OMB No. 0990-0115

Electronic Request for Proposal
SOLICITATION COVER PAGE

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OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE CMB WEBSITE http://www.niaid.nih.gov/contract/default.htm FOR ANY POSSIBLE SOLICITATION AMENDMENTS THAT MAY BE ISSUED. NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS WILL BE PROVIDED BY THIS OFFICE.

Purchase Authority: Public Law 92-218, as amended.
NOTE: The issuance of this solicitation does not commit the government to an award.

RFP Number:	*Just In Time:*	*Small Bus. Set-Aside* [ ] Yes [√] No *8(a) Set-Aside* [ ] Yes [√] No *SIC Code:* 8731 *Size Standard:* *500 employees*	*Level of Effort:* [ ] Yes [√] No *Total Effort:* N/A
NIH-NIAID-DMID-01-16	[ ] Yes [√] No		

TITLE: **"HEPATITIS C RECOVERY RESEARCH NETWORK (HC RRN)"**

Issue Date:	*Due Date/Time:*	*Technical Proposal Page Limits:*
July 26, 2000	**December 15, 2000**	[√] Yes *(see "How to Prepare and Submit Electronic Proposals")* [ ] No

ISSUED BY:

Barbara A. Shadrick, SCO
Contract Management Branch, DEA
NIH, NIAID
6700-B Rockledge Drive
Room 2230, MSC 7612
Bethesda, MD 20892-7612

[√] ***We reserve the right to make awards without discussion.***

NO. OF AWARDS:

[√] Only 1 Award
[ ] Multiple Awards

PERIOD OF PERFORMANCE:

5 Years beginning on or about August 1, 2001.

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)

The Official Point of Receipt for the purpose of determining timely delivery is the Contract Management Branch as stated above. If 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 PHS Clause 352.215-10 entitled "Late Proposals, Modifications of Proposals and Withdrawals of Proposals" located in this Solicitation.

POINT OF CONTACT **-- Janet M. Mattson, Contracting Officer**
[COLLECT CALLS WILL NOT BE ACCEPTED.]

Telephone:	*Fax*	*E-Mail*
Direct **(301) 496-0993** ***Main*** **(301) 496-0612**	**(301) 480-5253**	**jm32u@nih.gov**

THIRTY (30) DAY COMMENT PERIOD

The NIAID will be allotting offerors a period of approximately 5 months to prepare and submit their proposal in response to this solicitation. During the first 30 days, all recipients of this solicitation package and potential offerors will be provided an opportunity to review the solicitation package with regard to the conduct of this project and provide feedback.

We are looking for feedback with regards to the overall scope of work, approach, evaluation criteria, proposal submission, etc. in order to improve the understanding of the Government requirements and enhance the Government's ability to obtain quality services and increase efficiency in proposal preparation, proposal evaluation, negotiation and contract award.

We will utilize feedback to identify and resolve concerns regarding the acquisition strategy, including terms and conditions, schedules, the feasibility of the requirement (including performance, statement of work and data requirements), the suitability of the proposal instructions and evaluation criteria. This information will be utilized to amend the solicitation if the recommendations are determined by the contracts and program office to be an improvement.

ALL COMMENTS ARE DUE ON/BEFORE AUGUST 24, 2000.

Any resultant Amendments will be released within approximately 15 days from the closing of this comment period and will be posted on the CMB/RFP website.

Comments should be forwarded by e-mail to:

Janet M. Mattson, Contracting Officer jm32u@nih.gov

With a carbon copy (cc) to:

Barbara A. Shadrick, Senior Contracting Officer bs92y@nih.gov

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BACKGROUND / STATEMENT OF WORK

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BACKGROUND

Hepatitis C is a blood-borne, liver-targeting viral infection. Hepatitis C virus (HCV) infection and disease are important causes of morbidity and mortality in this country. The Centers for Disease Control (CDC) conservatively estimates that 2.7 million of the 4 million Americans exposed to HCV are chronic carriers. While 1.5% of non-Hispanic whites are infected with HCV, just over 3% of African-Americans and about 2% of Hispanic-Americans are infected. Persistent infection can lead to serious liver disease. Individuals have different rates of progression and currently no predictors of severe outcome are known. On the average, by the time infection has persisted for 20 years, about 20% of these chronic carriers will have developed cirrhosis, and 4% hepatocellular carcinoma. Estimates are that between 8,000 to 10,000 people die annually of HCV either from liver failure or cancer.

Data from numerous studies indicate that the majority (85%) of those infected with HCV develop a persistent infection; the remaining 15% recover. Thus, recovery itself is a rare event. Recovery from infection is currently defined as the loss of detectable viral RNA. Understanding the recovery process is crucial for rational vaccine development and for improvement of therapies. It is feasible to study the recovery process at two junctures – at the time of initial infection and when therapy is administered.

Recognizing or identifying initial infection is difficult. The symptoms are most often indistinguishable from other mild infections or aches and tiredness associated with daily life. It is difficult for individuals to recognize that they have been infected and; therefore, they are not aware that they should seek health care. An important "early warning system" for physicians is elevated liver enzymes – the clinical hallmark of liver injury. These are often minimally elevated, just above baseline, until significant liver damage is present making physician diagnosis problematic.

From other infectious diseases, we have learned that obtaining appropriate specimens as early as possible and continuing with intensive specimen collection are critical for understanding infection outcomes (recovery and persistence) and disease outcomes (pathogenesis and progression). For HCV, this would enable investigators to identify and study markers and mechanisms that determine whether an individual recovers or develops a persistent HCV infection. Such information may suggest new ways to enhance the recovery outcome. Defining important host variables and responses will form a starting point for the rational development of vaccine candidates. Careful study may provide information on mechanisms important to the variation in symptoms and progression seen with HCV infection and disease.

The very nature of this infection has made it extraordinarily difficult to study the early disease course except in the subset of patients with definitive early symptoms and diagnosis. The little available information does not represent the full patient spectrum, limiting applicability to the general infected population.

Since it is so difficult to identify initial infection, the development of prospectively followed cohorts at risk of HCV infection because of a definitive exposure is crucial to:

- identifying and characterizing exposure events including source patient information and relating these characteristics to both infection and its outcome;
- studying recovery and persistence outcomes in a multi-disciplinary fashion exploring virologic, immunologic and genetic variables and mechanisms;
- identifying possible predictors of outcome and validating them;
- studying natural history; and
- developing and evaluating early interventions that enhance the recovery outcome.

Although transmission to health-care workers (HCWs) is not a major form of transmission, this population does have both a definite risk of exposure and identifiable exposure events. This risk is determined by multiple factors including the nature of the patients in their care and the possibility of high-risk exposure events such as needle-stick. Hospitals provide screening and counseling for work-place exposures but generally not follow-up. **This RFP targets this health-care worker population.**

There are licensed therapies that are somewhat effective when used to treat HCV chronic carriers. Their impact, when used to treat early infections, is unknown. Because no substantive trials have been conducted, it is impossible to know if treatment would enhance recovery, have no impact, increase persistence, or cause greater liver disease. Individual patients and their health care providers are faced with venturing into uncharted waters. It is important to perform an early treatment intervention study to determine if it is beneficial for the patient. It is also important to determine when it is best to begin therapy.

The second event that allows evaluation of recovery responses is in chronic HCV carriers undergoing therapy. Recovery is termed a "sustained" response, i.e., loss of viral RNA during therapy and continued absence for six (6) months after therapeutic regimen is completed. In most patients, it does not return after this six-month period. Liver histology also improves and long-term sequelae are averted.

The problem is that the therapies are not very effective. Interferon therapy has led to a "sustained" response in ~15% of volunteers in Phase III trials. Factors associated with recovery included: infection with HCV non-genotype 1, early stage of disease (fibrosis stages 1 and 2), female and early age at acquisition. Treatment with the combination interferon-ribavirin improved the sustained response rate to ~ 48% in Phase III trials. However, only 20% of patients infected with genotype 1 developed a "sustained" response. This is especially important because genotype 1 predominates in the U.S. and many other parts of the world. Additionally, some studies have shown that African-Americans have a response rate that is 5-10 fold less. Information on the mechanism(s) of recovery is lacking because detailed virologic, immunologic, pharmacodynamic and genetic studies were not performed in conjunction with these studies. Additionally, understanding these mechanisms of recovery is anticipated to suggest new therapy options.

This RFP focuses on recovery research designed to enhance NIAID's response to the Framework for Progress for Hepatitis C first formulated by the Institute in 1997 as articulated at http://www.niaid.nih.gov/dmid/hepcframe.htm. Several grant initiatives have sought applications to address these areas, however, the difficulty in obtaining human clinical specimens for research purposes has slowed progress. In addition, there is a tendency to focus on evaluating the importance of only a single parameter such as quasispecies or cytotoxic T cells in the recovery process. It is clear that greater resources for accessing acute infection cases and performing basic research are required in order to begin to understand recovery. **This RFP also seeks to fill the gap in an important public health area - the impact of interventions such as early treatment of acute infection cases on the outcome of infection and early disease course.**

Over the years the National Institutes of Health and especially the NIAID have funded basic research grants interested in addressing the recovery issue from an immunological and virological basis. Access to specimens has been limited. In addition, not all potentially important areas of study are included. For example, there is no innate or B cell immunity research**. It is the intent of this solicitation to broaden the areas of expertise being applied to understanding the mechanisms of recovery.** NIH funded grants with Principal Investigators having an interest in recovery processes and mechanisms are identified in APPENDIX A.

Last year, NIAID funded a grant at the University of Maryland that developed a protocol that enrolls, follows, and studies outcome of infection in health-care workers with identified exposures at Baltimore area hospitals.

- Baltimore, MD, University of Maryland, (R01-AI-47364), **P.I. David Oldach, Study Contact;** ~ infections/year ~ 4.

Realizing that a larger cohort is necessary to meet the overall objectives identified in the Framework for Progress, three of NIAID's Vaccine and Treatment Evaluation Units (VTEUs) are adopting the existing protocol to initiate this study at hospital locations in Los Angeles, St. Louis and Cincinnati.

- Los Angeles, CA, University of California at Los Angeles (N01-AI-45249), P.I. Joel Ward, **Study Contact – Sylvia Yeh;** infections/year ~ 11
- St. Louis, MO, St. Louis University (N01-AI-45250), P.I. Robert Belshe, **Study Contact – Adrian Di Bisceglie;** infections/year ~ 2
- Cinncinati, OH, Cincinnati Children's Medical Center (N01-AI-45252), **P.I. Gilbert Schiff;** infections/year ~ 2

However, recruitment capabilities still will not amass the number of subjects estimated as needed to perform a definitive early intervention trial. Therefore, the HC RRN's (Hepatitis C Recovery Research Network) mandate is to link to, incorporate and build on these existing and funded grant and contract activities to create a complete, integrated research effort based on adequate numbers of well-characterized events, outcomes and specimens.

The objective of this Request for Proposals (RFP) is to solicit proposals that would establish a complete, integrated, single Hepatitis C Recovery Research Network (HC RRN), i.e., a flexible network of collaborative clinical studies/trials and research. The HC RRN will bring together the epidemiological, basic science, patient management and clinical trial expertise necessary to make advances in our understanding of recovery. A critical aspect of this network will be linking of clinical expertise and clinical specimens to a multi-disciplinary basic research team that will examine the mechanisms of recovery. To create a complete picture of the recovery process, it is necessary that both patient characteristics and infection outcome be integrated with multiple basic research approaches focused, for example, on virology, immunology and genetics. An early treatment/intervention trial will be part of this effort. The HC RRN will have an option to design and implement additional clinical trials in acutely infected patients and/or HCV chronic carriers in order to understand the basis of recovery and explore modalities with promise of enhancing the recovery outcome. Finally, the network will be responsible for evaluating the composite data and defining the critical features and components of the recovery process in multiple situations.

For additional information concerning the preparation, review and evaluation of proposals, please see Section L.2.c. Additional Technical Proposal Instructions and Evaluation Information.

STATEMENT OF WORK

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

Specifically, the Contractor shall establish a collaborative network for clinical research on recovery from hepatitis C virus infection and disease; hereafter referred to as the Hepatitis C Recovery Research Network (HC RRN). It shall consist of a consortium of institutions and sites capable of providing the scientific, clinical, technical and administrative expertise and requisite numbers of human subjects necessary to develop and carry out a scientific plan to:

- delineate the factors affecting transmission via percutaneous and permucosal exposure in the health-care worker population;
- design and conduct a clinical trial to evaluate the role of early therapy in enhancing recovery and improving natural history in the exposed health-care worker population;
- delineate the mechanisms of recovery and disease progression in concert with the HC RRN trial and, at the direction of the Project Officer, in other clinical trials in these areas sponsored by other Federal and private sector organizations and companies; and
- design and conduct clinical trials to evaluate promising new approaches to enhance recovery from infection and/or recovery with therapy.

A. HEALTH-CARE WORKER ACUTE INFECTION COHORT STUDY AND TRIAL (BASIC REQUIREMENT)

The Contractor shall:

1. Develop and implement a highly efficient multi-site clinical study and trial that shall:

    a. prospectively recruit, follow and evaluate health-care workers (HCW) with percutaneous and permucosal exposures resulting from contact with blood from source patients who are infected with HCV;
    b. incorporate a clinical trial that assesses natural history with and without early treatment; and
    c. collect and provide specimens that enable basic scientists to perform assays that will delineate the mechanisms impacting the outcome of infection and disease.

2. Design and power the protocol to obtain meaningful information on but not be limited to, the following:

    a. epidemiology of transmission including, but not limited to: transmission rates as well as source patient and subject factors involved in determining whether or not infection occurs;
    b. natural history of asymptomatic and symptomatic infections;
    c. impact of intervention on the outcome of infection and natural history; and
    d. mechanisms of recovery and persistence.

3. Develop the final protocol, all questionnaires, consent and report forms, Manual of Operations, Standard Operating Procedures (SOPs) and other documents needed for the study within three (3) months of award. Work with NIAID staff as directed by the Project Officer to develop information needed for submission of an Investigational New Drug Application (INDA) to the Food and Drug Administration (FDA). Implement the study within one (1) month of the FDA approval.

4. Prepare and implement effective clinical trial plans to:

    a. train study staff;
    identify source patients (obtain or use blood specimens to determine if they are infected with HCV or other infectious agents using, but not limited to: ELISA and RIBA tests); in addition, quantify viral load, determine genotype, antibodies, free and antibody bound HCV;
    b. recruit, enroll, collect initial demographic and exposure information and obtain clinical specimens of health-care workers;

c. retain subjects so as to obtain additional clinical information and specimens; and
d. perform the clinical trial and follow-up.

5. Determine clinical history and laboratory parameters validated across laboratories including, but not limited to: ALT, AST, creatinine, total bilirubin, total leukocyte count. Quantitate viral load. Perform liver biopsies as clinically necessary or according to protocol. Supply qualified central pathology expertise and evaluate liver pathology by means including, but not limited to, histology.

6. Obtain, process, and store clinical specimens including, but not limited to:

   a. as specified by the protocol and the Manual of Operations/Standard Operating Procedures;
   b. as clinically necessary; and
   c. as needed for recovery and progression research.

7. Develop and implement a plan for distribution and utilization of specimens. Ship specimens as specified in the protocol and Manual of Operations/Standard Operating Procedures to:

   a. collaborating investigators who are performing analyses of viral, immune response and host parameters in order to understand the mechanisms of recovery, persistence and progression (See SOW Item B.);
   b. repository contractors; and/or
   c. other locations, as identified by the Project Officer.

B. RECOVERY RESEARCH

The Contractor shall:

1. Develop, implement and provide an efficient, systematic, flexible, multi-disciplinary, comprehensive approach towards understanding the mechanisms involved in recovery from HCV infection and disease as well as disease progression. Make use of state-of-the-art technologies. Approaches shall include, but not be limited to, the following:

   a. evaluating the impact of viral factors including, but not limited to: viral genotype, quasispecies and load, antibodies, immune evasion tactics and gene expression;
   b. evaluating the immune response to HCV to include, but not be limited to: innate, humoral and cellular responses;
   c. analyzing involvement of different immune cell types using cell surface markers that identify function;
   d. determining and quantitating the immunoregulatory pathways using modern techniques including but not limited to, Elispot assays;
   e. exploring the impact of host genetics including but not limited to: HLA, T cell receptor usage and T cell epitope usage by means of novel approaches using positional scanning peptide combinatorial libraries; and
   f. identifying potential genes and their products that are involved in and might serve as early and/or surrogate markers of recovery and progression.

2. Implement these efforts with carefully collected specimens from:

   a. the Health-Care Worker Acute Infection Cohort Trial efforts in Item A of the SOW; and
   b. additional studies/trials including, but not limited to, those in Item F. of the SOW, at the direction of the Project Officer.

3. Develop and implement an external peer-reviewed pilot project program that enables exploration of new research ideas and permits application of new technologies. The Project Officer shall have final approval authority.

C. DATA BASES AND DATA ANALYSES

The Contractor shall:

1. Develop and implement a plan to modify or use existing data collection and computer-based data management system(s) in order to collect data that includes, but is not limited to: epidemiological, clinical, histologic, virologic, immunologic, genetic and pharmacodynamic information. Modify and/or use existing data forms. Perform data entry, checks, and quality control.

2. Provide tracking capabilities with respect to subjects, information and biospecimens that include, but are not limited to: study arm (if appropriate), laboratory results, site, accrual, trial status and adverse events.

3. Provide for data entry and system access at cooperating clinical and research sites.

4. Provide for integration of research results with patient and trial information

5. Develop and implement a uni-variate and multi-variate, as appropriate, data analysis plan that shall include, but not be limited to, evaluation of the:

    a. risk of HCV transmission through high-risk percutaneous and permucosal events as well as infection rates;
    b. influence of source patient characteristics on outcome of infection;
    c. overall outcomes of infection; i.e., recovery and persistence, as well as time to recovery;
    d. time course, both appearance and disappearance, and strength of virological and immunological events;
    e. extent and timing of symptoms and pathology; and
    f. nature, extent and timing of laboratory values and physical symptoms, including, but not limited to: liver enzymes (ALT, AST), total bilirubin, total leukocyte count, creatinine, fatigue, weakness, joint pain, rashes, fever, headache, nausea/vomiting, diarrhea, anxiety/depression, right-upper-quadrant pain, and jaundice.

6. Provide an advance copy of draft manuscripts (including abstracts and public presentations) resulting from this contract to the Project Officer and obtain clearance in writing before submitting for publication or presentation. Acknowledge support from the Government contract in all abstracts, presentations, and publications.

D. MANAGEMENT AND COORDINATION

The Contractor shall:

1. Develop and implement an overall plan and structure for management and coordination of all aspects of this effort including, but not limited to:

    a. definition of individual and collective responsibilities as well as lines of authority;
    b. a timeline;
    c. monitoring and evaluating progress and performance of: activities, accrual, compliance, staffing at multiple sites, the study/trial, data collection and entry, mechanistic research efforts at multiple sites, and pilot projects;
    d. providing flexibility via augmenting the Network (HC RRN), discontinuing, temporarily or permanently, the services of subcontractors and terminating or curtailing research projects;
    e. identifying scientific and technological advances applicable to this project;
    f. setting priorities;
    g. redirecting focus and allocating resources;
    h. integration with other funded efforts; and
    i. regular communication.

2. Coordinate with other contractors/grantees to organize and attend meetings for the purposes of future planning, protocol and study development and/or evaluation, data discussions between contract/grant groups, investigators and other essential persons, and meeting(s) with NIAID and FDA staff. These meetings shall be arranged at the direction of the Project Officer and shall include scientific advisors at the advisement of the Project Officer. The following trips/meetings are anticipated (but may be subject to change):

    a. Protocol finalization meetings - two trips of two full days duration in Bethesda, MD within the first three months.
    b. Start-up meeting - one trip of two days to Bethesda, MD within one month of FDA approval.
    c. Progress review - one trip per year for the Principal Investigator(s) and key personnel to attend a three-day meeting in Bethesda, MD.
    d. External scientists - one trip per year for up to five individuals to participate in the three-day review meeting. The timing and content of such meetings will be developed with and approved by the Project Officer. They will include other Government staff as necessary.

E. CONTRACT TRANSITION PERIOD

The Contractor shall:

1. Prepare a plan for orderly transition to a subsequent Contractor. This plan shall include provisions for transferring documents, electronic files and databases, computer programs and source codes, if required, and all relevant documentation for studies supported. The plan shall be submitted at least 45 days before the expiration of the contract period.

2. Carry out the plan as approved, providing detailed instructions and/or training for employees of the new Contractor on the functioning of data management systems, the adverse event reporting systems and regarding other essential information, such as study records, procedures and data sets.

F. OPTIONS: ADDITIONAL TRIALS TO DEFINE AND ENHANCE RECOVERY

The following three Options may be exercised by unilateral contract modification by the Government pursuant to FAR 52.217-7, Option for Increased Quantity – Separately Priced Line Item (MARCH 1989). The Contracting Officer may exercise the option by written notice to the Contractor within 60 days prior to the effective date of the Option period of performance. Unless the Government exercises these Options pursuant to FAR 52.217-8, the contract will consist only of the Statement of Work as defined in Items A through E. (hereafter referred to as the **Basis Requirement**) and any Options that may have been exercised.

OPTION 1: Develop and implement an additional trial (trials) using new treatment modalities thought to have greater promise for enhancing recovery in those acutely infected with HCV including, but not limited to, exposed health-care workers. Link the trial and its clinical outcomes with mechanistic basic research as required in SOW Item B. as well as data and management systems as required in SOW Items C. and D.

OPTION 2: Develop and implement an additional trial (trials) using new treatment modalities thought to have promise for enhancing recovery in well-characterized HCV chronic carriers. Link the trial and its clinical outcomes with mechanistic basic research as required in SOW Item B. as well as data and management systems as required in SOW Items C. and D. Document patient characteristics to include, but not be limited to: approximate length of time infected, risk factor history, clinical laboratory values including liver function tests, stage and grade of liver disease and detailed history of alcohol use.

OPTION 3: Develop and implement a clinical study/trial of a current therapy or current therapies in HCV chronic carrier patients so as to provide specimens for thorough evaluation of potential virologic, immunologic, pharmacologic and genetic mechanisms involved in recovery. Prepare for multiple types of trials including, but not limited to, non-randomized, randomized, single or multi-site. Link the trial and its clinical outcomes with mechanistic basic research as required in SOW Item B as well as data and management systems as required in SOW Items C. and D.

[END OF STATEMENT OF WORK]

REPORTING REQUIREMENTS AND OTHER DELIVERABLES

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The Contractor shall submit to the Contracting Officer and to the Project Officer technical progress reports covering the work accomplished during each reporting period. These reports are subject to the technical inspection and requests for clarification by the Project Officer. These shall be brief and factual and prepared in accordance with the following format:

A. Deliverables (Provide to the Project Officer only)

1. Within 60 days of the award of the contract the Contractor shall provide final documents describing:

   - collaborative arrangements with other NIH grantees and contractors, NIH intramural staff, industry, small business and other governmental agencies to support the conduct of the HCV acute infection intervention study;
   - a final scientific agenda for the HCV acute infection intervention study; and
   - a Directory of HC RRN Investigators to include: name, address, contact information, and area of responsibility.

   In addition, the Contractor shall submit:

   - a pent-ultimate protocol for the acute infection intervention trial as well as associated documents; and
   - draft SOPs, Manual of Operations and Study Training Manual

2. Within 90 days of the award of the contract, the Contractor shall submit:

   - the final protocol for the acute infection intervention trial as well as associated documents;
   - the final SOPs and Manual of Operations;
   - the final Study Training Manual; and
   - plans for the study initiation meeting to be held within one (1) month of FDA approval.

