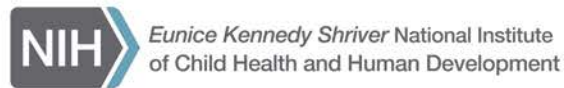# TECHNICAL ASSISTANCE WEBINAR
Pediatric HIV/AIDS Cohort Study (PHACS): 2020
Research Program Project (P01)
RFA-HD-20-002

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Denise Russo, PhD, Deputy Branch Chief

Maternal and Pediatric Infectious Disease Branch

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development

October 29, 2019

Structure of the Webinar

- Agenda
  - Introductory slides
  - P01 FOA presentation
  - Selected FAQs

- **Questions during the webinar**?
  - We may get to some via the FAQs today;
  - **Please email:** NICHDPHACSP01Questions@mail.nih.gov

- Please **mute your phone** to minimize feedback or other technical difficulties

Evolution to new PHACS Project Cycle

- This FOA builds on prior work begun in 2005

  - Encourage more focused, innovative, basic and clinical research agenda

  - Strongly renewed focus on urgent public health issue in the US

    - Perinatal HIV exposure and acquisition

RFA-HD-20-002: Pediatric HIV/AIDS Cohort Study (PHACS): 2020 (P01 Clinical Trial Not Allowed)

TABLE OF CONTENTS

- Part 1. Overview Information
  - Key Dates

- Part 2. Full Text of the Announcement
  - Section I. Funding Opportunity Description
  - Section II. Award Information
  - Section III. Eligibility Information
  - Section IV. Application and Submission Information
  - Section V. Application Review Information
  - Section VI. Award Administration Information
  - Section VII. Agency Contacts
  - Section VIII. Other Information

The PHACS Research Program Project (P01)

RFA-HD-20-002 (P01) Part 1

Overview Information

- **Activity code**: **P01 (Research Program Project)**
- Released October 7, 2019
- **Key Dates**
  - Open Date (Earliest Submission Date) November 5, 2020
  - LOI due November 5, 2019 (Not required, More on this later)
  - Application due December 5, 2019
  - Peer Review February 2020
  - Council May 2020
  - Earliest funding July 2020
- **Award**
  - Up to $12M (*Direct Costs*) to fund 1 award in 2020
  - Maximum Project period is 5 years
- **Partner organizations**
  - National Cancer Institute (NCI),
  - National Institute on Alcohol Abuse and Alcoholism (NIAAA),
  - National Institute of Allergy and Infectious Diseases (NIAID),
  - National Institute on Deafness and Other Communication Disorders (NIDCD),
  - National Institute of Dental and Craniofacial Research (NIDCR),
  - National Institute on Drug Abuse (NIDA),
  - National Institute of Mental Health (NIMH),
  - National Institute of Neurological Disorders and Stroke (NINDS)

Funding Opportunity Description

- **Purpose**
  - The PHACS Program Project will continue to addresses the clinical course of perinatally acquired HIV (PHIV) in adolescents and young adults and the oral and systemic health consequences of *in utero* and infant exposure to antiretroviral therapy in cohorts of children in the US.

- **Background**
  - Individuals with PHIV survive to adulthood <u>but</u> can have health consequences of prolonged HIV, ART and co-morbidities
  - Widespread use of ARVs for treatment and prevention <u>but</u> paucity of data on long-term toxicities in infants & children

RFA-HD-20-002 (P01) Part 2. Section I

Research Objectives and Scope

- **Cohorts:**
  - **HEU** infants and children
  - Adolescents and young adults with **PHIV**
  - Appropriate control groups

- **Protocols (Research Projects):**
  - **Surveillance Monitoring for Antiretroviral Treatment Toxicity** (SMARTT)
    - Drug toxicity surveillance system study in children exposed to prophylactic antiretroviral therapy (ART)
  - **The Adolescent Master Protocol** series (AMP, AMP Up, and AMP Up Lite)
    - Impact of HIV disease and ART on health outcomes of preadolescents, adolescents and young adults with PHIV
      - Sexual maturation, pubertal development, cardiovascular disease risk, bone and oral health, substance use, neurological and mental health outcomes, HIV-risk behaviors, cognitive, emotional, social, academic, and vocational functioning.

