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

RFP-NIH-NIAID-DMID-05-12
Animal Models for the Prevention and Treatment of Hepatitis B and Hepatitis C

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.niaid.nih.gov/contract/default.htm		
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:** September 30, 2004	4. **Due Date:** January 5, 2005 **Time:** 3:00 PM, EST	5. **Small Bus. Set-Aside:** [ ]Yes [X] No **8(a) Set-Aside:** [ ]Yes [X] No **NAICS #:** 541710 (See Section L.)
6. **Just In Time:** [X] No [ ] Yes (See Section L.)	7. **Number of Awards:** [ ] Only 1 Award [X] Multiple Awards	8. **Technical Proposal Page Limits:** Number of Copies: See Section J Page Limitations: 100 Pages Electronic File Size: 5 mega-bytes
9. **Issued By:** Paul D. McFarlane Contracting Officer Contract Management Program, DEA NIH, NIAID 6700-B Rockledge Drive Room 3214, MSC 7612 Bethesda, MD 20892-7612	10. [X] **NIAID reserves the right to make awards without discussion.** 11. **Options:** **[X] No** **[ ] Yes**	12. **Period of Performance:** 5 years beginning on/about September 1, 2005
13. **Primary Point of Contact:** **Name :** Yvette R. Brown **Phone:** (301) 451-3686 **Fax:** (301) 480-4675 **E-Mail:** ybrown@niaid.nih.gov	14. **Secondary Point of Contact:** **Name:** Paul D. McFarlane **Phone:** (301) 496-0612 **Fax:** (301) 480-4675 **E-Mail:** pmcfarlane@niaid.nih.gov	15. **Protest Officer:** 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 SECTION J – Attachments)		
18. **DELIVERY ADDRESS INFORMATION**		
19. **Hand Delivery or Overnight Service:** Yvette Brown, Contract Specialist Contract Management Program, DEA NIAID, NIH 6700-B Rockledge Drive, Room 3214 Bethesda, MD 20817	20. **U.S. Postal Service or an Express Delivery Service** Yvette Brown, Contract Specialist 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.		

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INTRODUCTION/BACKGROUND

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The National Institute of Allergy and Infectious Diseases (NIAID) supports research to understand, treat, and prevent the infectious diseases caused by two different hepatitis viruses, hepatitis B (HBV) and hepatitis C (HCV). Chronic infections by either virus affect hundreds of millions of people worldwide and may lead to life-threatening conditions like cirrhosis and cancer. Currently licensed therapies against either virus fall short of being curative, may have adverse side effects, and are further complicated by the development of resistant strains or coinfections with other viruses, such as HIV. New safer and more effective therapies are needed to prevent the end stage liver diseases that cause one million hepatitis-related deaths a year. Appropriate animal models are needed to test them.

Animal Models to Evaluate New Therapeutic Candidates for HBV and/or HCV. Small mammalian animal models (e.g.: mice, rats, small primates such as tamarins, tupaias, or marmosets, etc.) of HBV or HCV infection and disease are sought to evaluate new therapeutic candidates (drugs, immunomodulators, therapeutic vaccines, etc.) that may reduce or eliminate viral replication or prevent progression of liver disease. Results from testing a therapeutic in the animal model should predict human responses. Important considerations for selecting a model include the guaranteed provision of ample numbers of animals, and the availability of well-documented tools and assays for analysis of outcomes. As dose requirements are based usually on body weight, lighter is better. Endangered mammals or mammals over five (5) kilograms are excluded. All proposals submitted in response to this RFP must include one or more small animal models capable of evaluating therapeutic candidates against either hepatitis B or hepatitis C.

Animal Models to Evaluate Protective Vaccine Candidates for HCV. Small mammalian animal models are also sought to evaluate protective vaccine candidates for HCV. Proposals submitted in response to this RFP for HCV may propose to include one or more small animal models capable of evaluating protective vaccine candidates against HCV in addition to animal models for evaluating HCV therapeutic candidates. The same or different animal models may be proposed for the evaluation of HCV therapeutic candidates and protective vaccine candidates.

The long-standing woodchuck animal model will not be supported under this RFP. Work on this animal model will be continued through a separate mechanism concurrent with contracts awarded under this RFP.

In the early 1980s, the NIAID and the National Cancer Institute worked together to support and develop the eastern woodchuck (*Marmota monax*) infected with Woodchuck Hepatitis Virus (WHV) as a novel mammalian infection model for persistent hepadnaviral infection and disease. In addition to quickly establishing a colony-bred resource, critical experiments were performed to study the natural history, pathogenesis, and immune responses to well-characterized pools of WHV. By 1988, the model was supported solely by the NIAID and evaluations of candidate drugs became more common. Drug sponsors from academia to large drug companies have sought and used this resource. Today, the woodchuck is considered the gold standard for preclinical testing of HBV therapies for new drug submissions to the U.S. Food and Drug Administration (FDA). Not only does the woodchuck model mimic human disease progression, but it also parallels human responses to licensed HBV treatments, including the incidence of resistant viral strains.

The NIAID has supported additional animal model development for both HBV and HCV through diverse grant award mechanisms, including cooperative agreement awards (U19s), investigator-initiated awards (R01s) and small business innovative research awards (R43-R44s). Animal models specific for HCV or even a close surrogate were sought in the two previous NIAID contract competitions; however, no contracts were awarded as the models were not well developed at the time. Cornell and Georgetown Universities have been awarded a succession of contracts to characterize and maximize the utility of the WHV/woodchuck model as a surrogate model for HBV. The current contracts, N01-AI-05399 and N01-AI-95390 respectively, network to design creative protocols that include novel antivirals, vaccines and adjuvants tested alone and in combinations. A third contract, N01-AI-05404 to Utah State University, was also awarded to test therapeutics in an HBV transgenic mouse model originating from the Scripps Research Institute. These three awards were made from the same fiscal year 1999 competition. This virus-producing mouse model, initially created through NIAID grant support, was an important addition for several reasons including the ease and speed of breeding sufficient numbers, the reduction in the amount of drug needed for evaluation, and the ability to assess hepatitis B-specific therapies.

