The Early Stage Investigator (ESI) Scholar Award: Pilot Studies to Advance Non-Human Primate Models in Support of HIV Vaccine Clinical Research

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PART I – OVERVIEW INFORMATION

Funding Organization
National Institute of Allergy and Infectious Diseases (NIAID), (www.niaid.nih.gov)

Participating Groups
HIV Vaccine Trials Network (HVTN), (www.hvtn.org)
Center for HIV-AIDS Vaccine Immunology (www.chavi.org)
National Center for Research Resources (NCRR) (www.ncrr.nih.gov)

Key Dates
Release/Posted Date: October 1, 2010
Letters of Intent Receipt Date: November 30, 2010
Application Due Date: January 5, 2011
Peer Review Date: January 2011
HVTN and CHAVI Leadership Review Dates: February 2011
Earliest Anticipated Start Date: March 2011

Executive Summary

- **Purpose.** This Request for Applications (RFA) issued by the Center for HIV/AIDS Vaccine Immunology (CHAVI) in collaboration with the HIV Vaccine Trials Network (HVTN) under the sponsorship of the National Institute of Allergy and Infectious Disease (NIAID) of the National Institutes of Health (NIH) solicits pilot study proposals that aim to strengthen bridges between non-human primate (NHP) and human research by addressing key questions that may lead to the rational development of a safe and effective preventive HIV vaccine. Early Stage Investigators (ESIs) in collaboration with designated clinical and NHP scientist mentors are sought to propose innovative projects. This initiative seeks to promote the ultimate goal of developing a cadre of investigators committed to advancing our understanding of NHPs to predict immunogenicity and efficacy of candidate vaccines in humans, to develop novel models of pre-clinical evaluation of candidate vaccines, and to define new concepts in correlates of protection from infection or immune control after acquisition. The recent finding that the simian-human immunodeficiency virus (SHIV) NHP challenge model is unsuited to evaluate the efficacy of T cell-based vaccines has raised several questions about the comparability of NHP and clinical studies and argues for greater coordination of scientific inquiry across clinical and NHP research communities. The research proposed is expected to generate preliminary data and will likely be linked to existing NHP, clinical trial, or observational studies; stand-alone pilot studies can also be proposed and are encouraged. Selected clinical and NHP scientist mentors may hail from the same or different institutions. See Section III for eligibility criteria. This RFA solicits applications for a third cohort of scholars. The first cohort of five scholars was awarded in 2009 and a second cohort of four scholars was awarded in 2010. In addition to conducting the proposed research, selected scholars are required to participate in the ESI Scholar Program, which includes semi-annual workshops and formalized mentorship activities. As this program is open to new investigators, research expertise in the area of HIV vaccines or NHP models is not required as a prerequisite for submitting a proposal.
• **Funds Available and Anticipated Number of Awards.** CHAVI through its cooperative agreement with NIAID intends to commit approximately $1.35M in total costs in 2011 to fund 4-8 applications submitted in response to this RFA. Awards issued under this funding mechanism are contingent upon the availability of funds and the submission of a sufficient number of meritorious applications.

• **Budget and Project Period.** Budgets for direct and indirect costs of up to $200,000 (Total costs) for one year may be requested. Support up to $300,000 (Total costs) will be considered for special circumstances should Research Development Support be critical for NHP experiments. Sufficient justification including how existing resources will be leveraged to conduct the work must be included.

• **Application Research and Mentor Plan Component Length:** ESI Scholar proposals must include a Research Plan (Research Design and Methods), limited to 10 pages, and Mentorship Plan, limited to 2 pages.

• **Eligible Institutions/Organizations.** Institutions/organizations listed in Section III are eligible to apply.

• **Eligible Project Directors/Principal Investigators (PDs/PIs).** Individuals with the skills, knowledge, and resources necessary to carry out the proposed research under the mentorship of established clinical and NHP scientists are invited to work with their institution/organization to develop an application for support. Eligible applicants for the Early Stage Investigator awards will include those at the post-doctoral trainee, clinical instructor, or assistant professor level. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are encouraged to apply. Individuals in the first cohort of ESI Scholars are eligible for this 1-year award to expand upon their current project.