3. Within 30 days of FDA approval of the protocol, the Contractor shall hold the study initiation and training meeting.

4. Bi-monthly, starting two months after the study begins, the Contractor shall provide a brief summary of progress as well as problems encountered and proposed solutions.

B. Technical Reports (Provide to Project Officer and Contracting Officer)

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

1. Bi-monthly Update – by the fifteenth calendar day following each two-month period, the Contractor shall submit three (3) copies of a Bi-monthly Update, comprised of two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. This shall include a concise update of enrollment, trial progress and site performance.

2. Semiannual Technical Progress Reports - by the fifteenth calendar day of the month following the end of each six month period, the Contractor shall submit five (5) copies of a Semiannual Technical Progress Report, comprised of four (4) copies to the Project Officer and one (1) copy to the Contracting Officer. Semi-annual Technical Progress Reports are not due for periods in which an annual or final report is due. Each report 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 HC RRN and a brief description of new opportunities and technologies, recommended changes in scientific direction and ideas with respect to trial OPTIONS.

c. SECTION II - A description of project status and overall progress as well as a separate description of all identified work tasks including the clinical trial, research areas (results and their significance), pilot projects and, as appropriate, other logical segments of work on which effort was expended during the report period.

d. SECTION III - A brief description of all problems or impediments in carrying out the work tasks, whether affecting performance or costs, and recommendations for corrective action/resolution. This should include a summary assessment of the performance of all sites and scientific areas.

Each clinical study should be reported separately according to the number assigned by the Project Officer. The Contractor should address patient accrual and retention on protocols, adherence to protocols and research standards, and timeliness and accuracy of completion of case report forms. The summary shall document how accrual meets the current guidelines for inclusion of minorities and both genders. An explanation of any difference between planned progress and actual progress, why the differences have occurred, and if behind planned progress what corrective steps are planned. Status shall be summarized in terms of study results and publications.

Evaluation of progress with respect to the overall scientific agenda and individual projects should be included. The Contractor should discuss: successes, difficulties and proposed solutions.

e. SECTION IV – A brief description of tasks to be completed during the next year and of any difficulties anticipated.

f. Preprints, reprints and abstracts of all contract-supported work resulting in publication or presentation in the reporting period shall be submitted along with the report.

3. Annual Technical Progress Reports - within 30 calendar days following each anniversary date of the contract, the Contractor shall submit five (5) copies of an Annual Technical Progress Report, comprised of four (4) copies to the Project Officer and one (1) copy to the Contracting Officer. Such reports shall detail, document, and summarize the results of the entire contract work for the period covered. These reports shall be in sufficient detail to explain comprehensively the results achieved. Also to be included in the report is a summary of work proposed for the next reporting period. 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 not submitted in the semi-annual report shall be submitted.

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.

4. Final Report - on or before the completion date of the contract, the Contractor shall submit five (5) copies of a comprehensive Final Report, comprised of four (4) copies to the Project Officer and one (1) copy to the Contracting Officer. This final 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. Preprints and reprints not previously submitted shall also be included.

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.

5. Transition Plan - Submit a Transition Plan for transfer of the functions specified in the Statement of Work at least 45 days prior to the completion date of the contract at the request of the Project Officer. The Project Officer should request this plan at least 60 days before it is due. The Transition Plan shall be subject to review and approval of the Project Officer.

C. Timely Delivery

If the Contractor becomes unable to deliver the reports specified hereunder within the period of performance because of unforeseen difficulties, notwithstanding the exercise of good faith and diligent efforts in performance of the work, the Contractor shall give the Contracting Officer immediate written notice of anticipated delays with reasons, therefore.

D. Technical Report Distribution

Deliverable	No. of Copies	Addressee/Distribution	Due Dates
All deliverables in paragraphs A.1. – A.4.	As stated	Project Officer	As stated
Bi-Monthly Update	2 1	Project Officer Contracting Officer	Within 15 calendar days following each two-month reporting period.
Semiannual Report	2 1	Project Officer Contracting Officer	Within 15 calendar days following each six-month period. Not due when Annual or Final Reports are due.
Annual Report	2 1	Project Officer Contracting Officer	Within 30 calendar days following each Anniversary date of the contract. Not due when Final Report is due.
Final Report	2 1	Project Officer Contracting Officer	Due on/before the completion date of the contract.

E. Addressees

Project Officer: DMID, NIAID, NIH
Room _____, MSC _
6700-B Rockledge Drive
Bethesda, MD 20892-7640

Contracting Officer: CMB, DEA, NIAID, NIH
Room 2230, MSC 7612
6700-B Rockledge Drive
Bethesda, MD 20892-7612

NOTE: Electronic e-mail addresses will be provided at the time of award for electronic transmission of deliverables.

TECHNICAL EVALUATION FACTORS FOR AWARD

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1. GENERAL

SELECTION OF AN OFFEROR for contract award will be based on an evaluation of the proposal(s) for the Basic Requirement against three factors. The factors in order of importance are: Technical, Cost/Price 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.

The EVALUATION will be based on the demonstrated capabilities of the prospective Offeror(s) in relation to the needs of the Basic Requirement and all Options as set forth in the RFP. The merits of each proposal will be carefully evaluated. Each proposal must document the feasibility of successful implementation of the Basic Requirement and all Options of the RFP. Offerors must submit information sufficient to evaluate their proposals based on the detailed criteria listed below.

This research project involves human subjects. NIH Policy requires that women and members of minority groups and their subpopulations and children must be included in the study population of research involving human subjects.

Where inclusion of women, minority populations, and/or children is not feasible, a detailed rationale and justification for exclusion of one or both groups from the study population must be submitted with the technical proposal. The NIAID 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. If the rationale is not considered acceptable by the Government and you are included in the competitive range, you will be afforded the opportunity to further discuss and/or clarify your position during discussions or include women, minorities and/or children in your Final Proposal Revision (FPR). If your exclusion position is still considered unacceptable by the Government after discussions, your proposal may not be considered further for award.

2. EVALUATION OF OPTIONS

It is anticipated that any contract(s) awarded from this solicitation will contain Option provision(s) and period(s).

In accordance with FAR Clause 52.217-5, Evaluation of Options, (July 1990), the Government will evaluate offers for award purposes by adding the total price for all options to the total price for the basic requirement, except when it is determined in accordance with FAR 17.206(b) not to be in the Government's best interests. Evaluation of Options will not obligate the Government to exercise the Option(s). **Options will be evaluated separately and will not be a factor in source selection.**

3. EVALUATION OF TARGETS FOR EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION

SDB participation will not be scored, but the Government's conclusion about overall commitment and realism of the Offeror's SDB participation targets will be highly influential 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 SDB participation targets will be evaluated before determination of the competitive range. The evaluation will be based on information provided by the Offeror in their technical proposal. Evaluation of SDB participation will be a subjective assessment based on consideration of all relevant facts and circumstances. 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 as the prime contractor.

Offers will be evaluated on the following sub-factors:

a. The extent of participation of SDB concerns in terms of the value of the total acquisition.

b. The complexity and variety of the work SDB concerns are to perform. Greater emphasis will be given for arrangements where the SDB shall be performing work appropriate to the scientific objectives expressed in the statement of work.

4. TECHNICAL EVALUATION CRITERIA

The evaluation criteria are used by the technical evaluation committee 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.

OFFEROR(S) AND REVIEWERS ARE ADVISED TO REFER TO SECTION L.2.c. OF THIS SOLICITATION PACKAGE FOR GUIDANCE AND INFORMATON RELATED TO THE PREPARATION AND EVALUATION OF PROPOSALS.

CRITERIA – [FOR BASIC REQUIREMENT AWARD]	Sub Weight	TOTAL WEIGHT
A. TECHNICAL APPROACH		**55**
• **Documented adequacy and feasibility of plan and actual ability to identify, access, recruit and retain exposed health care workers and overall quality of the acute infection protocol in terms of scientific and clinical rationale, design, suitability and feasibility to:** • Identify critical factors of the exposure event that impact on infection and its outcome. • Determine the natural course of infection and its outcome. • Assess the impact of the proposed intervention on infection and disease outcomes. • Provide specimens for recovery research.	**25**	
• **Documented rationale for completeness, quality and feasibility of the proposed recovery research with respect to:** • Understanding mechanisms of recovery; • Scientific rationale for and completeness of the proposed disciplines and approaches; • Use of state-of-the-art technologies; • Validity of proposed methods; • Integrating across disciplines; and • Pilot projects.	**20**	
• **Suitability and feasibility of the Manual of Operations/Standard Operating Procedures, Data and Data Analysis Plan with respect to:** • Adequacy and feasibility of the Manual of Operations/SOPs; • Documented evidence of database capabilities; and • Quality and completeness of proposed data analysis plan.	**10**	
B. QUALIFICATIONS, EXPERIENCE AND AVAILABILITY OF PROPOSED STAFF		**35**
• **Documented relevant scientific qualifications, expertise, experience, availability of the overall Project Director and the overall Study Coordinator. Managerial abilities for multi-site and multi-disciplinary research as documented by the adequacy, feasibility and quality of the plans for staffing, flexibility, coordination, communication, incorporation of existing projects, timelines and training**	**15**	
• **Documented relevant scientific qualifications, training, expertise, experience and availability of co-Investigator(s) and other senior staff including subcontractors**	**10**	
• **Documented relevant qualifications, training, expertise, experience and availability of other professional staff, nurses, coordinators, technical and administrative staff.**	**10**	

C. FACILITIES AND INSTITUTIONAL SUPPORT		10
Documented availability and adequacy of facilities, equipment, and resources and liaisons necessary to carry out the Statement of Work at all sites.		
TOTAL		**100**

OPTIONS WILL BE EVALUATED SEPARATELY AND WILL NOT BE A FACTOR IN SOURCE SELECTION. SEPARATE TECHNICAL AND BUSINESS PROPOSALS ARE REQUIRED FOR EACH OPTION.	
CRITERIA – [FOR OPTIONS]	**TOTAL WEIGHT**
<u>OPTION 1:</u> • **Documented quality of the OPTION 1 concept including scientific rationale, suitability and feasibility;** • **Documented access to the appropriate type and number of patients; and** *Documented qualifications of staff and adequacy of time commitment.*	**25**
<u>OPTION 2:</u> • **Documented quality of the Option 2 protocol including scientific and clinical rationale, design, suitability, and feasibility;** • **Documented access to appropriate type and number of patients; and** *Documented qualifications of staff and adequacy of time commitment.*	**25**
<u>OPTION 3:</u> • **Documented quality of the Option 3 concept for additional studies;** • **Documented access to the appropriate number and type of patients; and** • **Documented qualifications of staff and adequacy of time commitment**	**25**

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.

SECTION I. GENERAL CLAUSES

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ARTICLE I.1. GENERAL CLAUSES FOR A NEGOTIATED COST-REIMBURSEMENT CONTRACT WITH EDUCATIONAL INSTITUTIONS - FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

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

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

FAR CLAUSE	DATE	TITLE
52.202-1	Oct 1995	Definitions
52.203-3	Apr 1984	Gratuities (Over $100,000)
52.203-5	Apr 1984	Covenant Against Contingent Fees (Over $100,000)
52.203-6	Jul 1995	Restrictions on Subcontractor Sales to the Government (Over $100,000)
52.203-7	Jul 1995	Anti-Kickback Procedures(Over $100,000)
52.203-8	Jan 1997	Cancellation, Rescisison, and Recovery of Funds for Illegal or Improper Activity (Over $100,000)
52.203-10	Jan 1997	Price or Fee Adjustment for Illegal or Improper Activity (Over $100,000)
52.203-12	Jun 1997	Limitation on Payments to Influence Certain Federal Transactions (Over $100,000)
52.204-4	Jun 1996	Printing/Copying Double-Sided on Recycled Paper (Over $100,000)
52.209-6	Jul 1995	Protecting the Government's Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment (Over $25,000)
52.215-2	Jun 1999	Audit and Records - Negotiation (Over $100,000), Alternate II (Apr 1998)
52.215-8	Oct 1997	Order of Precedence - Uniform Contract Format
52.215-10	Oct 1997	Price Reduction for Defective Cost or Pricing Data
52.215-12	Oct 1997	Subcontractor Cost or Pricing Data (Over $500,000)
52.215-14	Oct 1997	Integrity of Unit Prices (Over $100,000)
52.215-15	Dec 1998	Pension Adjustments and Asset Reversions
52.215-18	Oct 1997	Reversion or Adjustment of Plans for Post-Retirement Benefits (PRB) other than Pensions
52.215-19	Oct 1997	Notification of Ownership Changes

52.215-21	Oct 1997	Requirements for Cost or Pricing Data or Information Other Than Cost or Pricing Data – Modifications
52.216-7	Mar 2000	Allowable Cost and Payment (Paragraph (a) is modified to delete the words "Subpart 31.2" and to add the words "Subpart 31.3")
52.216-11	Apr 1984	Cost Contract - No Fee
52.219-8	Oct 1999	Utilization of Small Business Concerns (Over $100,000)
52.219-9	Oct 1999	Small Business Subcontracting Plan (Over $500,000)
52.219-16	Jan 1999	Liquidated Damages - Subcontracting Plan (Over $500,000)
52.222-2	Jul 1990	Payment for Overtime Premium (Over $100,000) (Note: The dollar amount in paragraph (a) of this clause is $0 unless otherwise specified in the contract.)
52.222-3	Aug 1996	Convict Labor
52.222-26	Feb 1999	Equal Opportunity
52.222-35	Apr 1998	Affirmative Action for Disabled Veterans and Veterans of the Vietnam Era
52.222-36	Jun 1998	Affirmative Action for Workers with Disabilities
52.222-37	Jan 1999	Employment Reports on Disabled Veterans and Veterans of the Vietnam Era
52.223-6	Jan 1997	Drug-Free Workplace
52.223-14	Oct 1996	Toxic Chemical Release Reporting
52.225-1	Feb 2000	Buy American Act – Balance of Payments Program - Supplies
52.225-13	Feb 2000	Restrictions on Certain Foreign Purchases
52.227-1	Jul 1995	Authorization and Consent, Alternate I (Apr 1984)
52.227-2	Aug 1996	Notice and Assistance Regarding Patent and Copyright Infringement (Over $100,000)
52.227-11	Jun 1997	Patent Rights - Retention by the Contractor (Short Form) (Note: In accordance with FAR 27.303(a)(2), paragraph (f) is modified to include the requirements in FAR 27.303(a)(2)(i) through (iv). The frequency of reporting in (i) is annual.
52.227-14	Jun 1987	Rights in Data - General, Alternate IV (Jun 1987)
52.232-9	Apr 1984	Limitation on Withholding of Payments
52.232-20	Apr 1984	Limitation of Cost
52.232-23	Jan 1986	Assignment of Claims
52.232-25	Jun 1997	Prompt Payment
52.232-34	May 1999	Payment by Electronic Funds Transfer--Other Than Central Contractor Registration
52.233-1	Dec 1998	Disputes
52.233-3	Aug 1996	Protest After Award, Alternate I (Jun 1985)
52.242-1	Apr 1984	Notice of Intent to Disallow Costs
52.242-4	Jan 1997	Certification of Final Indirect Costs
52.242-13	Jul 1995	Bankruptcy (Over $100,000)

52.244-2	Aug 1998	Subcontracts, Alternate II (Aug 1998) *If written consent to subcontract is required, the identified subcontracts are listed in ARTICLE B, Advance Understandings.
52.244-5	Dec 1996	Competition in Subcontracting (Over $100,000)
52.245-5	Jan 1986	Government Property (Cost-Reimbursement, Time and Material, or Labor-Hour Contract), Alternate I (Jul 1985)
52.246-23	Feb 1997	Limitation of Liability (Over $100,000)
52.249-5	Sep 1996	Termination for the Convenience of the Government (Educational and Other Nonprofit Institutions)
52.253-1	Jan 1991	Computer Generated Forms

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

HHSAR CLAUSE	DATE	TITLE
352.202-1	Apr 1984	Definitions - Alternate I (Apr 1984)
352.228-7	Dec 1991	Insurance - Liability to Third Persons
352.232-9	Apr 1984	Withholding of Contract Payments
352.233-70	Apr 1984	Litigation and Claims
352.242-71	Apr 1984	Final Decisions on Audit Findings
352.249-14	Apr 1984	Excusable Delays
352.270-5	Apr 1984	Key Personnel
352.270-6	Jul 1991	Publication and Publicity
352.270-7	Apr 1984	Paperwork Reduction Act

[End of GENERAL CLAUSES FOR A NEGOTIATED COST-REIMBURSEMENT CONTRACT WITH EDUCATIONAL INSTITUTIONS - Rev. 3/2000].

ARTICLE I.2. AUTHORIZED SUBSTITUTIONS OF CLAUSES

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

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

ALTERNATE IV (OCTOBER 1997) of FAR Clause 52.215-21, REQUIREMENTS FOR COST OR PRICING DATA OR INFORMATION OTHER THAN COST OR PRICING DATA--MODIFICATIONS (OCTOBER 1997) is added.

FAR Clause 52.216-7, ALLOWABLE COST AND PAYMENT (MARCH 2000), is modified in paragraph (a). The reference to Subpart 31.2 is changed to Subpart 31.3.

FAR Clause 52.216-7, ALLOWABLE COST AND PAYMENT (MARCH 2000), is modified in paragraph (a) to delete the words "subpart 31.2 of the Federal Acquisition Regulation (FAR)" and substitute the words "45 CFR part 74, appendix E".

FAR Clause 52.232-20, LIMITATION OF COST, is deleted in its entirety and FAR Clause 52.232-22, LIMITATION OF FUNDS (APRIL 1984) is substituted therefor. **Note: When this contract is fully funded, FAR Clause 52.232-22, LIMITATION OF FUNDS will no longer apply and FAR Clause 52.232-20, LIMITATION OF COST will become applicable.**

FAR Clause 52.232-34, PAYMENT BY ELECTRONIC FUNDS TRANSFER--OTHER THAN CENTRAL CONTRACTOR REGISTRATION (MAY 1999) , is deleted in its entirety and FAR Clause 52.232-36, PAYMENT BY THIRD PARTY (MAY 1999) is substituted therefor.

ARTICLE I.3. ADDITIONAL CONTRACT CLAUSES

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

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

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

FAR 52.216-15, Predetermined Indirect Cost Rates (APRIL 1998).

FAR 52.217-7, Option for Increased Quantity - Separately Priced Line Item (MARCH 1989).

> "....The Contracting Officer may exercise the option by written notice to the Contractor within [INSERT THE PERIOD OF TIME IN WHICH THE CONTRACTING OFFICER HAS TO EXERCISE THE OPTION] ...."

FAR 52.219-4, Notice of Price Evaluation Preference for HUBZone Small Business Concerns (JANUARY 1999).

> "(c) Waiver of evaluation preference.....
>
> **[ ]** Offeror elects to waive the evaluation preference."

FAR 52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns (OCTOBER 1999).

> "(b) Evaluation adjustment. (1) The Contracting Officer will evaluate offers by adding a factor of [*Contracting Officer insert the percentage*] percent to the price of all offers, except--..."

ALTERNATE I (OCTOBER 1998), FAR Clause 52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns (OCTOBER 1999).

FAR 52.223-3, Hazardous Material Identification and Material Safety Data (JANUARY 1997), ALTERNATE I (JULY 1995).

FAR 52.224-1, Privacy Act Notification (APRIL 1984).

FAR 52.224-2, Privacy Act (APRIL 1984).

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

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

Additions to, or limitations on, the restricted rights set forth in the Restricted Rights Notice of subparagraph (g)(3) of the clause are expressly stated as follows:

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

FAR 52.227-17, Rights in Data--Special Works (JUNE 1987).

FAR 52.230-5, Cost Accounting Standards - Educational Institution (APRIL 1998).

FAR 52.230-6, Administration of Cost Accounting Standards (NOVEMBER 1999).

FAR 52.239-1, Privacy or Security Safeguards (AUGUST 1996).

FAR 52.243-2, Changes--Cost Reimbursement (AUGUST 1987), Alternate V (APRIL 1984).

FAR 52.247-63, Preference for U.S. Flag Air Carriers (JANUARY 1997).

FAR 52.247-67, Submission of commercial Transportation Bills to the General Services Administration for Audit (JUNE 1997).

FAR 52.251-1, Government Supply Sources (APRIL 1984).

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

(1) PHS 352.223-70, Safety and Health (Deviation) (AUGUST 1997).

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

(3) HHSAR 352.270-1, Accessibility of Meetings, Conferences and Seminars to Persons with Disabilities (APRIL 1984).

(4) PHS 352.280-1b, Protection of Human Subjects (OCTOBER 1986).

(5) PHS 352.280-3, Maximum Allowable Costs for Drugs (APRIL 1984).

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

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

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

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

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

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

This contract incorporates the following clauses in full text.

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

1. FAR Clause 52.244-6, **SUBCONTRACTS FOR COMMERCIAL ITEMS AND COMMERCIAL COMPONENTS** (OCTOBER 1998)

(a) **Definition**.

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

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

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

(c) Notwithstanding any other clause of this contract, the Contractor is not required to include any FAR provision or clause, other than those listed below to the extent they are applicable and as may be required to establish the reasonableness of prices under Part 15, in a subcontract at any tier for commercial items or commercial components:
   (1) 52.222-26, Equal Opportunity (E.O. 11246);
   (2) 52.222-35, Affirmative Action for Disabled Veterans and Veterans of the Vietnam Era (38 U.S.C. 4212(a));
   (3) 52.222-36, Affirmative Action for Workers with Disabilities (29 U.S.C. 793); and
   (4) 52.247-64, Preference for Privately Owned U.S.-Flagged Commercial Vessels (46 U.S.C. 1241) (flow down not required for subcontracts awarded beginning May 1, 1996).

