Pilot Research Awards for Children's National Health System and The George Washington University

Information and Instructions for the 2019-2020 Pilot Application

The goal of this document is to provide the information you need to successfully complete your application for the CTSI-CN v2.0 Pilot Research Award.

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I. INTRODUCTION

National Center for Advancing Translational Sciences

The National Center for Advancing Translational Sciences (NCATS) was officially established in fiscal year 2012 to focus on the translation of science and discovery into clinical practice and improved health outcomes. NCATS defines translational research broadly to include the early steps necessary to develop new therapeutics, devices, and diagnostics from basic discoveries, the steps necessary to establish real world efficacy, and the research needed to improve the practical implementation and dissemination of improved approaches to care. The mission of NCATS includes strengthening the entire spectrum of translational research as defined below.

- **BASIC RESEARCH:** Scientific exploration that can reveal fundamental mechanisms of biology, disease, or behavior. Every stage of the translational research spectrum builds upon and informs basic research.
- **PRE-CLINICAL RESEARCH:** Pre-clinical research connects the basic science of disease with human medicine. During this stage, scientists develop model interventions to further understand the basis of a disease or disorder and find ways to treat it.
- **CLINICAL RESEARCH:** Clinical research includes studies to better understand a disease in humans and relate this knowledge to findings in cell or animal models; testing and refinement of new technologies in people; testing of interventions for safety and effectiveness in those with or without disease; behavioral and observational studies; and outcomes and health services research.
- **CLINICAL IMPLEMENTATION:** Adoption of interventions that have been demonstrated to be useful in a research environment into routine clinical care for the general population.
- **PUBLIC HEALTH:** Study of health outcomes at the population level to determine the effects of diseases and efforts to prevent, diagnose, and treat them. Findings help guide scientists working to assess the effects of current interventions and to develop new ones.

To achieve its mission, NCATS established The Clinical and Translational Science Award (CTSA) Program. The CTSA Program supports a national network of medical research institutions – called hubs – that work locally, regionally, and nationally to improve the translational research process to get more treatments to more patients more quickly by catalyzing innovation in training, research tools, and processes. The CTSA program hubs make up the CTSA Consortium.

Clinical and Translational Science Institute at Children's National v2.0

The Clinical and Translational Science Institute at Children's National (CTSI-CN) was established in 2010 as a collaboration between Children's National Health System (CNHS) and our academic partner, The George Washington University (GW). While Children's National researchers focus on pediatrics issues, the CTSI-CN does **not** focus exclusively on pediatrics.

The vision of CTSI-CN v2.0 is to promote innovations that speed the translation of research into improved child, family, and community health.

To realize this vision, the CTSI-CN v2.0 serves as a catalyst for clinical and translational research (CTR) by focusing on four major themes:

- Improving child, family, and community health, particularly for under-served populations;
- Developing novel treatment strategies for rare genetic diseases;

- Designing new devices for pediatric care; and
- Characterizing disease and disorders along the lifespan.

II. PILOT TRANSLATIONAL AND CLINICAL STUDIES PROGRAM

The CTSI-CN Pilot Translational and Clinical Studies Program (PTC) offers three distinct awards for pilot funding on an annual basis. Research supported through this mechanism should provide critical preliminary data to support an extramural research application within two years of the completion of this award.

CTSI-CN funds any impactful research, not just that which focuses on pediatric populations. Please visit the CTSI-CN website for a list of prior pilot awards.

Translation Acceleration Pilot Program

The Translation Acceleration Pilot (TAP) Program of the CTSI-CN is focused on barriers that involve methodological issues, institutional structures, and early clinical feasibility. This program is designed to challenge investigators to identify issues that hinder CTR. The TAP Program would not typically support translational research itself, but would support efforts to identify solutions to these barriers. The immediate goal is to accelerate CTR and the development of clinical trials. Multi-disciplinary and highly collaborative projects are especially encouraged.

III. IMPORTANT DATES

RFA Release	December 7, 2018
Letters of Intent Due	January 4, 2018 by COB (5:00 pm EST)
Full Proposal Invitation	January 14, 2019
Open Studios	TBD
CTSI-CN Symposium	TBD
Full Proposals Due	March 6, 2019 by COB (5:00 pm EST)
Funding Announcement	April 5, 2019
Award Date	June 1, 2019

IV. ANTICIPATED NUMBER OF AWARDS AND FUNDS AVAILABLE

Translation-Acceleration Pilot Program will award a maximum of 4 proposals up to $25,000 per award.