The ideal small model is one infected with the human hepatitis virus and one that subsequently expresses human-like symptoms and outcomes. To date, infections by HBV or HCV, complete with their associated disease progressions, are unique to humans. As evidenced by the woodchuck model for HBV, surrogate infection models such as the marmoset or tamarin infected with the related flavivirus GBV-B are plausible contenders for HCV. Offerors may propose, however, any small mammalian animal model, including genetically altered or transplant models, which represents aspects of the human infection or viral hepatitis disease process and also mimics the human response to licensed therapies.

Although more than one model may be proposed for a single virus, separate business and technical proposals for HBV or HCV are required. NIAID may establish separate Scientific Review Groups to evaluate proposals for HBV and HCV. The Government anticipates awarding at least one contract for HBV and at least one contract for HCV.

STATEMENT OF WORK

Animal Models for the Prevention and Treatment of Hepatitis B and Hepatitis C
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Independently, and not as an agent of the Government, the Contractor shall furnish all the services, qualified professional and technical personnel, material, equipment, and facilities not otherwise provided by the Government under the terms of this contract as needed to perform the work set forth below. Specifically, the Contractor shall carry out the tasks specified below.

1. **Provision of Animal Models:** Provide a well-characterized, efficient, small (less than 5 kilograms) mammalian animal model(s) for screening hepatitis therapeutics and vaccines. Infection models, including those for closely related surrogate viruses, shall be established and proven to respond to at least one currently licensed therapy. Genetically altered or fabricated models, such as mice transgenic with hepatitis viral gene(s) or mice/rats implanted with hepatitis-infected human liver/tissues, must be proven to demonstrate consistent reproducibility. Models may include those capable of testing therapies in the background of known antiviral resistance mutations. The Contractor shall:

    a) Provide adequate numbers of the hepatitis virus animal model as well as naïve animals for treatment and control use.

    b) Maintain the health of the breeding and experimental animals through proper veterinary care and animal husbandry; maintain standardized living conditions to meet the specific needs of the animal model (e.g., air, temperature, light, humidity, feed, isolation chambers); and prevent animal and staff exposure to adventitious agents.

        i. Document and report any adverse conditions and/or infections in the separate Monthly Report to the NIAID Project Officer as required under this contract. Include in this report a breakout of numbers of animals on hand either as breeders/controls, on protocols, or awaiting new protocols.

        ii. Whenever possible, establish cause of death for animals on active protocols and report findings in the Monthly Report to the Project Officer.

    c) Provide all the reagents/assays needed to perpetuate the model over the life of the contract, e.g. well-characterized pools of relevant virus to reproduce consistent levels of chronicity/carriage in experimental animals or stores of human liver for transplant.

    d) Provide the NIAID Project Officer with ready access to animals and information during business hours and during off-hours with reasonable advance notice to the Contractor.

    The Contractor may be required to use animal models other than the one(s) proposed in the event that better models become available. Additional costs and access to a better model will be addressed by the NIAID Contracting Officer should this option occur.

2. **Evaluation of Experimental Therapeutic Agents:** Using a hepatitis animal model, evaluate experimental therapeutic agents for safety and efficacy. Conduct studies to assess novel strategies for drug delivery and dosing, including combination or sequential drug administration. These studies shall include appropriate positive and negative controls.

    The number of therapeutic agents available for assessment will vary with the model and the nature and availability of appropriate agents. It is anticipated that the experimental therapeutic agents will include nucleosides, nucleotides, peptides, RNA inhibitors (siRNAs), ribozymes/dnazymes, cytokines/chemokines, immunomodulators, protease and polymerase inhibitors, therapeutic vaccines, and novel chemical entities. Agent acquisition usually results from NIAID staff contacts with drug sponsors, from the Contractor's direct contacts with drug sponsors, and from identification of *in vitro* activity in one of the NIAID-supported screening contracts. These agents may be irritating, toxic, and/or potentially carcinogenic or hazardous.

3. Study of Mechanics and Immunology: Design and conduct mechanistic and immunological studies of the animal model responses to varying classes of therapeutics and vaccines. These studies may include T cell responses (CD4+, CD8+) induced upon treatment with therapeutic vaccines or other immune enhancers, or the analyses of cytokines/chemokines affected by vaccines, drugs, or immunomodulators, etc.

4. Evaluation of Candidate HCV Protective Vaccines: Use HCV animal models to evaluate candidate HCV protective vaccines for: a) safety and toxicity; b) dose and schedule of administration, c) efficacy to include challenge studies, and d) immune responses.

5. Collection and Storage of Specimens: Collect and store specimens from each protocol:

a) Gather, prepare, and store animal specimens using methods that preserve both functions and structures, both tissue and fluid as appropriate, for in-house or external studies, to include serum, cells and liver tissues collected pre, during and post treatment.

b) Maintain an inventory, in a Microsoft Access database or Excel spreadsheet (Microsoft Office 2000 is currently in use at NIAID), of fluids/tissue samples, with unique identifiers, for future in-house use or for transportation to other sites. Labels shall include protocol number, animal number, and collection date. Provide the year's inventory as an appendix in the Annual Report required under this Contract.

6. Testing of Blood and Liver Specimens: Provide and use sensitive, documented assays, methodologies and procedures to test blood and liver specimens to determine the safety and efficacy of candidate therapeutics and vaccines. Multiple methods shall be provided to monitor the various effects of treatment on the disease process and virus replication. Assays shall include quantitative as well as qualitative assessments that statistically demonstrate differences between treatment and control groups of animals, to include:

a) Quantitative assessments that detect differences, with a statistically relevant level of confidence, between treatment groups of animals and appropriate controls. Use relevant discrete indicators including confirmation and status of viremia, quantitation of viral DNA/RNA/replicative intermediates, viral proteins and antibodies, immunological markers, immunohistostaining for key viral antigens, *in situ* hybridization when applicable, and other markers of disease progression or diminution. When viral levels drop below the level of detection of less sensitive measurements, polymerase chain reaction (PCR) analysis shall be used. Analysis of cccDNA levels of HBV may be required. Heteroduplex mobility assays or other determinations of quasispecies of HCV, before, during, and after treatment, may be required.

b) Appropriate observations and measures of general toxicity specific for the animal species, to include body weight, blood chemistries (AST, ALT, BUN, GGT, etc.), hematologic measures, body temperatures, behavior and other indicators of general health. Other specific toxicity tests may be required.

c) Appropriate analyses of gross pathology and histopathology from different sites in the liver to include, whenever possible, separate isolations of normal and diseased areas of inflammation or necrosis. Perform studies of other tissues when applicable to the model proposed or the therapeutic studied, as required.

d) Characterize, as required, a collected pool(s) of virus which demonstrates drug resistance or attenuation from exposure to certain treatments. This may include sequencing and determination of infectious dose.