• **Number of PDs/PIs.** Only one ESI may be designated on the application. One primary clinical and one NHP scientist mentor must be designated.

• **Number of Applications.** Applicants may submit more than one application, provided each application is scientifically distinct.

• **Application Materials.** See Section IV.1 for application materials.
PART II – FULL TEXT OF ANNOUNCEMENT

Section I. Funding Opportunity Description

1. Research Objectives

This novel collaborative funding initiative entitled “The Early Stage Investigator Scholar Award: Pilot Studies to Advance Non-Human Primate Models in Support of HIV Vaccine Clinical Research” has two primary objectives: (1) to attract and retain promising Early Stage Investigators (ESIs) interested in improving non-human primate models that support preventive HIV vaccine development, and (2) to provide a framework for ongoing ESI mentorship that will foster increased collaboration between clinical and NHP scientists addressing common questions in vaccine discovery.

Background

With over 6500 new HIV infections occurring daily across the globe, identifying effective prevention strategies continues to be an urgent public health priority. An HIV vaccine represents our best hope to combat this global pandemic, yet its discovery has been elusive. Correlates of immune protection remain undefined and this has challenged the rational development of antibody or T cell-based vaccines that can protect against infection or affect post-infection viral dynamics or disease course. Animal models, particularly non-human primate (NHP) systems, have led to key advances in vaccine development. While HIV fails to replicate and cause disease except in humans and chimpanzees, NHP lentivirus models have been used to recapitulate HIV’s modes of infection, pathogenesis, and antiviral immunity. NHP models have proven to be important platforms to test the immunogenicity and efficacy of a wide range of HIV vaccine candidates. But the validation of any animal model, including NHPs, requires a successful human trial and the determination of correlates of immunity. This feedback loop was highlighted by the finding in 2007 that the MRKAd5 HIV-1 Gag/Pol/Nef candidate vaccine failed to prevent HIV infection and disease progression in the STEP phase 2b test-of-concept efficacy trial conducted by the HVTN and Merck & Co., Inc., despite encouraging data from an NHP simian-human deficiency virus (SHIV) 89.6 challenge model. Thus, we can conclude the SHIV challenge model is inappropriate for evaluating the efficacy of T-cell based vaccines, while the SIV challenge model, which did not show demonstrable differences in viral load in vaccinated macaques, appears more predictive of what was eventually observed in the pivotal STEP study.

How NHP models can best be utilized to promote vaccine discovery was a key focus of the March 2008 NIAID HIV Vaccine Summit. A critical theme that emerged from these discussions was the importance of strengthening the linkages between the NHP and clinical researchers to collaboratively tackle key areas of scientific inquiry. Parallel NHP and clinical studies were promoted as a way to generate comparable data across systems in order to evaluate testable hypotheses.

Another key theme to emerge from the Vaccine Summit was the desire to attract and retain new talented investigators to the HIV vaccine field. Two areas of major work were identified: young investigators who would study novel approaches to the immunobiology of HIV including B and T cell biology, and the interface between the pathogenesis and vaccinology of the non-human primate and human vaccine response. It is also recognized that early stage investigators bring fresh and innovative ideas to address these key scientific areas.

The ESI Scholar Program

The NIAID-sponsored HVTN proposed the Early Stage Investigator Scholar Award Program to the Vaccine Research Program of the Division of AIDS in NIAID to address both of the important themes that emerged from the Vaccine Summit. Since NHP research is outside of the scope of the HVTN cooperative agreement award, the HVTN enlisted the assistance of CHAVI to make this Award Program a reality. A
novel feature of the ESI Scholar Program is the requirement that scholars develop and execute research proposals under the guidance of both a clinical and a NHP scientist mentor. Thus, an important byproduct of this initiative will be greater collaboration across these spheres through the novel research proposed in response to this RFA and through a series of forums organized by NIAID, the HVTN and CHAVI including conference plenaries, working groups, and seminars. The linkages between the NHP and clinical research areas will be a critical component of the initiative, and applicants are encouraged to proscribe how mentors in each area will contribute to the success of the award.