CTSI-CN pilot funding is contributed through cost share from both Children's National Health System and The George Washington University. Therefore, it is the goal of CTSI-CN to elicit sufficient pilot applications from both organizations to utilize the dedicated funds of each.

Per NCATS, CTSI-CN pilot awards cannot support clinical trial activity beyond phase IIA.

Faculty salary of any investigator and indirect costs are **not** allowed.

Individual awards are available to cover direct research costs. Allowable expenses include salaries and fringe benefits for personnel other than faculty investigators working on this project (e.g., post-doctoral fellow); project-related supplies/small equipment for the project; costs for

patients/subjects (including subject recruiting); consulting costs for statistical and/or informatics support; project-related charges to utilize equipment/core services; and other appropriate costs for necessary services based on justification. Travel costs are allowed when reasonable and justified.

V. AWARD PERIOD

The award period is for twelve months, from June 1, 2019 to May 31, 2020. The funds used to support pilot awards are subject to institutional funding period requirements.

In addition, the CTSI-CN is required to comply with the NCATS policy regarding human subjects and animal research. According to the policy, all CTSI-CN-funded Pilot and K projects that involve human or animal subjects are required to secure prior approval from NCATS before funds can be released and project work can begin.

This process enables NCATS to ensure that human and animal subjects are protected and appropriate data safety monitoring is used. Spending of pilot funds cannot be authorized until approval is secured. Please note that IRB approval is required ***before*** submission to NCATS and that NCATS prior approval takes a minimum of 30 days. Often NCATS prior approval can take 60 days or more. CTSI-CN staff will work with pilot awardees to expedite the process and to compile and submit the necessary documents to NCATS. Detailed information about the necessary documentation will be sent to pilot awardees as applicable. Once the documentation is gathered, the official award letters will be released to the impacted awardees.

VI. ELIGIBILITY CRITERIA

Following are the eligibility criteria for all applicants:

- All applicants must become a CTSI-CN member. If not done previously, applicants will be automatically subscribed to CTSI-CN emails when they submit their application.
- Principal Investigators (PI) must have a PhD, MD, or equivalent doctoral-level degree and must be faculty members at either CNHS or GW.
- Co-PIs are permitted, but each individual may submit one application only, whether as PI or Co-PI. Prior awardees are not allowed to serve as Co-PI.
- Co-Investigators must be faculty at either CNHS or GW, and their salary may not be included in the budget. Prior awardees may serve as Co-Investigators.
- Applications from Associate or full Professors are allowed if they propose a substantively new direction for the PI's research. This new direction must be explicitly stated and justified. Applicants unsure of their eligibility are encouraged to inquire with program staff, listed at the end of this section, prior to applying.
- Previous CTSI-CN pilot awardees are **not** eligible for a second award unless they propose a substantively new direction for the investigator's research. This new direction must be explicitly stated and justified. Applicants unsure of their eligibility are encouraged to inquire with program staff, listed at the end of this section, prior to applying.
- Current CTSI-CN KL2 awardees and NIH K awardees are **not** eligible for this program.
- Before re-submitting any proposal substantively similar to a proposal previously submitted to the PTC, a PI must obtain the written permission of a PTC Lead.

The PTC faculty and staff are:

- PTC Co-Lead: Tim McCaffrey, PhD (mcc@email.gwu.edu)
- PTC Co-Lead: Maureen Monaghan, PhD (MMonagha@childrensnational.org)
- Program Leads: Christina Robinson, MA (cgrobins@childrensnational.org)
  Valery Yankov (vyankov@childrensnational.org)

VII. GENERAL INSTRUCTIONS

The PTC Pilot Program uses a two-phase approach. In Phase I, applicants must submit a two-page Letter of Intent (LOI). All submitted LOIs will be reviewed by the PTC Leadership and select content experts as required. A subset of applicants will be invited to submit a full proposal.

Phase I applications for the 2019-2020 Pilot Award must be submitted electronically using the REDCap application form included in the Phase I instructions below. Applicants must complete the entire form and include a single PDF document.

Phase II applicants will receive additional instructions when they are invited to submit a full proposal.

The format requirements for all submitted documents are as follows:

- Arial, 11-point font
- Margins should be 0.5 inch
- Single spaced

Please adhere to the page limitations specified below. Appendices are not allowed.