7. Pharmacology: Perform limited pharmacologic studies, as appropriate. The Contractor is required to have the capability of dosing animals (intravenously as well as orally or intramuscularly) and collecting and preparing appropriate tissue samples for analysis in order to ship them to another site to determine the results.

8. Additional Studies: Perform additional studies, as required, to characterize, refine, and validate the proposed experimental mammalian model(s) as applicable. Additional activities related to experimental models may include optimizing protocols and assays to improve the utility of the model. These studies may include the characterization and definition of the model system in terms of the disease pathogenesis (steatosis, fibrosis, cirrhosis and/or hepatocellular carcinoma) and host responses (innate/adaptive, cellular and humoral). Delineation of the role of virus gene expression and replication, virus genotype and host differences, and the significance of virus resistance may be included in these studies.

9. Collaborations: Collaborate with other groups, as requested by the Project Officer, at no additional cost to the Contractor. Collaborators may be NIAID grantees, applicants or foreign investigators, and collaborations may include (1) supplying collected nonproprietary samples from hepatitis models for additional assays, (2) supplying nonproprietary animals in accordance to biosafety and animal care and welfare guidelines, or (3) planning to evaluate a novel therapy currently in development under a grant if it proves to be a good candidate for *in vivo* evaluation of efficacy against viral hepatitis.

10. Protocol Approval: A draft of each protocol, accompanied by a protocol approval form, shall be submitted to the Project Officer for review and approval prior to initiation. Drug or vaccine sponsors will provide agents for evaluation by the Contractor through the NIAID Project Officer at no cost to the Contractor.

11. Message and Document Transfer: Establish electronic message and document transfer capability with the NIAID Project Officer. Organize, maintain, and transfer information on protocols and test results and provide electronic copies of all reports to the NIAID Project Officer.

12. Confidentiality Agreements: Abide by terms of Confidentiality Agreements with drug sponsors signed by the DMID, NIAID Division Director. Copies of agreements will be provided to the Contractor prior to, or simultaneous with, the delivery of the biological agents covered by the agreements. The Contractor shall provide a plan of specific procedures to include labeling and locking designated file cabinets and protecting electronic databases by unique passwords to safeguard proprietary information. The Contractor shall maintain all confidential data and information in files accessible only to the NIAID Project Officer, the Contractor's Principal Investigator, and integral Contractor contract staff as identified in writing by the Principal Investigator and approved by the Project Officer.

13. Electronic Records: Maintain a secure electronic record of all therapeutics and vaccines received for testing in an Excel spreadsheet, compatible with Microsoft Office XP. Yearly copies of data, recorded on a CD, shall be sent with the annual progress report.

14. Manuscripts, Abstracts and Presentation Materials: Prepare manuscripts for submission to peer-reviewed journals. Provide advance copies of all draft manuscripts, abstracts and presentation materials based on results generated through the Contract to the NIAID Project Officer for approval. NIAID Contract support must be clearly acknowledged on all written and oral presentations.

15. Compliance with Biosafety in Microbiological and Biomedical Laboratory Guidelines: Conduct work in accordance with the Biosafety in Microbiological and Biomedical Laboratories guidelines (including working in the proper Biosafety Level for the viruses being used) as outlined at http://www.nih.gov/od/ors/ds/safetymgt.html, and conduct all animal work according to the NIH guidelines for animal care and use as outlined in http://grants.nih.gov/grants/olaw/references/phspol.htm. Follow the Federal Guidelines for Research involving Recombinant DNA molecules at http://www4.od.nih.gov/oba/guidelines.html when appropriate. Provide training and protective gear for all Contractor personnel involved at all stages of the research pathway from receipt of drugs or vaccines to shipping of samples. Abide by the requirements for researchers developing resources with NIH funding as explained in the new NIH Policy on Sharing of Model Organisms for Biomedical Research, published on May 7, 2004: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html .

16. Annual Meetings: Participate in two (2) annual meetings each year—one meeting in the fall and the second in conjunction with the annual meeting of the Collaborative Antiviral Testing Group (CATG), which usually occurs in the spring.

Meetings will be closed to the public and will involve oral and electronic presentations including: (1) a summary of the status of the colony since the last meeting (include summaries of breeding records, animals used on protocols, animals available for future protocols); (2) updates specific to each site to include results of recently completed studies; (3) interim reports on active protocols; (4) a summary of assays currently in use on site; (5) a description of any problem that may have arisen; and (6) a discussion of future protocols or other action items.

17. Transition: Ensure an orderly transition to a successor contractor or to the Government. A Transition Plan shall be submitted to the NIAID Project Officer three months prior to the completion date of the Contract. The Transition Plan shall include: transportation of all deliverables listed under the Deliverables and Reporting Requirements section of the Contract; relocation/disposition of animals and frozen specimens, equipment, unused materials and supplies; inventory status of materials within repository of specimens, animal profiles, materials, manuals and directories developed by the Contractor, Contract-developed data base programs, entries, and files necessary for an orderly transition of this work to a new contractor or to the Government.

The Transition Plan shall also include: movement of all Government property not specifically identified above; the manner of operations by the Contractor during the transition period; the proposed training time and the nature of the interactions with the subsequent contractor or the Government.