The primary goals of this funding opportunity are to address high priority scientific questions relevant to NHP models and vaccine discovery and to provide novel opportunities to investigators willing to dedicate their efforts to this fundamental area of research. The focus of the current awards, which will be limited to one year of funding, will be on studies to better understand how research observations relevant to HIV vaccine development can be better translated between NHP and humans. Recognizing the significant resources required to conduct de novo NHP studies as well as required laboratory reagents, it is envisaged that proposed projects would be embedded within larger existing or proposed NHP studies, clinical trials, or observational cohort studies. However, novel standalone pilot studies are highly encouraged, targeting either significant technical and/or scientific hurdles facing the field.

Research projects and studies may include, but are not limited to, the following topics:

1. Translation of research tools or assays that are specific for one species to the other, with particular emphasis on development of platforms that allow better comparisons of immune responses between NHP and humans.
2. Defining similarities and differences in vaccine-elicited immune responses in NHP versus humans by directly comparing responses to candidate immunogens.
3. Comparative studies that elucidate the role of innate or mucosal immunity in control of HIV/SIV infection and vaccine-induced protection in NHP and humans.
4. Development of new approaches to analyze the role of neutralizing or non-neutralizing antibodies play in host resistance that could be applied to both NHP and humans.

The above list is not intended to emphasize or limit applications to any specific area of research, but only to serve as a set of examples of potentially responsive research projects. For reference, a brief description of ESI Scholar projects awarded under both the 2008 and 2009 calls for applications can be found at http://www.hvtn.org/science/esiprofiles.html. Previous ESI Scholars will be eligible to apply for an additional year of support but will need to submit a new application that clearly identifies a novel area of research that is responsive to the revised focus stated above.

Note: Applications proposing any of the following research topics will be identified as non-responsive and will not be reviewed. Applicants will be notified via email if an application is deemed non-responsive.

- Incremental improvements of approaches already under development
- Research projects currently being conducted in the applicant's laboratory that are supported by NIH or other funding entities
- Purely descriptive basic research or structural studies not addressing a clear hypothesis

Section II. Award Information

1. Mechanism of Support

This initiative will use a novel grant award administered by CHAVI through a cooperative agreement with the Division of AIDS, NIAID. As an applicant, the candidate and his/her mentors are jointly responsible for the planning, directing, and executing the proposed project and career development activities.
2. Funds Available

NIAID has committed approximately $1.35M in total costs for this funding initiative for 2011 to fund 4-8 applications. Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary.

Budgets for direct and indirect costs of up to $200,000 (Total costs) with a project duration of one year may be requested. Support up to $300,000 (Total costs) will be considered for special circumstances should Research Development Support be critical for NHP experiments. Awards are not renewable. Sufficient justification including how existing resources will be leveraged to conduct the work must be included.

NIH grants policies as described in the NIH Grants Policy Statement will apply to the applications submitted and awards made in response to this RFA.

Allowable Costs:

Salary: This funding mechanism will provide salary and fringe benefits for the ESI Scholar Award recipient. The total salary requested must be based on a full-time, 12 month staff appointment requiring the candidate to devote a minimum of 50% of full-time professional effort to conducting the proposed research project and mentorship activities with the expectation that ~50-100% of effort will be devoted to this project. The salary must be consistent both with the established salary structure at the institution and with salaries actually provided by the institution from its own funds to other staff members of equivalent qualifications, rank, and responsibilities in the department concerned. If full-time, 12-month salaries are not currently paid to comparable staff members, the salary proposed must be appropriately related to the existing salary structure. Confirmation of salary is required prior to the issuance of an award. Fringe benefits, based on the sponsoring institution's rate and the percent of effort, are provided in addition to the salary.

