE

(The Contractor may attach additional sheets to this form to present the requested data.)

A. Actual Cost and Effort

1. Labor hours - list specific assigned individuals, labor category, and actual hours worked.
2. Labor costs - list labor category, individual, and total amount.
3. Employee benefits
4. Direct Materials
5. Travel
6. Subcontracts
7. Other direct costs
8. Indirect costs
9. Total costs for this W.A.

B. Report of Deliverables

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REVIEW AND APPROVAL OF SATISFACTORY PERFORMANCE

The signatures below indicate that the services/products required under Work Assignment No. __ have been delivered, received and satisfactorily meet the requirements of this Work Assignment.

==========

l. For the Contractor: _____ Date:
(Signature)
Typed name:

2. For the Government: _____ Date:
(Project Officer)

_____ Date:
(Contracting Officer)

APPENDIX B

ADDITIONAL BUSINESS PROPOSAL INSTRUCTIONS
UNIFORM BUDGET ASSUMPTIONS

IN ADDITION TO THE FORMAT REQUIREMENTS FOR THE BUSINESS PROPOSAL THAT ARE CONTAINED IN SECTION L OF THE SOLICITATION, THE INFORMATION PROVIDED IN THIS APPENDIX IS INTENDED TO PROVIDE UNIFORM COST ASSUMPTIONS AND BUSINESS CLARIFICATIONS.

OFFERORS ARE ADVISED TO GIVE CAREFUL CONSIDERATION TO THE STATEMENT OF WORK, ALL REFERENCE MATERIAL PROVIDED AS APPENDICES AND ATTACHMENTS, AND THE TECHNICAL EVALUATION CRITERIA, AND, THE RFP AS A WHOLE, IN THE DEVELOPMENT OF YOUR PROPOSAL. THE INFORMATION REQUESTED IN THESE INSTRUCTIONS SHOULD BE USED AS A GUIDE FOR THE DEVELOPMENT AND FORMATTING OF YOUR BUSINESS PROPOSAL. OFFERORS SHOULD CONSIDER AND INCLUDE THE INFORMATION REQUESTED IN THIS APPENDIX, AS WELL AS *ANY OTHER* INFORMATION WHICH WILL BENEFIT THE PROPOSAL.

- **For the purposes of budget preparation, the Offeror shall assume the following activities will occur in the years indicated.**

Year 1
UNIFORM BUDGET ASSUMPTIONS

Develop a hematological model and screen candidate compounds for efficacy:	Fifteen (15) compounds
Develop a GI model and screen candidate compounds for efficacy:	Five (5) compounds
Formulate and demonstrate oral bioavailability:	Two (2) compounds
Develop stability indicating methods and initiate stability studies:	Two (2) compounds
Compare nonclinical efficacy in rodent model:	Two (2) compounds
Conduct nonclinical safety pharmacology and toxicology to support IND:	Two (2) compounds
Conduct nonclinical PK/ADME study:	Two (2) compounds
Design and initiate nonclinical, GLP efficacy study in Non-human primates:	One (1) compound
Arrange and manage Pre-IND meeting with FDA:	One (1) Pre-IND meeting and package
Develop Phase I clinical human safety and pharmacokinetic study protocol:	One (1) licensed product (new label indication)
Prepare and submit documents for NDA/BLA submission:	One (1) licensed product (new label indication)

Provide QAU and QA services to monitor and maintain GLP, cGMP and GCP.

Provide resources for management of program and program reporting/deliverables.

Years 2 - 5

Assume twice the effort of year one for subsequent years.

The number and type of actual tasks are unknown at this time and will be dependent on availability of funding, number and type of candidate products, stage of development of candidate products and regulatory issues.

TRAVEL

- In year 1, budget five trips of 4 people (PI and 3 additional employees of Contractor or subcontractor) to Bethesda, Maryland for 2 days to meet with the PO (Kickoff meeting and four (4) quarterly meetings). In years 2-5 budget four trips of 4 people (PI and 3 additional employees of Contractor or subcontractor) to Bethesda for 2 days to see PO (each Quarter). For each year of the Contract, budget four trips trips of 2 people (for budgeting purposes two East

coast and two West coast) for two days to visit subcontractors and one trip for 2 persons to location TBD for 4 days to attend scientific conferences related to radiological medical countermeasure product development.