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

SECTON J
LIST OF ATTACHMENTS

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

- Packaging and Delivery of Proposals
- Proposal Intent Response Sheet ***Submit on/before: October 15, 2000***
  Your attention is directed to the "proposal intent response sheet". If you intend to submit a proposal, you must complete this form and return it to this office via fax or e-mail on or before the date identified above. The receipt of this form is critical as it contains information essential for CMB's coordination of the electronic submission and review of proposals.
- How to Prepare and Submit an Electronic Proposal

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 - 1

Appendices to Introduction/Statement of Work

- **APPENDIX A: Table listing NIH funded grants with Principal Investigators having an interest in recovery processes and mechanisms.**
- **APPENDIX B: Guidance for Clinical Protocol Development (June 19, 2000)**
- **APPENDIX C: Sample Concept Sheet**

Applicable to Technical Proposal

- **Technical Proposal Cover Sheet**
- **Technical Proposal Cost Summary**
- **Summary of Related Activities**
- **Optional Form 310, Protection of Human Subjects Assurance Identification/Certification/Declaration** *[When applicable, all institutions must have the form reviewed and approved by their Institutional Review Committee.]*
- **Government Notice for Handling Proposals**

Applicable to Business Proposal

- **NIH-2043, Proposal Summary and Data Record**
- **Small Business Subcontracting Plan**
- **Summary of Proposed Estimated Cost (plus fee) and Labor Hours**
- **Detailed Breakdown of Proposed Costs (Excel cost spreadsheet template)**
- **Offeror's Points of Contact**

To Become Contract Attachments and Reports Required During Contract Performance (as applicable)

- **Annual Technical Progress Report Format for Each Study** *[Applicable when contract involves Human Subjects unless it has been determined by the Government that the inclusion of Women and Minority Groups in the Study Population is not appropriate.]*
- **NIH(RC)-4: Invoice/Financing Request and Contract Financial Reporting Instructions for NIH Cost-Reimbursement Type Contracts**
- **NIH(RC)-11: Research Patient Care Costs**
- **Privacy Act System of Records, #09-25-0200**
- **Safety and Health (Deviation), PHS Clause 352.223-70**
- **Procurement of Certain Equipment, NIH(RC)-7 (OMB Bulletin 81-16)**

HOW TO PREPARE AND SUBMIT AN ELECTRONIC PROPOSAL

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ELECTRONIC SUBMISSION INSTRUCTIONS

PAGE LIMITS

- **THE NARRATIVE PORTION OF THE TECHNICAL PROPOSAL SHALL NOT EXCEED 100 PAGES.**
- **BASIC REQUIREMENT: SAMPLE PROTOCOL, CONSENT FORMS, STUDY SCHEDULE AND TIMELINE SHALL NOT EXCEED 50 PAGES AND BE SUBMITTED AS A SEPARATE DOCUMENT.**
- **OPTIONS 1 and 3 BRIEF TRIAL CONCEPTS FOR OPTIONS SHALL NOT EXCEED 6 PAGES EACH.**
- **OPTION 2 PHASE I/II PROTOCOL SHALL NOT EXCEED 15 PAGES.**
- **APPENDICES, ATTACHMENTS, OPERATING MANUALS, NON-SCANNABLE FIGURES OR DATA, LETTERS OF INTENT, ETC., SHALL NOT EXCEED A TOTAL OF 30 PAGES.**
- **CURRICULUM VITAEs (CVs) SHALL NOT EXCEED 2 PAGES EACH.**

Pages in excess of this will be removed from the proposal and will not be read or evaluated. Offerors are encouraged to limit the overall size of the Technical Proposal (excluding appendices, attachments, operating manuals, non-scannable figures or data, letters of collaboration/intent, etc.). 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.

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.

GENERAL --- To submit a proposal electronically under this RFP, Offerors will need to prepare the proposal on a word processor or spreadsheet program (for the cost portions) and convert them to Adobe Acrobat Portable Document Format (PDF). THE TECHNICAL PROPOSAL AND BUSINESS PROPOSAL MUST BE CONTAINED ON SEPARATE FILES. Further, to expedite the file transferring process, the two files must be named using the following:

- **Technical Proposal: c:\rfpDMID01_16techprop.pdf**
- **Business Proposal: c:\rfpDMID01_16busiprop.pdf**

If your organization does not have the capability to submit electronically, or unforeseen difficulties occur during transmission, you may submit the electronic copy of your proposal with the original proposal on a diskette, CD-Rom or ZipDisk, in lieu of the internet. The Contract Specialist/Contracting Officer must be notified in advance of using these optional methods.

Approximately TWO weeks prior to the due date of proposals, all offerors will be provided with 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 Contracting Officer identified in this RFP and **complete and submit the attached Proposal Intent Form by the date provided on that Attachment.**.

NOTE: There is no limit to the size (MB) of the two electronic PDF files to be submitted; however, the size of the technical proposal is limited to the page limitation language outlined below. For purposes of assessing compliance with the page count, technical proposals will be viewed using the print function of the Adobe Acrobat Reader, Version 3.0.

ADDITIONAL SUGGESTIONS --- Do not embed sound or video (e.g., MPEG) files into the proposal documents. The evaluation system will not incorporate a capability to read these files. Graphics which are embedded into documents should be kept 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. Suggestions include:

- 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).

PROPOSAL INTENT RESPONSE SHEET

[Return to Table of Contents] or [Return to List of Attachments]

RFP No.: NIH-NIAID-DMID-01-16
RFP Title: "Hepatitis C Research Recovery Network"

Please review the attached Request for Proposal. Furnish the information requested below and return this page by **October 15, 2000**. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

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

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

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

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

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

RETURN VIA FAX OR E-MAIL TO:
CMB, NIAID, NIH
Room 2230
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn: Janet M. Mattson, Contracting Officer
RFP-NIH-NIAID-DMID-01-16
FAX# (301) 480-5253
Email : jm32u@nih.gov

PACKAGING AND DELIVERY OF THE PROPOSAL

[Return to Table of Contents] or [Return to List of Attachments]

[Note to Offeror: Listed below are delivery instructions for the submission of the PAPER copies of your proposal. Instructions for your electronic submission are described above in Electronic Submission Instructions.]

Shipment and marking shall be as indicated below:

A. EXTERNAL PACKAGE MARKING:

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

"RFP NO. NIH-NIAID-DMID-01-16
TO BE OPENED BY AUTHORIZED GOVERNMENT PERSONNEL ONLY"

B. NUMBER OF COPIES:

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

Technical Proposal: One (1) unbound signed original and 5 unbound copies, with 10 copies of items excluded from electronic submission requirement that you choose to provide in paper format (SOPs, PERTINENT MANUALS, NONSCANNABLE FIGURES OR DATA, AND LETTERS OF COLLABORATION/INTENT.)

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

C. PAPER COPIES TO:

If hand delivery or express service	*If using U.S. Postal Service*
Janet M. Mattson Contracting Officer Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230 Bethesda, Maryland 20817	Janet M. Mattson Contracting Officer Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230, MSC 7612 Bethesda, Maryland 20892-7612

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

NOTE: The U.S. Postal Service's "Express Mail" does not deliver to the hand delivered (20817 zip code) address. Any package sent to this address via this service will be held at a local post office for pick-up. THE GOVERNMENT IS NOT RESPONSIBLE FOR PICKING UP ANY MAIL AT A LOCAL POST OFFICE. If a proposal is not received at the place, date, and time specified herein, it will be considered a "late proposal," in accordance with PHSAR 352.215-10, Late Proposals, Modifications of Proposals and Withdrawals of Proposals (NOV 1986).

SECTION K

REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

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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://www4.od.nih.gov/ocm/contracts/rfps/REPCERT.htm

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

IF YOU INTEND TO SUBMIT A PROPOSAL, YOU MUST COMPLETE THE REPRESENTATIONS AND CERTIFICATIONS AND SUBMIT THEM AS PART OF YOUR BUSINESS PROPOSAL.

SECTION L
INSTRUCTIONS, CONDITIONS AND NOTICES TO OFFERORS

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1. GENERAL INFORMATION

a. **INSTRUCTIONS TO OFFERORS--COMPETITIVE ACQUISITION** [FAR Clause 52.215-1 (February 2000)]

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

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

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

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

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

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

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

(c) Submission, modification, revision, and withdrawal of proposals.

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

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

(3) Submission, modification, revision, and withdrawal of proposals.

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

(ii) (A) Any proposal, modification, or revision received at the Government office designated in the solicitation after the exact time specified for receipt of offers is "late" and will not be considered unless it is received before award is made, the Contracting Officer determines that accepting the late offer would not unduly delay the acquisition; and--

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

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

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

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

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

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

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

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

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

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

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

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

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

(e) Restriction on disclosure and use of data. Offerors that include in their proposals data that they do not want disclosed to the public for any purpose, or used by the Government except for evaluation purposes, shall--

(1) Mark the title page with the following legend:

This proposal includes data that shall not be disclosed outside the Government and shall not be duplicated, used, or disclosed--in whole or in part--for any purpose other than to evaluate this proposal. If, however, a contract is awarded to this offeror as a result of--or in connection with--the submission of this data, the Government shall have the right to duplicate, use, or disclose the data to the extent provided in the resulting contract. This restriction does not limit the Government's right to use information contained in this data if it is obtained from another source without restriction. The data subject to this restriction are contained in sheets [*insert numbers or other identification of sheets*]; and

(2) Mark each sheet of data it wishes to restrict with the following legend:

Use or disclosure of data contained on this sheet is subject to the restriction on the title page of this proposal.

(f) Contract award.

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

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

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

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

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

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

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

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

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

(10) The Government may disclose the following information in postaward debriefings to other offerors:

(i) The overall evaluated cost or price and technical rating of the successful offeror;
(ii) The overall ranking of all offerors, when any ranking was developed by the agency during source selection;
(iii) A summary of the rationale for award; and
(iv) For acquisitions of commercial items, the make and model of the item to be delivered by the successful offeror.

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

(f) (4) The Government intends to evaluate proposals and award a contract after conducting discussions with offerors whose proposals have been determined to be within the competitive range. If the Contracting Officer determines that the number of proposals that would otherwise be in the competitive range exceeds the number at which an efficient competition can be conducted, the Contracting Officer may limit the number of proposals in the competitive range to the greatest number that will permit an efficient competition among the most highly rated proposals. Therefore, the offeror's initial proposal should contain the offeror's best terms from a price and technical standpoint.

b. **SIC 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 standard industrial classification (SIC) code for this acquisition is **8731**.

(2) The small business size standard is **500 employees**.

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

c. **NOTICE OF PRICE EVALUATION ADJUSTMENT FOR SMALL DISADVANTAGED BUSINESS CONCERNS**

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

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

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

d. **TYPE OF CONTRACT AND NUMBER OF AWARD(S)**

It is anticipated that ONE AWARD will be made from this solicitation and that the award(s) will be made on/about **August 1, 2001**.

It is anticipated that the award(s) from this solicitation will be a MULTIPLE-YEAR, COST REIMBURSEMENT, COMPLETION TYPE CONTRACT with a PERIOD OF PERFORMANCE OF FIVE (5) YEARS, and that incremental funding will be used [see Section L.2.d. Business Proposal Instructions].

e. **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 total five-year effort to be approximately 4,190 total labor hours/year (20,950 total labor hours for all five-years). This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

f. **COMMITMENT OF PUBLIC FUNDS**

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

g. **COMMUNICATIONS PRIOR TO CONTRACT AWARD**

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

h. **RELEASE OF INFORMATION**

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

i. **COMPARATIVE IMPORTANCE OF PROPOSALS**

You are advised that paramount consideration shall be given to the evaluation of technical proposals. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. The relative importance of the evaluation factors are specified in the TECHNICAL EVALUATION FACTORS FOR AWARD 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.

j. **PREPARATION COSTS**

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

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

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

Brenda J. Velez
Chief, Contract Management Branch
National Institutes of Allergies and Infectious Diseases
6700 B Rockledge Dr., Room 2230 MSC 7612
BETHESDA MD 20892-7612

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

(End of Provision)

l. **LATE PROPOSALS, MODIFICATIONS OF PROPOSAL, AND WITHDRAWALS OF PROPOSALS, PHS 352.215-10**

Notwithstanding the procedures contained in the provision of this solicitation entitled Late Submissions, Modifications, and Withdrawals of Proposals, a proposal received after the date specified for receipt may be considered if it offers significant cost or technical advantages to the Government, and it was received before proposals were distributed for evaluation, or within five calendar days after the exact time specified for receipt, whichever is earlier.

(End of provision)

2. INSTRUCTIONS TO OFFERORS

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a. GENERAL INSTRUCTIONS

INTRODUCTION

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

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

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

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

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

I. COVER PAGE

Include RFP title, number, name of organization, identification of the proposal part, and indicate whether the proposal is an original or a copy.

II. TECHNICAL PROPOSAL

It is recommended that the technical proposal consist of a cover page, a table of contents, and the information requested in the Technical Proposal Instructions.

III. BUSINESS PROPOSAL

It is recommended that the business proposal consist of a cover page, a table of contents, and the information requested in the Business Proposal Instructions.

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

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

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

The proposal must be prepared in two parts: a "Technical Proposal" and a "Business Proposal." The Technical Proposal must be further divided to separately propose for the “Base Contract” and each of “Options 1, 2 and 3”. Each of the parts shall be separate and complete in itself so that evaluation of one may be accomplished independently of, and concurrently with, evaluation of the other. The technical proposal must include direct cost and resources information, such as labor-hours and categories and applicable rates, materials, subcontracts, travel, etc., and associated costs so that the offeror's understanding of the project may be evaluated (See Attachment entitled, TECHNICAL PROPOSAL COST INFORMATION/SUMMARY OF LABOR AND DIRECT COSTS). However, the technical proposal should **not** include pricing data relating to individual salary information, indirect cost rates or amounts, fee amounts (if any), and total costs. The technical proposal should disclose your technical approach in as much detail as possible, including, but not limited to, the requirements of the technical proposal instructions.

(5) **Alternate Proposals**

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

(6) **Confidentiality of Proposals --HHSAR 352.215-12, Restriction on Disclosure and Use of Data (April 1984)**

The proposal submitted in response to this request for proposals may contain data (trade secrets; business data, e.g., commercial information, financial information, and cost and pricing data; and technical data) which the offeror, including its prospective subcontractor(s), does not want used or disclosed for any purpose other than for evaluation of the proposal. The use and disclosure of any data may be so restricted; **provided**, that the Government determines that the data is not required to be disclosed under the Freedom of Information Act, 5 U.S.C. 552, as amended, and the offeror marks the cover sheet of the proposal with the following legend, specifying the particular portions of the proposal which are to be restricted in accordance with the conditions of the legend. The Government's determination to withhold or disclose a record will be based upon the particular circumstances involving the record in question and whether the record may be exempted from disclosure under the Freedom of Information Act:

Unless disclosure is required by the Freedom of Information Act, 5 U.S.C. 552, as amended, (the Act) as determined by Freedom of Information (FOI) Officials of the Department of Health and Human Services, data contained in the portions of this proposal which have been specifically identified by page number, paragraph, etc. by the offeror as containing restricted information shall not be used or disclosed except for evaluation purposes.

The offeror acknowledges that the Department may not be able to withhold a record (data, document, etc.) nor deny access to a record requested pursuant to the Act, and that the Department's FOI officials must make that determination. The offeror hereby agrees that the Government is not liable for disclosure if the Department has determined that disclosure is required by the Act.

If a contract is awarded to the offeror as a result of, or in connection with, the submission of this proposal; the Government shall have the right to use or disclose the data to the extent provided in the contract. Proposals not resulting in a contract remain subject to the Act.

The offeror also agrees that the Government is not liable for disclosure or use of unmarked data and may use or disclose the data for any purpose, including the release of the information pursuant to requests under the Act.

The data subject to this restriction are contained in pages (insert page numbers, paragraph designations, etc. or other identification)

In addition, the offeror should mark each page of data it wishes to restrict with the following legend:

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

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

(7) **Evaluation of Proposals**

The Government will evaluate technical proposals in accordance with the criteria set forth in the Technical Evaluation Factors for Award.

(8) **Potential Award Without Discussions**

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

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

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

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

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

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

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

(10) **Human Subjects**

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

Notice to Offerors of Requirements of 45 CFR Part 46, Protection of Human Subjects (SEPTEMBER 1985)

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

b) The regulations define a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. The regulations extend to the use of human organs, tissue and body fluids from individually identifiable human subjects as well as to graphic, written or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable State and local law and is not directly regulated by 45 CFR, Part 46.

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

d) Inappropriate designations of the noninvolvement of human subjects or of exempt categories of research in a project may result in delays in the review of a proposal. The Public Health Service will make a final determination of whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the proposal. In doubtful cases, prior consideration with OPRR, (telephone: 301-496-7041), is recommended.

e) In accordance with 45 CFR, Part 46, prospective Contractors being considered for award shall be required to file with OPRR an acceptable Assurance of Compliance with the regulations, specifying review procedures and assigning responsibilities for the protection of human subjects. The initial and continuing review of a research project by an institutional review board shall assure that the rights and welfare of the human subjects involved are adequately protected, that the risks to the subjects are reasonable in relation to the potential benefits, if any, to the subjects and the importance of the knowledge to be gained, and that informed consent will be obtained by methods that are adequate and appropriate. Prospective Contractors proposing research that involves human subjects shall be contacted by OPRR and given detailed instructions for establishing an institutional review board and filing an Assurance of Compliance.

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

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

Prior to award of any contract for research involving human subjects, the offeror must provide a description of education in the protection of human subjects that the Principal Investigator and all individuals identified as "Key Personnel" have completed. Curricula that are readily available and meet the educational requirement include the NIH on-line tutorial, titled "Protection of Human Research Subjects: Comoputer-Based Training for Researchers," available at http://helix.nih.gov.8001/ohsr/newcbt/ . This site may be downloaded at no cost and modified for use by the offeror, if desired. In addition, the University of Rochester has made available its training program for individual investigators, and completion of this program will also satisfy the educational requirement. The University of Rochester's website is http://www.centerwatch.com . If an institution has already developed educational programs on the protection of research participants, completion of these programs will also satisfy the educational requirement.

Additionally, prior to any substitution of the Principal Investigator or Key Personnel, the contractor must provide information in writing to the Contracting Officer describing the education in the protection of human subjects that has been completed by successor personnel.

Any contract awarded as a result of the solicitation will require the contractor to provide a written report, on an annual basis, which includes, by individual, a description of completed education in the protection of human subjects.

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

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This new policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43) and supersedes and strengthens the previous policies (Concerning the Inclusion of Women in Study Populations, and Concerning the Inclusion of Minorities in Study Populations) which have been in effect since 1990. The new policy contains some new provisions that are substantially different from the 1990 policies.

All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research" which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513), [(this was reprinted to correct typesetting errors from Federal Register dated March 9, 1994 (FR 59 11146-11151)], and reprinted in the NIH GUIDE FOR GRANTS AND CONTRACTS of March 18, 1994, Volume 23, Number 11.

Offerors may obtain copies from these sources or from the contact person listed in the RFP.

Unless otherwise specified in this solicitation, the Government has determined that the work set forth herein does not involve a gender specific study or a single or limited number of minority population groups. Therefore, the Institute believes that the inclusion of women and minority populations is appropriate for this project.

The format for the Annual Technical Progress Report for Clinical Research Study Populations (See LIST OF ATTACHMENTS of this RFP) shall be used in proposal preparation.

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

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

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

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

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" which was published in the NIH Guide for Grants and Contracts on March 6, 1998 and is available at the following URL address:

http://www.nih.gov/grants/guide/notice-files/not98-024.html

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

(14) **Privacy Act**

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

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

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

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

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

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

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

-to the cognizant audit agency and the General Accounting Office for auditing.

-to the Department of Justice as required for litigation.

-to respond to congressional inquiries.

-to qualified experts, not within the definition of Department employees, for opinions as a part of the review process.

(15) **Selection of Offerors**

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

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

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

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

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

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

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

While it is the Institute's policy to conduct discussions with all offerors in the competitive range, the Institute reserves the right, in special circumstances, to limit the number of proposals included in the competitive range to the greatest number that will permit an efficient competition. All aspects of the proposals are subject to discussions, including cost, technical approach, past performance, and contractual terms and conditions. At the conclusion of discussions, each offeror still in the competitive range shall be given an opportunity to submit a written Final Proposal Revision (FPR) with the reservation of the right to conduct limited negotiations after Final Proposal Revisions (FPRs) in accordance with HHSAR 315.670.

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

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

(16) **Small Business Subcontracting Plan**

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

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

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

c) The offeror understands that:

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

(2) An acceptable plan must, in the determination of the Contracting Officer, provide the maximum practicable opportunity for small business concerns and small business concerns owned and controlled by socially and economically disadvantaged persons to participate in the performance of the contract.

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

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

(5) It is the offeror's responsibility to develop a satisfactory subcontracting plan with respect to small business concerns and small business concerns owned and controlled by socially and economically disadvantaged individuals, and women-owned small business concerns, and that each such aspect of the offeror's plan will be judged independent of the other.

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

d) Each plan must contain the following:

(1) Goals, expressed in terms of percentages of total planned subcontracting dollars, for the use of Small, small disadvantaged, women-owned, and HUBZone small business concerns as subcontractors.

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

(3) A description of the principal types of supplies and services to be subcontracted with an identification of which supplies and services are expected to be subcontracted to small, small disadvantaged, women-owned and/or HUBZone small business concerns.

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

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

(6) A statement as to whether or not indirect costs were included in establishing subcontracting goals. If they were, a description of the method used to determine the proportionate share of indirect costs to be incurred with small, small disadvantaged, women-owned, and HUBZone small business concerns.

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

(8) A description of the efforts the offeror will make to assure that small, small disadvantaged, women-owned, and HUBZone small business concerns have an equitable chance to compete for subcontracts.

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

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

(11) List the types of records the offeror will maintain to demonstrate procedures that have been adopted to comply with the requirement and goals in the plan, including establishing source lists. Also, the offeror shall describe its efforts to locate small, small disadvantaged, women-owned, and HUBZone small business concerns and award subcontracts to them.

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

(17) **HUBZone Small Business Concerns**

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

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

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

The factor entitled “Extent of Small Disadvantaged Business Participation” as set forth under the **Technical Evaluation Criteria**, shall be used for evaluation purposes. Credit under this evaluation factor is not available to SDB concerns that receive a Price Evaluation Adjustment (PEA) under FAR 19.11. Therefore, an SDB will be evaluated on this factor only if that SDB concern waives the PEA. **Waiver of the price evaluation adjustment shall be clearly stated in the proposal.**

The Department of Commerce determines, on an annual basis, by Major Groups, as contained in the Standard Industrial Classification (SIC) Manual, and region, if any, the authorized SDB procurement mechanisms and applicable factors (percentages). The SIC codes can be found at: http://www.sba.gov/regulations/siccodes/siccodes.pdf or http://www.sba.gov/regulations/siccodes/siccodes.doc

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

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

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

EXAMPLE

Targets for SDB Participation - SIC Major Group 87

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

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

(19) **Salary Rate Limitation in Fiscal Year 2000**

Offerors are advised that pursuant to P.L. 106-113, no NIH Fiscal Year 2000 (October 1, 1999 - September 30, 2000) funds may be used to pay the direct annual salary of an individual through any contract awarded as a result of this solicitation at a rate in excess of the Executive Schedule, Level II* (direct salary is exclusive of Overhead, Fringe Benefits and General and Administrative expenses). This does not preclude the offeror from absorbing that portion of an employee's annual salary (plus the dollar amount for fringe benefits and associated indirect costs) that exceeds a rate of the Executive Schedule, Level II*. The salary rate limitation set by P.L. 106-113 applies only to Fiscal Year 2000 funds, however, salary rate ceilings for subsequent years may be included in future DHHS appropriation acts. Multi-year contracts awarded pursuant to this solicitation may be subject to unilateral modifications by the Government if an individual's annual salary exceeds any salary rate ceiling established in future appropriations acts. The Executive Schedule, Level II* annual salary rate limit also applies to individuals proposed under subcontracts. P.L. 106-113 states in pertinent part:

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

***This rate may change periodically. For your information, the rate can be found at: http://www.opm.gov/oca/2000tbls/Execses/html/execschd.htm**

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

EACH INSTITUTION MUST:

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

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

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

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

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

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

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

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

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

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

4) the Institution will otherwise comply with the regulations.

Institutional Management of Conflicting Interests

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

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

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

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

(21) **ROTC Access and Federal Military Recruiting on Campus**

Section 514 of the FY 1997 Appropriations Act prohibits NIH from providing contract funds to educational institutions that the Secretary of Defense determines have a policy or practice (regardless of when implemented) that either prohibits, or in effect prevents (1) the maintaining, establishing, or operation of a unit of the Senior Reserve Officer Training Corps at the covered education entity; or (2) a student at the covered educational entity from enrolling in a unit of the Senior Reserve Officer Training Corps at another institution of higher education.