Essential Features of PHACS

P01 Program Project

- P01 PI/PD (multiple PI/PD(s) encouraged)
- P01 Research Project Lead(s)
  - 3 - 4 Research Projects
- PHACS Scientific Leadership Committee (SLC)
- Scientific Administrative Core (SAC)
- Data Resources Core (DRC)
- Optional Core(s)

- Semi-Annual Programmatic Meetings

- External Advisory Group

- NIH PHACS Management and Oversight Committee (NIH PMOC)

RFA-HD-20-002 (P01) Part 2. Section III

Eligibility Information

- Eligible organizations
  - All US
  - No foreign institutions or components

- Eligible individuals
  - Broadly inclusive (PI/PD with knowledge, skills, resources)
  - Multi-PI applications accepted

- Number of applications
  - Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

RFA-HD-20-002 (P01) Part 2. Section IV

Application and Submission Information

- Letters of Intent (LOI)
  - Due by **COB November 5th, 2019**
  - Not required and not binding. Helps to plan review but does not impact it

- Include:
  - Description
  - Name(s), address(es), telephone(s) of PI/PD(s)
  - Name(s) of other key personnel
  - Participating institution(s)
  - Number & title of this FOA

- Letters of Intent (LOI) should be submitted to:

      Bill G. Kapogiannis, M.D.
      Email: kapogiannisb@mail.nih.gov

RFA-HD-20-002 (P01) Part 2. Section IV

Application and Submission Information

Page Limitations

Available Component Types	Research Strategy/Program Plan Page Limits
Overall	12 pages
Sci Admin Core (Scientific Administrative Core)	12 pages
Data Resources Core	12 pages
Research Projects	12 pages (per project)
Optional Core	6 pages (per core)

RFA-HD-20-002 (P01) Part 2. Section IV

Application and Submission Information

- The application should consist of the following components:
  - **Overall Research Plan**:
    - P01 PI/PD is expected to provide oversight of all Cores and projects
    - Summarize overall research objectives and describe a **<u>Project Management Plan</u>** for the multi-project application
    - Describe the central theme of the Program and how the research projects, cores and other program infrastructure will synergize so that the Program's overall scientific merit is greater than the sum of its parts.

RFA-HD-20-002 (P01) Part 2. Section IV

Application and Submission Information

- The application should consist of the following components (cont'd):
    - **Scientific Administrative Core (SAC)** - <u>required</u>
        - The P01 PD(s)/PI(s) expected to lead this core (≥25%FTE to the Program)
        - Responsible for managing, coordinating, and supervising all program activities:
            - Assemble the necessary multidisciplinary team of established investigators to institute the **PHACS Scientific Leadership Committee (SLC).**
            - Maintain the **PHACS SLC** and establish collaborations with other research networks
            - Monitor progress against milestones, implementation of **overall Project Management Plan**, and proposed timelines.
        - A discretionary budget should be requested for focused **Emerging Research Pilots**, collaborations & other costs after PHACS begins
        - Include plan for determining how the research pilots will be identified, reviewed and funded
        - Describe plan for mentoring new and early stage investigators

RFA-HD-20-002 (P01) Part 2. Section IV

Application and Submission Information

- The application should consist of the following components (cont'd):
  - **Scientific Administrative Core (SAC)** (cont'd)
    - **PHACS Scientific Leadership Committee (SLC)**
      - *Composition:* PD(s)/PI(s) of the SAC and DRC, research project and other representatives from clinical sites, non-voting NIH staff
      - Responsible for PHACS governance, oversight & coordination
      - Develops and implements PHACS research agenda
      - Convene scientific working groups → expand / contract
      - Establish and enforce PHACS policies and procedures