NOTES TO OFFERORS

Animal Models for the Prevention and Treatment of Hepatitis B and Hepatitis C
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NOTE 1 TO OFFEROR: The purpose of this solicitation is to obtain proven, characterized hepatitis animal model systems to evaluate the clinical potential of experimental therapeutic agents for HBV and HCV and prophylactic HCV vaccines for the treatment and prevention of human chronic hepatitis viral infectious diseases and to facilitate the entry of these therapeutic and protective agents into clinical trials. The expertise of the Offeror and the utility of models proposed shall be fully discussed and may be accompanied by peer-reviewed journal articles describing the model or demonstrating the Offeror's success at evaluating therapeutics in the proposed model. If an Offeror wishes to respond with models for both HBV and HCV, separate Technical and Business Proposals are required.

The model system employed shall have features relevant to the corresponding infection in humans. The Offeror shall explain in detail why the model proposed is suitable to predict clinical effectiveness of experimental therapeutics or candidate vaccines. The virus shall be either HBV or HCV or an animal virus with considerable similarity to the comparable human virus. For example, an animal model using Bovine Viral Diarrhea Virus (BVDV) alone is NOT considered responsive to this RFP. The Offeror shall anticipate ~10 % effort for mechanistic/immunologic studies performed in experimental models.

NOTE 2 TO OFFEROR: In the Technical Proposal, Offerors must submit **a complete report on a "proof of concept" drug study** performed by the Offeror with a licensed therapeutic and tested in the model being proposed. Include in the report a thorough discussion of the hypothesis being tested, the objectives of the study, the endpoints, the rationale for selecting specific types of animals for treatment and controls, quantitative and qualitative tests and assays performed on blood and liver tissues, and a thorough discussion of results seen in treatment and control groups. Peer-reviewed publications describing the proposed model and successes by the Offeror for screening therapeutics may be submitted to supplement this requirement.

The Offeror shall list the assays proposed to monitor the effect(s) of treatment on viral replication as well as the disease process when relevant, and describe the procedures to be used to apply these assays within the context of the animal model proposed. Offerors shall provide proof they can perform histologic analyses (by stains, *in situ* hybridization, etc.) to show markers of liver pathology.

NOTE 3 TO OFFEROR: Offerors must submit the following **three sample protocols** in the Technical Proposal:

(1) a combination study (i.e., two drugs or a drug and immunomodulator or therapeutic vaccine, etc.);
(2) a prophylactic vaccine study to assess safety and determine protection from hepatitis C infection/disease, or a therapeutic vaccine study for HBV which detects immune responses leading to reduced viremia, retarded progression to liver disease, or amelioration of current liver disease; and
(3) a pharmacologic study outlining the methods of administration and sample collection.

Offerors shall include a discussion of the logistical problems associated with implementing the proposed protocols, along with a schedule showing timelines and specimen collections, and an estimate of the total number of agents that could be examined at one time. The capability to dose and collect samples for others to complete pharmacologic studies is a requirement at a projected effort of ~1-2 percent.

The number of therapeutic agents available for assessment will vary for each model and the nature and availability of appropriate agents. It is estimated that ~6-8 therapeutic agents per year will be evaluated for efficacy and ~1-2 therapeutic agents will be more extensively evaluated annually. These secondary studies may include optimal dose determination, or combination with another therapeutic.

Offerors must **provide a brief plan** outlining the methods proposed to store, retrieve, and safeguard animal specimens and test biologicals.

NOTE 4 TO OFFEROR: Protective HCV vaccines shall be evaluated for their ability to prevent infection or alter its course, and to study specific immune responses. Descriptions of assays used to assess protective attributes of an HCV vaccine candidate, if proposed, must be included in the Technical Proposal. It is estimated that ~5 HCV vaccine candidates/year may be evaluated.

Although protective vaccines will not be tested in HBV models, assays to assess therapeutic vaccines for HBV must be included in Technical Proposals proposing animal models to evaluate therapeutics against HBV.

NOTE 5 TO OFFEROR: It is important to focus on the HCV genotypes that are most refractive to current therapies. These studies may include the characterization and definition of the model system in terms of the disease pathogenesis and host immune responses. Studies on viral gene expression and replication, virus and host strain differences, and viral resistance may be included. Part of this work may necessitate looking at other tissues, in addition to blood and liver, and this too may vary depending on the animal model(s) proposed. Additional funding should not be required; rather, workloads will be altered to accommodate this change, should it occur. It is anticipated that 10% of contract resources will be utilized to perform these studies annually, as approved by the Project Officer.

NOTE 6 TO OFFEROR: The NIAID is connected to the INTERNET and uses IBM-compatible computers that currently run the Microsoft XP operating system and Microsoft Office 2000 software. MAC users must guarantee that data can be transferred to the Project Officer without corruption of data or figures.

NOTE 7 TO OFFEROR: The Director of the NIAID Division of Microbiology and Infectious Diseases is often required to sign a letter of agreement to ensure the sponsor of a candidate therapeutic or vaccine that the patenting and future development of an experimental agent shall not be jeopardized by Contractor involvement or by premature disclosure of results. Each Offeror is required to **provide a brief plan** for how the intellectual property of each sponsor's data shall be safeguarded. Primary data shall remain with the Contractor; the information required by the Government will be obtained through the required reports.

NOTE 7A TO OFFEROR: By providing information on antiviral activity developed under these Contracts to suppliers of testing substances, the NIAID seeks to stimulate research and development in all sectors of the antiviral scientific community.

Because the goal of this NIAID *in vivo* antiviral screening program is to promote the determination of critical biological information, it will be necessary to restrict certain rights of the Contractor providing *in vivo* testing to either attract suppliers of proprietary compositions or enable NIAID to offer a package of intellectual property rights to a collaborator for commercialization. It is anticipated that the great majority of substances submitted to the NIAID for testing will be proprietary in nature, and our experience has demonstrated that suppliers are reluctant to provide testing substances or ideas without complete assurance that their intellectual property rights are protected. In addition to the need to protect third party suppliers' proprietary rights, it is also necessary to consolidate into a single package the intellectual property rights that may arise in the performance of multiple contracts within this NIAID program.