Further, contract funds may not be provided to educational institutions that have a policy or practice that prohibits or prevents (1) entry to campuses, or access to students (who are 17 years of age or older) on campuses, for purposes of Federal military recruiting; or (2) access by military recruiters for purposes of Federal military recruiting to information pertaining to students (who are 17 years of age or older) enrolled at the covered educational entity.

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

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

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1):

a) Order of Precedence-Uniform Contract Format, FAR Clause 52.215-8, (October 1997).
b) Preaward On-Site Equal Opportunity Compliance Evaluation, (Over $10,000,000), FAR Clause 52.222-24, (February 1999).

b. TECHNICAL PROPOSAL INSTRUCTIONS

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

(1) **Technical Discussions**

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

a) **Statement of Work**

(1) Objectives

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

(2) Approach

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

(3) Methods

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

(4) Schedule

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

b) **Personnel**

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

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

(1) Principal Investigator/Project Director

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

(2) Other Investigators

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

(3) Additional Personnel

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

-The specific items or expertise they will provide.
-Their availability to the project and the amount of time anticipated.
-Willingness to act as a consultant.
-How rights to publications and patents will be handled.

(4) Resumes

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

(2) **Technical Evaluation**

Proposals will be technically evaluated in accordance with the factors, weights, and order of relative importance as described in the TECHNICAL EVALUATION FACTORS FOR AWARD.

(3) **Additional Technical Proposal Information**

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

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

(4) **Other Considerations**

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

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

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

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

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

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

(5) **Information Technology Systems Security**

If this project involves Information Technology, the proposal must present a detailed outline of its proposed Information Technology systems security program which complies with the requirements of the Statement of Work, the Computer Security Act of 1987 Office of Management and Budget (OMB) Circular A-130, Appendix III, "Security of Federal Automated Information Systems," and the DHHS Automated Information Systems Security Program Handbook (Release 2.0, dated May, 1994). The proposal will also need to include similar information for any subcontract proposed.

NOTE: OMB A-130 is accessible via web site: http://www.whitehouse.gov/WH/EOP/OMB/html/circular.html

c. ADDITIONAL TECHNICAL PROPOSAL INSTRUCTIONS AND EVALUATION INFORMATION

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THE FOLLOWING INFORMATION IS SPECIFIC FOR PURPOSES OF RESPONDING TO THIS RFP. ALL OFFEROR(S) SHOULD PROVIDE SPECIFIC DOCUMENTATION IN THEIR PROPOSAL WITH REGARDS TO THESE ITEMS.

1. Biohazard Protection

   Offeror(s) must outline potential biohazards to workers and outline steps to minimize these risks under this contract, particularly with respect to inadvertent needle stick injuries.

2. Clinical Trial Protocols: Format and Information

   DMID has developed comprehensive guidelines on what the Offeror(s) needs to include in proposals that include clinical studies and trials. See APPENDIX B. Offeror(s) should carefully review this information so as to be able to provide an adequate proposal. These guidelines include information such as: suggested format, required components and explanations, sample informed consents, human subjects and biohazards protection clinical terms of award, NIAID protocol review process, safety and monitoring, adverse event reporting, project assurances, data and safety monitoring board guidelines and helpful internet sites.

3. Personnel

   Describe the experience and qualifications of personnel who will be assigned to this project, as well as the percentage of the total time each will be committed to the project. Identify the composition of the task or work group, its general qualifications and recent experience with similar efforts. As a minimum, this effort will require different staff/areas of expertise at different times over the course of the contract based on:

   - completion of the primary acute infection cohort trial,
   - evaluation of performance at the sites,
   - the performance as well as the completion of specific scientific activities, and
   - the need to add additional sites or expertise.

   [See paragraph 5.e), Management Approaches and Plans, below: The Offeror(s) are charged with providing a plan capable of identifying the need to add, replace, or remove scientific and technical staff, especially the proposed subcontractor(s), depending on progress or changes in scientific direction.]

   Several high-level or lead personnel will be required for this contract. Some will be named as key personnel:

   a) Overall Project Director (Key Personnel): The Project Director will have ultimate responsibility for organizing and overseeing the professional, epidemiological, clinical trial, basic research, administrative, laboratory, budgetary and personnel management of the contract. The Project Director must be able to comprehend and respond adequately to many complex scientific issues that impact staffing, budgeting, and the overall conduct of a large (multi-site) and complex (multi-disciplinary) study having epidemiological, clinical trial, and basic research components. Related experience, expertise and educational background should be clearly documented.

      Offeror(s) should document:

      - Qualifications and experience as supported by academic degree(s) and expertise, specialized training, relevant collaborative work involving clinical research, proven ability to provide the necessary scientific leadership/management in designing, managing and coordinating the epidemiological, clinical and research components of this multi-site and multi-disciplinary effort.
      - Relevant work in planning and/or supporting clinical research as appropriate to the proposed role in the project.
      - Availability for the proposed project.
      - Managerial ability to achieve delivery or performance requirements as demonstrated by the proposed use of management and other personnel resources and to successfully manage the Project as demonstrated by the management plan and previous relevant experience.

b) Overall Study Coordinator (Key Personnel): The Study Coordinator will bear day-to-day responsibility for study management and will monitor all aspects of field operations as well as monitor and ensure both quality and progress of enrollment, transmission epidemiology, clinical trial, laboratory, data management and all other components of the study. The Study Coordinator will be in regular communication with the Project Director; will serve as a member of a key liaison team with the NIAID Project Officer in weekly and other conference calls providing information needed for assessment; and be in regular communication with the study manager(s) responsible for field operations and other components of the study. The Study Coordinator must be able to comprehend, respond, and communicate, to both NIAID and Study Manager(s), the many complex scientific issues involved in staffing, budgeting and the overall conduct of a large complex study.

Offeror(s) should document relevant training, qualifications, expertise, experience, education, competence, and availability to perform the requirements of the work statement.

c) Study Managers: Identify and propose, as key personnel, additional staff in specialized areas such as epidemiological studies, clinical trials and research studies. These Study Managers must be active participants in this project in the area for which they will be serving on the Management Team. Offeror(s) should document relevant education and training, qualifications, expertise, vision, experience with similar projects/competence, suitable time commitment and ability to perform as a member of the proposed management team.

d) Co-Investigators/Subcontractors: Documented relevant training, education, qualifications, expertise, experience, competence, and availability of the proposed staff, ability to perform their roles in the proposed effort with respect to the requirements of the SOW.

e) Nursing, Coordinator, Technical and Administrative Staff/Subcontractors: Documented relevant training, education, expertise, experience, competence and availability of the proposed staff to perform their roles in the proposed effort.

4. Organizational Experience and Related Performance

Documented experience and performance relevant to this study.

5. Further Study Details

a) Collaborative Arrangement:

Research scientists find it difficult to access appropriate patient specimens. It is the intent of this RFP to provide access to patient specimens to as many of these investigators as possible as well as to coordinate and integrate their results into the overall picture. See APPENDIX A. The Government anticipates that the Offeror(s) will incorporate existing NIH supported efforts harnessing all available resources whether they are grants, other contracts, or NIH intramural activities, in order to quickly achieve Government objectives. Most of these investigators are focused on quasispecies or cellular immunity. This RFP specifically seeks to integrate investigation of additional aspects of the immune response with the existing approaches.

The proposal must contain signed letters of collaboration from both new and existing sites/investigators/consultants that are proposed to be part of the HC RRN. Discussion as to how these activities would be coordinated and managed is required.

b) Study populations

Offeror(s) are responsible for determining the number and type of human subjects appropriate for the two (2) protocols:

- The primary HCV acute infection cohort protocol that includes evaluation of the impact of treatment on natural history (SOW, Item A), and
- The innovative Phase I/II protocol designed to enhance recovery in HCV chronic carriers (SOW, Item F, Option 1).

Based on their proposed numbers, Offeror(s) are responsible for efficient enrollment of subjects that meet the Government's needs in terms of women, minorities, and children. APPENDIX B provides additional information. Offeror(s) should describe how they developed and implemented criteria for selecting sites, how the sites included in the Proposal meet those criteria, how site flexibility will be implemented to meet rapid accrual objectives, and procedures for discontinuing and/or adding sites. Offeror(s) need to describe the experience-based capabilities of the participating sites in terms of implementation and performance of clinical research in compliance with protocols or alternatively how this requirement will be met.

For the acute infection cohort, the sites that participate in the study need to be identified based on projected availability of sufficient numbers of new HCV infections in health-care workers with exposures to patients infected with HCV. The proposal must contain the requisite documentation. **The Government has a goal of enrollment completion within 2 years of award.** The sites must be able to proactively access exposed health-care workers as well as source patients and blood, and to have the cooperation, participation, and full support of employee health and other pertinent organizations.

[NOTE: The numbers of subjects anticipated from other collaborating sites are identified above in the BACKGROUND].

So as to fulfill the need for rapid accrual, as well as to provide comprehensive collection of specimens and subject monitoring, there is a need for strong collaboration and coordination among the following: employee health and protocol staff, appropriate medical subspecialties such as infectious diseases and gastroenterology, and specimen preparation and research laboratories.

For the chronic HCV carrier subjects, the sites that participate need to be identified based on documented access to suitable numbers of the type of well-characterized patients needed for the proposed Option 1 protocol. These sites may be the same as or different than the sites suitable for SOW Item A. In addition, Offeror(s) are encouraged to categorize and present other types of available patients.

A higher score would be given to Offeror(s) who provide thorough documentation of access to the required populations as well as a detailed and realistic plan to recruit and retain subjects.

c) Protocols

BASE PROTOCOL: THE ACUTE INFECTION INTERVENTION TRIAL:

Offeror(s) must provide a complete protocol, etc. in the format provided in APPENDIX B. and be responsible for full implementation. It is anticipated that this protocol will require submission of an Investigational New Drug Application (INDA) to the Food and Drug Administration (FDA). The type and extent of support that NIAID can supply in terms of regulatory activities is described in APPENDIX B. NIAID will have the responsibility for final submission of the INDA to the FDA.

The rationale for the trial needs to be clearly defined. The trial must address the epidemiology of transmission, early natural history, and outcome of infection and disease with and without early treatment. In addition, the protocol must collect specimens for and be integrated with research on mechanisms of recovery. A complete submission is one having all the required elements sufficiently described, a strong rationale for the study design and the capability to provide definitive answers.

OPTIONS PROTOCOL:

In addition to the BASE proposal requirements covered in SOW, ITEMS A-E, Offeror(s) must propose efforts to accomplish SOW ITEM F, OPTIONS. OPTIONS are considered to be additional activities that provide the Government with the capability to request additional clinical trial efforts in order to further define and enhance recovery. The Government exercises OPTIONS if and when needed. Offeror(s) should delineate their capabilities to access the required subjects and patient populations, staffing needs including those that would differ from those in the BASE proposal. Offeror(s) capabilities to meet each of the OPTION requirements will be assessed individually and separately from the BASE requirement. Separate technical and cost proposals are required to be submitted for each OPTION. Further information is presented below.

OPTION 1 will be carried out in additional acute infection subjects and will require populations and staffing similar to those in the BASE portion of the contract. Offeror(s) should assume that this OPTION would be exercised after the enrollment and treatment phases of the BASE protocol are concluded and that recovery research, managerial and trial support would derive from the BASE portion of the contract. Offeror(s) do not need to provide a protocol for this OPTION but should submit a brief trial concept (See APPENDIX C). Offeror(s) should indicate basic research components they believe would be critical to include. Offeror(s) should propose the participation of specific sites/groups/staff for involvement in this OPTION and describe their qualifications**. For costing purposes, Offeror(s) should assume that an additional 30 subjects would be needed to study a potentially improved intervention. Separate technical and business proposals are required.** Receipt of an award does not represent a commitment to doing the proposed study. Actual implementation of such an OPTION 1 protocol can only be performed if the Government requests it, requiring the written approval and involvement of the Project Officer and Contract Officer.

OPTIONS 2 and 3 require access to a different population group, i.e., well-characterized HCV chronic carriers, and may have different staffing requirements.

OPTION 2 involves innovative protocols/approaches to increasing the sustained recovery response of HCV chronic carriers. Offeror(s) are required to submit one (1) innovative protocol designed to explore ways to enhance recovery in HCV chronic carriers. (See APPENDIX B.) The protocol proposal should be for a Phase I/II study but should not be based on an intervention that has already been or is being evaluated clinically. Offeror(s) should indicate preliminary information that would be needed before such a protocol could be implemented. The protocol will be evaluated based on adequacy and appropriateness including its rationale, innovative nature, design, feasibility and completeness. At this point, the intervention is unknown making it impossible to precisely specify patient characteristics that might be required. Therefore, Offeror(s) should document both the characteristics of and access to the HCV chronic carrier populations that they propose to use. Offeror(s) should propose the participation of specific sites/groups/staff for involvement in this OPTION and describe their qualifications. **Separate technical and business proposals are required. For costing purposes, Offeror(s) should provide a budget for a study using fifty (50) HCV chronic carriers**. Receipt of an award does not represent a commitment to doing the proposed study. Actual implementation of such an OPTION 2 protocol can only be performed if the Government requests it, requiring the written approval and involvement of the Project Officer and Contract Officer.

OPTION 3 provides for the Government to request additional studies for treatment of HCV chronic carriers with FDA approved therapies in order to further define the recovery process. Offeror(s) do not need to provide a protocol for this OPTION but should submit a brief trial concept (See Appendix C). They should indicate basic research components they believe would be critical to include. It is impossible to precisely specify patient characteristics that might be required. Therefore, Offeror(s) should document both the characteristics of, and access to the HCV chronic carrier populations that they propose to use. Offeror(s) should propose the participation of specific sites/groups/staff for involvement in this OPTION and describe their qualifications. **Separate technical and business proposals are required. For costing purposes, Offeror(s) should provide a budget for a study using thirty (30) HCV chronic carriers.** Receipt of an award does not represent a commitment to doing the proposed study. Actual implementation of such an OPTION 3 protocol can only be performed if the Government requests it, requiring the written approval and involvement of the Project Officer and Contract Officer.

d) Recovery Research

- Offeror(s) are charged with employing state-of-the-art, multi-disciplinary approaches to understanding the variables and mechanisms of recovery, persistence, and progression in human subjects.
- Offeror(s) should provide a conceptual framework of approaches to understand the mechanisms of recovery, describe knowledge gaps and scientific opportunities, discuss specific scientific areas/hypotheses, indicate rationale and feasibility for approaches proposed and integrate these into a cohesive plan.
- Offeror(s) should provide both prioritization and a timeline for implementing the proposed research areas/activities//approaches.
- Offeror(s) should employ state-of-the-art technologies that provide maximal information with minimal specimens.
- Offeror(s) should describe three (3) potential pilot projects.

- Offeror(s) should understand that the primary focus is recovery and persistence. Progression represents a secondary focus to be implemented with stored specimens.
- The score given during proposal evaluation will be based on the rationale for the overall scientific approach, its completeness and feasibility, the application of newer technologies and the quality of three (3) required pilot project proposals. In addition, the individual research components will contribute to the overall score. This will be based on their relative strengths in terms of rationale, feasibility, and appropriateness of the proposed specimens, methodologies, controls, and alternative approaches. See also paragraph e., Management Approaches and Plans, below.

e) Management Approaches and Plans

Offeror(s) are required to develop and submit complete working plans that describe how this contract and its activities will be implemented, managed, coordinated, and integrated. Scores will be based on completeness and feasibility. These plans relate to and need to include:

i. Overall Management

- Manual of Standard Operations and Procedures;
- Management of site participation and quality of performance; and
- Staffing, responsibilities, lines of authority.

ii. Scientific Management

- Ensuring multi-disciplinary research and application of new approaches and technologies;
- Integration of basic research findings with clinical parameters; and
- Pilot project submission, rating and prioritization.

iii. Trial Management:

- Training manual for and training of study personnel;
- Data entry, quality control, management plan;
- Data analysis plan describing the types and methods of analyses as well as a schedule for analyses;
- Study initiation, tracking, and completion;
- Obtaining epidemiological information; and
- Recruitment, retention and follow-up of subjects.

iv. Specimen Management

f) Standard Operating Procedures (SOPs)

SOP documents designate safe, sequential, numbered series of steps that allow tasks to be conducted in a standardized manner. SOPs are required procedures that include, but are not limited to, such things as: data collection and entry, drug usage, collection, processing, storage and shipping of biospecimens, etc. The Contractor monitors adherence to procedures and evaluates untoward events in terms of whether the procedure was followed or not. In the event of problems, the Contractor takes appropriate action based in part on an analysis of the SOP, i.e., revise the procedure, conduct quality control as required, and other measures as needed to resolve any detected discrepancies.

Offeror(s) are expected to provide SOP quality control plans with the proposal, to integrate them into the training program and manuals and to fully implement them.

g) Informed Consents

Offeror(s) are responsible for obtaining Institutional Review Board (IRB) approvals for the study(ies) and providing them to the NIAID. An example of an acceptable informed consent is found in APPENDIX B and at http://cancertrials.nci.nih.gov/understanding/index.html. Signed informed consents are required for all study participants. The consent instrument should include provision for permission to obtain questionnaire data, medical record information, pathology documentation, phlebotomy for analyses and storage and liver biopsy per protocol for the clinical and research purposes defined in the protocol. Separate consent for source patients is required.

h) Forms

Offeror(s) are responsible for providing all forms needed for the study. These should be listed and provided with the proposal. Examples should include:

- Abstracting of medical record information and pathology
- Transmission
- Clinical data
- Pathology data
- Adverse Events
- Biospecimen collection, tracking, and shipping

i) Computerized Data Management System

See also paragraph e), Management Approaches and Plans, above. Offeror(s) should provide adequate information on the proposed database; indicate the state of its development and how it would be used at multiple sites. The system must include data tracking forms to monitor the flow of information and materials (biospecimens) from subject identification through creation of the final database. Forms shall include but not be limited to those required to track biospecimens, monitor the specimen transportation and shipping process, and document subject recruitment and participation rate.

The system must track all study forms and biospecimens. It must generate reports of the status of enrollment, trial, data and biospecimen collection for study participants as well as summary reports and other reports on the status of data collection activities across subjects and research investigations, as well as other reports as required by the NIAID Project Officer. This system is used to generate the required bi-monthly reports.

j) Laboratory and Recovery Research Studies

The selected Contractor will collect biospecimens on all study participants in the volumes and types as described in the protocol. These biospecimens will be identified, processed, packaged, stored, shipped, and tracked. See paragraph e), Management Approaches and Plans, above.

k) Abstracts and Manuscripts

Thirty (30) days prior to submission the selected Contractor will provide an advance copy of draft manuscripts (including abstracts and public presentations) resulting from data generated under this contract to the Project Officer in order to allow an opportunity for written review, comment and clearance. Support from the Government Contract and any other Government support should be acknowledged in all abstracts, presentations, and publications.

d. BUSINESS PROPOSAL INSTRUCTIONS

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(1) **Basic Cost/Price Information**

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

(2) **Proposal Cover Sheet**

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

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

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

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

1. **Direct Labor**

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

2. **Materials**

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

3. **Subcontracted Items**

Include parts, components, assemblies, and services that are to be produced or performed by others in accordance with offeror's design, specifications, or direction and that are applicable only to the prime contract. For each subcontract over $500,000, the support should provide a listing by source, item, quantity, price, type of subcontract, degree of competition, and basis for establishing source and reasonableness of price, as well as the results of review and evaluation of subcontract proposals when required by FAR 15.806.

4. **Raw Materials**

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

5. **Purchased Parts**

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

6. **Fringe Benefits**

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

7. **Indirect Costs**

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

8. **Special Equipment**

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

9. **Travel**

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

10. **Other Costs**

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

To assist in the preparation of future cost estimates, the Projected Consumer Price Index may be accessed at: http://amb.nci.nih.gov/cpi.htm

(3) **Qualifications of the Offeror**

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

(1) **General Experience**

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

(2) **Organizational Experience Related to the RFP**

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

(3) **Performance History**

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

(4) **Pertinent Contracts**

Pertinent contracts is defined as a listing of each related contract completed within the last three years or currently in process. The listing should include: 1) the contract number; 2) contracting agency; 3) contract dollar value; 4) dates contract began and ended (or ends); 5) description of contract work; 6) explanation of

relevance of work to this RFP; 7) actual delivery and cost performance versus delivery and cost agreed to in the contract(s). For award fee contracts, separately state in dollars the base fee and award fee available and the award fee actually received. The same type of organizational experience and past performance data should be submitted.

(5) **Pertinent Grants**

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

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

(4) **Other Administrative Data**

a) **Property**

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

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

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

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

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

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

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

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

c) Financial Capacity

The offeror shall indicate if it has the necessary financial capacity, working capital, and other resources to perform the contract without assistance from any outside source. If not, indicate the amount required and the anticipated source.

d) **Incremental Funding**

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

> Sufficient funds are not presently available to cover the total cost of the complete multiple year project described in this solicitation. However, it is the Government's intention to negotiate and award a contract using the incremental funding concepts described in the clause entitled "Limitation of Funds." Under that clause, which will be included in the resultant contract, initial funds will be obligated under the contract to cover an initial period of performance. Additional funds are intended to be allotted from time to time, to the contract by contract modification, up to and including the full estimated cost of the contract, to accomplish the entire project. While it is the Government's intention to progressively fund this contract over the entire period of performance up to and including the full estimated cost, the Government will not be obligated to reimburse the Contractor for costs incurred in excess of the periodic allotments, nor will the Contractor be obligated to perform in excess of the amount allotted.

The "Limitation of Funds" clause to be included in the resultant contract shall supersede the "Limitation of Cost" clause found in the General Clauses.

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

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

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

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

(End of Provision)

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

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

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

(5) **Subcontractors**

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

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

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

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

d) Information on their cognizant field audit offices.

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

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

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

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

(7) **Representations and Certifications**

One copy of the Representations and Certifications attached as SECTION K shall be completed and be signed by an official authorized to bind your organization. Additionally, a completed copy of the Representations and Certifications shall be submitted from any proposed subcontractor.