We anticipate that a wide range of applicants including post-doctoral trainees, clinical instructors, and assistant professor level faculty members may apply for funding through this mechanism. Thus, the award will provide support ranging from $40,000 to $100,000 to help offset the full-time salary requirement of the ESI candidate. The sponsoring institution, or other funds from federal or non-federal sources, may supplement the award salary contribution up to a level that is consistent with the institution's salary scale. Institutional supplementation of salary must not require extra duties or responsibilities that would interfere with the purpose of the ESI Scholar Award.

Research Development Support: The ESI Scholar Award will provide support ranging from $50,000 to $200,000 (including F&A) per year for the following expenses: (a) research expenses, such as reagents, supplies, equipment, and technical personnel; (b) travel to relevant meetings including required semi-annual ESI Scholar seminars; (c) expenses associated with dedicated time at a mentor's clinical and/or NHP research facility if proposed in the mentorship plan; and (d) NB statistical services in experimental design will be provided by the CHAVI biostatistical unit and their support will come from CHAVI core funds. If the research development support is requested in excess of $100,000 per year, a thorough rationale for the proposed study and costs therein is expected. Of note, applicants are encouraged to seek additional statistical input from the Statistical Center for HIV/AIDS Research Programs (SCHARP) early in concept development, particularly for proposals involving comparative studies involving human trials and NHPs. SCHARP staff can work in close collaboration with statisticians from the applicants’ institutions on the design and analysis plans, if requested. Please refer to Section VII for contact information.

Ancillary Personnel Support: Salary for mentors, secretarial and administrative assistance, etc., is not allowed.
Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

Individuals from the following organizations/institutions are eligible to apply:

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education
- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions
- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Small Businesses
- For-Profit Organizations (Other than Small Businesses)
- State Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribally Designated Organizations
- County Governments
- City or Township Governments
- Special District Governments
- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- U.S. Territory or Possession
- Indian/Native American Tribal Governments (Other than Federally Recognized)
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Organizations)
- Other(s):
  - Eligible Agencies of the Federal Government
  - Faith-based or Community-based Organizations

1.B. Eligible Individuals

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the ESI Applicant is invited to work with his/her organization as well as two designated mentors, preferably a clinician scientist and NHP scientist experts, to develop an application for support. Current ESI Scholars from the first cohort are eligible for this award. Mentors must have extensive research experience. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for support.

For this initiative, “early stage” investigators are candidates who at the time of application are within 10 years post-subspecialty fellowship or completion of doctoral training, and cannot have been the recipient of R01 or equivalent mechanism of independent funding. Candidates for this award may possess a health-professional doctoral degree or its equivalent. Such degrees include but are not limited to the M.D., D.O., D.D.S., D.M.D., O.D., D.C., Pharm.D., as well as a doctoral degree in nursing research or practice. Candidates with a Ph.D. degree may also apply for this award. For those candidates proposing clinically-oriented research, they must have completed their clinical training, including specialty and, if applicable, subspecialty training prior to receiving an award. However, candidates may submit an application prior to the completion of clinical training. The NIH definition of “Early Stage Investigators” can
be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-013.html. For the policy on requesting an extension of the ESI period see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-034.html. Current HVTN/CHAVI NHP ESI Scholars from the first cohort, awarded in 2009, are eligible to apply for this funding as long as the project proposed is distinct from their currently funded project (e.g. adding new aims).

Candidates must be able to commit to a minimum of 50 percent of full-time professional effort conducting the proposed research project and engaging in mentorship and structured learning activities as part of the ESI Scholar Program. The remaining effort can be divided among other research, clinical and teaching activities and should not restrict the applicant’s ability to complete the proposed research or pre-specified mentorship activities, including field placements at collaborating clinical and/or NHP research sites. The candidate must have a “full time” appointment at the academic institution that is the applicant institution. Candidates who have VA appointments may not consider part of the VA effort toward satisfying the “full time” requirement at the applicant institution. Candidates with VA appointments should contact the staff person in the relevant Institute or Centers prior to preparing an application to discuss their eligibility, see http://grants.nih.gov/grants/guide/contacts/pa-05-143_contacts.htm. Individuals with an active K-award must seek approval from their program officer prior to submitting an application under this program. This approval should be included as an appendix to the application.

