CFAR Supplement Announcement in HIV/AIDS – FY2018

The CFAR Program at the National Institutes of Health (NIH) invites applications from currently funded CFARs that are eligible for administrative supplements. CFARs in the last year of their funding cycle or in a bridge period are NOT eligible to apply. Each CFAR can submit a maximum of four supplement applications. There are six scientific areas of interest in total.

Supplement awards are for up to one year with maximum funding per application of up to $150,000 Direct Costs, not including third party indirect costs.

Purpose and Scientific Areas of Interest

The purpose of this administrative supplement opportunity is to **support innovative research from basic science through implementation research** that address key gaps in HIV/AIDS and will advance the field. This opportunity should build research capacity and be consistent with the recent NIH HIV/AIDS research priorities (NOT-OD-15-137).

Basic Research on HIV Infection and Persistence

In recent years the balance between basic and translational HIV research has shifted heavily towards the translational side, with increased focus on prevention modalities and curative strategies. While this is a natural progression given the maturity of the field, it is important to maintain a strong basic research foundation to fuel future innovation and discovery. The goal of this topic is to bolster basic research in new and emerging areas of HIV biology and immunology and leverage innovative technologies to address remaining scientific gaps in our understanding of either HIV infection or HIV persistence during long-term ART, including virus-host interactions and both innate and adaptive immune responses.

Supplement requests addressing one or more of the following topics will be of greatest interest:

- Mechanisms and host factors involved in post-fusion intracellular transit, uncoating, and nuclear import of the HIV pre-integration complex
- The role of novel, biologically active host and/or viral RNA species, RNA modifications, or extracellular vesicles in HIV infection or persistence
- Application of innovative single-cell analysis approaches to the study of HIV infection, persistence, or host immune response
- Utilization of innovative technologies for intracellular, intravital, or whole-body imaging to study HIV infection or persistence
- Virologic or immunologic mechanisms or predictive markers associated with spontaneous control of HIV or SIV observed in some individuals after ART interruption
- Novel assays for monitoring HIV persistence and predicting or detecting the earliest stages of viral rebound including the use of oral tissues and fluids

Infant Immunity for HIV Vaccine Development

The development of the fetal immune system is an area of great interest especially since new tools have been developed for interrogation before or at birth. It is also important to understand the impact of maternal immunity on the fetus during infection. Information on the fetal exposure to HIV before ARVs are delivered is especially important since the virus targets immune cells. Knowledge of the maternal and fetal response to HIV in utero would be helpful in the development of a vaccine and would inform our understanding of the development of the immune system.

Responsive studies could include, but are not limited to:

- Research on the timing, development and maturation of immune system cells and cytokines, in HIV infected or exposed uninfected infants
- Studies of fetal innate and cellular component development and susceptibility during maternal/placental HIV infection
- In HIV infection, what really passes the placenta? Is the response enhanced or dampened?
- Studies to examine the maternal seeding and evolution of the fetal microbiome in infection/health and the impact on the developing brain
- Monitoring vaccine response or immune status in the oral cavity

Studies to Delineate Sex Differences in the Incidence of Heart, Lung, Blood, and Sleep Comorbidities in People Living with HIV

In recent years, sex has become a well-recognized biological variable. In fact, sex is defined as an independent risk factor for the development of a number of heart, lung, blood, and sleep (HLBS) diseases and has been found to play a role not only in disease prevalence but also in disease symptomatology, disease progression, and treatment outcomes. For example, women have a higher prevalence of autoimmune disease, non-obstructive coronary artery disease, and hereditable pulmonary arterial hypertension than men, while males are at a higher risk for developing atrial fibrillation and exhibit a doubled risk of myocardial infarction. In terms of HIV infection, it is well-known that sex differences exist in rates of HIV acquisition, immune responses to infection and protective immune correlates associated with HIV vaccination, and HIV disease progression. To date, very few studies have been conducted to determine sex differences in the incidence of heart, lung, blood, and sleep comorbidities in the context of HIV infection despite overwhelming evidence indicating that people living with HIV (PLWH) are at a much higher risk of developing these comorbidities in general. To inform best treatment practices and reduce disease burden in PLWH, it is of considerable interest to identify and characterize sex differences in the incidence of HLBS comorbidities in the context of HIV infection. Supplement requests addressing one or more of the following HIV-related HLBS comorbidities will be of greatest interest: heart failure and/or coronary artery disease, chronic lung disease (including tobacco use-induced lung disease in PLWH), sleep apnea and other sleep-related disorders, and platelet and endothelial cell dysfunction.