(8) Travel Costs/Travel Policy

a) **Travel Policy**

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

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PROJECT	PI NAME	INSTITUTION	TITLE
[Return to List of Attachments]			
1 P50 AA11999-01 SUB:0006	LAI, MICHAEL 323-442-1748 michlai@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	CENTER FOR ALCOHOLIC LIVER AND PANCREATIC INJURY SUB TITLE PILOT--HCV AND ALCOHOL SENSITIZE HEPATOCYTES FOR TNF-A MEDIATED CYTOTOXICITY
5 K08 AI01410-03	OLDACH, DAVID W 410-706-4609 oldach@umbi.umd.edu	UNIVERSITY OF MARYLAND BALT PROF SCHOOL	MURINE MODEL FOR HEPATITIS C VIRUS INVESTIGATIONS
5 K08 AI01460-03	SCHMIDT, WARREN N 319-353-7048 warren-schmidt@uiowa.edu	UNIVERSITY OF IOWA	HEPATITIS C AND CRYOGLOBULINEMIA
1 K08 AI01685-01	ANTHONY, DONALD D 216-844-3211 dda3@po.cwru.edu	CASE WESTERN RESERVE UNIVERSITY	CHARACTERIZATION OF CD8 T-CELL IMMUNITY TO HEPATITIS C
5 R01 AI20001-16	CHISARI, FRANCIS V 858-784-8228 fchisari@scripps.edu	SCRIPPS RESEARCH INSTITUTE	PATHOGENESIS OF LIVER DISEASE IN HEPATITIS
5 R01 AI31168-08	PARHAM, PETER R 415-723-6224 peropa@leland.stanford.edu	STANFORD UNIVERSITY	EVOLUTION, SELECTION AND ORIGINS OF CLASS I MHC MOLECULE
5 R01 AI31563-07	WALKER, BRUCE D 617-726-3812 bwalker@helix.mgh.harvard.edu	MASSACHUSETTS GENERAL HOSPITAL	CELL MEDIATED IMMUNITY IN HEPATITIS C VIRUS INFECTION
5 U01 AI31834-07	MINKOFF, HOWARD L 718-270-2860 hminkoff@netmail.hscbklyn.edu	HEALTH SCIENCE CENTER AT BROOKLYN	WOMEN'S INTERAGENCY HIV STUDY
5 U01 AI35004-06	ANASTOS, KATHRYN M 718-920-6635 kanasto@aol.com	MONTEFIORE MEDICAL CENTER (BRONX, NY)	NATURAL HISTORY OF HIV INFECTION IN WOMEN
5 R44 AI38620-03	SETTE, ALESSANDRO D 858-860-2516 asette@epimmune.com	CYTEL CORPORATION	VACCINE APPROACHES TO TREATMENT OF HEPATITIS C INFECTION
5 R29 AI39049-04	GRETCH, DAVID R 206-341-5216 gretch@u.washington.edu	UNIVERSITY OF WASHINGTON	HCV PATHOGENESIS IN LIVER TRANSPLANT RECIPIENTS
5 U19 AI40034-04 SUB 0001	GREENBERG, HARRY B 415-493-5000 X63122 hbgreen@leland.stanford.edu	STANFORD UNIVERSITY	HEPATITIS C--STUDIES OF IMMUNITY AND PATHOGENESIS TITLE: HEPATITIS C--EARLY EVENTS IN CELL INFECTION
5 U19 AI40034-04 SUB:0002	WRIGHT, TERESA L 415-750-2105 twright@itsa.ucsf.edu	STANFORD UNIVERSITY/UCSF	HEPATITIS C--STUDIES OF IMMUNITY AND PATHOGENESIS FACTOR SUB TITLE IMMUNE PATHOGENESIS OF HEPATITIS C VIRUS--THE HUMAN
5 U19 AI40035-04	LEMON, STANLEY M 409-772-2324 smlemon@utmb.edu	UNIVERSITY OF TEXAS MEDICAL BR GALVESTON	
5 U19 AI40035-04 SUB:0003	THOMAS, DAVID 410-955-0349 dthomas@jhmi.edu	UTMB/Johns Hopkins University	SOUTHEASTERN COOPERATIVE HEPATITIS C RESEARCH GROUP SUB TITLE PATHOGENESIS OF HEPATITIS C VIRUS INFECTION AMONG INTRAVENOUS DRUG USERS
5 U19 AI40038-04	LAI, MICHAEL M 323-442-1748 michlai@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	HEPATITIS C VIRUS PERSISTENCE AND PATHOGENESIS

PROJECT	PI NAME	INSTITUTION	TITLE
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5 U19 AI40038-04 SUB:0001	LAI, MICHAEL 323-442-1748 michlai@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	HEPATITIS C VIRUS PERSISTENCE AND PATHOGENESIS SUB TITLE HEPATITIS C VIRUS CORE PROTEIN AND HOST DEFENSE
5 U19 AI40038-04 SUB:0002	DENNERT, GUNTHER 323-865-0621 dennert@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	HEPATITIS C VIRUS PERSISTENCE AND PATHOGENESIS SUB TITLE TRANSGENIC MICE AS A MODEL TO STUDY HCV IMMUNOPATHOGENESIS
5 U19 AI40038-04 SUB:0003	OU, JING-HSIUNG JAMES 323-442-1720 jamesou@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	HEPATITIS C VIRUS PERSISTENCE AND PATHOGENESIS SUB TITLE GENE EXPRESSION AND REPLICATION OF HEPATITIS C VIRUS
5 U19 AI40038-04 SUB:0004	LINDSAY, KAREN 323-342-5577 klindsay@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	HEPATITIS C VIRUS PERSISTENCE AND PATHOGENESIS SUB TITLE HEPATITIS C VIRUS MECHANISMS OF LIVER INJURY--EFFECTS OF THERAPY IN HUMANS
1 R01 AI40672-01A2	AGNELLO, VINCENT 617-273-8887 vincent.agnello@lahey.org	LAHEY HITCHCOCK MEDICAL CENTER	HEPATITIS C VIRUS IN ETIOLOGY OF WA RHEUMATOID FACTORS
5 R01 AI41219-04	KAO, KUO-JANG J 352-392-7841 kjkao@ufl.edu	UNIVERSITY OF FLORIDA	DEFINING HEPATITIS C VIRUS-SPECIFIC CTL ACTIVITY IN MAN
5 U19 AI41320-04	FAUSTO, NELSON 206-685-1221 nfausto@u.washington.edu	UNIVERSITY OF WASHINGTON	EXPERIMENTAL MODELS AND CLINICAL VIROLOGY OF HEPATITIS C
5 U19 AI41320-04 SUB:0001	GRETCH, DAVID R 206-341-5216 gretch@u.washington.edu	UNIVERSITY OF WASHINGTON	EXPERIMENTAL MODELS AND CLINICAL VIROLOGY OF HEPATITIS C SUB TITLE CLINICAL VIROLOGY
5 U19 AI41320-04 SUB:0002	FAUSTO, NELSON 206-685-1221 nfausto@u.washington.edu	UNIVERSITY OF WASHINGTON	EXPERIMENTAL MODELS AND CLINICAL VIROLOGY OF HEPATITIS C SUB TITLE TISSUE CULTURE MODELS
5 U19 AI41320-04 SUB:0003	KAY, MARK 650-498-6531 Markay@Stanford.edu	UNIVERSITY OF WASHINGTON	EXPERIMENTAL MODELS AND CLINICAL VIROLOGY OF HEPATITIS C SUB TITLE ANIMAL MODELS
5 U19 AI41320-04 SUB:0004	KAY, MARK 650-498-6531 Markay@Stanford.edu	UNIVERSITY OF WASHINGTON	EXPERIMENTAL MODELS AND CLINICAL VIROLOGY OF HEPATITIS C SUB TITLE GENE THERAPY
5 U19 AI41320-04 SUB:9001	GRETCH, DAVID R 206-341-5216 gretch@u.washington.edu	UNIVERSITY OF WASHINGTON	EXPERIMENTAL MODELS AND CLINICAL VIROLOGY OF HEPATITIS C SUB TITLE CORE--MOLECULAR VIROLOGY
5 R29 AI41563-03	KOZIEL, MARGARET J 617-632-0133 mkoziel@bidmc.harvard.edu	BETH ISRAEL DEACONESS MEDICAL CENTER	IMMUNITY TO HEPATITIS C IN LIVER TRANSPLANT RECIPIENTS
5 R01 AI41629-03	KATZE, MICHAEL G 206-543-8837 honey@u.washington.edu	UNIVERSITY OF WASHINGTON	HEPATITIS C VIRUS AND INTERFERON--CONTROL OF PKR BY NS5A
5 R01 AI43478-02	SCHMIDT, EMMETT V 617-726-5707 schmidt@helix.mgh.harvard.edu	MASSACHUSETTS GENERAL HOSPITAL	HEPATITIS C TRANSGENIC MICE AS MODEL OF LIVER INJURY
1 R03 AI44036-01	PADMANABHAN, RADHAKRISHNAN K 913-588-7018 rpadmana@kumc.edu	UNIVERSITY OF KANSAS MEDICAL CENTER	VIRUS/HOST INTERACTIONS MODULATED BY HEPATITIC C VIRUS

PROJECT	PI NAME	INSTITUTION	TITLE
[Return to List of Attachments]			
5 R03 AI44679-02	GAUR, LAKSHMI K (206) 292-1866 lgaur@u.washington.edu	PUGET SOUND BLOODCENTER AND PROGRAM	DECREASING SEVERITY OF RECURRENT HEPATITIS C IN LIVER ALLOGRAFT
1 R03 AI45873-01	YEN, TIEN-SZE B 415-476-5334 yen@itsa.ucsf.edu	NORTHERN CALIFORNIA INSTITUTE RES & EDUC	PATHOGENESIS OF CHRONIC HEPATITIS AND HEPATOMA
1 R01 AI47348-01	LAI, MICHAEL M 323-442-1748 michlai@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	REPLICATION OF HEPATITIS C VIRUS RNA
1 R01 AI47349-01 C VIRUS	PRINCE, ALFRED M (212) 570-3279 aprince@server.nybc.org	NEW YORK BLOOD CENTER	PROPHYLACTIC & THERPEUTIC DNA IMMUNIZATION AGAINST HEPATITIS
1 R01 AI47364-01	OLDACH, DAVID W 410-706-4609 oldach@umbi.umd.edu	UNIVERSITY OF MARYLAND BALT PROF SCHOOL	NEEDLESTICK HCV EXPOSURE--VIROLOGIC & IMMUNOLOGIC EVENTS
1 R01 AI47367-01	WALKER, CHRISTOPHER 614-722-2735 Walkerc@pediatrics.ohio-state.edu	CHILDREN'S HOSPITAL (COLUMBUS	HCV SPECIFIC T CELL RESPONSES
1 R01 AI47519-01	CHANG, KYONG-M (215) 823-5893 kmchang@mail.med.upenn.edu	UNIVERSITY OF PENNSYLVANIA	CELLULAR IMMUNITY--OUTCOME HEPATITIS C VIRUS INFECTION
5 N01 AI95362-001	HAHN, BEATRICE 205-934-0412 bhahn@shaw-hahn.dom.uab.edu	EPIMMUNE, INC.	BAA-APPLICATION OF HLA DATA TO DEVELOP & IMPROVE VACCINE
5 R01 CA38450-14	STUVER, SHERRI O 617-432-4591 sstuver@hsph.harvard.edu	HARVARD UNIVERSITY (MEDICAL SCHOOL)	NATURAL HISTORY OF HTLV-I AND HCV INFECTION
5 R01 CA57973-08	RICE, CHARLES M 314-362-2842 rice@borcim.wustl.edu	WASHINGTON UNIVERSITY	HEPATITIS C VIRUS--DEVELOPING ANTIVIRALS AND VACCINES
5 R01 CA76403-02	CHISARI, FRANCIS V 858-784-8228 fchisari@scripps.edu	SCRIPPS RESEARCH INSTITUTE	HEPATITIS C VIRUS IMMUNOBIOLOGY AND PATHOGENESIS
1 U01 CA84951-01	BLOCK, TIMOTHY M 215-489-4948 block@lac.jci.tju.edu	THOMAS JEFFERSON UNIVERSITY	EARLY DETECTION OF LIVER CANCER AND HEPATITIS
1 R01 CA85883-01	RICE, CHARLES M 314-362-2842 rice@borcim.wustl.edu	WASHINGTON UNIVERSITY	IMMUNOTHERAPY PROTECTION AND VACCINES FOR HEPATITIS C
3 R37 DA04334-13	VLAHOV, DAVID 410-955-1848 DVLAHOV@PHNET.SPH.JHU.EDU	JOHNS HOPKINS UNIVERSITY	NATURAL HISTORY OF HIV INFECTION AMONG DRUG USERS
5 R01 DA10627-02	THOMAS, DAVID L 410-955-0349 dthomas@jhmi.edu	JOHNS HOPKINS UNIVERSITY	HIV, DRUG USE AND HEPATITIS C PATHOGENESIS
5 R01 DA10646-03	BORKOWSKY, WILLIAM 212-263-6426 borkow01@mcgc16.med.nyu.edu	NEW YORK UNIVERSITY SCHOOL OF MEDICINE	BIOLOGY OF PEDIATRIC HEPATITIS C INFECTION

PROJECT	PI NAME	INSTITUTION	TITLE
[Return to List of Attachments]			
1 R01 DA11447-01A1	HAGAN, HOLLY C 206-591-6552 holly.hagan@metrokc.gov	SEATTLE-KING COUNTY PUBLIC HEALTH DEPT	HEPATITIS C IN IV DRUG USERS--EPIDEMIOLOGY AND PREVENTION
3 R01 DA12568-01S2	STRATHDEE, STEFFANIE A 410-614-4255	JOHNS HOPKINS UNIVERSITY	INCIDENCE OF HIV INFECTIONS IN A COHORT OF IV DRUG USERS
1 U01 DA13032-01	NELSON, KENRAD E (410) 955-1296 kenelson@jhsph.edu	JOHNS HOPKINS UNIVERSITY	THE EPIDEMIOLOGY OF HEPATITIS C INFECTION IN THAILAND
7 R01 DA13242-02	RUSSELL, MARCIA T russell@ria.org	PACIFIC INSTITUTE FOR RES AND EVALUATION	HCV TRANSMISSION: SEX, VIOLENCE ALCOHOL & DRUG USE
1 R01 DA13245-01	EDLIN, BRIAN R 415-476-3400	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	CLINICAL AND HISTOLOGIC SPECTRUM OF HCV LIVER DISEASE IN IDU
1 R01 DA13324-01	THOMAS, DAVID D\ 410-955-0349 dthomas@jhmi.edu	JOHNS HOPKINS UNIVERSITY	HEPATITIS C PATHOGENESIS AND THE HUMAN GENOME
1 K08 DK02595-01A1	NELSON, DAVID R 352-392-7353	UNIVERSITY OF FLORIDA	CELLULAR IMMUNE RESPONSE IN CHRONIC HEPATITIS C
1 R03 DK54842-01	SCHMIDT, WARREN N 319-353-7048 warren-schmidt@uiowa.edu	UNIVERSITY OF IOWA	QUANTITATION OF HEPATITIS C VIRUS IN PERIPHERAL BLOOD
1 R01 DK56388-01	CARITHERS, JR R 206-548-4956 doctorc@u.washington.edu	UNIVERSITY OF WASHINGTON	STUDIES OF THE NATURAL HISTORY OF HEPATITIS C IN LIVER
1 R01 DK56402-01	FARRELL, GEOFFREY C 612-984-5770 geofff@westmed.wh.usyd.edu.au	UNIVERSITY OF SYDNEY	CHRONIC HEPATITIS C--MOLECULAR AND CELLULAR MARKERS
1 R01 DK56435-01	DI BISCEGLIE, ADRIAN M 314-577-8762 dibiscam@wpogate.slu.edu	ST. LOUIS UNIVERSITY	HEPATITIS C VIRAL QUASISPECIES WITHIN THE LIVER
1 R21 DK57939-01	HAHN, YOUNG S 804-924-1155 ysh5e@virginia.edu	UNIVERSITY OF VIRGINIA CHARLOTTESVILLE	IMMUNOMODULATORY ROLE OF HCV CORE ON AUTOIMMUNE HEPATITIS
1 R01 DK57998-01	RAY, STUART C 410-614-2891 sray@jhmi.edu	JOHNS HOPKINS UNIVERSITY	SEQUENCE SELECTION AND PERSISTENCE OF HEPATITIS C
5 N01 DK92318-001	GRETCH, DAVID R 206-341-5216 gretch@u.washington.edu	UNIVERSITY OF WASHINGTON	HEPATITIS C CLINICAL TRIAL--VIROLOGY LABORATORY
5 N01 DK92319-002	DIENSTAG, JULES L 617-726-7450	MASSACHUSETTS GENERAL HOSPITAL	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTERS
3 N01 DK92320-001	HOEFS, JOHN 714-456-7518 jchoefs@uci.edu	UNIVERSITY OF CALIFORNIA IRVINE	HEPATITIS C CLINICAL TRIALS--CLINICAL CENTERS
5 N01 DK92321-002	LEE, WILLIAM H 214-648-6830 lee03@utsw.swmed.edu	UNIVERSITY OF TEXAS SW MED CTR/DALLAS	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTER

PROJECT	PI NAME	INSTITUTION	TITLE
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3 N01 DK92322-001 UNIVERSITY	SHIFFMAN, MITCHELL 804-828-4060 mshiffma@hsc.vcu.edu	VIRGINIA COMMONWEALTH	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTERS
3 N01 DK92323-002	LOK, ANNA 734-936-4780 alok@umich.edu	UNIVERSITY OF MICHIGAN AT ANN ARBOR	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTERS
3 N01 DK92324-001	DIBISCEGLIE, ADRIAN 314-577-8762 dibiscam@wpogate.slu.edu	ST. LOUIS UNIVERSITY	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTERS
2 N01 DK92325-002	LINDSAY, KAREN 323-342-5577 klindsay@hsc.usc.edu	UNIVERSITY OF SOUTHERN CALIFORNIA	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTERS
5 N01 DK92326-002	BONKOVSKY, HERBERT 508-856-3068 Herbert.bonkovsky@banyan.ummed.edu	UNIVERSITY OF MASSACHUSETTS MEDICAL SCH	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTERS
3 N01 DK92327-002	EVERSON, GREGORY T	UNIVERSITY OF COLORADO HLTH SCIENCES CTR	HEPATITIS C CLINICAL TRIAL--CLINICAL CENTERS
1 N01 DK92328-000	WRIGHT, ELIZABETH 617-923-7747 libbyw@neri.org	NEW ENGLAND RESEARCH INSTITUTES, INC.	HEPATITIS C CLINICAL TRIAL--DATA COORDINATING CENTER
3 N01 HB67130-008	MIMMS, LARRY T	GEN-PROBE, INC.	NEW ASSAYS FOR DIRECT DETECTION OF VIRAL N
5 P01 HL44612-10 SUB:0006	ECKELS, DAVID D 414-937-6310 david@smtpgate.bcsew.edu	BLOOD CENTER OF SOUTHEASTERN WISCONSIN	MOLECULAR AND CELLULAR MECHANISMS IN TRANSFUSION MEDICINE SUB TITLE IMMUNOBIOLOGY OF HCV IN TRANSFUSION MEDICINE
1 R01 HL64817-01	FRIED, MICHAEL W 404-727-7021 mfried.@med.unc.edu	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	HEPATITIS C IN CLINICALLY DISCORDANT HEMOPHILIC SIBLINGS
5 R01 OH03459-02	GERSHON, ROBYN 410-955-3046 rgershon@jhsph.edu	JOHNS HOPKINS UNIVERSITY	RISK OF INFECTIOUS DISEASE IN PRISON BASED HCWS
1 Z01 AI00311-18	PURCELL, ROBERT 301-496-6227 rp18p@nih.gov	DIR, NIAID, NIH	SEARCH FOR NEW HEPATITIS AGENTS
1 Z01 AI00570-10	PURCELL, ROBERT 301-496-6227 rp18p@nih.gov	DIR, NIAID, NIH	MOLECULAR BIOLOGY OF HEPATITIS C VIRUS
1 Z01 AI00823-02	PURCELL, ROBERT 301-496-6227 rp18p@nih.gov	DIR, NIAID, NIH	NEW APPROACHES TO PASSIVE AND ACTIVE IMMUNOPROPHYLAXIS
1 Z01 BC10318-01	WINKLER, CHERYL ANN 301-846-5747 cw209r@nih.gov	NCI, FCRDC	INTERACTIONS BETWEEN HIV AND HCV IN HEMOPHILIACS
1 Z01 BK04001-07	FEINSTONE, STEPHEN 301-496-3200 sf3x@nih.gov	CBER, FDA	ANTIGENIC STRUCTURE OF HEPATITIS C VIRUS

PROJECT	PI NAME	INSTITUTION	TITLE
[Return to List of Attachments]			
1 Z01 CL02005-30	ALTER, HARVEY J 301-402-7144 halter@dtm.cc.nih.gov	CC, NIH	A CONTROLLED PROSPECTIVE STUDY OF TRANSFUSION-ASSOCIATED HEPATITIS
1 Z01 CL02064-08	SHIH, JAMES W 301-496-4506 js204s@nih.gov	CC, NIH	QUANTITATIVE ANALYSIS OF VIRAL GENOMES & THEIR CLINICAL CORRELATIONS
1 Z01 CL02068-08	ALTER, HARVEY J 301-402-7144 halter@dtm.cc.nih.gov	CC, NIH	A PROSPECTIVE STUDY OF ANTI-HEPATITIS C VIRUS POSITIVE BLOOD DONORS
1 Z01 CL02078-04	ALTER, HARVEY J 301-402-7144 halter@dtm.cc.nih.gov	CC, NIH	VIRAL AND IMMUNE FACTORS THAT INFLUENCE RECOVERY OR PROGRESSION OF HEPATITIS C
1 Z01 CL02080-04	ALTER, HARVEY J 301-402-7144 halter@dtm.cc.nih.gov	CC, NIH	NATURAL HISTORY OF HEPATITIS C VIRUS INFECTION
1 Z01 DK54509-02	REHERMANN, BARBARA 301-402-7144 br81y@nih.gov	NIDDK, NIH	HCV SPECIFIC CYTOTOXIC T CELL RESPONSE IN PATIENTS AND TRANSGENIC MICE

TAB A Protocol Development Guidance **APPENDIX B**

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TABLE OF CONTENTS

FACE PAGE

The face page should follow a standard format as illustrated here:

TITLE

A (Single/Multicenter) Study of the
NIAID Cooperative Hepatitis C Recovery Research Network

Supported by Contract #(leave blank for now) from:
The National Institute of Allergy and Infectious Diseases

Contractee Organization:

Principal Investigator:

DMID Project Officer: (leave blank for now)
DMID Study Number: (To be assigned by DMID)
Draft version number:
Date:

PRÉCIS

The précis is a short section summarizing the objectives, design, population, and outcomes of the trial. This "snapshot" of the protocol should include the full protocol title.

General Objective

- Describe the type of trial (Treatment, Vaccine, Prevention).
- Identify the phase of the study.
- Identify the study agent including dose and route of administration (if applicable)

Study Design

- Describe design in broad terms (randomized, placebo-controlled, multi-armed).
- Include the planned duration of the study and the duration of each subject's participation in the study.

Population

- Identify the group to be studied.
- Identify the physical location of the population (single site, multi-centered, international).
- Include number of participants to be recruited.

Outcome Parameters

- Identify the specific outcomes (laboratory/clinical endpoints) to be measured and analyzed

1.0 INTRODUCTION/RATIONALE

For Phase I studies should present summary data of pre-clinical studies (*in-vivo* and *in vitro*) or data that support the safety, effectiveness and/or immunogenicity (if relevant) of the investigational study agent. For other phase studies, the results of previous human experiences should also be summarized. Discuss relevant issues and compellingly present why the proposed trial is considered worthwhile. This is the section in which it is appropriate to describe the natural history of the infection, relevant treatment issues and prevailing controversies. This section should be concise and not include unnecessary information – try to limit this section to no more than 3-4 pages.

2.0 STUDY OBJECTIVES

The objectives of the study should be clearly stated. The statement of the primary objective is the most important specification in the trial. The statement should indicate:

- the type of subject to be evaluated;
- the class of treatment to be evaluated; and
- the primary outcome measure or primary endpoint.

> For example: The primary objective is to estimate the efficacy of 3 doses of an investigational acellular pertussis vaccine, compared with placebo, administered to Swedish infants in the prevention of "typical" pertussis; i.e. cough lasting longer than 21 days.

It may be appropriate to have secondary objectives as well. In the preceding example, such secondary objectives could include vaccine efficacy against confirmed pertussis infection with varying definitions, as well as safety as measured by adverse events.