VIII. PHASE I: LETTER OF INTENT

LOIs should be submitted **by 5:00 pm EST on January 4, 2019** through the REDCap application form. If applicants meet all eligibility criteria listed above, the LOI should be submitted as a single PDF document and should include the following items in the order listed:

- Cover Page: On a **single page**, applicants should provide information regarding all investigators' position and rank, primary organization and primary unit (i.e., department, center, or institute), and their contact information (email, office phone, physical address). Each PI should provide his or her signature (e-signature will suffice) acknowledging agreement to submit the proposal.
- Letter of Intent: All eligible applicants are encouraged to submit a document, **no more than two pages**, with the following elements:
  - Title
  - Brief Background
  - Hypothesis and Specific Aims
  - Experimental Approach
  - Future Directions (i.e., a brief description of how successful completion of the project will result in a proposal for extramural funding)
  - References

Note: Cover page, references, and NIH Biosketches do not count toward the page limit.

- NIH Biosketch: Biosketches for the PI and Lead Mentor must be provided and adhere to the **new** NIH biosketch format with a maximum of five pages each. The PI **must** provide an ORCID number next to their eRA Commons user name on their Biosketch. Any applicant who does not have an ORCID number should register to get one.

All submitted LOIs will be reviewed by the PTC Leadership and select content experts as required. A subset of applicants will be invited to submit a full proposal. Each will receive an overall impact score reflecting the merit using the NIH scoring system.

The CTSI-CN will **not** provide reviews to LOI applicants.

Applicants who meet all of the eligibility requirements and who have LOIs that meet the requirements for pilot awards will be invited to submit a full application. If further consultation is needed, applicants are encouraged to take advantage of two offerings new for this grant year. During Phase II, the PTC will offer Open Studios for project formulation and a Symposium of CTSI-CN resources. Details around these offerings are available in the next section(s). Additionally, applicants may seek support from the CTSI-CN Grants Enhancement Program (See Section X. CTSI-CN Resources).

IX. APPLICATION DEVELOPMENT SUPPORT

Applicants who move on to Phase II will have the opportunity to take advantage of two new offerings from the PTC. The **Open Studio** grew from a recognized need for earlier exposure to the process of project formulation (i.e., conceptualizing and formulating viable, realistic, and promising research proposals).

- The PTC will offer two Open Studios: one at CNHS and one at GW.
- Participation in the Open Studios is strictly voluntary.
- Applicants who choose to participate will have 20-30 minutes of presentation and discussion around their study concept.

The PTC will invite senior investigators and key faculty in specialized services such as biostatistics, informatics, community engagement, team science and more. Before the meeting these faculty will review the LOI of each applicant who chooses to participate.

In addition, the PTC will offer a **CTSI-CN Symposium** where faculty leads will present the vast array of CTSI-CN tools, resources, services, and funding opportunities. The symposium will be open to all faculty, but Phase II pilot applicants are strongly encouraged to attend. CTSI-CN offers some services at no or reduced costs. Early engagement of relevant CTSI-CN modules allows applicants to budget for necessary, but often overlooked study pieces.

X. PHASE II: INVITED FULL PROPOSALS

Applicants who are invited to submit a full proposal in Phase II will be provided additional instructions at that time. Full proposals must be submitted no later than **5:00 pm EST on March 6, 2019**. The full proposal should be submitted as a single PDF document and should include the following items in the order listed:

- Full Proposal: The full proposal should be **no more than seven pages** and submitted as a single PDF document that includes the following elements:

- Title
- Background
- Hypothesis and Specific Aims
- Significance
- Innovation
- Experimental Approach
- Future Directions (i.e., description of how successful completion of the project will result in a proposal for extramural funding)
- References

Note: References, budget/budget justification, NIH biosketches, and lead mentor/co-mentor statements do not count toward the page limit.