Responsive studies (utilizing existing cohort data and/or pilot, ancillary studies) could include but are not limited to:

- Investigations into the incidence rates of HLBS comorbidities in the context of HIV infection stratified by sex
- The identification of sex-specific risk factors that increase the likelihood of developing HIV-related HLBS comorbidities
- Investigations into the effects of HLBS comorbid conditions on HIV disease progression (evidenced by $CD4^+$ T cell counts, viral loads, ART failure, progression to AIDS, etc.) in PLWH stratified by sex
- Sickle cell disease

Formative Research on Behavioral Aspects of Novel Biomedical HIV Prevention and Treatment Regimens

Although current oral drug regimens for HIV prevention and treatment are highly efficacious, there is significant work to be done to optimize uptake and adherence. To help overcome these barriers,

researchers are advancing novel products, long-acting drug regimens and drug delivery systems for HIV prevention and treatment, including long-acting injectable PrEP and ART, sustained-release drug delivery systems, broadly neutralizing monoclonal antibodies, and prime-boost vaccines. Although these methods reduce the burden of daily pill taking, they have other features that may lead to new uptake, adherence, and use challenges. Greater input from end-users and prescribers could lead to the advancement of HIV prevention and treatment technologies that are optimally designed for maximum uptake and adherence and could help prepare the way for any future implementation of long-acting regimens.

Responsive studies could include, but are not limited to:

- Studies to identify product attribute and drug delivery system preferences, and to understand which products and delivery systems are preferred by whom, with which partners, in which contexts
- Studies to understand the trade-offs people are willing (and not willing) to make for their preferred products and delivery systems
- Studies to understand how to optimize or combine existing delivery systems
- Qualitative studies designed to conceptualize novel products and delivery systems not currently in the pipeline that align with end-user preferences and sexual scripts in key populations
- Studies to understand social, contextual and structural influences (e.g., partners, family, sexual and social network, providers, and community) on drug regimen and delivery system preferences
- Studies to investigate patient, provider, and healthcare system delivery factors that may facilitate or impede implementation of HIV prevention and treatment products with non-daily dosing schedules
- Studies to develop behavioral, care, and systems interventions that will facilitate patient use and healthcare delivery of HIV prevention and treatment products with non-daily dosing schedules

The Evolving Opioid Epidemic and its HIV Consequences

The opioid epidemic in the US appears dynamic with many different components and considerations. Continuing high rates of opioid overdose death in rural areas have been joined by increased overdose deaths in urban centers among long-term people who inject drugs (PWID) and non-injection drug users. Synthetic opioids and their widespread availability seem to be fueling these epidemics of overdose and there is some evidence that urban, suburban, and rural opioid epidemics may have increasing areas of overlap and there is potential for newer opioid epidemics to be joined with established HIV epidemics among PWID and users of other drugs. Current trends increase the likelihood that the newer opioid epidemics may see more HIV cases and suggest more attention needs to be given to the needs of long-term drug users living with HIV to reduce the potential consequences of opioid use, including overdose and problems adhering to HIV care. The complexity of the current opioid epidemics may benefit from cross-CFAR collaboration and the inclusion of colleagues from AIDS Centers funded by NIDA (e.g., CDUHR/NYU) and NIMH (e.g., UCSF/CAPS, Yale/CIRA, UCLA/CHIPTS, CAIR/MCW, PMHARC/Penn, HIV Center/Columbia). Multidisciplinary investigator teams working together with clinicians, local community stakeholders, and public health officials are encouraged. The application should include a description of collaborative activities, including any prior relationships with these collaborators.

Projects should be responsive to the opioid epidemic and its recent evolution with particular consideration of preventing HIV and other infectious disease consequences. There is a continuing need to implement evidence-based interventions such as integrated drug/HIV treatment, needle/syringe services, and overdose prevention, particularly outside of urban areas with established opioid-driven HIV epidemics. Prevention of opioid injection in established drug using populations is needed. There needs to be a better understanding of how current opioid use trends may intersect with populations of long-term drug users living with HIV, as well as other risk groups. Note that projects related to needle exchange and syringe services need to be consistent with US Department of Health & Human Services policy: https://www.aids.gov/pdf/hhs-ssp-guidance.pdf.