2. Cost Sharing or Matching

This program does not require cost sharing as defined in the current NIH Grants Policy Statement.

3. Other-Special Eligibility Criteria

**Mentorship:** A key feature of the ESI Scholar Program is the role of the clinical and NHP mentors. The ESI Scholar must name two mentors, who, together with the applicant are responsible for the planning, direction, and execution of the proposed research project. This initiative seeks to strengthen the link between non-human primate research and clinical trials, in part, through jointly conceived and implemented research projects. This link is also fostered by the shared responsibility of mentoring the ESI Scholar by the established clinician and NHP scientists. The mentors should be recognized as accomplished investigators in some aspect of the proposed research area and have a track record of success in training independent investigators in patient-oriented research or working with NHP models in immunology and/or infectious disease. Either one of the mentors should have sufficient independent research support to cover the costs of the proposed research project in excess of the allowable costs of this award. It is anticipated that this will be relevant to many applications for funding under this initiative as ancillary studies or projects embedded within larger experiments (NHP studies, clinical trials, or observational studies). Where feasible, women, individuals from diverse race and ethnic groups, and individuals with disabilities should be involved as mentors to serve as role models.
Section IV. Application and Submission Information

1. Content and Form of Application Submission

Prepare all applications using the ESI application forms (http://www.hvtn.org/science/esi.html).

Required Components:

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<tr>
<th>Document</th>
<th>Required</th>
<th>Optional</th>
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<tr>
<td>ESI Application Form</td>
<td>x</td>
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<tr>
<td>ESI Letter of Intent</td>
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<td>x</td>
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<tr>
<td>ESI Biographical Sketch for applicant and mentors</td>
<td>x</td>
<td></td>
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<tr>
<td>Letters of Reference</td>
<td>x</td>
<td></td>
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<tr>
<td>ESI Detailed Budget</td>
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ESI Additional Forms (includes the sections listed below)

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<tr>
<th>Document</th>
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<th>Optional</th>
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</thead>
<tbody>
<tr>
<td>ESI Research Plan: includes Background &amp; Significance, Preliminary Studies, Research Design &amp; Methods, and the References Cited sections</td>
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<tr>
<td>ESI Mentoring Plan</td>
<td>x</td>
<td></td>
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<tr>
<td>ESI Resource Sharing Plan</td>
<td>x</td>
<td></td>
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<tr>
<td>ESI Facilities and Resources</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>ESI Budget Justification</td>
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</table>

Foreign Organizations (Non-Domestic [non-U.S.] Entities)

CHAVI adheres to NIH policies concerning grants to Foreign (non-U.S.) organizations can be found in the NIH Grants Policy Statement at: http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part12.htm#Toc54600260.

Applications from Foreign organizations must:

- Request budgets in U.S. dollars;
- Prepare detailed budgets for all applications;
- Not include any charge-back of customs and import fees;
- Comply with the format specifications, which are based upon a standard U.S. paper size of 8.5” x 11” within each PDF;
- If appropriate, request funds for up to 8% administrative costs (excluding equipment) (see NOT-OD-01-028, March 29, 2001);
- Comply with Federal/NIH policies on human subjects, animals, and biohazards; and
• Comply with Federal/NIH biosafety and biosecurity regulations (see Section VI.2, “Administrative and National Policy Requirements”).

Proposed research should provide special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions in other countries that are not readily available in the United States (U.S.) or that augment existing U.S. resources.

Applications Involving Multiple Institutions

When multiple institutions are involved, one institution must be identified as the prime institution and funding for the other institution(s) must be requested via a separate subcontract to be administered by CHAVI. When submitting a detailed budget, each institution should submit its budget using the Research & Related Budget component.

2. Submission Dates and Times

2.A. Submission, Review, and Anticipated Start Dates

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
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<tbody>
<tr>
<td>Release/Posted Date</td>
<td>October 1, 2010</td>
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<td>February 2011</td>
</tr>
<tr>
<td>Earliest Anticipated Start Date</td>
<td>March 2011</td>
</tr>
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2.A.1. Letter of Intent

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed research.
- Name, address, and telephone number of the ESI Scholar candidate
- Names of other key personnel, including designated mentors
- Participating institutions.
- Title of this funding opportunity.