- Budget and Justification: Using PHS 398 Form Page 4 (Rev. 06/09), complete the budget template with accompanying budget justification.
- NIH Biosketches: NIH biosketches of all investigators must be provided and adhere to the **new** NIH biosketch format with a maximum of five pages each. If available, biosketches of any key personnel (e.g., postdoctoral fellows) to be supported by the proposed budget should be included as well.
- Lead Mentor and Co-Mentor(s) Statement: A **single** letter, signed by the Mentor and any Co-Mentor(s), should be included and **not** exceed two pages. The statement should include the following:
  - A description of the research and all other developmental activities such as seminars, scientific meetings, training in the responsible conduct of research, and presentations. It should discuss expectations for publications over the period of the proposed project.
  - The source of anticipated additional support (aside from the pilot funds) for the applicant's research project over the one-year award period.
  - The nature and extent of supervision and mentoring of the candidate and commitment to the candidate's development that will occur during the award period.
  - The candidate's anticipated portion of time available for research.
  - The mentors' experience as a mentor, including type of mentoring (e.g., graduate students, career development awardees, postdoctoral students), number of persons mentored, and career outcomes.

The PTC strongly encourages all applicants, but in particular those with human subject and animal studies, to submit their protocol to the IRB before or near the time of submitting their full proposal application. Human subject and animal studies **must get** NCATS prior approval, which requires an IRB approval letter, before spending can be authorized.

At least two members of the CTSI-CN Scientific Review Group with relevant content expertise will assess the scientific merit of all proposals. Each proposal will receive an overall impact score reflecting scientific merit using the NIH scoring system. The CTSI-CN will provide de-identified proposal reviews to all applicants invited to submit a full proposal.

Final funding decisions will be made at the discretion of Lisa Guay-Woodford, MD,

Principal Investigator of the CTSI-CN, based on the recommendations of the PTC and Community Engagement leadership.

XI. PROGRESS REPORTING

Pilot awardees are expected to present a Mid-Year Progress Report approximately six months into the award. The mid-year progress report will be a combined presentation and discussion. The goal of this presentation will be for CTSI-CN leadership to troubleshoot potential problems and assess progress. Awardees will be contacted directly by a PTC Program Lead with guidelines and to schedule the progress presentations. A final presentation will be scheduled roughly three months after award completion. This will be in a symposium format.

To allow tracking of progress/success of each project, funded investigators will be required to submit data on all relevant work products related to their awards (e.g., abstracts, manuscripts, submitted grants, and funding notifications) at regular intervals via a REDCap survey. The PTC may request additional information from funded investigators.

Each publication, press release, or other document that cites results from the pilot award must include an acknowledgement of our CTSI-CN grant as follows:

> ***"This publication [or project] was supported by Award Number UL1TR001876 from the NIH National Center for Advancing Translational Sciences. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Advancing Translational Sciences or the National Institutes of Health."***

XII. CTSI-CN RESOURCES

The mission of the CTSI-CN is to foster broad collaborative investigation that accelerates discovery and drives dialogue across the bench, bedside, and community continuum. Applicants are encouraged to consult with CTSI-CN modules, listed below, to access resources and further develop their proposals. More information can be found and contacts can be found at http://ctsicn.org/.

The Biostatistics, Epidemiology and Research Design (BERD) provides high quality biostatistical and epidemiological expertise for the development and design of pediatric and lifespan CTR. All requestors can be provided with up to four hours of free support. Additional free support can be provided on a case-by-case basis especially for proposal development or for K-awardees. Where appropriate, GW Biostatistics Practicum graduate students provide additional data analysis needs to CTSI-CN investigators, and K awardees receive more support, should they require it. Consultations are coordinated through the CTSI-CN supported Services, Pricing, & Application for Research Centers (SPARC) portal.

The Child Health Research Acceleration through Multisite Planning (CHAMP) module seeks to provide the infrastructure, assistance, and training for CTR investigators in the performance of multi-site clinical studies. The CHAMP program seeks to develop the infrastructure and training program for multi-center trials initially involving CTSA hubs that have a strong pediatric focus. For rare genetic diseases and other childhood disorders, natural history studies, in combination with clinical trials, are essential for advancing child health.

The goal of the Collaboration and Multidisciplinary Team Science (CMTS) module is to foster collaborative research teams among the varied scientific and clinical disciplines and the broad community (e.g., lay public, patient advocacy groups, foundations, and industry). The strategy

involves identifying, training, utilizing, and disseminating best practice in team science as applied to child health CTR. It also includes crediting each member of the team appropriately in recognition of his/her contribution.

The Community Engagement module focuses on two communities and their intersection in support of CTR: the lay public in the Washington, DC region and the multidisciplinary academic community of the CTSI-CN. In a broad sense, community engagement starts at the early stages of a research project's development and continues through its completion and dissemination.