Responsive studies could include, but are not limited to:

- Addressing knowledge gaps regarding HIV transmission among PWID, including identification of possible transmission networks that connect opioid epidemics in rural areas to established HIV epidemics
- Analysis of phylogenetic HIV transmission networks among PWID exploring spread between rural and historical urban opioid epidemics or how PWID cases may reflect networks that include other risks
- Rapid policy and epidemiology assessments that can inform implementation of evidence-based practices (e.g. PrEP, syringe services)
- Identification of promising approaches for implementing evidence-based infectious disease prevention interventions (e.g., PrEP) in rural or other non-urban areas
- Development of interventions to prevent opioid uptake among long-term drug users living with HIV
- Addressing the impact of pain management practices on the development of opioid use/misuse among PLWH

Implementation of Evidence-Based HIV Interventions and Treatments for Health Disparity Populations

There are a variety of evidence-based interventions and treatments to prevent HIV infection/transmission, and to achieve viral suppression in individuals infected with HIV. However, significant racial/ethnic, socioeconomic, and geographic disparities in new HIV infections and attainment of viral suppression persist in the US. Health disparity populations in the US still often lack access to culturally appropriate interventions and services, and service providers that serve these populations may lack resources to offer the most efficacious interventions and services. Thus, there is considerable need to conduct research regarding the implementation of evidence-based HIV interventions and treatments for health disparity populations.

The supplement will support pilot and feasibility studies to prepare for implementation science research proposals to understand how to best deliver evidence-based interventions and services for targeted health disparity populations, which include racial/ethnic minorities, socioeconomically disadvantaged populations, underserved rural populations, and sexual and gender minorities. This initiative targets behavioral and health services interventions to prevent HIV infection, increase engagement and retention in HIV care, and increase adherence to ART.

Responsive studies could include, but are not limited to:

- Systematic review and evaluation of adapted evidence-based interventions/services tailored to be culturally appropriate, acceptable, or feasible in settings that serve health disparity populations
- Systematic review and evaluation of strategies to increase uptake of evidence-based interventions or treatments such as PrEP or ART by health disparity populations.
- Feasibility study to guide protocol development of comparative effectiveness research that would assess which evidence-based interventions/services in real-world settings are most effective for targeted health disparity populations
- Feasibility study to provide evidence and data to support the design and implementation of optimization research that identifies which elements of multi-component interventions/service models may be most effective or cost-effective in low-resource settings or for particular health disparity populations

Eligibility

Project leaders for all scientific areas of interest are restricted to early career investigators who have never received an R-series research grant and to established investigators in non-HIV fields who have never received an NIH research award for HIV/AIDS studies. Post-doctoral fellows are eligible to apply if they will assume a faculty position by the time the supplement project and funding begins.

Studies that are a continuation of previously funded CFAR supplements or funded NIH applications that do not address new specific aims are not eligible for funding under this announcement. Additionally, a proposed supplement application that is linked to a proposed application not yet funded is not eligible for funding under this announcement.

Application Instructions

Requests submitted in response to this opportunity must use the PHS 398 forms (rev. 1/2018) and include the elements in the request packet as described below. Applicants must submit each application as an e-mail attachment, in one file, in PDF format; however, the signature of the institutional official must be clearly visible. Font size restrictions apply as designated within the PHS 398 instructions

1) **Cover Letter** – Citing this Supplement Announcement, a request for an Administrative Supplement, and the following information:

- CFAR Principal Investigator and Supplement Project Director names
- Parent grant number and title
- Scientific area of interest for this supplement request
- Amount of the requested supplement
- Name and title of the authorized institutional official
- Phone, email, and address information for the PI, the PD and the institutional official

The cover letter must be signed by the authorized organizational representative/institutional official.

2) **PHS 398 Form Page 1** (Face page) (MS Word PDF) – Provide requested information as follows:

- The title of the project (Box 1) should be the title of the parent award and a descriptive title of the supplement application.
- The scientific area of interest should be cited under title in Box 2, and the “yes” box should be checked.

- Enter name of CFAR PI and the name of the project director. (Example: Dr. Bill Jones (CFAR PI) and Dr. John Smith (Project Director).
- The remaining items on the face page should be filled out in accordance with the PHS 398 application instructions.

3) **PHS 398 Form page 2**

Note: The project "summary" is that of the administrative supplement, not the parent grant. All other information requested on Form Page 2 should be provided.