RFA-HD-20-002 (P01) Part 2. Section IV

Application and Submission Information

- The application should consist of the following components (cont'd):
  - **Data Resources Core (DRC)** - <u>required</u>
    - Multiple leads [PD(s)/PI(s)] allowed; Identify & establish relationships with current PHACS sites for continued cohort follow-up
    - The DRC is a centralized data and resource management entity with direct access to clinical sites for this large, prospective observational multi-cohort Program:
      - Support sample tracking and laboratory data management, data storage, access and transfer, and integrated data analysis as a shared resource to the Research Projects and other Program components.
      - Execute and manage performance-based subcontracts and conduct oversight of all clinical sites and personnel - **Clinical Investigators**, **Study Coordinators** and **Community Advisory Board (CAB) members**, associated with recruitment and retention of the PHACS cohorts into all Research Projects.
      - Monitor progress against milestones, implementation of **overall Project Management Plan**, and proposed timelines.
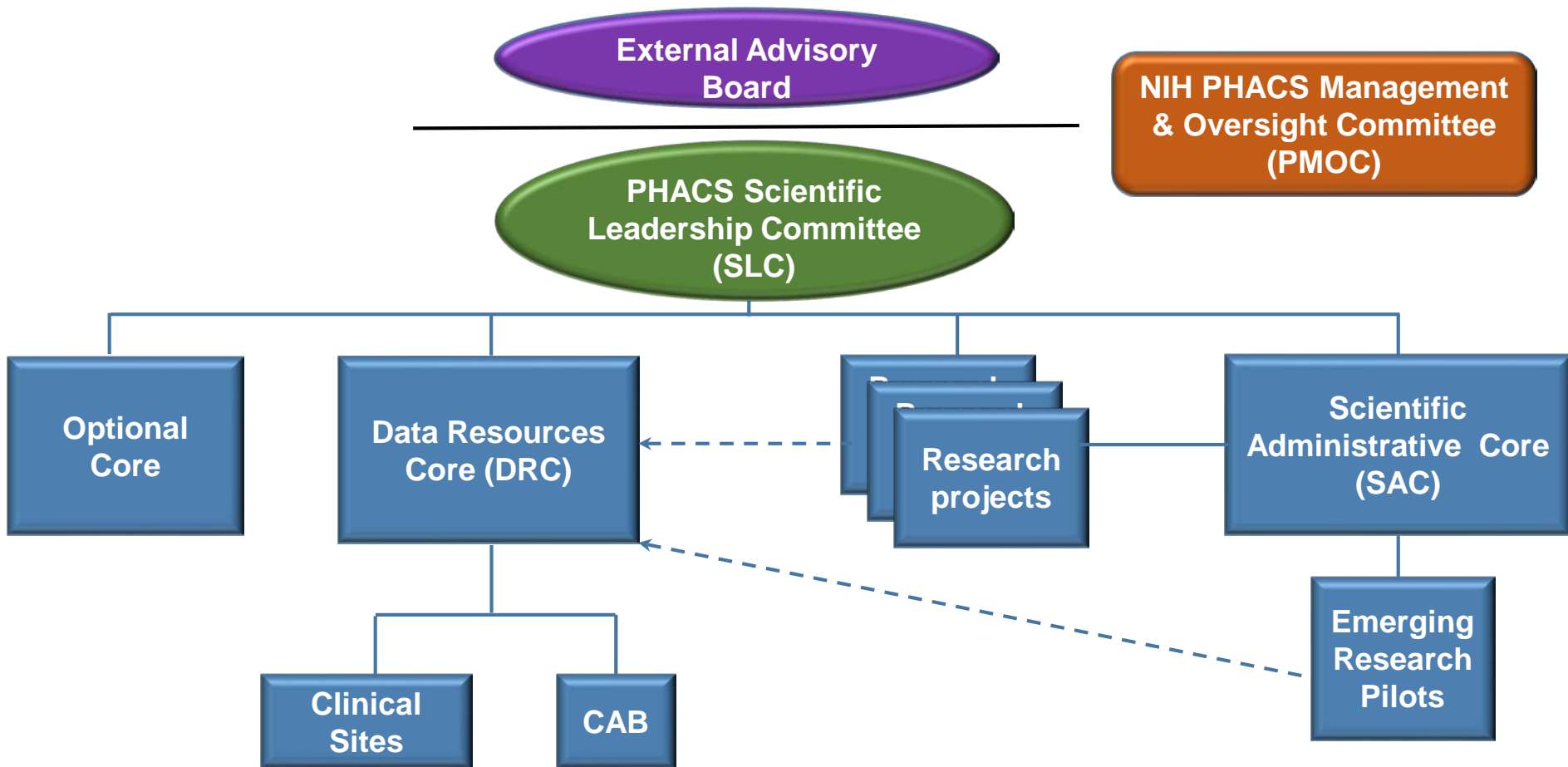
RFA-HD-20-002 (P01) Part 2. Section IV