Letters of intent are not required, but are highly recommended. They are not binding, and do not enter into the review of a subsequent application. The information that an LOI contains allows CHAVI and HVTN staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed in Section IV.2.A and should be e-mailed to vtn.research@hvtn.org to the attention of Blythe Adamson.

2.B. Submitting an Application to the ESI Scholars Program

To submit an application in response to this RFA, applicants should submit their application, combined into one PDF document, via email to vtn.research@hvtn.org to the attention of Blythe Adamson.

PAPER APPLICATIONS WILL NOT BE ACCEPTED.
2.C. Application Processing

Applications may be submitted on or after the opening date and must be successfully received by HVTN no later than 5:00 p.m. local time (of the applicant institution/organization) on the application due date(s). (See Section IV.2.A. for all dates.) If an application is not submitted by the due date(s) and time, the application may be delayed in the review process or not reviewed. There will be an acknowledgement of receipt of applications from Blythe Adamson.

Upon receipt, applications will be evaluated for completeness and responsiveness by HVTN and CHAVI. Incomplete and non-responsive applications will not be reviewed.

The HVTN and CHAVI will not accept any application in response to this RFA that is essentially the same as one currently pending initial review by NIH or other funders, unless the applicant withdraws the pending application. When a previously unfunded application, originally submitted as an investigator-initiated application, is to be submitted in response to a funding opportunity, it is to be prepared as a NEW application. That is, the application for the funding opportunity must not include an “Introduction” describing the changes and improvements made, and the text must not be marked to indicate the changes from the previous unfunded version of the application.

3. Intergovernmental Review

This initiative is not subject to intergovernmental review.

4. Funding Restrictions

This award is subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement.

Pre-award costs are allowable. A grantee may, at its own risk and without CHAVI prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new or competing renewal award if such costs: 1) are necessary to conduct the project, and 2) would be allowable under the grant, if awarded, without CHAVI prior approval. If specific expenditures would otherwise require prior approval, the grantee must obtain CHAVI approval before incurring the cost. CHAVI prior approval is required for any costs to be incurred more than 90 days before the beginning date of the initial budget period of a new or competing renewal award.

The incurrence of pre-award costs in anticipation of a competing or non-competing award imposes no obligation on CHAVI either to make the award or to increase the amount of the approved budget if an award is made for less than the amount anticipated and is inadequate to cover the pre-award costs incurred. CHAVI expects the grantee to be fully aware that pre-award costs result in borrowing against future support and that such borrowing must not impair the grantee's ability to accomplish the project objectives in the approved time frame or in any way adversely affect the conduct of the project (this is outlined in the NIH Grants Policy Statement).

5. Other Submission Requirements and Information

5.A. Format Specifications for ESI Application

All components of the application should be submitted as one PDF or Microsoft Word file using the ESI application forms (available at http://www.hvtn.org/science/esi.html), and must conform to the formatting requirements noted below. Failure to follow these requirements may delay the review process.
Early Stage Investigator (ESI) Scholar Award Request for Applications

Font
- Use an Arial, Helvetica, Palatino Linotype, or Georgia typeface, a black font color, and a font size of 11 points or larger. (A Symbol font may be used to insert Greek letters or special characters; the font size requirement still applies.)
- Type density, including characters and spaces, must be no more than 15 characters per inch.
- Type may be no more than six lines per inch.

Page Margins
- Use standard paper size (8 ½” x 11).
- Use at least one-half inch margins (top, bottom, left, and right) for all pages.

Page Formatting
Use only a standard, single-column format for the text.

Figures, Graphs, Diagrams, Charts, Tables, Figure Legends, and Footnotes
You may use a smaller type size but it must be in a black font color, readily legible, and follow the font typeface requirement. Color can be used in figures; however, all text must be in a black font color, clear and legible. All figures, graphs, diagrams, charts, and tables must fit within the page limits outlined below.