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

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

Potential Offerors are advised that a Determination of Exceptional Circumstances (DEC), signed by the Director, NIH, along with the aforementioned FAR clause deviations will be sought for this initiative. Because these clause deviations are not yet approved, their text is not available for publication. (However, it is NIAID's intention that the finalized versions of the

deviated FAR clauses will be available before award of any contract resulting from this solicitation.) Instead, the aforementioned description of how these clause deviations will be practiced under the resultant Contract is provided. Potential Offerors are afforded an opportunity to comment on their understanding of what NIAID is planning and to identify what impact these deviations may have on their conduct of the work should they be awarded a contract. Responses should be provided, in writing, to the Point of Contact for this RFP. See the bottom of the front page of this RFP for this individual's name and contact information. Comments should be provided within 30 days of the issue date of this RFP. Thereafter, NIAID will consider potential Offeror's comments and determine whether alternative courses of action may be necessary.

NOTE 8 TO OFFEROR: Offerors are advised to study the information on the websites listed in the SOW. The web-based guidelines for biosafety, animal welfare, use of recombinant reagents, and plans for sharing resource reagents shall apply to the animal models used in the contracts to be awarded under this RFP. The experience and standard operations of the Offeror in working with potential biohazards, such as viruses and infectious animals, toxic chemicals, and radioisotopes shall be addressed in the Technical Proposal, along with relevant safety procedures. In addition, procedures for the care and housing of breeding and experimental animals, the extent of appropriate veterinary coverage, and a description of the physical plant housing all animals and laboratories and the expertise and training of the technical staff employed shall be provided in the Technical Proposal. Therefore, **include Standard Operating Procedures** (SOPS) in the Technical Proposal that apply the guidelines of Section 15 in the SOW to assure the safety and welfare of personnel and animals.

Please note that the Offerors are to **provide a plan** for sharing and distributing hepatitis animal models, if appropriate, as per the new NIH Policy on Sharing of Model Organisms for Biomedical Research, published on May 7, 2004, located at **http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html .**

NOTE 9 TO OFFEROR: Funds to support travel to the two annual meetings for the Principal Investigator, and a Co-Investigator, if desired, shall be included in the Business Proposal. For cost estimating purposes, assume that each meeting will last two full days and will be held in Bethesda, MD.

NOTE 10 TO THE OFFEROR: The Offeror shall include a proposed transition plan in the Technical Proposal (and transition-associated costs in the Business Proposal) as follows:

a) In the event that this Contract is recompeted, and an organization other than the existing Contractor is selected, the incumbent Contractor shall move all Government property to the new site by the completion date of the Contract. It is estimated that this shall take no longer than 45 calendar days.

b) For purposes of preparing a cost proposal, assume that the transition will cost $20,000.

c) The Offeror shall provide, in the Technical Proposal, a transition plan which shall include: moving all Government property; all tasks associated with this relocation effort; the manner of operations by the Offeror during the transition period; and any proposed training time and interaction with the subsequent Contractor.

REPORTING REQUIREMENTS

Animal Models for the Prevention and Treatment of Hepatitis B and Hepatitis C
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A. Technical Reporting Requirements

The Contractor shall submit, by e-mail, CD, or hard copy (as specified below), to the NIAID Contracting Officer and to the NIAID Project Officer, progress reports covering the work accomplished during each reporting period. These reports are subject to technical inspection and requests for clarification by the Project Officer or the Contracting Officer. These shall be brief and factual and prepared in accordance with the following format:

(1) **Drug and Vaccine Sponsor Reports** - These reports cover all aspects of evaluation of candidate drugs such as antivirals/immunomodulators/adjuvants or evaluation of protective HCV vaccines. A "Sponsor" is generally the company or university that supplies the candidate but can also be the NIAID Project Officer. Reports include: cover page, rationale, product information, protocol, methods, data/results, interpretation, conclusions/ summary, references, tables/graphs, and histology pictures. Reports shall be sent in draft form electronically to the NIAID Project Officer within three (3) months of protocol termination. After the NIAID Project Officer reviews the draft, the Contractor shall edit to produce a Final Drug Sponsor Report or a Final Vaccine Sponsor Report as applicable. The Contractor shall then provide an electronic version and two (2) hard copies to the Project Officer within two weeks. There may be a need to respond directly to Sponsor inquiries after the final report is provided.

(2) **Special Reports** – Up to four (4) special reports may be requested each year by the NIAID Project Officer. These reports shall be due within five (5) working days of receipt of the request. These reports are not specifically scheduled, and may include, for example, an update on the Contract/protocol progress, current compilations of raw data, or an overview of the work in progress to be used for presentations for Sponsors, Congress, or other groups. The reports shall be brief and shall be submitted electronically. Hard copies may be necessary if transmission issues arise.

(3) **Submission of papers/abstracts and communication of pre-prints/reprints** – At least two weeks prior to submission of papers or abstracts, the Contractor shall send a copy to the NIAID Project Officer for review. The NIAID Project Officer shall be informed when and where each is submitted and shall be kept current by full disclosure of all outcomes including any follow-up issues such as a change in submission site or acceptance of an abstract for presentation at a meeting.

(4) **Monthly Protocol Reports** - The monthly protocol report shall be submitted electronically to the NIAID Project Officer for format approval within thirty (30) days after Contract award and monthly thereafter for each active protocol. The first report for an active study shall include the approved protocol used to secure the IACUC approval. Subsequent monthly reports shall include only updates to the original and are due electronically each thirty (30) days thereafter. Monthly reports shall be received until the final report-to-sponsor is prepared. A separate Monthly Report shall include a breakout of numbers of animals on hand as breeders/controls, on active protocols, or available for new protocols.

(5) **Annual Reports** –Annual Reports shall be a compilation of reports throughout the year, excluding monthly reports, but including protocols, drug or vaccine reports, animal data, publications, etc. A specific format shall be followed as specified below. Two (2) hard copies and an electronic copy on a CD shall be sent to the NIAID Project Officer and one (1) hard copy original to the NIAID Contracting Officer. The reports are due one month (30 days) after the yearly anniversary of the Contract award.