4) A **brief proposal** describing the request (with parts 4a and 4b **not exceeding five pages** in total), should include:

a. An introduction that clearly states the **scope of the overall request,** the anticipated contribution of the requested supplement, and how the project addresses the NIH HIV/AIDS Research Priorities (NOT-15-137).

b. The **research project plan** should include the background and rationale for the proposed application; a description of the activities to be undertaken, and roles of key staff; expected outcome of these activities; expected follow-up plan upon completion of the supplement; a description of how the supplement and follow-up plan are expected to achieve this outcome ("value-added"); and plans to monitor and evaluate the ability of the activities to achieve the outcome. Most importantly, applicants must clearly indicate how the proposed activities outlined in the supplement requests are expected to lead to development of the stated goals. Mentorship and collaborations must be explained.

c. **Budget** for the supplement with a justification that details the items requested, including Facilities and Administrative costs and a justification for all personnel and their role(s) in this project. Note the budget should be **appropriate for the work proposed** in the supplement request. If funding for travel to a scientific meeting is included, it must be for the early stage investigator and must be for the purpose of presenting data from this supplement award.

   A statement regarding the expenditure of currently available unobligated grant funds of the parent CFAR grant. The CFAR must include a description of the plans to spend remaining funds in order to demonstrate the need for additional funds.

d. **Biographical Sketch** for all new Senior/Key Personnel and for mentors. Use the new biosketch format in MS Word. Please note the personal statement should be related to the CFAR supplement project.

e. **Human Subjects/Vertebrate Animal documentation** (if applicable). Include a current Human Subjects/Institutional Review Board (IRB) or Vertebrate Animals/Institutional Animal Care and Use Committee (IACUC) approval date, if applicable. Otherwise, this information will be required at time of funding. All appropriate IRB and IACUC approvals must be in place prior to the initiation of a project. NOTE: Studies involving clinical trials are not allowed.

f. Further NIH-initiated administrative actions and approvals are required for ALL international studies (NOTE: this also includes the CFAR International Checklist requirement) and any clinical studies deemed above minimal risk or involving vulnerable populations.

g. **PHS 398 Checklist Form** MS Word PDF

i. TYPE OF APPLICATION. Check REVISION box and enter your CFAR grant number;
ii. Applicants must state that all federal citations for PHS grants will be met (e.g., human subjects, animal welfare, data sharing, etc.

h. NO other support. This information will be required for all applications that will be funded. NIH will request complete and up to date "other support" information at an appropriate time after review.

i. NO resource page (unless there are new resources that will be used for this request)

j. NO appendices

k. Submit a letter(s) of collaboration endorsing the proposed request from all substantial participants. For the Evolving Opioid Epidemic and its HIV Consequences topic, a letter of support must be provided from the collaborating stakeholder(s), if applicable.

l. If applicable, please include letters of support for projects requiring access to data, samples, tissues, or etc. Include evidence to support the feasibility of enrollment, including descriptions of prior experiences and yield from research efforts employing similar referral sources and/or strategies for projects involving recruitment of participants.

m. For transitioning post-doctoral fellows, please include a letter from your institution confirming the transition to a faculty position that includes the start date.

Budget and Funding Information

Funding for supplements will be supported by the CFAR NIH co-funding Institutes. The maximum funding allowed per application is $150,000 Direct Costs. Funding for administrative supplements to existing CFAR grants will be available for up to one year in FY2018.

Supplemental funds for these supplements will be provided to the Developmental Core of the CFARs.

How to Apply

This is a one-time announcement.

Do not send applications to the NIH Center for Scientific Review.

Applications must be signed by the authorized institutional official and submitted on or before **May 14, 2018**. If an application is received after that date, it will be returned to the applicant without review.

Applications should be emailed to:

Elaine Wong
National Institute of Allergy and Infectious Disease
Telephone: 240-627-3100
Email: wongelai@niaid.nih.gov

Applicants must submit each application electronically as an e-mail attachment in a single PDF file to the Program Officer; however, the signature of the institutional official must be clearly visible. Files should be named [XYZ] CFAR – [Project PI Last Name] [Indicate topic: Basic/Infant Immunity/Sex

Differences/Behavioral Aspects/Opioid/Health Disparities] [2018]. Example: “University CFAR – Smith Infant Immunity 2018.”

Review Considerations

Upon receipt, applications will be reviewed by the CFAR Program Officers for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to this announcement, the application will be returned without review.