5.B. ESI Research Plan Component Sections

Full application instructions are provided below:

Research Plan:
- The Research Plan is limited to 10 pages and should be focused on verifying a hypothesis; appendices and additional supportive materials are permitted, but limited to 5 additional pages.
- The Background and Significance section must specifically address the approach proposed and must provide a sound rationale.
- The Preliminary Studies section is not required, however, if preliminary data are available to support the rationale for the proposed study, they should be highlighted.
- The Research Design and Methods section must identify a single hypothesis or issue to be addressed.

The plan should also:
- Describe any potential cross-disciplinary collaborations (collaborations are strongly recommended/encouraged; this is included in the 10 page limit).
- Signed letters of collaboration and agreements addressing the proposed research, where appropriate, should be included as a PDF attachment; these letters do not count toward the Research Plan 10 page limit.

Bibliography and References Cited: Limit the number of cited references to 25 and include the title of the reference cited. Note that the ten page limit for the Research Plan does not include the Bibliography and References Cited section.

Career Development and Mentoring Plan:
- The ESI applicant should submit a 2 page overview of their career development and mentoring plan.
- The plan should summarize his/her prior research and training, describe a commitment to devote at least 50% effort to the research and career development/mentoring activities proposed herein, and outline a plan, if applicable, to pursue field placement at an NHP center and/or clinical site for a portion or all of the proposed award period, any additional didactic research training, etc. Cohort 1 scholars applying for an extension should include justification on how this award would support their existing project and career development plan.

**Statements by Mentors/Supervisors**

- Letters of reference should be submitted by each proposed mentor. If the ESI candidate proposes two mentors that do not hail from their primary institution, a third letter is required from a supervising research director or mentor that endorses the ESI applicant’s plan including any proposed time away from the primary institution as part of a field placement experience outlined in the career development and mentoring plan.

**Biographical Sketches:** A limited biographical sketch is required for the ESI Applicant and mentors ONLY. The biographical sketch may not exceed 2 pages per investigator. List no more than 15 publications per individual.

Potential applicants are strongly encouraged to phone the Program Contact listed in Section VII “Agency Contacts”, of this RFA to discuss the responsiveness of their proposed work scope.

**5.C. Resource Sharing Plan(s)**

The HVTN and CHAVI adhere to NIH policies regarding sharing of research resources using NIH resources. NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. Selected applicants will participate in the CHAVI resource sharing plan by becoming members of the CHAVI Research Consortium. (for more information, refer to http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm).

(a) **Data Sharing Plan:** Investigators are expected to include a brief 1-paragraph description of how research data will be shared with the CHAVI Statistical and Data Management Center, or explain why data-sharing is not possible. Applicants are encouraged to discuss data-sharing plans with their CHAVI program contact (see Data-Sharing Policy or http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html).

(b) **Sharing Model Organisms:** Regardless of the amount requested, all applications where the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organisms and related resources, or state appropriate reasons why such sharing is restricted or not possible. See Sharing Model Organisms Policy, and NIH Guide NOT-OD-04-042.

(c) **Genome-Wide Association Studies (GWAS):** Regardless of the amount requested, applicants seeking funding for a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. A genome-wide association study is defined as any study of genetic variation across the entire genome that is designed to identify genetic associations with observable traits (e.g., blood pressure or weight) or the presence or absence of a disease or condition. For further information see Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (go to NOT-OD-07-088, and http://grants.nih.gov/grants/gwas/).
5.D. Foreign Applications (Non-Domestic [non-U.S.] Entities)

Indicate how the proposed project has specific relevance to the mission and objectives of the NIH and has the potential for significantly advancing the health sciences in the United States.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process.

2. Review and Selection Process

Applications that are complete and responsive to this RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by CHAVI with the HVTN and in accordance with NIH peer review procedures (http://grants1.nih.gov/grants/peer/), using the review criteria stated below.