Annual reports shall include the following specific information:

a) A cover page that lists the Contract number and title, the period of performance being reported, the Contractor's name and address, the author(s), and the date of submission;

b) SECTION I - An introduction covering the purpose and scope of the Contract effort;

c) SECTION II – The report shall detail, document, and summarize the results of the entire Contract work for the period covered. This report shall be in sufficient detail to explain comprehensively the results achieved. The description shall include pertinent data and/or graphs in sufficient detail

to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the Contract. Include in the report a summary of the work proposed for the next reporting period. Specific requirements are set forth in the Work Statement. A one-page summary of each ongoing and completed protocol shall be submitted at this time. An Annual Report will not be required for the period when the Final Report is due. Preprints and reprints of papers and abstracts shall be submitted with the Annual Report; and

d) SECTION III - Substantive performance; a description of current technical or substantive performance and any problems encountered together with proposed corrective action; an explanation of any difference between planned progress and actual progress; the causes of the differences; and if behind planned progress the corrective steps to be taken.

e) Electronic submission of annual inventory of therapeutics and vaccines received and characterized animal specimens collected and stored.

(6) **Final Report** - By the completion date of the Contract, the Contractor shall submit a comprehensive Final Report, in the same format as the Annual Report, with two (2) hard copies and one electronic copy on CD to the NIAID Project Officer and one (1) hard copy original to the NIAID Contracting Officer. This Final Report shall detail, document and summarize the results of the entire Contract period of performance. The Final Report shall be in sufficient detail to explain comprehensively the results achieved. Pre-prints and reprints not included previously shall also be submitted with the Final Report.

(7) **Summary of Salient Results** - With the annual and final reports, the Contractor shall submit a summary (not to exceed 200 words) of salient results achieved during performance period

B. Other Deliverables

1. Materials, manuals and directories developed by the Contractor, Contract-developed data base programs, other software, entries, and files related to protocol development and endpoints.
2. Frozen specimens, pathogen stocks, and other inventory developed under this Contract, with complete animal profiles for each specimen.
3. Any live useable animals supported by Contract funds.
4. All useable Government-owned equipment, materials and supplies.
5. All Contract-related papers submitted for publication and all Contract-related abstracts submitted for presentation.
6. A Transition Plan, submitted three (3) months prior to the completion date of the Contract.

C. Report Distribution/Deliverables

Copies of the written technical reports shall be submitted as follows:

	Deliverable	No. of Copies	Addressee	Due Dates
(1)	Drug /Vaccine Sponsor Reports	1 draft 2 finals (one to be sent to Sponsor by PO)	Project Officer	Draft: 3 months after end date of protocol Final: two weeks after all comments are received by Contractor
(2)	Special Reports	1 electronic copy (e-mail delivery)	Project Officer	Within 5 working days
(3)	Papers/Talks/ Abstracts	1 electronic copy (e-mail delivery)	Project Officer	Two weeks before submission.
(4)	Monthly Protocol Reports	1 electronic copy (e-mail delivery)	Project Officer	Within 30 days after contract award and each month after the original report and protocol are submitted.
(5) & (7)	Annual Report and Summary of Salient Results	1 original, 1 hard copy and 1 electronic copy on CD. 1 original	Project Officer & Contracting Officer	30 days after the yearly anniversary of the contract award date
(6) & (7)	Final Report and Summary of Salient Results	1 original, 1 hard copy, and 1 electronic copy on CD. 1 original	Project Officer & Contracting Officer	On the contract completion date.

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 CLAUSES 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 9: **Alternate II** (OCTOBER 2001) of FAR Clause **52.219-9, Small Business Subcontracting Plan** (OCTOBER 2001) is added.

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 34: FAR Clause **52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns** (JUNE 2003), is applicable to this solicitation.

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

ITEM 35: FAR Clause **52.219-25, Small Disadvantaged Business Participation Program--Disadvantaged Status and Reporting** (OCTOBER 1999), is applicable to this solicitation.

ITEM 46: The following Alternate is applicable to this solicitation:

Alternate I (JUNE 1987), **FAR Clause 52.227-14, Rights in Data--General** (JUNE 1987).

ITEM 54: FAR Clause **52.237-3, Continuity of Services** (JANUARY 1991), is 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:

ITEM 79: FAR Clause **52.244-6, Subcontracts for Commercial Items** (JULY 2004), is 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 AND SUBMIT AN ELECTRONIC PROPOSAL:
(http://www.niaid.nih.gov/contract/eproposal.htm#electronic)

PROPOSAL INTENT RESPONSE SHEET [SUBMIT ON/BEFORE: December 6, 2004] (Attached to this listing)

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

RFP FORMS AND ATTACHMENTS:

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

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

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

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

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

- **NIH-2043, Proposal Summary and Data Record**
- **Small Business Subcontracting Plan Format *[if applicable]***
- **Breakdown of Proposed Estimated Cost (plus fee) and Labor Hours**
- **Offeror's Points of Contact**
- **OMB Form SF-LLL, Disclosure of Lobbying Activities**

TO BECOME CONTRACT ATTACHMENTS (INFORMATION ONLY):

- **NIH(RC)-4, Invoice/Financing Request and Contract Financial Reporting Instructions for NIH Cost-Reimbursement Type Contracts**
- **HHSAR Clause 352.223-70, Safety and Health**
- **NIH(RC)-7, Procurement of Certain Equipment**
- **OMB Form SF-LLL, Disclosure of Lobbying Activities**

- **PACKAGING/DELIVERY/ELECTRONIC SUBMISSION OF THE PROPOSAL**

Please refer to http://www.niaid.nih.gov/contract/eproposal.htm for delivery instructions for the submission of both PAPER and ELECTRONIC COPIES of your proposal.

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

ELECTRONIC SUBMISSION: In addition to the paper submission, you are requested to submit your proposal electronically through the CRON (Contracts Review Online) in accordance with the instructions provided at the above-referenced weblink. You must certify that both the original paper and electronic versions of the proposal are identical.

The electronic submission is solely for the benefit of the Agency. Such submission is still in a "test" stage, and the electronic submissions may or may not be utilized, at the sole discretion of the Agency.