Applications that are complete and responsive to the announcement will be evaluated for scientific and technical merit, and alignment with the NIH AIDS research priorities by an internal NIH review group convened by the NIAID in accordance with standard NIH review procedures.

Review Criteria

The following criteria apply to all applications, unless noted. Reviewers will also examine the appropriateness of the budget, in consideration of the research environment and the supplement request.

1. Evidence that the proposed project will enhance new multidisciplinary collaborations and exert a sustained, powerful influence on HIV/AIDS research;
2. Extent to which the supplement will address scientific gaps and/or development of new strategies which include a variety of scientific disciplines;
3. Adequacy that the strategy, methodology, and analyses are well reasoned and appropriate to accomplish the specific aims;
4. Utilization of existing resources (including CFAR Cores) and/or development of unique and appropriate expertise, technology, and resources at the CFAR institution(s) and other sites, as appropriate;
5. Degree of innovation in project selection and experimental design;
6. Quality and appropriateness of mentorship and collaboration for the research project;
7. Choice of appropriate project PI and co-investigators (e.g., scientific qualifications, commitment, and experience), as well as the collaborations with other institutions, if applicable;
8. Appropriateness of the budget, in consideration of the research environment, for the scientific projects and cores.
9. Feasibility to complete the project within the FY18 project period (e.g., this will range between 8-12 months depending on the parent CFAR grant).

Allowable Costs

Funding may be requested for any category normally funded by a CFAR grant that is required to fulfill the goals of the proposed request and must be fully justified.

Schedule for Applications

Announcement Release Date: ***2/21/18***

Application Receipt Date: ***5/14/18***

Review Date: ***6/19/18***

Earliest Anticipated Award (Start) Date: ***6/29/18***

Terms of Award

A formal notification in the form of a Notice of Award (NoA) will be provided to the grantee organization. The NoA signed by the grants management officer 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.

Reporting

Awarded administrative supplements will be required to submit a progress report to be included in the annual progress report of the parent grant. Progress reports should include a summary of the supplement projects and outcomes.

Award Criteria

The following will be considered in making awards:

- Relevance to NIH HIV/AIDS research priorities;
- Scientific and technical merit of the proposed project as determined by NIH convened internal review panel;
- Funding availability and;
- Program balance.

Inquiries

Prospective applicants are encouraged to discuss their applications, including proposed collaborators, with the NIH contacts below.

For questions concerning eligibility of the CFAR to respond to this announcement, and any other administrative issues:

Candice Beaubien, M.P.H.
National Institute of Allergy and Infectious Diseases
Telephone: 240-627-3098
Email: candice.beaubien@nih.gov

For questions concerning a specific scientific area of interest, please communicate with the appropriate scientific contact below:

Basic Research on HIV Infection and Persistence

Karl Salzwedel, Ph.D.
National Institute of Allergy and Infectious Diseases
Telephone: 301-496-5332
Email: salzwedelkd@niaid.nih.gov

Infant Immunity for HIV Vaccine Development

Denise A. Russo, Ph.D.
National Institute of Child Health and Human Development
Telephone: 301-435-6871
Email: drusso1@mail.nih.gov

Studies to Delineate Sex Differences in the Incidence of Heart, Lung, Blood, and Sleep Comorbidities in People Living with HIV

Lis Caler, PhD
National Heart, Lung, and Blood Institute
Tel: 301-435-0222
Email: lis.caler@nih.gov

Formative Research on Behavioral Aspects of Novel Biomedical HIV Prevention and Treatment Regimens

Teri Senn, Ph.D.
National Institute of Mental Health
Telephone: 301-761-7852
Email: teri.senn@nih.gov

The Evolving Opioid Epidemic and its HIV Consequences

Richard A. Jenkins, Ph.D.
National Institute on Drug Abuse
Telephone: 301-443-1923
Email: jenkinsri@mail.nih.gov

Implementation of Evidence-Based HIV Interventions and Treatments for Health Disparity Populations

Rick Berzon, Dr.P.H., PA
National Institute on Minority Health and Health Disparities
Telephone: 301-594-5949
Email: rick.berzon@nih.gov

For questions concerning budget and fiscal matters:

Roberta Wolcott, J.D.
National Institute of Allergy and Infectious Diseases
Telephone: 240-669-2964
Email: wolcottr@niaid.nih.gov