As part of the scientific peer review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific and technical merit will be discussed and assigned a priority score;
- Receive a written critique; and
- Receive a second level of review by the CHAVI Scientific Leadership Group and the HVTN Scientific Steering Committee.

The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review.
- Merit of the proposed career development/mentoring plan
- Availability of funds.
- Relevance of the proposed project to program priorities.
- Research portfolio balance across the different scientific priorities addressed in the proposals solicited through this RFA. Thus CHAVI reserves the right to make awards to cover significantly different concepts as a mechanism to achieve balance through this pilot initiative.

In their written critiques, reviewers will be asked to comment on each of the following criteria in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, and weighted as appropriate for each application. Note that an application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a meritorious priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

**Significance:** Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? How will the link between the NHP models and its clinical application be strengthened? If the applicant is attempting to verify a novel hypothesis, is it critical for the field that the hypothesis be verified or disproved? Is the significance of the hypothesis or problem clearly addressed in the application? Does the project promise to generate data that will ultimately support future research in this area?

**Approach:** Are the conceptual design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? If proposed as an ancillary study to an existing
project, do the experimental methods adequately account for the parent research protocol? Does the applicant acknowledge potential problem areas and consider alternative tactics? Does the approach taken succinctly address either a rationale for developing a hypothesis, or identify a problem for which solutions are sought? Will the approach taken provide a reasonable expectation of an outcome within the duration of the proposed timeline?

Innovation: Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

Investigators: Reviewers recognize that an individual with limited research experience is less likely to be able to prepare a research plan with the breadth and depth of a more experienced researcher. Considering the proposed mentorship and mentorship plan, are the ESI applicant and other key personnel appropriately trained and well suited to carry out this work? Does the proposed research team bring complementary and integrated expertise to the project (if applicable)?

Environment: Do(es) the scientific environment(s) in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support? Is there evidence of strong, appropriate, cross-disciplinary collaborations?

2.A. Additional Review Criteria

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the rating:

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. Refer to the guidelines for the “Human Subjects Sections” of the PHS398 Research Plan component of the SF424 (R&R).

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated. Refer to the guidelines for the “Human Subjects Sections” of the PHS398 Research Plan component of the SF424 (R&R).

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the adequacy of the plans for their care and use will be assessed. Refer to the guidelines for the “Human Subjects Sections” of the PHS398 Research Plan component of the SF424 (R&R).

Biohazards: If materials or procedures are proposed that are potentially hazardous to research personnel and/or the environment, determine if the proposed protection is adequate.

2.B. Additional Review Considerations

Budget and Period of Support: The reasonableness of the proposed budget and the appropriateness of the requested period of support in relation to the proposed research may be assessed by the reviewers. The priority score should not be affected by the evaluation of the budget.

Applications from Foreign Organizations: Whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental
conditions in other countries that are not readily available in the United States or that augment existing U.S. resources will be assessed.

2.C. Resource Sharing Plan(s)

When relevant, reviewers will be instructed to comment on the reasonableness of the following Resource Sharing Plans, or the rationale for not sharing the following types of resources. However, reviewers will not factor the proposed resource sharing plan(s) into the determination of scientific merit or priority score, unless noted otherwise in the RFA. Program staff within the institute/center will be responsible for monitoring the resource sharing.


3. Anticipated Announcement and Award Dates

Awards letters will be distributed by e-mail no later than April 1, 2011.

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, HVTN and CHAVI will share comment sheets with the ESI Applicant via email. If the application is under consideration for funding, additional information may be requested by CHAVI, as needed.

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization. The NoA signed by the finance officer at CHAVI is the authorizing document. Once all administrative and programmatic issues have been resolved, the NoA will be generated via email notification from the awarding component to the grantee business official.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs. See Section IV.4., Funding Restrictions.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the NoA. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities.

3. Reporting

Awardees will be required to submit to the CHAVI the Non-Competing Continuation Grant Progress Report (PHS 2590) annually and financial statements.

A final progress report, invention statement, and Financial Status Report are required when an award is relinquished when a recipient changes institutions or when an award is terminated.
Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Please contact:

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