Epidemic Interventions Demonstration Project Research Award

2011 Special Call for Applications
One-Time Special Opportunities Award

The California HIV/AIDS Research Program at the University of California requests proposals for research to test and evaluate innovative approaches toward implementation of interventions, as described below, intended to improve health outcomes and curb the HIV epidemic in California. This initiative focuses on two prevention intervention approaches for which there is evidence of efficacy in certain settings.

Proposals must address both of the following intervention approaches:

1. Testing and Linkage to Care plus Treatment (TLC+). Approaches to strengthening and improving HIV testing among high risk populations, and efforts toward establishing a seamless system to link HIV positive persons to continuous and coordinated quality care and services including antiretroviral treatment.
2. Pre-Exposure Prophylaxis (PrEP). Approaches to engaging high-risk HIV-negative persons in prophylactic antiretroviral medication, prevention counseling, and other appropriate services.

The intention is to fund demonstration projects that combine both intervention approaches such that enrollees will be directed, through a triage approach, to the appropriate intervention based on serostatus. For the TLC+ arm of the demonstration project, funding will support efforts in outreach, data collection and integration with existing care and service programs, and the augmentation of the effectiveness of such programs, but will not cover the cost of antiretrovirals, or the cost of existing care and service efforts. For the PrEP arm of the demonstration project, funds may be used to provide outreach, data collection, prevention counseling, and medical monitoring services to participants as they directly relate to the project. For this arm of the study, Gilead Sciences will provide prophylactic antiretroviral medication for study participants, pending final approval of associated protocols. The results of this research will advance the body of knowledge as applied to the effective implementation of these evidence-based interventions in California as part of focused efforts to have a significant impact on incidence and prevalence, as well as improving quality of life for those living with HIV.

Important Dates

- September 13, 2011: Release of the Call for Applications, application instructions posted.
- September 27, 2011: Prospective Applicant Webinar (3:00 PM Pacific Time). See the CHRP Website for details.
- October 11, 2011: Letters of Intent due before noon, Pacific Time.
- November 17, 2011: Applications due before noon, Pacific Time.
- March, 2012: Funding notification
- April 1, 2012: Award start date

Additional information is available in the *General Information* section later in this document.

For more information about the California HIV/AIDS Research Program at the University of California, please visit the Program Web Site.

Research Rationale and Framing

Testing and Linkage to Care plus Treatment (TLC+): CHRP, in collaboration with the California Council for Local AIDS Directors (CCLAD), co-sponsored a TLC+ think tank meeting on May 18, 2010 to address the benefits and challenges of TLC+ implementation in California. This intervention approach, where effective testing is linked to the immediate availability of a range of care and services including antiretroviral therapy, is increasingly compelling based on the confluence of several very hopeful research results. These results have strongly suggested that, with effective implementation, a coordinated, contemporaneous, and multi-faceted intervention can both improve long term health and quality of life outcomes to those who are diagnosed, while also decreasing transmission levels sufficiently to have a significant impact on incidence and ultimately prevalence of infections. The approach also has the potential to increase cost effectiveness, both through the prevention of new infections, and increasing the effectiveness of systems of delivery of care and services through enhanced coordination and collaboration. The advent of Highly Active Anti-Retroviral Therapy (HAART) has markedly and steadily improved the prognosis for People Living with HIV/AIDS (PLWHA) over the past 15 years. Over this time, the greater availability of improved drugs and regimens has led to both reduced viral loads and decreased treatment-associated morbidities. In addition, evidence is increasing that earlier treatment provides long term health benefits to the individual that generally outweigh the drawbacks. This includes achieving a lower long term viral load and higher CD4+ T-cell counts, which correlate with less severe long term morbidities, the importance of which is growing as the HIV positive population ages. This has led to a growing shift toward early treatment in the provider community. At the same time, epidemiologic studies of populations with a high prevalence of adherent drug therapy strongly suggest a striking concurrent benefit: a significantly decreased rate of transmission due to lowered individual and community viral load (cVL). A recent study funded by CHRP showed that cVL in San Francisco declined significantly between 2004 and 2009, and was associated with reductions in newly diagnosed and reported HIV cases. In addition, improvements in the technology of testing and diagnosis has both decreased the detection window (the amount of time between infection and the ability to detect the infection), and decreased the time to results, such that accurate results are often available during the same visit for sample collection and analysis, helping to prevent a loss to follow up. Taken together, these technological improvements, shifts in treatment modalities, and epidemiological effects on disease dynamics, make TLC+ a highly compelling approach to help curb the epidemic.