3.0 STUDY DESIGN

The study design section should be a comprehensive summary of how the study will be conducted. It should describe the components, phases, procedures and sequence of the study. Standard and experimental aspects of the study should be separated as much as possible. The following elements should be included as applicable:

Subjects:

- Specific study population (e.g. adults, children, infants; other special populations such as persons with a specific disease)
- Number of subjects (total study and projected number at each site)

Test Agent Administration:

- How administered (i.e. oral, IV, intramuscular, etc.)
- How often administered
- Who administers

Duration:

- Duration of entire study
- Duration of each individual subject's participation in the study (include the length of time receiving test agent and the length of time in follow-up after test agent is discontinued)

Analysis :

- When will analysis occur (e.g. interim analyses or only at end of study)?
- DSMB review?

Other relevant design components

4.0 STUDY AGENT (can be vaccine or drug)

Preparation

The following items should be considered when writing the Study Intervention section:

- Will the study agent be supplied in single doses or multiple doses?
- Will dilution or reconstitution be required?
- Will the study agent be masked? How?

Administration and Duration

- How will the study agent be administered? (oral, IV, intramuscular, subcutaneous, special preparation or shipping procedures)
- How often will it be administered?
- How long will the study agent be administered?

Drug Formulation

- Human Safety
- Dosages
- Usage
- Warnings and Contraindications
- Reactions and side effects that might be expected during use of study agent

Compliance Monitoring

- Describe how compliance will be monitored, i.e. staff phone, diary cards,

5.0 SELECTION AND ENROLLMENT OF SUBJECTS

Selection of Population

The study population and inclusion/exclusion criteria should be clearly defined in this section of the protocol.

- Include percentages of women, minorities and children expected to be recruited. If women, minorities and children will not be recruited, explain why not. (refer to Protection of Human Subjects, Section 11.0).

- Indicate where the study population will be recruited, e.g. inpatient hospital setting, outpatient clinics, student health service? Where possible, include names of hospitals, clinics, etc.

- Provide the sample size.

- Identify strategies for subject recruitment and retention.

- Distinguish between screening subjects, e.g. discussing study with them vs. enrolling subjects, e.g. signing informed consent, obtaining necessary information, drawing bloods, randomizing to test article vs. placebo, giving test article. Note: if subjects are screened, e.g. blood is drawn, prior to informed consent for the study, there must be a separate screening consent form. Also note: a separate consent form is needed for the source patient.

- The inclusion criteria and exclusion criteria should provide a definition of subject characteristics required for study entry. Some examples may include the following: age, presence of a medical condition/disease, understanding of study procedures, ability to comply with study procedures for the entire length of the study, given method of birth control being used (if applicable), informed consent received and signed, medical condition or laboratory finding that prevents participation, recent (with time frame) febrile illness that prevents participation, pregnancy if applicable, immunosuppressed household contacts (if applicable), known allergic reactions to study agent components, disallowed concomitant medication, etc.

6.0 STUDY PROCEDURES

This section provides a detailed list and description of the epidemiological and clinical procedures to be performed at each visit of the study. A table summarizing this information is particularly helpful to those conducting the study at clinical and laboratory sites and should be included as an appendix of the protocol. A sample appendix Table is included at the end of section 6.0.

Specific procedures can be organized by study visit or by type of evaluation. Typically, studies are ordered by study visit and include the following sections:

- Screening visit evaluations: (Only those evaluations necessary to determine if the subject is eligible. Can be combined with the baseline visit.)
- Baseline visit
- Evaluations on study
- Toxicity Management
  - Criteria for subject management and dose modification
  - Procedures for modification
- Post treatment evaluations/follow-up
- Evaluations for subjects who prematurely discontinue study treatment

All evaluations should be bulleted or numbered under each heading and should include information that is specific. For example, if the study collects blood chemistries, “blood chemistries” should be a bullet point and then a list of specific chemistries to be obtained should be included.

SAMPLE TABLE

SCHEDULE OF EVALUATIONS

Procedures	**Screening**	**Baseline**	**4 wks**	**8 wks**	**12 wks**	**16 wks**	**20 wks**	**24 wks**	**Premature discontinuation**
Obtain Informed Consent	**X**								
Medical History [1]	**X**								
Complete Physical Exam [2]	**X**								
Targeted Physical Exam [3]			**X**	**X**	X	**X**	**X**	**X**	**X**
Chemistries [4]	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Hematology [5]	**X**	**X**	**X**	**X**	X	**X**	**X**	**X**	**X**
LFTs [6]	**X**	**X**	**X**	**X**	X	**X**	X	**X**	**X**
Virology [7]		**X**			X			**X**	**X**
Immunology [8]		**X**			X			**X**	**X**
Questionnaire[9]									

1. Medical History: Any prescription or over-the counter medication. History of liver disease, cancer, etc.

2. Complete Physical Exam: Height, Weight, Temperature, Blood Pressure, etc.

3. Targeted Physical Exam: Weight, Temperature, Blood Pressure, etc (exam on study)

4. Chemistries: list tests

5. Hematology: list tests

6. Liver Function Tests: list tests

7. Virology: list tests, see Appendix X (if special instructions apply)

8. Immunology: list tests, see Appendix X (if special instructions apply)

9. Genetics: list tests

10. Questionnaire: See Appendix X

7.0 ADVERSE EVENT REPORTING

Serious Adverse Event Reporting

Guidelines for the reporting of Serious Adverse Events (SAEs) are set forward in the Terms of the Contract Award. Additional and more stringent reporting requirements may be necessary, particularly if a site is functioning as the coordinating center for multi-site trials. This might include non-serious events that will be closely monitored for trend analysis or product acceptability. Any additional requirements, such as these, should be clearly delineated in the protocol.

A toxicity table should be included in the study management section of the protocol to allow for uniform grading of events. If requested, DMID can suggest models of toxicity grading scales. Serious adverse events for unlicensed products should be submitted using the standard DMID Serious Adverse Event Reporting form.

For IND studies performed under contract, the Contractor reports to DMID all SAEs. Deaths and life-threatening events are reported to the DMID Project Officer or designee within 24 hours and SAEs possibly associated with the drug, vaccine, etc. are reported within 72 hours. The DMID, in turn, assumes all responsibilities for reporting to the FDA. The Investigator is responsible for all reporting obligations set forward in the Terms of Award (IRBs as well as Medwatch, VAERS, etc. if the product(s) under study are already licensed). The annual IND report should include a summary of all adverse experiences.

CRITERIA FOR TREATMENT DISCONTINUATION (EXAMPLES)

- Subjects who do not complete treatment as defined by protocol
- Subjects not eligible for study
- Death
- Study agent-related toxicity
- Subjects who are pregnant
- Subjects who require protocol disallowed concomitant medication
- Subject/Physician requests discontinuation of study treatment
- Subjects who are non-adherent with medications and/or clinic visits
- Premature closure of one or more treatment arms

8.0 DATA COLLECTION/MANAGEMENT

The following items should be included in this section. If already known, also include information on specific plans for data collection, entry, tracking, correction, quality control, quality assessment, storage, back-up, etc. Otherwise, this additional information will be requested later as a formal Data Management Plan.

<u>Records to be kept</u>

- Describe method of data collection (paper case report forms (CRFs), electronic, combination).
- Address method for assuring participant confidentiality in the study database.

<u>Data management</u>

- Identify the facility/team responsible for data management.
- List key data management activities.
- If multi-center, describe methods for ensuring uniformity of data collection and processing.

9.0 STATISTICS

This section should describe the number of subjects to be enrolled in the study and the projected time to complete enrollment. Points below that pertain to formal sample size calculations apply only where the objective is: 1.) to answer with a specified probability (i.e., power) a particular research question through some statistical test or 2.) to achieve a specified degree of precision of a key estimate. It may involve an efficacy endpoint or a serologic endpoint, for example, and typically applies only to some Phase II and all Phase III studies.

Study summary

Provide a brief summary of the study design and information pertinent to statistical issues, including:
- Key visits
- Number of study arms and enrollment ratio
- Stratification variables
- Whether study is randomized and if so, level of masking
- Number and nature of follow-up visits as they relate to primary and secondary endpoints

Endpoints

This section should be separated into primary and secondary endpoints. For each endpoint, include:
- A description of the endpoint (i.e., particular lab result, mortality, disease recurrence, drug reaction, etc.)
- Whether proportion (binomial), mean (continuous), or categorical
- Whether change in value (specify the visits compared) or level at a specific visit (specify visit)

Sample size and accrual

- Estimate expected data losses due to participant loss to follow-up, missing data, specimen quantity not sufficient or loss, etc.
- Specify Type 1 and Type 2 error rates and whether test is one- or two-sided.
- Provide sample size formula and reference.
- Provide sample size estimates for the entire study and for each intervention arm and stratification variable (each center if multi-center) if applicable, adjusting for estimated losses.
- Reference and justify parameter estimates used in the calculations.
- Provide a range of sample size estimates for several effect sizes, significance levels and power estimates.
- Calculate projected enrollment per year.

Analysis plan

Formal interim analysis, if planned
- Procedures for initiation (as requested by DSMB, at the study midpoint, etc.) and rationale
- Procedures for adjusting significance level of final analysis
- Stopping rule procedures
- Number of anticipated interim analyses

Final analysis

- Describe the specific analyses that will be used for the primary and secondary objectives in order of priority, including the specific tests used and references.

10.0 PROTECTION OF HUMAN SUBJECTS

Institutional Review Board (IRB) or Ethical Committee (EC)

- State that this protocol, the informed consent document, including any information sheets or pamphlets given to the patient in support of the informed consent process, and any advertisements or other recruitment material will be reviewed and approved by the local IRB or EC overseeing the study before beginning the study. Any amendments to this material will also be reviewed and approved by the IRB or EC prior to implementation.

Informed Consent and Assent Processes and Documents

- Describe the consent procedures to be followed, including the circumstances in which consent will be sought and obtained, who will seek it, and the nature of the information to be provided to prospective subjects.

  Note: The informed consent document will describe the purpose of the study, the procedures to be followed and the risks/benefits involved. Informed consent templates are provided for investigator use (Attachment Tab B). These templates may be adapted to the clinical site's institutional requirements. Sites are reminded that the consents should be written at 8th grade level or below. Written informed consent will be obtained from the subject (or parent, legal guardian, or person with power of attorney for subjects who cannot consent for themselves, such as those below the legal age.) For subjects who cannot legally give consent but who are able to understand the nature, significance and risks associated with the study, the subject's assent must also be obtained. Children are generally not legally empowered to give consent, but depending on their age, they may have the ability to give assent ("assent" means a child's affirmative agreement to participate in research). Every protocol involving children (those individuals under age 18) should include a discussion of how assent will be obtained for the particular study.

Evaluation of Benefits and Risks/Discomforts:

- Describe the potential benefits to subjects or to others that may reasonably be expected from the research. Specify compensation, if applicable.

- Describe any potential risks -- physical, psychological, social, legal, or other -- and assess their likelihood and seriousness. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects. Describe the procedures for protecting against or minimizing any potential risks, such as violations of confidentiality, and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and in relation to the importance of the knowledge that may reasonably be expected to result.

Safety Monitoring:

- Describe the provisions for monitoring the safety of subjects. *Independent safety monitoring mechanisms that may be used include a Data Safety Monitoring Board, and Independent Monitoring Board and/or an on-site Independent Safety Monitor*. Please review Attachment 3 for information on prevailing policy.

- Subject Confidentiality

  Describe how subject confidentiality will be maintained (storage, coding etc.) and who will have access to subject records and/or data (include pharmaceutical company, regulatory authorities and NIAID).

11.0 BIOHAZARD CONTAINMENT

This section will provide a discussion of technical risks. Technical risks include those associated with the use of investigational vaccines, handling of blood samples and human secretions that could potentially be contaminated with infectious agents, use of radioisotopes in immunologic assays, and nucleic acids detection procedures. A partial list of current references is provided for general information:

a. HHS publication #(CDC) 93-8395 "Biosafety in Microbiological and Biomedical Laboratories", 1993. Washington, D.C.: US Department of Health and Human Services, Public Health Service.
b. Centers for Disease Control. Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. MMWR 1988; 37:377-382, 387-388.
c. Occupational Safety and Health Administration. Occupational exposure to blood borne pathogens. Federal Register 1989; 54:23042-139.

Appropriate staff training, facilities and waste handling techniques will reduce risk.

12.0 REFERENCES

A list of scientific literature cited in the protocol should be included.

13.0 INFORMED CONSENT

An Informed Consent template is included under Tab B. A draft Informed Consent form appropriate for the proposed clinical trial must be submitted along with the clinical protocol.

14.0 CASE REPORT FORMS (CRFs)

Case report forms (CRF) are the documents that record all the protocol-required information for each study participant. Please include in your application a list of the case report forms planned for the trial along with a sample inclusion/exclusion form and a medical assessment form.

(Before enrollment of subjects into the clinical trial, all CRFs must be fully developed. DMID standard forms for serious adverse events and protocol deviations will be provided prior to the start of the clinical trials.)

15.0 QUESTIONAIRES

If the proposed effort requires questionnaires these must be supplied with the proposal.

RELEVANT TABLES AND FIGURES

GENERAL TIPS ON PREPARING A CLINICAL PROTOCOL :

- Indicate the date and version number of the protocol and consent in a header or footer
- Proof read protocol. Use a spell checker
- Use page numbers
- Consider the use of flow diagrams or algorithms within complex protocols.

TAB B INFORMED CONSENT TEMPLATES

Within this TAB are three sample consent form templates:

- A template suitable for drug studies
- A template suitable for vaccine studies
- A template suitable for future use of clinical specimens

Information on the future use of clinical specimens is also included.

NIAID CO-OPERATIVE HEPATITIS C …

INFORMED CONSENT TEMPLATE
FOR DRUG STUDIES
(ADAPTED FROM NCI MODEL)

NOTE:

- Model text in **bold**
- Instructions are in *[italics]*.
- _____ Indicates that the investigator should fill in the appropriate information.

STUDY TITLE

[Title]

This is a clinical trial (a type of research study). Clinical trials include only individuals who choose to take part. Please take your time to make your decision. Discuss it with your friends and family. It is important that you understand what will be done and the possible risks to you, so please ask questions at anytime.

DISEASE ***is a disease that****…[describe briefly in lay terms: e.g., how disease is contracted, who it affects and how.]*

You are being asked to take part in this study because you have (your child has) DISEASE**.**
Or
You are (Your child is) being asked to take part in this study because you are (your child is) a healthy adult (child) who *[e.g., is between x and x in age, is not taking other medication, etc.]*

[For a minor child, substitute "your child" for "you" and "child/children" for "person/people" throughout.]

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test the safety of an experimental drug/intervention, called name of *DRUG/INTERVENTION* **and** *[As appropriate, add from examples below)*

A. Phase 1 studies:

to see what effects (good or bad) it has on you.

This drug/intervention has not been given to people before. It has been studied in animals and *[Describe briefly the results of earlier trials, including significant side effects.]*

Or

This drug/intervention has been given to a small number of people. In those studies, *[Describe briefly the results of earlier trials, including significant side effects.]*

B. Phase 1 or 2 studies

to see what effects (good or bad) it has on you and look for the best dose that can be given without causing severe side effects. This drug/intervention has been given to a small number of people. In those studies, *[Describe briefly the results of earlier trials, including significant side effects.]*

C. Phase 2 studies:

to find out what effects (good or bad) that this drug/intervention has on you and your disease. Previous studies with this drug/intervention have shown that *[Describe briefly the results of earlier trials, including significant side effects.]*

D. Phase 3 studies:

to compare the effect (good or bad) of this drug/intervention with the effect of *COMPARISON (COMMONLY-USED DRUG/INTERVENTION, STANDARD OF CARE, PLACEBO, NO INTERVENTION)* **on you and your disease to see whether one is better than the other (or as good as the other).** *[Note: If there is a placebo, explain, "placebo", and define the placebo to be used--either here or in the description of study groups below.]*

This research is being done because_____.
[Explain in one or two sentences. Examples are: **"currently, there is no effective treatment for this disease (in this population),"** or **"we do not know which of these two commonly-used treatments is better,"** or "**we do not know what effect** *DRUG/INTERVENTION* **will have on people your age or in your (population group/country)."**

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY

[If appropriate:]
About _ people will take part in this study; ____ people here at *[NAME OF SITE].*

WHAT IS INVOLVED IN THE STUDY?

[Provide simplified schema and/or calendar, summarizing the number of visits, blood draws, etc.]

[For randomized studies:]
You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. A computer decides which group you are put in. Neither you nor the researcher will choose what group you will be in. You will have an *EQUAL/ONE IN THREE/ETC.* **chance of being placed in any group.**

[For single-blinded studies]
You will not know which group you are in until the end of the study.
Or
[For double-blinded studies] **Neither you nor the researcher will know which group you are in until the end of the study.**

[For all studies:
Describe what drug/intervention each group will be receiving, route of administration and schedule, using bullets, as
- *Group A: [description].*
- *Group B: [description].*
- *Group…*

If there is a placebo group, explain "placebo" and define the placebo to be used]

[For all studies:]
If you take part in this study, you will have the following tests and procedures:
[List procedures and their frequency under the categories below. Include whether a patient will be at home, in the hospital, or in an outpatient setting. If objectives include a comparison of interventions, list all procedures, including those considered standard therapy.]

- **Procedures that are part of your regular medical care and may be done even if you do not join the study.** *{If applicable, add "and will be billed to you or your insurance company."]*
- **Additional procedures being done because you are in this study.**
- **Procedures that are being tested in this study.**

HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for *MONTHS/WEEKS, UNTIL A CERTAIN EVENT.* *[Where appropriate, state that the study will involve long-term follow-up and for how long.]*

The researcher may decide to take you off this study if _____.
[List circumstances, such as in the participant's medical best interest, funding is stopped, drug supply is insufficient, patient's condition worsens, new information becomes available.]

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.

[Describe any serious consequences of sudden withdrawal from the study.]

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you may be at risk for some side effects. **You should discuss these with the researcher and/or your regular doctor. There also may be other side effects that we cannot predict. Many side effects go away shortly after the** *INTERVENTION/DRUGS* **are stopped, but in some cases, side effects can be serious or long lasting or permanent**.

Risks and side effects related to the *PROCEDURES, DRUGS, OR DEVICES* **we are studying include:**

[List physical and nonphysical risks related to the investigational aspects of the trial including risks noted in the investigator brochure and identify as "very likely" and "less likely but serious". Specifically highlight or otherwise identify those that may not be reversible or are long-term or life threatening. If drug/intervention has not been used in people before, list what side effects might be expected based on animal data. Include nonphysical risks, such as, psychological stress and the inability to work. Describe what may be done to make side effects less severe and uncomfortable.]

[Include if applicable, or if unknown]
Reproductive risks: Because it is not known if the drugs in this study can affect an unborn baby,
Or
Reproductive risks: Because the drugs in this study can affect an unborn baby,

you should not become pregnant or father a baby while on this study *[and for x time after completion of study or stopping study drug]***. You should not nurse your baby while on this study. You may ask one of the study staff about counseling or for information about preventing pregnancy.** *[Include a statement about possible sterility when appropriate.]*

Other risks of participating in this study are:
[List other risks not mentioned above identifying the seriousness and likelihood of the risk, including risks to privacy.]

For more information about risks and side effects, ask the researcher or contact NAME AND PHONE NUMBER.
[*Reference and attach drug sheets, pharmaceutical information for the public, or other material on risks.]*

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit other patients with *DISEASE* **in the future.** *[Add possible benefits]*

Or

[For Phase I studies, healthy volunteers]
There are no direct benefits of taking part in this study. We hope the information learned from this study will help patients with *DISEASE* **in the future.**

[For Phase I and 2 studies, where appropriate]
NAME OF INTERVENTION/DRUG **may not help you get better and it might make your disease worse.**

WHAT WILL YOU DO WITH MY UNUSED *BLOOD, BIOPSY SAMPLES, ETC.* AT THE END OF THE STUDY?

At the end of this study, any of your unused *BLOOD, BIOPSY SAMPLES, ETC,* taken for research will be destroyed.
OR
[If samples will be stored after the end of the study]
At the end of this study, we would like to keep your unused *BLOOD, BIOPSY SAMPLES, ETC.***, taken for research. We will give you a separate consent document for this. Whether or not you agree to let us to store your samples and use them for other research in the future will have no effect on your taking part in this study or on your medical care at this institution.**

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:
[List alternatives including commonly used therapy and not participating in the study]

If appropriate (for noninvestigational treatments):]
You may get *STUDY TREATMENTS/DRUGS AT THIS CENTER AND OTHER CENTERS* **even if you do not take part in the study.**

Please talk to your regular doctor about these and other options.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

If a publication results from this study, you will not be identified by name.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

[List the National Institute of Allergy and Infectious Diseases, Food and Drug Administration and other relevant organizations like the pharmaceutical company, etc.]
[If appropriate, state what, if any, study information will be included in the subject's personal medical records.]

WHAT ARE THE COSTS OF PARTICIPATING IN THIS STUDY?

There will be no added costs to you or your insurance company for procedures and medications that are part of this study. *[If appropriate]* **Costs of your clinical care that are not related to this research may be charged to you or your insurance company.** *[List what will/will not be covered.]*

WHAT IF I AM INJURED OR BECOME ILL AS A RESULT OF BEING IN THIS STUDY?

In the case of injury or illness resulting from this study, *[List what will be available for care of injury resulting from study participation and what compensation. If any, is available.*

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits or legal rights to which you are entitled.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

WILL I BE GIVEN ANYTHING FOR BEING IN THE STUDY?

In return for being in this study, you will be given…*[Describe compensation.]*
Or
You will not be given money for being in this study, but you will be given…*[paid transportation, child care, etc.]*

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study, contact the researcher(s), *NAME(S) at TELEPHONE NUMBER*
For questions about a research-related injury or your rights as a research subject, contact NAME(S) *at* TELEPHONE NUMBER**.** [And If available, list patient representative (or other individual who is not on the research team or IRB).]

WHERE CAN I GET MORE INFORMATION?

You will get a signed copy of this form.

[Attach information materials (including updates) and checklist of attachments. If there are attachments, the signature page should be at the end of the consent package.

SIGNATURES

I have read this informed consent document and have had the opportunity to ask questions. I agree to take part in this study.

Participant _____ **Date** _____
Signature

[If minor subject]
Parent or legal guardian_____**Date** _____
Signature (relationship to subject)

Person obtaining informed consent _____**Date** _____
Signature

Principal Investigator _____**Date** _____
Signature

NIAID CO-OPERATIVE HEPATITIS C ..
INFORMED CONSENT TEMPLATE
FOR VACCINE STUDIES
(ADAPTED FROM NCI MODEL)

NOTE:

- Model text in **bold**
- Instructions are in *[italics]*.
- _____ Indicates that the investigator should fill in the appropriate information.

Study Title

*[Title]*_____

This is a clinical trial (a type of research study). Clinical trials include only individuals who choose to take part. Please take your time to make your decision. Discuss it with your friends and family. It is important that you understand what will be done and the possible risks to you, so please ask questions at anytime.

You are (Your child is) being asked to take part in this study because you are (your child is) a healthy adult (child) who *[e.g., is between x and x in age, is not taking other medication, etc.] [For a minor child, substitute "your child" for "you" and "child/children" for "person/people" throughout.]*

WHY IS THIS STUDY BEING DONE?

DISEASE **is a serious health problem that** *[describe disease, who it affects and how]*.

Vaccines prevent disease by making antibodies (germ fighters) in your blood to protect/fight against infections--so that when you are exposed to those germs, the antibodies will help keep you from becoming ill.