SUBMISSION OF PROPOSALS BY FACSIMILE IS NOT ACCEPTABLE. -- SUBMISSION OF ONLY ELECTRONIC PROPOSALS WITHOUT PAPER COPIES IS NOT ACCEPTABLE.

WARNING: You are advised to read and carefully follow the instructions listed in this RFP. Failure to adhere to these instructions and to the specified limitations for size of paper and electronic proposals may result in the rejection of your proposal.

NUMBER OF COPIES:

Document	Number of Copies	Page Limits	File Size
Technical Proposal	One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES	Limited to not-to-exceed 100 pages.	Limited to not-to-exceed 5 mega-bytes
Technical Proposal Appendices All materials not available electronically (i.e. SOPs, Pertinent Manuals, Nonscannable Figures or Data, and Letters of Collaboration/Intent).	One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES	This information is included in the total Technical Proposal page limit.	N/A
Business Proposal	One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES	N/A	Limited to not-to-exceed 5 mega-bytes
Representations and Certifications	One (1) Original required to be submitted with the Original Business Proposal. (Extra copies are optional.)	N/A	N/A
All offerors are required to submit three (3) CDs that each contain electronic versions of all proposal information (both technical and business – clearly named). If information appended to the paper version is not available electronically, the CD shall contain a file listing all documents that are submitted in paper format only. **The offeror shall include certification that the documents provided electronically match the paper version of those same documents.**		Technical Proposal: 2 Compact Discs (CDs) Business Proposal: 1 Compact Disc (CD)	

THE TECHNICAL PROPOSAL LIMIT INCLUDES: Appendices, Attachments, Operating Manuals, Non-Scannable Figures or Data, Letters of Intent, etc.. ANY PORTIONS OF YOUR TECHNICAL PROPOSAL NOT AVAILABLE ELECTRONICALLY ARE ALSO CONSIDERED TO BE INCLUDED IN THE TOTAL TECHNICAL PROPOSAL PAGE LIMITATION. **PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE TECHNICAL PROPOSAL AND WILL NOT BE READ OR EVALUATED.**

HOW TO PREPARE AND SUBMIT AN ELECTRONIC PROPOSAL

PAGE LIMITS -- THE TECHNICAL PROPOSAL IS LIMITED TO NOT-TO-EXCEED 100 PAGES. PAGES THAT ARE 2-SIDED WILL COUNT AS 2 PAGES. [THIS PAGE LIMIT INCLUDES: Appendices, Attachments, Operating Manuals, Non-Scannable Figures or Data, Letters of Intent, etc.] ANY PORTIONS OF YOUR TECHNICAL PROPOSAL NOT AVAILABLE ELECTRONICALLY ARE ALSO CONSIDERED TO BE INCLUDED IN THE TOTAL TECHNICAL PROPOSAL PAGE LIMITATION. PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE TECHNICAL PROPOSAL AND WILL NOT BE READ OR EVALUATED.

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

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

Please note that the electronic submission does not replace the requirement to submit a signed, unbound original paper copy of both your Technical and Business Proposal, along with any required unbound duplicate copies. These paper originals should be mailed or hand-delivered to the address provided in blocks 19. or 20. of the RFP cover page and must be received on/before the closing date and time.

There is a limit of ten (10) megabytes to the size (MB) of the two electronic PDF files to be submitted; however, the size of the technical proposal is limited to the page limitation language outlined above. For purposes of assessing compliance with the page count, technical proposals will be viewed using the print function of the Adobe Acrobat Reader, Version 4.0 (or higher).

Formatting Requirements:

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

SUBMISSION OF "PROPOSAL INTENT RESPONSE SHEET":

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

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

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

LOG-IN / TRANSMISSION INSTRUCTIONS:

1.	Log-in Site:	Will be provided by the Contract Specialist after receipt of the "Proposal Intent Response Sheet"
2.	Log-in Name:	Will be provided by the Contract Specialist via e-mail.
3.	Log-in Password:	Will be provided by the Contract Specialist via e-mail.

4. Procedure -- When your proposal is completed and converted to a PDF file using Adobe Acrobat, it is ready to be transmitted electronically. You must upload separate Technical and Business Proposal Files. It is recommended that proposals be transmitted a few days before the due date so that you will have sufficient time to overcome any transmission difficulties.

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

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

PROPOSAL INTENT RESPONSE SHEET

RFP No.: NIH-NIAID-DMID-05-12
RFP Title: "Animal Models for the Prevention and Treatment of Hepatitis B and Hepatitis C"

Please review the attached Request for Proposal. Furnish the information requested below and return this page by December 6, 2004. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

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

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

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

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

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

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

Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):

_____
_____
_____
_____
(Continue list on a separate page if necessary)

RETURN VIA FAX OR E-MAIL TO:
CMP, NIAID, NIH
Room 3214
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn: Yvette Brown
RFP-NIH-NIAID- DMID-05-12
FAX# (301) 480-4675
Email: ybrown@niaid.nih.gov

PART IV – REPRESENTATIONS AND INSTRUCTIONS

SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

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

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/forms/rcneg.pdf

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

IF YOU INTEND TO SUBMIT A PROPOSAL, YOU MUST COMPLETE AND SUBMIT ONE ORIGINAL OF THE REPRESENTATIONS AND CERTIFICATIONS AND SUBMIT IT AS PART OF YOUR ORIGINAL BUSINESS PROPOSAL. ADDITIONALLY, A COMPLETED ORIGINAL MUST BE SUBMITTED 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 employees.

ITEM 12: **TYPE OF CONTRACT AND NUMBER OF AWARD(S)**

It is anticipated that up to four awards will be made from this solicitation and that the awards will be made on/about September 1, 2005.

It is anticipated that the awards from this solicitation will be for multiple-year cost reimbursement type completion contracts with a period of performance of 5 years, and that incremental funding will be used.

ITEM 13: **ESTIMATE OF EFFORT**

It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the effort to be approximately 4.4 full time equivalents per year. This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

ITEM 17: **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.

ITEM 21: **LATE PROPOSALS AND REVISIONS,** HHSAR 352.215-70, is applicable to this solicitation.