Pre-Exposure Prophylaxis (PrEP): Building on existing evidence that antiretroviral treatment among HIV+ persons can decrease the transmission of HIV from infected to uninfected individuals, a recent international intervention trial, called iPrEx, has demonstrated that antiretrovirals, combined with standard prevention practices, can have a significant protective effect among HIV negative men who have sex with men, provided that adherence to the drug regimen is high. Efficacy was 47% overall among the trial participants, but rose to 73% among the subset who reported pill usage on 90% or more of the days in the study. Following the release of the promising results from the iPrEx study, a separate trial examining PrEP among women, called FEM-PrEP, was halted early (April 2011) when it was determined that it was insufficiently powered to show significant efficacy. More recently, however, encouraging results have been reported for two trials examining PrEP in at-risk heterosexuals. In the TDF2 study, a 63% reduction was observed in an African study population of heterosexual men and women. In the Partners PrEP study, a 73% reduction was observed in serodiscordant couples.

These studies taken as a whole suggest that, if implemented effectively in groups at high risk of infection, this intervention strategy has a strong potential to decrease HIV incidence. However, some concerns have been raised regarding the possible use of PrEP, including the benefits versus the cost of Truvada (Tenofovir and Emtricitabine, the two-drug combination used in these studies), community acceptability and willingness to participate, potential adverse effects including possible increases in high risk behavior, levels of adherence to the drug regimen and its impact on resistance, and others. Additional research is clearly needed to better assess the challenges and opportunities presented by this intervention approach in California.

Purpose

These grant funds are specifically intended to support innovative approaches and evaluate targeted modifications and enhancements to new or existing systems of testing and care for populations disproportionately affected by HIV. The approaches, modifications and enhancements will likely have a significant impact on the effective implementation of TLC+ and PrEP in areas and populations where the intervention(s) may be expected to have a measurable impact on the spread of HIV.

It is critical to stress that for the TLC+ arm of the studies, the initiative will **not** cover the cost of antiretrovirals, or the cost of existing care and service efforts, but instead will help fund and evaluate innovative approaches and enhancements (outreach, testing, triage, linkage to care, and systems to enhance retention in care and access to treatment) designed to substantively inform the use of TLC+, if significant feasibility is indicated. For the PrEP arm of the studies, Gilead Sciences will provide prophylactic antiretroviral medication for study participants, pending final approval of associated protocols, while CHRP funds may be used to provide outreach, testing, triage, prevention counseling, and medical monitoring and follow-up services to participants as they directly relate to the project.

Eligibility Requirements

***Institutional Eligibility*:** Institutions must be nonprofit 501(c) (3) community-based organizations, academic institutions, non-profit health service providers, or local health jurisdictions based in California. Also, demonstration projects funded through this initiative must exclusively serve persons in California. In order to achieve the research goals of the project, institutions must meet all eligibility requirements listed below.

Please note that institutions may apply for this program as a single Institution or as a Lead Institution of a Consortium of agencies. If applying as part of a Consortium, a Lead Institution must be identified to submit the application and receive grant funds, and all participating agencies must be identified in the application. In the case of a Lead Institution and Consortium, the Consortium as a whole can meet the requirements.

At least one of the applicant institutions, either the Lead Institution or a partner, must be a non-profit 501(c) (3) community-based organization or a local health jurisdiction based in California.

Investigator Eligibility: There must be one Project Director identified as the lead investigator responsible for the proposed project. The Project Director must have Principal Investigator status at the lead institution named in the application, and must devote a minimum of 10% effort to this project. For those applying as a Lead Institution and Consortium, a co-Project Director from each

consortium member must be identified. Other key investigators should be identified from both the lead and/or the partnering institutions.

Eligibility Requirements for the TLC+ Arm of Demonstration Projects:

- **A. Currently provide appropriate services comprising the basic components of TLC+ such as HIV testing, care and treatment.**
- **B. Enrollment Capacity**
  1) Demonstrated potential to establish or enhance outreach capacity to allow for the ability to locate, test, link to care, and treat traditionally hard-to-reach high-risk individuals.
  2) The overall enrolled study population for both study arms must be comprised of at least 40% individuals from ethnic minorities, with African Americans representing at least 15% of the total study population. Enrollment of a higher percentage of African Americans, if possible, is strongly encouraged.
  3) A sufficient sample size to provide statistical power to evaluate the proposed interventions and enhancements. Applicants must provide statistical power calculations to justify the proposed sample size.
- **C.** Capacity, including infrastructure, to establish or augment linkages to care and services and to follow and enhance continuity of care for participants.
- **D.** Availability of antiretroviral treatment for participants.
- **E. Have a demonstrated capacity to evaluate the effectiveness of all proposed approaches, targeted modifications, or enhancements. This includes the examination of psychosocial factors influencing study participant choices, including reasons for refusal, missed appointments, lack of continuity in care, loss to follow-up, etc.**

Eligibility Requirements for PrEP Arm of Demonstration Projects:

- **A. Current capacity for the following services**
  1) Regular medical monitoring of those enrolled in the study.
  2) Appropriate testing, prevention services, counseling, and health education, to be offered to all individuals who meet enrollment eligibility criteria.
- **B. Enrollment Capacity**
  1) Demonstrated potential to establish or enhance outreach capacity to allow for the ability to locate and test individuals at high risk for contracting HIV and to offer PrEP to those with confirmed negative serostatus.
  2) The overall enrolled study population for both study arms must be comprised of at least 40% individuals from ethnic minorities, with African Americans representing at least 15% of the total study population. Enrollment of a higher percentage of African Americans, if possible, is strongly encouraged.
  3) Plans to achieve enrollment of a sufficient sample size to provide statistical power to evaluate the proposed interventions and approaches. Applicants must provide statistical power calculations to justify the proposed sample size.
- **C. Have a demonstrated capacity to evaluate the effectiveness of all proposed approaches. This includes the examination of psychosocial factors influencing study participant choices, including reasons for refusal, non-adherence, missed appointments, and loss to follow-up, etc.**

Proposed Use of Funds

1. ***Allocation of Funds for Evaluation:*** As evaluation will be a crucial component of all demonstration projects, at least 15% of the first year budget must be allocated for evaluation activities, increasing to at least 20% for year two, and at least 25% for years three and four.

2. ***Funding of direct participant services***. For the TLC+ arm of demonstration projects, funding will support the Institutions' efforts in outreach, data collection and integration with existing care and service programs, and the augmentation of the effectiveness of such programs, but will not cover the cost of antiretrovirals, or the cost of existing care and service efforts. While funds cannot be used for existing patient care and services, funds can be used to support staff providing enhanced and innovative outreach, testing, triage, patient care and prevention activities needed for developing, improving, and evaluating the demonstration project activities. For the PrEP arm of demonstration projects, funding will support the institutions' efforts in outreach, testing, data collection and integration with existing or enhanced care and service programs, and the augmentation of the effectiveness of such programs, but will not cover the cost of antiretrovirals. Additionally, for the PrEP arm of demonstration projects, funds may be used to provide prevention counseling and medical monitoring services to participants as they directly relate to the project; prophylactic antiretroviral medication will be provided by Gilead Sciences, contingent upon final approval of protocols.

3. ***Performance-Based Renewal:*** Grantees will be subject to funding renewal on an annual basis contingent upon adequate performance, using metrics established with CHRP before the receipt of funding for the year. It is expected that outreach and enrollment will be a principal component of the first formal performance evaluation. Applicants will submit a detailed projected evaluation plan that may be modified during the course of the study in collaboration with CHRP.

4. ***Dissemination****:* Proposals should describe plans for dissemination of findings through print or online publications, creation and dissemination of training materials, and through presentation of findings to local, statewide, and national planning bodies and at meetings and conferences.

5. ***Collaborative Meetings:*** Projects approved for funding must adhere to the aims of the initiative and work collaboratively on study implementation to ensure that the goals of the research initiative and the scientific validity of the project are maintained, and that challenges encountered during implementation that could compromise achievement of intended outcomes are adequately addressed. To meet this requirement, grantees will attend regularly scheduled collaborative meetings with CHRP over the four-year grant period and participate in at least one annual site visit. Grantee expenses for these meetings will be covered by the CHRP award, and meetings will be jointly organized by the grantees and CHRP.

6. **Community Advisory Board (CAB):** Proposals must describe plans to recruit and convene a local community advisory board on a periodic basis meeting a minimum of four times per year to provide advice and community input, and to address concerns regarding plans, protocols, outcomes, and dissemination.

Award Amounts, Duration, and Requirements

1. The project start date is April 1, 2012, and the project period will span up to 48 months (4 years), ending March 31, 2016.
2. For each demonstration project, it is anticipated that the **annual** direct costs will be up to $1,200,000 per year for four years, contingent on available funding ($4.8 million maximum total direct costs over the entire four-year period). These costs are expected to cover both the TLC+ and PrEP arms of the demonstration project, in the areas outlined above, and do not include the costs of antiretroviral medication for either arm.
3. Non-University of California institutions are eligible for additional indirect costs of up to 25% of total eligible direct project costs, or at the rate established for the institution through a U.S. Department of Health and Human Services (DHHS) negotiated indirect cost rate agreement (or other similarly established rate), whichever is lower.
4. If multiple organizations apply as a Consortium, the Lead Institution will submit the application with the other Consortium members included as subcontractors.
5. CHRP anticipates funding up to 3 demonstration project awards, contingent upon receipt of a sufficient number of meritorious[1] applications. It is the intent of CHRP to fund at least one meritorious Institution or Lead Institution and Consortium each from Northern and Southern California.
6. Grants are one-time, non-renewable grants.
7. CHRP reserves the right to reallocate research funds for other purposes if there are no institutions that meet qualifying standards for research funding under this initiative.
8. Grantees will be subject to funding renewal on an annual basis contingent upon adequate performance, using metrics established with CHRP before the receipt of funding for the year.
9. Availability of funds is contingent upon receipt of a sufficient allocation to CHRP from the State of California.