The purpose of this study is to test the safety of an experimental vaccine, called *NAME OF VACCINE* and *[As appropriate, add from examples below]***...**

A. Phase 1 studies:
to see if what effects (good or bad) it has on you.

This vaccine has not been given to people before. It has been studied in animals and *[Describe briefly the results of earlier trials, including significant side effects.]*

Or

This vaccine has been given to a small number of people/children. In those studies, *[Describe briefly the results of earlier trials, including significant side effects.]*

B. Phase 1 or 2 studies
to see what effects (good or bad) it has on you and look for the best dose that does not cause serious side effects. This vaccine has been given to a small number of people/children. In those studies, *[Describe briefly the results of earlier trials, including significant side effects.]*

C. Phase 2 studies:
to find out what effects (either good or bad) this vaccine has on you and whether it helps prevent *DISEASE*.
Previous studies with this vaccine have shown that *[Describe briefly the results of earlier trials, including significant side effects.]*

D. Phase 3 studies:
compare the protection of this vaccine with that of *COMPARISON: COMMONLY-USED VACCINE, STANDARD OF CARE, PLACEBO, NO VACCINE)* **to see if one is better than the other (or as good as the other) at preventing** *DISEASE***.**
[Note: If there is a placebo, explain, "placebo", and define the placebo to be used--either here or in the description of study groups below.]

This research is being done because_____
_____.
[Explain in one or two sentences. Examples are: **"currently, there is no effective vaccine for this disease (in this population),"** or **"we do not know which of these two commonly-used vaccines is better,"** or "**we do not know how well** *VACCINE* **will work or the possible effects (good or bad) in people your age or in your (population group/country)."**

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY

[If appropriate:]
About _ people will take part in this study; ____ people here at *[NAME OF SITE].*

WHAT IS INVOLVED IN THE STUDY?

[Provide simplified schema and/or calendar, summarizing the number of visits, blood draws, etc.]

[For randomized studies:]
You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. A computer decides which group you are put in. Neither you nor the researcher will choose what group you will be in. You will have an *EQUAL/ONE IN THREE/ETC.* **chance of being placed in any group.**

[For single-blinded studies]
You will not know which group you are in until the end of the study.
Or
[For double-blinded studies]
Neither you nor the researcher will know which group you are in until the end of the study.

[For all studies:
Describe what vaccine each group will be receiving, route of administration, and schedule, using bullets, as
- *Group A: [description].*
- *Group B: [description].*
- *Group…*

If there is a placebo group, explain "placebo" and define the placebo to be used]

[For all studies:]
If you take part in this study, you will have the following tests and procedures:
[List procedures and their frequency under the categories below.]

- ***Routine procedures being done as part of this study.*** [if any, e.g., well-baby visits]
- **Additional procedures that are being done because you are in this study.** *[e.g., blood samples, HIV testing, pregnancy testing, quarantine or other special measures that would not be taken except for participation in this study]***.**

HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for *MONTHS/WEEKS, UNTIL A CERTAIN EVENT.* *[Distinguish between active participation and follow up.]*

You will be asked to return to the clinic at _____.
And/Or
You will be asked to keep a diary of how you feel for ___days.
And/Or
A nurse will call you ___days after you receive the vaccine.
[As applicable]
The researcher may decide to take you off this study if _____.
[List circumstances, such as in the participant's medical best interest, funding is stopped, vaccine supply is insufficient, new information becomes available.]

The researcher may decide to not to give you any more doses of the vaccine if _____. [List circumstances under which subject would discontinue vaccine but remain on study, such as in the participant's medical best interest, because of a adverse reaction to an early dose in multi-dose study, because of a concurrent illness, new information becomes available.]

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.
[Describe any serious consequences of sudden withdrawal from the study.]

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you may be at risk for some side effects. **You should discuss these with the researcher and/or your regular doctor. There also may be other side effects that we cannot predict. Many side effects go away shortly after the vaccine is given, but in some cases, side effects can be serious or long lasting or permanent**.

Risks and side effects related to *NAME OF VACCINE* **include:**

[List physical and nonphysical risks related to the investigational aspects of the trial including risks noted in the investigator brochure and identify as "very likely" and "less likely but serious". Specifically highlight or otherwise identify those that may not be reversible or are long-term or life threatening. If this vaccine has not been used in people before, list what side effects might be expected based on animal data or experience with similar vaccines. Describe what may be done to make side effects less serious and uncomfortable.]

[Include if applicable, or if unknown]
Reproductive risks: Because it is not known how the vaccine in this study might affect an unborn baby,
Or
Reproductive risks: Because the vaccine in this study can affect an unborn baby,

you should not become pregnant or father a baby while on this study *[and for x time after completion of study or stopping study vaccine]***. You should not nurse your baby while on this study. You may ask one of the study staff about counseling or for information about preventing pregnancy.** *[Include a statement about possible sterility when appropriate.]*

Other risks of participating in this study are:
[List other risks not mentioned above, including risks associated with blood drawing and, including risks to privacy, identifying the seriousness and likelihood of the risk, including risks to privacy.]

For more information about risks and side effects, ask the researcher or contact____NAME AND PHONE NUMBER **_____**.
[*Reference and attach vaccine information sheets, pharmaceutical information for the public, or other material on risks.]*

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit *[describe who will benefit from this vaccine if it proves effective, e.g., "persons living in areas where there is a lot of DISEASE"]* **in the future.** *[Add possible benefits]*

OR
[For Phase I studies]
There are no direct benefits of taking part in this study. We hope the information learned from this study will help *[describe target group who will benefit* **in the future.**

WHAT WILL YOU DO WITH MY UNUSED ***BLOOD, BIOPSY SAMPLES, ETC.*** AT THE END OF THE STUDY?

At the end of this study, any of your unused *BLOOD, BIOPSY SAMPLES, ETC,* taken for research will be destroyed.
OR
[If samples will be stored after the end of the study]
At the end of this study, we would like to keep your unused *BLOOD, BIOPSY SAMPLES, ETC.*, taken for research. We will give you a separate consent document for this. Whether or not you agree to let us to store your samples and use them for other research in the future will have no effect on your taking part in this study or on your medical care at this institution.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:
[List alternatives, including getting standard vaccine from personal physician and not participating in the study]

If appropriate (for noninvestigational treatments):]

You may get *VACCINE* at this center or other centers even if you do not take part in the study.

Please talk to your regular doctor about these and other options.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

If a publication results from this study, you will not be identified by name.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

[List the National Institute of Allergy and Infectious Diseases, Food and Drug Administration and other relevant organizations like the pharmaceutical company, etc.]

[If appropriate, state what, if any, study information will be included in the subject's personal medical records.]

WHAT ARE THE COSTS OF PARTICIPATING IN THIS STUDY?

There will be no added costs to you or your insurance company for the vaccines or procedures that are part of this study. *[List what will/will not be covered.]*

WHAT IF I AM INJURED OR BECOME ILL AS A RESULT OF BEING IN THIS STUDY?

In the case of injury or illness resulting from this study, *[List what will be available for care of injury resulting from study participation and what compensation. If any, is available.*

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits or legal rights to which you are entitled.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

WILL I BE GIVEN ANYTHING FOR BEING IN THE STUDY?

In return for being in this study, you will be given…*[Describe compensation.]*
Or
You will not be given money for being in this study, but you will be given…*[paid transportation, child care, etc.]*

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study, contact the researcher(s), *NAME(S) at TELEPHONE NUMBER*
For questions about a research-related injury or your rights as a research subject, contact NAME(S) *at* TELEPHONE NUMBER**.** [And If available, list patient representative (or other individual who is not on the research team or IRB).]

WHERE CAN I GET MORE INFORMATION?

You will get a signed copy of this form.

[Attach information materials (including updates) and checklist of attachments. If there are attachments, the signature page should be at the end of the consent package.

SIGNATURES

I have read this informed consent document and have had the opportunity to ask questions. I agree to take part in this study.

Participant _____ **Date** _____
Signature

[If minor subject]
Parent or legal guardian_____**Date** _____
Signature (relationship to subject)

Person obtaining informed consent _____**Date** _____
Signature

Principal Investigator _____**Date** _____
Signature

SUGGESTED LANGUAGE FOR INFORMED CONSENT FOR FUTURE USE OF BIOLOGICAL SPECIMENS COLLECTED UNDER CLINICAL PROTOCOLS

BACKGROUND

There has been increasing concern in the biomedical community about the use of biological specimens obtained during clinical research. Current Federal regulations set out criteria for the use of subject specimens. These criteria include: 1) subject specimens can only be used for research that is described in the protocol and consent; and 2) any new research use of identifiable specimens must be approved by the IRB. Furthermore, the National Bioethics Advisory Commission (NBAC), which was established by the President to make recommendations concerning bioethical issues arising from research on human biology and behavior, has released its recommendations on stored biological specimens. [http://bioethics.gov/pubs.html]

PURPOSE

DMID is providing this consent language template to assist the investigator in meeting federal guidelines and regulations for providing informed consent of study participants for the storage and use of their biological specimens for purposes other than those defined in the protocol. This guidance applies to storage and research use of specimens outside of and/or after the clinical trial for which they were originally collected. It does not apply to specimens collected and used for protocol-specified assays.

The following guide is provided for DMID investigators who anticipate:

- Using leftover biological specimens that contain identifiers or are coded in any way that can be traced to the subject, or
- Taking extra biological specimens (in addition to what is needed for protocol defined-research), whether they are identifiable or anonymized. *[Note: You may not take extra specimens for future research unless it is stated in the main protocol consent.]*

These recommendations are based on current federal regulations and the NBAC draft recommendations.

DEFINITIONS

Biological specimens:	*Tissues, bodily fluids (such as blood, saliva), and excreta (such as, stool and urine).*
Microbial organism Specimens:	*Bacteria, fungi, virus and parasitic specimens that are stored in artificial culture or biological cell culture*
Identifiers:	Data that directly identifies the individual from whom a sample is obtained, such as, name, initials, Social Security Number, Hospital Patient Number, address, telephone number. Identifiable specimens: Biological specimens that are identified either directly or through a code. It is possible to determine the individual's identity from the identifying information.
Coded specimens:	Biological specimens that are identified only by a code key that can be linked to the individual directly or through an intermediary (e.g., a repository). These are **identifiable** specimens.
Anonymized specimens:	Biological specimens that have been stripped of all identifiers (including codes) that would link directly to the individual. Please note that health and demographic data may be retained, such as height, weight, age, diagnosis, socio-ethnic group, zipcode, etc.).

GUIDANCE

DMID recommends that consent for retention and future use of biological specimen taken in conjunction with a clinical protocol be documented as a supplemental consent and attached to the main study consent. Both of these informed consent documents must be reviewed and approved by the local IRB before use. However, information from this supplemental consent may be incorporated into the main consent if that is preferred by your IRB.

At the close of the study, consent for future use of biological specimens should be placed in a file and retained under lock by investigator/facility responsible for their use and maintained for at least two years after the last specimen has been used.

Anonymized biological specimens

Consent to obtain biological specimens is required if additional specimens, other than those required for study related purposes, are obtained, even if these specimens are then anonymized. *[Note: Sites should have an SOP for anonymization of specimens.]*

Consenting Participants

It should be made clear to subject/volunteers that they may refuse permission for future research use of their biological specimens without affecting their participation in the study or their care by the health provider. It should also be made clear to subject/volunteers that they may change their mind and refuse to permit their specimens to be used at some time in the future.

Re-consenting Participants

By not requesting and obtaining proper consent from the subject/volunteers at the time that the specimen is obtained, an investigator runs the risk of not being able to use valuable biological specimens later without re-consenting the participants—a procedure that may be problematic because it may be construed as a breach of confidentiality. If re-consenting a participant is planned, it is important to include in the main protocol consent or in a separate consent, permission to re-contact the participant for future studies of stored biological specimens.

Minors as Subjects

If consent was given by a parent or guardian on behalf of a minor child, the child subject as an adult may rescind the permission to use the identifiable biological specimens (just as an adult participant could change their mind about use of their biological specimens). In the event that re-contact is required for the research, the investigator would need to attempt to contact the child/now adult whose identifiable biological specimens were kept.

Research Populations

Special consideration should be given to the handling of the information obtained from research with biological specimens, even if not individually identified, in cases in which the subjects' socio-economic or ethnic community might be harmed by the disclosure of data for that community as a group (for example, a study linking incidence of a specific disease with subject zipcodes, or with an ethnic group). A statement that there might be unintended harm to the individual or group as a result of disclosure of data or research results should be included in the Risk Section of the supplemental consent.

Previously Collected Biological Specimens

If the investigator plans to use already collected identifiable biological specimens in research not specifically defined in the protocol, the investigator must consult with their IRB. If the IRB finds that an existing consent covers the intended research use, then no further action is necessary. If there was no prior consent, or if the IRB finds that the consent does not cover the intended use, then consent must be obtained, or waived by the IRB, as appropriate.

Microbial Organisms Derived from Biological Specimens

Additional consent is not required for microorganisms that are stored without information that identifies the subject or a link to an identified specimen after the study is completed.

Permission to retain microorganisms with links to identifiable specimens after the study is completed, or to send them to a repository with information linking them to identifiable specimens, must be included in the informed consent document.

No Biological Specimens To Be Stored

If no biological specimens are to be stored after a study is completed, then there should be a statement in both the protocol and informed consent that all biological specimens will be destroyed at the end of the study.

USE OF TEMPLATE

If biological specimens are to be kept for non-protocol-defined research, the investigator should create a consent document covering each of the sections in the attached consent template. Examples of acceptable statements are included for each paragraph or section. At the very least, subjects should be told:

- What kind of specimens will be collected and the means of collection.
- What type of research will be done with the specimens,
- Whether the biological specimens will be shared with other investigators,
- Whether biological specimens will be coded or anonymized (no way of tracing back to subject/uncoded or code destroyed),
- Whether the subject may be contacted for additional consent.
- If possible, how long the biological specimens will be stored. (Short-term: current protocol only or other current research; Long-term: future studies on disease or condition, repository, etc.)
- Foreseeable risks or benefits to subjects in the collection, storage, and subsequent research use of specimens.
- What will be done with the biological specimens if the subject refuses permission ("anonymized"—stripped of identifiers--or destroyed).
- What will be done with the research results. (Research results should not be placed in the individual subject's medical record.)

[Note: A version number and/or date for the consent must be included on the consent form.]

DMID staff will help you customize this consent if you wish.

NIAID CO-OPERATIVE HEPATITIS C …..
INFORMED CONSENT TEMPLATE
FOR FUTURE USE OF STORED SPECIMENS OBTAINED DURING RESEARCH STUDIES
(ADAPTED FROM NCI MODEL)

Supplemental Consent to: ***(Name of protocol)*****--Future use of (T*****ype of sample)***

[TO BE PLACED ON YOUR INSTITUTIONAL LETTERHEAD IF YOU HAVE ONE]

1. INTRODUCTION

While you are in this study, there may be **type of sample(s)** taken from you that may be useful for future research. These samples will be stored at **(Institution)**. Samples **may/will not** also be shared with investigators at other institutions. Organisms derived from your samples may also be stored in cultures for future research.

2. WHAT WILL THE SAMPLES/CULTURES BE USED FOR? *(If you know what this research will be, provide a description, e.g., "Your blood and body fluid will be used to study the changes that occur in 'disease'" using genetic markers. Specific results are not likely to affect you as an individual patient."*

a. These **(samples/cultures)** will be used for future **(subject)** studies ONLY.

OR

These **(samples/cultures)** will be used for future research to learn more about **(disease)** and other diseases.

b. Your **(samples/cultures)** will be used only for research and will not be sold or used directly for the production of commercial products. The research done with your **(samples/cultures)** may help to develop new products in the future. *(Use this statement only if you can guarantee that it is true.)*

OR

In some research using **(samples/cultures)**, the samples/cultures may enable researchers to develop medical tests or treatments that have commercial value. You will not receive any money that may result from any such commercial tests or treatments.

c. There will be no human genetic tests performed on your samples/cultures.

OR

Genetic research may be performed on samples/cultures to study the nature of **(disease**) in people. However, no genetic information obtained from this research will be placed in your medical records. These **(samples/cultures)** will be identified only by codes so that they cannot be readily identified with you personally.

3. WHAT ABOUT CONFIDENTIALITY?

a. Your **(samples/cultures)** will be coded so that your name cannot be readily identified. Reports about research done with your samples/cultures will not be put in your health/medical record and will be kept confidential to the best of our ability within state and federal law.

AND (if applicable)

In the future, researchers studying your (samples/cultures) may need to know more about you, such as whether you smoke or not, and other information such as your age, gender, race. If this information is already available because of your participation in a study, it may be provided to the researcher. Your name, social security number or anything that might identify you personally will NOT be provided. If you agree to be recontacted, you may still change your mind about providing information in the future.

AND (if applicable)

If the researcher needs other information about you

(*Please check below to indicate whether or not you may be contacted in the future by the investigator conducting this study.)*

___I may be re-contacted for information.

___I may not be re-contacted for information

Subject Initials_____ Date_____

OR

b. Your **(samples/cultures)** will be kept with no identifiers that can be traced to you. *(Note--this need only be used if extra amounts are taken specifically for future use and all identifiers and codes are removed at the time of collection)*

4. WHAT ARE THE RISKS?

There are few risks to you from future use of your samples/cultures. A potential risk might be the release of information from your health or study records. Reports about research done with your samples will not be put in your health record, but will be kept with the study records. The study records will be kept confidential as far as possible within state and federal law.

For research in which the subjects' socio-economic or ethnic community might be harmed by the disclosure of data for that community as a group:

There is a risk by (being a/living in) _____ that the results of the study may effect you, because you (are _____or live _____. [Explain impact, *i.e.*, we may find that people of your ethnic background have because of their gene a greater chance of getting (**disease**), therefore it might impact of your insurance—or—Because of where you live people may know that many people have (**condition**) and may assume you have it.]

5. ARE THERE BENEFITS TO ALLOWING MY SAMPLES/CULTURES TO BE STORED?

There will be no direct benefit to you. From studying your **(samples/cultures)** we may learn more about **(disease)** or other diseases: how to prevent them, how to treat them, how to cure them.

6. WHAT WILL HAPPEN TO THE RESULTS FROM RESEARCH WITH MY SAMPLES/CULTURES?

a. Results from future research using your samples/cultures may be presented in publications and meetings but your name will not be identified.

AND

b. If future research on your (samples/cultures) provides meaningful information related to your health, the investigator will try to contact you. If you wish to be contacted, you must notify **name and phone number** of changes in your address or telephone number.

OR

Reports from future research done with your **samples/cultures** will **NOT** be given to you or your doctor. These reports will **NOT** be put in your health/medical record.

OR

Reports from future research done with your **samples/cultures** may be given to your doctor to assist you in making health care decisions. If you wish your doctor to be contacted, you must provide your doctor's address and telephone number to **name and phone number**.

7. WHAT HAPPENS IF SOMEONE WANTS TO DO MORE RESEARCH WITH MY SAMPLES/CULTURES?

Any additional research studies beyond the current study using your identifiable samples/cultures will be reviewed by the investigator's Institutional Review Board (IRB), a special committee that oversees medical research studies to protect the rights and welfare of the human subject volunteers.

8. WHAT ARE MY RIGHTS AS A PARTICIPANT?

You can change your mind at any time about allowing your identifiable **samples/cultures** to be used for future research. If you do, contact the study doctor or nurse and let them know. Then your **samples/cultures** will no longer be made available for research and will be destroyed.

You are free to refuse to allow us to use your identifiable **(samples/cultures)** in future research. Whether or not you allow us to use your identifiable **(samples/cultures)** in future research, your decision will not have any effect on your participation in this study or future participation in other studies.

9. CONSENT

I give permission for the use of my identifiable **(samples/cultures)** in future research for the purposes described above. *(Please check one)*

_____ YES

_____ YES (but my study **(samples/cultures)** will be stripped of identifiers)

_____ NO (My study **(samples/cultures)** will be destroyed.

_____ _____
Participant Signature Date

(If subject is a minor or cognitively unable to give consent)

_____
Parent or Guardian Signature (relationship to participant) Date

_____ _____
Signature of Person Administering Consent Date

PLEASE RETAIN A SIGNED COPY OF THIS DOCUMENT IN YOUR PERSONAL FILE. NO COPY WILL BE PLACED IN YOUR MEDICAL RECORD.

TAB C REGULATORY PLAN

Clinical Trials supported under grants from the Division of Microbiology and Infectious Diseases, NIAID, are expected to be conducted under the highest standards following the guidelines and regulations set forth by the International Congress of Harmonization Guidelines for Good Clinical Practice, Food and Drug Administration (FDA) and the Office for the Protection from Research Risks (OPRR) (see web sites in Attachment 4). The principles set forth in these documents provide assurance that there are procedures in place to protect the safety and integrity of subjects participating in DMID-sponsored studies, as well as to produce meaningful data.

Applicants are required to submit a regulatory plan that will detail how they will meet these standards. U.S based studies involving investigational agents or off label use of a licensed pharmaceutical should be done under an Investigational New Drug Application (IND), thereby invoking the FDA regulations found in 21CFR 312. FDA information sheets are also available on the web. DMID also prefers that international studies be conducted under IND. If the applicant does not intend to perform the study under IND (either in U.S. or international sites), the applicant must submit a rationale for DMID review and concurrence prior to enrollment of subjects.

Federally funded studies (the awardee and all collaborating sites) must also meet the requirements for OPRR for Project Assurances (see Attachment 2 and associated web site) and informed consents. Requirements for consents are set forth in 45CFR 46 and 21CFR 50. If you plan to store left over biological samples for future research, please see the OPRR guidance and decision tree and DMID's template for informed consent to store such samples.

At the time of proposal, the following parts of the regulatory plan should be submitted:

- A clinical product development plan. Include a timeline for projected product development. State if there is a current IND or Master File (MF) for the product and identify the sponsor.

- Information about where and how the test article is manufactured, including whether under GLP or GMP. *Note: Labels for non-licensed products must meet the specifications listed in the FDA guidelines.*

- A feasibility assessment plan. Describe how the selection of investigators and sites will be made, including a list of potential sites. The plan should include the sites' demonstrated ability to recruit and enroll subjects that will satisfy the criteria of the study design in sufficient numbers and in the proposed timeframe.

- International studies should include a plan with a timetable for obtaining required clearances from the international sites. Applicants should address their experience in conducting international studies and their experience with the designated site and investigators. Documentation of notification and/or approval, as applicable, from the host country must be submitted to the DMID program officer prior to the beginning the study.

An awardee must complete and submit the following components of the plan to the NIAID/DMID Project Officer prior to initiation of the study:

- A standard operating procedure for safety assessments and reporting. This should include investigator oversight, as well as the establishment of independent safety and data monitoring. Details of the plan will be reviewed and approved by the NIAID/DMID Project Officer. Award funds will be used to support data safety monitoring activities.

- A standard operating procedure for the accountability, handling and shipping of test article and biological samples.

- Development of the regulatory file; including where it will be maintained and policies for record retention. An individual should be identified who will maintain the file and has responsibility for IRB, FDA, DSMB (if applicable), and NIAID/DMID correspondence.

- The Awardee will be responsible for developing an internal quality assurance program, including an internal clinical monitoring plan, and an internal data quality assurance system. This quality assurance program, including the structure and defined responsibilities of clinical trial investigators, should provide the framework for all quality control and assurance activities related to the conduct of the clinical trial protocol. These processes or systems must ensure that work is being done according to the clinical trial protocol and standard operating procedures and that corrective action will be taken by the clinical trial investigators when it is not. DMID, NIAID will retain the option of performing audits, which entail auditing the internal clinical monitoring established under the internal quality assurance program.

- A standard operating procedure for data management.