II. GENERAL INSTRUCTIONS

ITEM 24: **Potential Award Without Discussions** is applicable to this solicitation.

ITEM 30: **Sharing Research Data** is applicable to this solicitation.

ITEM 31: **Sharing of Model Organisms for Biomedical Research** is applicable to this solicitation.

ITEM 34: **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 Disadvantage 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 36: **Extent of Small Disadvantaged Business Participation** is applicable to this solicitation.

ITEM 38: **Salary Rate Limitation in Fiscal Year 2004** is applicable to this solicitation.

ITEM 50: **Prohibition on Contractor Involvement with Terrorist Activities** is applicable to this solicitation.

ITEM 51: **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).

III. TECHNICAL PROPOSAL INSTRUCTIONS

ITEM 53: **Project Objectives, NIH-1688-1, is** applicable to this solicitation.

IV. BUSINESS PROPOSAL INSTRUCTIONS

ITEM 58: **Proposal Cover Sheet,** is applicable to this solicitation.

ITEM 61: **Cost and Pricing Data** is applicable to this solicitation.

Subparagraph 3. Formats for Submission of Line Item Summaries:

[x] The format specified in SECTION L at http://rcb.cancer.gov/rcb-internet/wkf/sectionl.pdf is applicable to this solicitation.

ITEM 62: **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 67: **Incremental Funding,** is applicable to this solicitation.

SECTION M - EVALUATION FACTORS FOR AWARD

1. **GENERAL**

The major evaluation factors for this solicitation include technical (which encompasses experience and past performance factors) cost/price factors and Small Disadvantaged Business (SDB) participation. Although technical factors are of paramount consideration in the award of the contract, 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 Contractor 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. Proposals will be judged solely on the written material provided by the Offeror. Failure to provide the information required to evaluate the proposal may result in rejection of that proposal without further consideration.

NIAID may establish separate Scientific Review Groups to evaluate proposals for hepatitis B and hepatitis C.

2. **MANDATORY QUALIFICATION CRITERIA**

Listed below are mandatory qualification criteria. **THE OFFEROR SHALL INCLUDE ALL INFORMATION WHICH DOCUMENTS AND/OR SUPPORTS THE QUALIFICATION CRITERIA IN ONE CLEARLY MARKED SECTION OF ITS PROPOSAL.**

The qualification criteria establish conditions that must be met at the time of submission of the Technical Proposal in order for your proposal to be considered for award.

The Offeror shall demonstrate the availability of a small mammalian viral hepatitis model and all laboratory facilities necessary to perform the tasks set forth in the Statement of Work. This includes continuous daily access to an AAALAC-accredited (or equivalent for non-US institutions) animal facility throughout the Contract period. The vivarium shall be approved for housing either an HBV model or HCV model or a comparable surrogate virus model of HBV or HCV.

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," 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. TECHNICAL EVALUATION CRITERIA

The evaluation criteria are used by the Technical Evaluation Committee when reviewing the technical proposals. The criteria below are listed in the order of relative importance with weights assigned for evaluation purposes. Proposals will be judged solely on the written proposals and materials provided by the Offerors.

1. Technical Approach—listed in descending order of importance **65**

METHODS, STUDY DESIGNS & ANALYSES: (35 points)

Completeness and rigor of the "proof-of-concept" efficacy study of a licensed therapy tested in the animal model to include critical and incisive analysis of the data, proper use of controls, and optimal use of available tools to reach the final conclusion

Adequacy and feasibility of the methods proposed to measure outcomes, including sensitivity, specificity, dynamic range, and reproducibility of: 1) viral assays (nucleic acids, antigens and antibodies in sera and liver), 2) liver injury and disease progression, 3) gross pathology and

histopathology, and 4) safety/toxicity

Adequacy and feasibility of the sample protocols and methods of data analysis for (1) combinations of therapeutics, (2) vaccine study, or (3) dosing and collecting samples for pharmacologic studies.

Adequacy of standard operating procedures (SOPS) for the safety and welfare of personnel and animals.

ANIMAL MODEL: (30 points)

Suitability, feasibility, reproducibility and availability of the animal model(s) for the evaluation of broadly different classes of therapeutics and/or vaccines, and predictability of the test results on future clinical responses by patients

Adequacy of the animal model to imitate important aspects of the human infection including similar host immune responses to infection and treatment

Adequacy of an HCV animal model to assess protection by a candidate vaccine.

2. Personnel **25**

1. PROFESSIONAL PERSONNEL: (15 points)

Adequacy and appropriateness of the training, expertise, experience, availability and capability of the Principal Investigator in conducting and managing an integrated project as well as planning and conducting animal model protocols. Expertise and experience of the Principal Investigator and the team of professional personnel in:

a. characterizing, developing and maintaining a hepatitis B or hepatitis C animal model;
b. protocol design for the *in vivo* evaluations of therapeutics or vaccines;
c. the design, use and analysis of assays and diagnostics;
d. accountability for all phases of project management including preparation of deliverables and reports; and
e. optimized production and care of animals.

2. TECHNICAL SUPPORT PERSONNEL: (10 points)

Adequacy and appropriateness of training, education, and experience of the technical personnel to:

a. provide routine and special care for the animals;
b. perform the variety of required animal protocols and associated clinical procedures;
c. conduct laboratory assays, techniques and;
d. handle infectious agents.

3. Resources and Administration: **10**

Adequacy and feasibility of the infrastructure for the Offeror to coordinate and administer the multiple aspects of the proposed contract as evidenced by:

1. Quality and safety of facilities including lab space to conduct proposed research and prevent unintended spread of infectious agents;
2. In place procedures and practices to ensure rapid communication, report dissemination, and coordination of activities;
3. Electronic tracking of animal specimens both stored and sent;
4. Capacity to safeguard, manage, enter, exchange, analyze, and communicate data; and
5. Standard operating procedures in place for monitoring personnel health with respect to infectious agents.

Total Possible Points **100**

5. EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION

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

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

Offers will be evaluated on the following sub-factors:

(a) Extent of commitment to use SDB concerns
(b) Realism of the proposal
(c) Extent of participation of SDB concerns in terms of the value of the total acquisition.