Application and Submission Information

- The application should consist of the following components (cont'd):
    - **Research Projects** – <u>required</u> – min of **3**, max of **4**
        - Contribute materially and intellectually with expertise and resources to overall theme and specific objectives of PHACS
        - Emphasize cross-component collaboration to meet FOA objectives of synergy and cost-effectiveness
        - Include recruitment objectives, timelines, milestones and plans for data sharing
    - **Optional Core(s)** – *<u>optional</u>* – max of 2
        - Specialized, <u>unique</u> services or resources to Research Projects

PHACS P01 **Example** Structure

RFA-HD-20-002 (P01) Part 2. Section V

Application Review Information - Overall

- **Standard plus RFA-specific Review Criteria**
  - **Significance** (address important problem, critical barrier to progress; advance knowledge & practice)
  - **Investigators** (appropriate experience; complementary, integrated expertise; leadership)

    Are Early stage investigators (ESI) involved in leading different components of the program application? If a multi PD/PI application, are they part of the leadership plan?

  - **Innovation** (novelty of approaches and interventions)
  - **Approach** (methods appropriate to achieve aims; problems and alternatives)
  - **Environment** (benefit from unique features of scientific environment, subject populations, collaborative arrangements)

RFA-HD-20-002 (P01) Part 2. Section V

Application Review Information

- **Review Criteria - Scientific Administrative Core (SAC)**
  - **Planning and coordination of research activities adequately described?**
  - **Strategies for P01 management, including monitoring progress against Milestones, implementation of the Project Management Plan, and Timelines discussed?**
  - Information on integration of cross-disciplinary research, fund allocation & management, and QC provided?
  - Plans for ongoing communication, and evaluation of the Program Project by internal or external advisory board clearly delineated?
  - **Qualifications, experience, and commitment of the Core lead and other Core personnel appropriate?**
  - Are the Core's governance and organizational structure appropriate?
  - Is the Core cost-effective, and are there appropriate QC measures?
  - **Evaluate how decisions will be made for identifying, reviewing and funding pilot projects and describe their adequacy and rigor.**
  - Plan provided to mentor new and early stage investigators to promote junior investigators into leadership roles and independent research careers?

RFA-HD-20-002 (P01) Part 2. Section V

Application Review Information

- **Review Criteria – Data Resource Core (DRC)**
    - Plan for services provided to the other Core, Research Projects, and process for prioritizing requests for use of Core facilities by various Research Projects adequately formulated?
    - Design of overall management of DRC, decision-making process for use of DRC services, and plans for cost-effectiveness and QC included?
    - Rationale provided for how DRC resources contribute to the objectives of the Research Projects?
    - **Discussion of how DRC will implement new and enhanced bioinformatics analysis pipelines and web-based screening and follow-up of enrolled patients?**
    - Description of innovative capabilities in data analysis and visualization, including artificial intelligence (AI) strategies to enhance data integration workflows and pipelines?
    - **Description of plans for statistical and data management support and for creating and maintaining the necessary clinical infrastructure provided?**
    - **Strategies for maintenance and oversight of clinical sites associated with PHACS cohorts described?**
    - **Personnel in maintaining and operating the clinical sites and the Community Advisory Board (CAB) described?**
    - Plans for outreach & Information dissemination by maintaining a functional website addressed?
    - **Are the qualifications, experience, and commitment of the Core director and other Core personnel appropriate?** Are the Core's governance and organizational structure appropriate?
    - Is the Core cost-effective, and are there appropriate QC measures?