- If an IND is required, an awardee will work with the DMID Project Officer and other DMID staff to prepare an INDA filing or seek other options such as contracting from the award to an existing DMID contractor.

After the award has been made, it is expected that:

- For studies conducted under IND the sponsor will copy the DMID program officer on all correspondence with the FDA.

- An analysis plan will be developed.

A list of all ICH available guidelines is available on the Internet (Attachment 4). DMID encourages you to use these documents in preparation and execution of your study.

ATTACHMENT 1 CLINICAL TERMS OF AWARD

NIAID POLICY: MONITORING GRANTS SUPPORTING CLINICAL TRIALS AND STUDIES
(Single Site, Multi-Center or Multi-National Clinical Trial/Research)

The National Institute of Allergy and Infectious Diseases (NIAID) supports clinical trials and studies and must ensure compliance with law and government regulations including procedures to protect the safety of all participants. To assist the NIAID and investigators in properly monitoring studies, additional information beyond what is normally submitted with a competitive grant application and the annual noncompetitive renewal application is required.

Applicants for clinical trials and studies must take these policies into consideration in the preparation of their applications. Awardees must adhere to terms of award that will be incorporated in their notice of grant award. Potential applicants are encouraged to contact NIAID concerning this policy.

NIAID terms of award are presented below; they delineate awardee responsibilities including submission of the required documentation to NIAID. These terms apply to all NIAID-supported clinical research including: Patient-Oriented Research including the development of new technologies using human subjects or materials derived from patients or volunteers, studies into the mechanisms of human disease using patient or volunteer samples, therapeutic interventions, clinical trials, and any studies that require IRB approval to collect samples from patients or volunteers; Epidemiologic and Behavioral Studies; and Outcomes and Health Services Research. The terms of award delineate specific time lines for approvals related to the initiation of the trial or study and time lines for reporting events related to the progress of the trial or study. It is the responsibility of the awardee to send the requested documentation and/or information to NIAID according to these time lines.

NIAID-supported clinical research must adhere to all appropriate human subjects requirements. NIH information and guidance on human subject protection, informed consent, and IRB review can be found at http://grants.nih.gov/grants/oprr/library_human.htm. Within that site is a link to FDA INFORMATION SHEETS Guidance for Institutional Review Boards and Clinical Investigators at: http://www.fda.gov/oc/oha/IRB/toc.html. All clinical research projects must comply with the universally accepted principles of Good Clinical Practice (GCP) as outlined in Title 21 of the CFR (http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr312_99.html). International studies must adhere to the above-cited regulations or the International Congress on Harmonization's Guidelines to Good Clinical Practice (http://www.ifpma.org/pdfifpma/e6.pdf).

INQUIRIES
General inquiries related to this notice may be directed to:
Office of the Director
Division of Extramural Activities, NIAID
Telephone: (301) 496-7291
FAX: (301) 402-0369
E-mail: ac20a@nih.gov or jm80c@nih.gov
Inquiries about a specific grant should be directed to the NIAID Program Officer for that grant.

2 - TERMS OF AWARD

These Terms of Award are in addition to and not in lieu of other NIH grant administration policies, such as written assurance of compliance with the Office of Protection from Research Risks regulations (45 CFR 46), PHS guidelines, HHS grant administration regulations (45 CFR parts 74 and 92), and Office of Management and Budget administrative guidelines.

In accordance with Department of Health and Human Services regulations for the protection of human subjects (45 CFR 46) and ensuring objectivity in research (42 CFR 50, Subpart F), Terms of Award details the agreements between the National Institute of Allergy and Infectious Diseases (NIAID) and (Name of Grantee Institution, Grant Number, and Principal Investigator [PI]) for the conduct of all clinical research, studies or trials supported by (Grant Title and Number).

NIAID Point of Contact:
All information and documentation requested by NIAID in this document must be forwarded electronically or by mail to the following address:
TERMS OF AWARD FOR NIAID GRANTS COORDINATOR (specific NIAID staff member will be assigned for each award)
Division of XXXXXX
6700-B Rockledge Drive
RoomXXXX
BETHESDA, MARYLAND 20892-76XX
USA
If non-US Postal Service mail carrier- use 20817 Zipcode
FAX: 301-XXX-XXXX
Telephone: 301-XXX-XXXX
E-mail: xxxxxx@nih.gov

The NIAID coordinator will ensure that the documents are entered into a grant terms of award tracking system and will forward them to the appropriate program officer in NIAID.

A. NIAID Review Process Prior to Study Initiation

The NIAID has a responsibility to ensure that mechanisms and procedures are in place to protect the safety of participants in NIAID-supported studies. Therefore, prior to patient accrual/participant enrollment, the grantee will provide the following (as applicable) for review and approval by the NIAID:

a) Data Safety and Monitoring Board (DSMB) organization and responsibilities (see D. below);

b) the clinical research protocol, including details of study design, proposed interventions, patient eligibility and exclusion criteria; plan for the management of side effects; procedures for assessing and reporting adverse events; site monitoring plan; the informed consent document, and documentation of IRB approval. To assist you in preparing these materials for submission, a checklist and other guidances are provided (Attachment 1). NIAID staff comments will be forwarded to the grantee within 3 (three) weeks of receipt of the above information. The grantee must address in writing all safety, regulatory, ethical, and conflict of interest concerns raised by NIAID staff to the satisfaction of the NIAID before patient accrual and participant enrollment can begin.

c) Clinical research projects involving the testing of new investigational therapeutics, vaccines or other medical interventions under a research protocol should be performed under an IND, unless otherwise agreed-upon by the NIAID and the Principal Investigator (PI).

B. Required Reporting
The NIAID is required to report the number and demographics of participants enrolled in NIAID-supported studies.

Clinical Trials. To aid the NIAID in fulfilling these reporting requirements, the grantee must complete the table below showing cumulative accrual information for each clinical trial protocol semi-annually.
This submission should be made 6 **(six)** months after enrollment opens and each 6 **(six)** months thereafter for clinical trials.

Clinical Studies. For all other clinical studies, yearly submission of the table with the non-competitive grant renewal is required.

Current Accrual Information and Demographics of Subjects Enrolled in the Study

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	Total
Female 0-20 years							
Female 21-above							
Male 0-20							
Male 21-above							
Total							

C. Time-sensitive Notification

To help ensure the safety of subjects enrolled in NIAID-funded studies, the following information must be sent to NIAID in a timely manner as specified in this section. The NIAID program officer must be informed of all major changes in the status of ongoing protocols, including:

- all amendments to the protocol
- termination of the protocol
- temporary suspension of the protocol
- any change in informed consent or IRB approval status
- temporary suspension or permanent termination of patient accrual
- any other problems or issues that could affect the human subjects in the studies.

Notification of any of the above changes must be made within three (3) **working days** by e-mail, followed by a signed letter cosigned by the Principal Investigator and the institutional business official, detailing the change of status notification to or from the local IRB.

IND studies: A copy of the seven-day telephone or facsimile safety reports sent to the FDA must be submitted to the NIAID Grants Coordinator **within 24 hours of FDA notification.**

IND studies: A copy of the fifteen-day written safety reports submitted to the FDA must be submitted to the NIAID Grants Coordinator **within 24 hours of FDA notification.**

In case of specific problems or issues, the NIAID program officer will contact the grantee within ten (10) **working days** (by e-mail or FAX), followed by an official letter to the Principal Investigator, with a copy to the institutions grants office, within thirty (30) calendar days to discuss appropriate actions.

D. Safety and Monitoring Issues, including multicenter trials and/or international sites:

1. Data and Safety Monitoring Board requirements:

Independent monitoring is essential for all clinical trials involving investigational drugs, devices or biologics and other clinical research perceived to involve more than a minimal risk **(Minimal Risk**: *A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination*). Decisions regarding the type of review committee to employ will be made jointly by the NIAID and the PI prior to study initiation. Discussions with the responsible NIAID Program Official regarding the appropriate safety monitoring will occur before patient enrollment may commence and include discussions about the appointment of:

a. Independent Safety Monitor – an individual physician who is independent of the study and available in real time to review and recommend appropriate action regarding adverse events and other safety issues;

b. Data and Safety Monitoring Board (DSMB) – an independent committee charged with reviewing safety and trial progress and providing advice with respect to study continuation, modification and/or termination. Decisions are made according to preset stopping rules.

The grantee may be required to use an established NIAID DSMB or to organize an independent DSMB. When the monitoring board is organized by the grantee, a description of the board, its operating procedures (including proposed meeting schedule and plan for review of adverse events) and roster and CV from all members must be submitted to and approved by the NIAID prior to study initiation. Additionally, the grantee will submit written summaries of all open sessions to the Grants Coordinator within **30 (thirty) days** of meetings.

2. IRB Approval:

Annually, the grantee will submit to the NIAID documentation of current approval from the local IRB, including a copy of the current informed consent document submitted as part of the IRB package. Where there are other institutions involved in the research, the protocol must be approved by each institution's IRB and initial and annual documentation from these institutions must also be provided to the NIAID. For international sites, initial approval and annual documentation from the local IRB is required, along with approval from a National IRB if applicable.

3. Other: *To be determined on a case-by-case basis.*

Clinical Research Information Report

Prior to protocol implementation, submit Attachment I to the following address:
TERMS OF AWARD FOR GRANTS COORDINATOR
(NIAID staff member will be identified for each award)
Division of . . . . .
6700-B Rockledge Drive
Room . . . .
BETHESDA, MARYLAND 20892-76xx
USA
If FedEx, UPS, etc.,- use 20817 Zipcode
FAX: 301-xxx-xxxx
Telephone: 301-xxx-xxxx
Email: xxxxx@nih.gov
Date: _____

Principal Investigator: _____
phone _____ fax _____ email _____
Grant #: _____
Site Name: _____
Address: _____
_____
Study Title: _____

1. Study Agents or Intervention(s):_____
NA _____
Note: Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

2. Copy of the protocol:
Please provide a current, complete copy of the clinical/research protocol
Please note that for the duration of the grant it is the responsibility of the grantee to notify the NIAID of subsequent protocol amendments before implementation and provide documentation.

3. OPRR Assurance number:

4. IND Submission to FDA:
yes____ no____ NA _____

5. Name and institution of IND holder:_____

6. FDA IND Approval:
yes____ no____ Date:_____ attach copy of FDA IND number assignment and comments if available
7. IND#:_____

8. Initial IRB Protocol Approval:
yes____ no_____ Date:_____ attach all IRB documents
Annual Review
yes___ no_____ Date: attach all IRB documents

9. Recombinant DNA Advisory Committee Approval:
yes____ Date: _____ NA_____

cont'd.

10. DSMB established:
yes_____
Standing NIAID DSMB_____
(name of DSMB and NIAID contact person)
no _____
NA_____

11. Target Accrual and Demographics: _____ Date _____

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	Total
Female 0-20 years							
Female 21-above							
Male 0-20							
Male 21-above							
Total							

NA = not applicable

ADVERSE EVENT REPORTING

Division of Microbiology and Infectious Diseases
NIAID
REQUIRED REPORTING AND GUIDELINES FOR SERIOUS ADVERSE EVENTS

Regardless of whether a clinical study is filed under an IND or not, the DMID requires notification of the occurrence of Serious Adverse Events (SAE) within specific timeframes. The following sets forth DMID's expectations and provides guidance to meet the expectations.

Required Reporting to DMID

A written report or case report form (CRF) must be faxed in the stated timeframes to the DMID Program Officer or to assigned contact for the following events:

- Unexpected Fatal or Life Threatening events with any possible association with use of test article or participation in the study must be reported within *7 calendar days.*

- Events that are both Serious and Unexpected with any possible association with the use of the test article or study participation must be reported within *15 calendar days.*

Guidelines for Reporting

Standard Reporting Information

The following information should be included in the report/CRF (additional information may be requested):

- Description of the event
  Date, time of onset
  Clinical history
  Associated signs and symptoms
  Temporal association with study agent
  Medical management, including rationale
  Pertinent laboratory tests
  Severity – see definitions or toxicity score
  Casual relationship to the study agent

- Other Information
  Relevant past medical history
  Concomitant medications
  Autopsy report or expectation of an autopsy in the case of death

- Outcome of event
  Date, time of resolution, if resolved

- Plans for study subject
  Follow-up
  Treatment of event
  Return to treatment/Contraindicate

- Location/Study Center

- Reporting Physician

- Verification of notification to IRB and Safety Monitor or DSMB

Definitions

- Adverse Event [Experience] (AE):
  Any untoward medical occurrence, including dosing errors, that may arise during administration of the study agent, and which may or may not have a casual relationship with the study agent.

- Unexpected Adverse Event [Experience]:
  Any adverse experience that has not been previously observed (i.e., included in the labeling), whether or not the event is anticipated because of the pharmacologic properties of the study agent.

- Serious Adverse Experience (SAE):
  Any adverse experience occurring at any dose that results in any of the following outcomes:

  a. Death
  b. Life threatening - defined as an experience that places the patient or subject, in the view of the Investigator, at *immediate risk* of death from the reaction as it occurred. (Note; this does not include a reaction that, had it occurred in a more severe form, might have caused death.)
  c. Requires inpatient hospitalization or prolongation of existing hospitalization
  d. Results in a congenital anomaly or birth defect
  e. Results in a persistent or significant disability or incapacity

  Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse experience when, based upon appropriate medical judgement, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. (*The event might be defined as serious based on progression of grade if Toxicity Tables are being used*)

- Severity

Adverse experience/events should be assessed by the on-site investigator as to their severity or intensity.

a. Life Threatening
b. Severe: incapacitating with inability to work or do usual activity
c. Moderate: enough discomfort to cause interference with usual activity
d. Mild: awareness of sign or symptom, but easily tolerated

Relationship or Association with Use of Study Agent or Participation in the Study

Casual relationship with the investigational study treatment must be assessed by the on-site investigator using the following or similar terms:

- **Definite –** clear-cut temporal association, with a positive re-challenge test or laboratory confirmation
- **Probable –** clear-cut temporal association, with improvement upon study agent withdrawal, and not reasonably explained by the subject's known clinical state.
- **Possible –** less clear temporal association, other etiologies are possible
- **None –** no temporal association with the study agent; related to other etiologies such as concomitant medications or conditions, or subject's known clinical state

Other Reporting

Investigators are reminded that they may have other reporting obligations:

- For all studies, there must be compliance with the clinical site IRB's policy for reporting adverse events.
- For all IND studies, there must be compliance with FDA regulations found in 21 CFR 312.32
- For serious associated events with licensed drugs, a MedWatch form should be filed, and for licensed vaccines, a VAERS form should be filed with the FDA.

ATTACHMENT 2 PROJECT ASSURANCES

In order to receive NIH support for research studies involving human subjects, an applicant organization must agree to comply with the U.S. Department of Health and Human Services (DHHS) regulations for the Protection of Human Subjects. These regulations apply to all research that is conducted or supported, in whole or in part, by DHHS and involve human subjects at the awardee or any collaborating site, either U.S. or international. The definition of human subject research includes not only studies in which data are obtained through intervention or interaction with an individual, but also studies in which identifiable private information is obtained.

The DHHS Office of Protection from Research Risk (OPRR) is responsible for the oversight of compliance by awardee institutions. Each institution or organization and their collaborators on a DHHS-funded project involving human subjects in research must sign an agreement to protect the rights and welfare of human research subjects before the research begins. The document containing this legally binding commitment is called an Assurance. An Assurance approved by OPRR is a written document that commits the institution and its personnel to compliance with minimum standards for the protection of human subjects.

These ethical standards, Institutional Review Board (IRB) or Ethics Committee (EC) functions, and informed consent expectations are generally compatible with those of the U.S. Food and Drug Administration (FDA) and of the International Ethical Guidelines for Biomedical Research Involving Human Subjects published by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO).

Institutions that do not already have an applicable Assurance of Compliance on file with OPRR must provide an appropriate Assurance prior to funding. There are several types of Assurances. Some U.S. institutions have a Multiple Project Assurance (MPA), which is a standing agreement on file with OPRR and covers all human subject research at that site. DHHS-funded research at institutions with MPAs do not need to provide additional Assurance documents.

Sites that do not have MPAs will need to obtain an Assurance. In most cases, a Single Project Assurance (SPA) that is study specific will be required. An SPA application provides a list of IRB/EC members and their expertise and affiliation, which is signed by the IRB/EC Chairperson and Institutional Official. The Assurance application, IRB membership list, protocol and proposed informed consent document (English translation) for each site are forwarded to OPRR by the Principal Investigator.

An SPA application form for U.S. studies and one for international studies, as well as additional information about Assurance documents, can be found on the Internet at: http://grants.nih.gov/grants/oprr/humansubjects/assurance. The OPRR e-mail address is oprr@od.nih.gov.

ATTACHMENT 3 POLICY AND GUIDELINES FOR THE ESTABLISHMENT OF DATA AND SAFETY MONITORING FOR CLINICAL TRIALS

Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases

The Division of Microbiology and Infectious Diseases (DMID) supports clinical research studies and trials under both contract and grants. This support carries with it the responsibility to assure that mechanisms and procedures are in place to protect the safety and rights of human subjects who participate in clinical research. Therefore, DMID has established the policy of requiring the establishment of appropriate data and safety monitoring for all clinical studies that include investigational test articles, other clinical studies where there is a potential for harm to the participants, or where independent assessments are required to assure objectivity. This policy applies to all DMID sponsored research, regardless of funding mechanism and is consistent with the NIH Policy for Data and Safety Monitoring issued on June 10, 1998.

The purpose of data and safety monitoring is to provide an independent and objective review of interim safety information and, if appropriate, efficacy data to protect the safety and rights of volunteers, while assuring the integrity of the data. The primary charge to this group or individual (as defined below) is to provide advice to DMID and the study investigators on the appropriateness of continuing the study as designed. Independent monitoring committees/boards may also be tasked with providing recommendations concerning continuation or initiation of related studies based on the results of studies they are currently reviewing.

The monitoring guidelines provide that the DMID program officers have the authority to recommend and approve the type of monitoring appropriate for the proposed clinical research. Studies that are considered "minimal risk" would not require independent monitoring. "Minimal risk is defined as: *a risk where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than doing so as part of routine physical examination.* The three basic types of monitoring are summarized below.

1. Data Safety Monitoring Board (DSMB) - All phase 3 studies and most masked phase 2 studies would normally be supported by a DSMB. It may be appropriate to use a DSMB for other long-term studies that may require statistical input. The committee/board is charged with reviewing safety at defined intervals as the study progresses and providing advice as to whether a study should proceed as planned. The committee should include a statistician; decisions are made according to preset statistical rules for stopping the study. The committee convenes on a regular basis and on an *ad hoc* basis if necessary.

2. Internal Monitoring Board (IMB) – An IMB is a small committee similar to a DSMB. This type of monitoring group may be used for unblinded studies and for some masked studies that are not intended to evaluate efficacy. The committee/board may be composed of other staff from the investigator's institution who are not involved with the study. An IMB would generally include an independent safety monitor but not necessarily a statistician. This type of committee must be able to convene or confer on an *ad hoc* basis if immediate safety concerns arise.

3. Independent Safety Monitor (ISM) – An ISM is an individual who is independent of the study and available in real time to review adverse events and other safety issues. An ISM may be the sole monitor for some early phase studies, such as pharmacokinetics or immunogenicity studies. An ISM may also be utilized for other studies that are considered very low risk and of a short duration. The ISM may also be included as a member of an IMB or DSMB.

Neither the ISM nor any member of a safety monitoring board should be an employee of the manufacturer or any other individual with vested interests in the outcome of the study.

ATTACHMENT 4 USEFUL INTERNET SITES

ICH Guidelines
http://www.ifpma.org/ich5.html

NCI Consent Documents and Guidance
http://cancertrials.nci.nih.gov/understanding/index.html
http://cancertrials.nci.nih.gov/researchers/safeguards/consent/index.html

Cancer Toxicity Table
http://ctep.info.nih.gov/handbook/HandBookText/Appendix_XII.htm#Att_3
http://ctep.info.nih.gov/CTC3/ctc_ind_term.htm

FDA HomePage
http://www.fda.gov/default.htm

CBER Regulatory Page
http://www.fda.gov/cber/guidelines.htm
http://www.fda.gov/cber/points.htm
http://www.fda.gov/cber/infosheets.htm
http://www.fda.gov/cber/rules.htm

CDER Regulatory Page
http://www.fda.gov/cder/regulatory/default.htm

FDA Office of Health Affairs: Clinical Trials and Human Subjects Protection
http://www.fda.gov/oc/health/hsp.html

FDA IRB Operations and Clinical Investigations Requirements
http://www.fda.gov/oc/oha/IRB/toc.html

21CFR50-Informed Consent
http://www.fda.gov/oc/oha/IRB/toc10.html#AppendixB

21CFR56-IRBs
http://www.fda.gov/oc/oha/IRB/toc10.html#AppendixC

Belmont Report
http://www.fda.gov/oc/oha/IRB/toc11.html#The Belmont Report

Declaration of Helsinki
http://www.fda.gov/oc/oha/IRB/toc11.html#World Medical Association Declaration of Helsinki

OPRR HomePage
http://grants.nih.gov/grants/oprr/oprr.htm

45CFR46-Human Subjects Protection
http://grants.nih.gov/grants/oprr/humansubjects/45cfr46.htm

Human Subject Regulations Decision Charts
http://grants.nih.gov/grants/oprr/humansubjects/guidance/decisioncharts.htm

Involvement of Children in Research
http://grants.nih.gov/grants/guide/notice-files/not98-024.html

Categories Eligible for Expedited IRB Review
http://grants.nih.gov/grants/oprr/humansubjects/guidance/hsdc99-01.htm

Tips on Informed Consent
http://grants.nih.gov/grants/oprr/humansubjects/guidance/ictips.htm

Issues to Consider in the Research Use of Stored Data or Tissues (11/7/1997)
http://grants.nih.gov/grants/oprr/humansubjects/guidance/reposit.htm

Form 310: Certification of IRB approval
http://grants.nih.gov/grants/oprr/humansubjects/assurance/as-fm310.htm

CDC Human Subjects Requirements
http://www.cdc.gov/od/ads/hsr2.htm

NIH OHSR HomePage
http://helix.nih.gov:8001/ohsr/

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APPENDIX C

CONCEPT SHEET

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I. TITLE:

II. PRINCIPAL INVESTIGATOR:

III. PATIENT GROUP:

IV. AREA OF PROPOSED RESEARCH

V. PROPOSED INTERVENTION (PHARMACEUTICAL SPONSOR, IF APPLICABLE)

VI. BACKGROUND AND RATIONALE:

VII. SIGNIFICANCE

VIII. HYPOTHESIS (ES) TO BE TESTED:

IX. STUDY OBJECTIVES:

X. STUDY DESIGN:

A) Study Endpoints:
   1. Primary:
   2. Secondary

B) Statistical assumptions

C) Sample size with justification

D) Randomization/stratification, if applicable

E) Inclusion and exclusion criteria

F) Anticipated duration of:
   1. recruitment phase,
   2. study phase

G) Interim Monitoring plan, if applicable

H) Study visit schedule and primary evaluations

I) Study timeline

XI. PROPOSED MECHANISTIC STUDIES: DESCRIPTION AND RATIONALE

XII. DATA ANALYSES PLANNNED

XIII. PROPOSED COLLABORATORS

XIV. POTENTIAL ETHICAL ISSUES

XV. INCLUSION OF WOMEN AND MINORITIES

XVI. CONFLICT OF INTEREST DISCLOSURE

XVII. COMPETING STUDIES:

XVIII. KEY REFERENCES:

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