Merit Review Criteria

Reviewers will evaluate applications for:

1. Strength and feasibility of concept, approach and methods.
2. Experience and capacity to collect relevant data and evaluate the demonstration project, including structural and psychosocial factors influencing the choices of study participants.
3. Qualifications of the investigators and capacity and experience of the institution(s) to carry out the research. It is expected that expertise in clinical sciences will be represented among the investigators in order to monitor and evaluate the medical and clinical outcomes of the interventions. In addition, it is expected that expertise in the social and behavioral sciences will be represented among the investigators in order to assess structural and psychosocial factors that may affect the feasibility and acceptability of these intervention approaches.
4. Documentation of meeting the eligibility requirements outlined in this Call for Applications.
5. Capacity and readiness to implement proposed activities.

[1] 'Meritorious' is defined by an overall merit score in the very good, excellent, outstanding or exceptional range.

6. Qualifications and experience in providing various components of a robust TLC+ system and capacity to develop appropriate approaches for PrEP implementation.
7. Feasibility of the proposed plan to provide actionable information for the improved and practical implementation of TLC+ and PrEP in key populations in California.
8. Proven ability to recruit and enroll populations most highly impacted by HIV. The overall enrolled study population for both study arms must be comprised of at least 40% individuals from ethnic minorities, with African Americans representing at least 15% of the total study population. Additional consideration will be given for proposed proven ability to recruit and enroll African Americans at levels higher than the minimum of 15%. Capability to achieve stated accrual goals.
9. The capacity to form and continually engage an effective and representative community advisory board.
10. Capability and proposed plans for the timely dissemination of outcomes and results through the scientific literature, conference presentations, and lay communications and media.

General Information

Application Cycle Timeline: *Letter of Intent and Application deadline is 12:00 noon Pacific Time (3:00 p.m. Eastern Time). All LOI and application materials will be submitted electronically.*

- September 13, 2011: Call for Applications Release Date.
- September 27, 2011: Prospective Applicant Webinar (3:00 PM Pacific Time). See the CHRP Website for details.
- October 11, 2011: Letters of Intent (LOI) submission deadline. It is important to follow the instructions.
- November 17, 2011: Application submission deadline.
- March, 2012: Funding notification
- April 1, 2012: Award start date

Prospective Applicant Webinar: Information for participation in the Prospective Applicant Webinar will be posted on the CHRP website by September 20, 2011. The webinar is scheduled for September 27, 2011 at 3:00 PM (Pacific Time). Understanding of the intent of the award and the application review process is central to the success of applicants. Participation by prospective applicants is strongly encouraged. During this meeting, program representatives will answer questions about the application and review process.

How to Apply and Required Letter of Intent

A Letter of Intent (LOI) is required for all Demonstration Project Research Award applications. LOIs will be evaluated by CHRP for responsiveness to the Call for Applications to ensure that all full applications will qualify to be forwarded for peer review. Specific instructions for submitting a Letter of Intent are available from the CHRP web site. *It is important that LOI submissions follow these instructions*. LOIs must be submitted electronically before 12 noon Pacific Time (3 p.m. Eastern Time), October 11, 2011. Applicants with approved LOIs will be notified by e-mail, and will then have access to materials to prepare a full application. LOIs will be approved as they are received; therefore, earlier submission will potentially provide earlier access to the full application materials for approved LOIs. *NOTE: It is recommended that applicants review the instructions and the LOI submission web pages as soon as possible in order to allocate sufficient time for the completion of the process before the deadline*.

Applications are due on November 17, 2011 before noon, Pacific Time, and will also be submitted electronically. Application instructions and guidelines, templates and forms will be available upon approval of the LOI.

Contact Information:
For general questions regarding letter of intent or application preparation and submission, contact:

Research Grant Programs Office, Contracts and Grants Unit:

RGPOGrants@ucop.edu
510/987-9386

To obtain guidance or direction on the suitability of a proposed project for this funding opportunity, or for scientific questions regarding application preparation, contact:

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California HIV/AIDS Research Program

The California HIV/AIDS Research Program (CHRP; formerly UARP) at the University of California provides funding for the support of merit-reviewed HIV/AIDS-related research to be conducted at universities, non-profit research institutions and community organizations throughout California. The program's mission is to support excellent, timely, and innovative research that is attentive to the needs of California and will accelerate progress towards prevention and a cure for HIV/AIDS.

How to Contact CHRP

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