RFA-HD-20-002 (P01) Part 2. Section V

Application Review Information

- **Review Criteria – Optional Core**
    - Plan for services to the other Core and Research Projects, and process for prioritizing requests of Core facilities adequately formulated?
    - Design of overall management of the Core, decision-making process for use of Core services, and plans for cost-effectiveness and QC included?
    - Rationale provided for how Core resources will contribute to the objectives of the Research Projects and other Cores?
    - Information on innovative capabilities for services provided?
    - Plans for statistical and data management support provided?
    - Are the qualifications, experience, and commitment of the Core director and other Core personnel appropriate?
    - Are the Core's governance and organizational structure appropriate?
    - Is the Core cost-effective, and are there appropriate QC measures?

RFA-HD-20-002 (P01) Part 2. Section V

Application Review Information – Research Projects

- **Standard plus RFA-specific Review Criteria**
    - **Significance** (address important problem, critical barrier to progress; advance knowledge & practice)

    - **Investigators** (appropriate experience; complementary, integrated expertise; leadership)

    - **Innovation** (novelty of approaches and interventions)

    - **Approach** (strategy, methodology and analyses; problems, alternative strategies and benchmarks for success presented)

        Has the research project's use of the Core services, including why they are needed, been adequately explained?

    - **Environment** (institutional infrastructure and support; benefit from unique features of scientific environment, subject populations, collaborative arrangements)

Frequently Asked Questions

FAQs

1. Does the change in mechanism to a P01 have implications for NIH staff who previously collaborated with PHACS

   - NIH staff are not allowed to participate as **collaborating scientists** in a P01 (e.g. analysis, publications, etc)

   - NIH staff will participate in normal programmatic and other activities involved in the **stewardship** of the PHACS P01

     - Membership on NIH PMOC
     - Non-voting membership in PHACS committees (e.g. SLC, etc)

FAQs

2. What is a **Project Management Plan** and where does it fit?

- Describes the roles, responsibilities, strategies & processes to manage a successful multi-component P01
- **Research Plan (Overall)**

3. What key elements are in a **Project Management Plan?**

- Roles/areas of responsibility of the PIs
- Fiscal and management coordination
- Process for making decisions on scientific direction and allocation of resources
- Data sharing and communication among investigators
- Publication and intellectual property (if needed) policies
- Procedures for resolving conflicts

FAQs

4. Is it better to have 3 or 4 Research Projects?

    - It depends on the quality of the science proposed

5. Are the SMARTT and AMP series Protocols considered among the 3-4 Research Projects?

    - SMARTT is addressing specific scientific questions about HEU individuals → **1 Research Project**

    - The AMP series is addressing specific questions on adolescents with PHIV → **1 Research Project**

FAQs

6. If new scientific questions arise after PHACS begins, can these be addressed at that time?

- Yes, they can be addressed through proposals to conduct <u>Emerging Research Pilots</u> or by <u>external R01s</u>

- These proposals will come through the PHACS SLC and SAC – policies and procedures to be developed after the kick-off meeting

FAQs

7. What will reviewers expect to critique in plans for <u>Emerging Research Pilots</u>

- Discussion of how they will be identified, developed, reviewed and prioritized for funding by PHACS

- The Pilots will come through the PHACS SLC and SAC – policies and procedures to be developed after the kick-off meeting

FAQs

8. Can a Core propose more than one Lead?

    - Yes, as long as scientifically and methodologically justified and is feasible

9. When might it be beneficial to include Optional Core (s)?

    - P01 includes **≥ 2** Research Projects that would benefit from a common/unique source of resources and support (e.g. central lab)

FAQs

10. Are <u>signed</u> performance-based subcontracts required for the P01 application to be submitted

- No; executed subcontracts are not required to submit an application

FAQs

11. Is the membership of the External Advisory Board (EAB) to be identified on the application?

- This is discretionary, but not required

FAQs for Multi-project Applications

- https://grants.nih.gov/grants/ElectronicReceipt/faq_full.htm#multiproject

More Questions?

- Please submit to:

       Bill G. Kapogiannis, M.D.

       Telephone: 301-402-0698

       email: kapogiannisb@mail.nih.gov