The Grants Enhancement Program (GEP) provides critical support for junior faculty in writing successful grant applications. The GEP offers the following services:

- Open Studios for senior faculty input on early project formulation;
- Specific aims and proposal review by senior faculty;
- Monthly meetings for peer review of and by K- and R-focused junior faculty, facilitated by senior faculty members;
- Access to materials such as successful grant applications and guidance documents; and
- By request, external expert review of well-prepared grant applications and mock study sections for multidisciplinary input.

The Informatics Core provides a comprehensive, integrated informatics ecosystem to investigators and their study teams by unifying bioinformatics and medical informatics and provides investigators and their teams with easy access to data and analytic tools required for current and future CTR needs. The Informatics Core also provides investigators and their teams with training in informatics methods and tools in order to promote self-sufficiency among researchers in the use of informatics across the enterprise.

The Integrating Special Populations (ISP) module provides support, resources, and innovative tools to assist investigators in including special populations in CTR projects. Special populations are defined as:

- Children from underserved populations (i.e., those experiencing health disparities);
- Fetuses and their mothers; and
- Children with rare genetic disorders.

The goal of the Liaison to Trial Innovation Centers (LTIC) module is to provide trial readiness and an efficient and effective environment to participate in multicenter studies through the CTSA TIC streamlined procedures for the implementation of multicenter research projects. The primary objective of LTIC is to facilitate the initiation and implementation of clinical studies in CTSI-CN, functioning as a liaison between CTR investigators and the planned CTSA TICs.

The Liaison to Recruitment Innovation Centers (LRIC) assists with maximizing the recruitment to pediatric and rare genetic diseases studies by using a variety of existing and developing informatics tools, educating users on their use, and reaching out to the community to maximize the buy-in of community stakeholders and their encouragement of their constituents about participation in CTR.

The Orphan Product Accelerator – Innovations Incubator (OPA-II) provides the infrastructure, assistance, and training for CTR investigators in the development of orphan products, specifically those aimed at the diagnosis and treatment of rare diseases, many of which are

particularly relevant to children. The overarching goal of the OPA-II is to develop innovative methods for reducing both the cost and time required to bring orphan products to market.

The Participant and Clinical Interactions (PCI) module is a dedicated clinical research unit. The mission of the PCI is to provide a high-quality, safe, and welcoming environment for pediatric study participants and investigators. PCI encompasses a variety of resources and services divided into various components. Each component provides specialized services for investigators/research staff and their clinical research protocols. Services can be performed in the PCI or other hospital areas, both inpatient and outpatient. All PCI personnel have comprehensive training, including GCP, to perform each service/task with the highest level of efficiency, quality, and ethical standards. In addition, the PCI leadership and management team has many years of combined experience in clinical research in pediatrics and other vulnerable populations.

- ClinicalTrials.gov Support: In partnership with the IRB, PCI sends reminders to PIs to register and provide study results on ClinicalTrials.gov and in collaboration with the Informatics Core, ensures that the ClinicalTrials.gov NCT# is entered in our EHR for patients enrolled in research studies.
- Scientific Review Committee: The new Scientific Review Committee (SRC) pre-screens human research IRB submissions (i.e., pilot projects; clinical trials by K, T, or other trainees; and projects funded by foundation, small pharmaceutical, or biotech grants). The SRC exempts proposals with prior rigorous peer-review (e.g., NIH R, other federal awards) unless the associated human research protocol has not been reviewed.
- Bionutrition Services: This service provides:
    - Caloric intake assessment;
    - Special meal design;
    - Nutrient analysis;
    - Anthropometric measurements using stadiometers, length board, knee height and Lange calipers, infant and standing weight scales;
    - Body composition assessments using air displacement plethysmography and/or bioelectrical impedance analysis; and
    - Energy expenditure and fitness studies utilizing a metabolic cart.

  Up to 4-hours of free services are provided for preliminary data gathering with structured cost recovery built into subsequent grant budgets.

- Neurobehavioral and Psychosocial Evaluation Core: This Core function provides assessments of infants, children, adolescents, and adults, including cognition, behavior, social/environmental and family dynamics assessments, as well as consultation on behavioral phenotyping, selection of optimal assessment tools, and functional MRI applications for research on neurodevelopmental disorders.
- Biorepository: The CTSI-CN Biorepository provides expert assistance with:
    - Bio-specimen collection, processing (e.g., DNA and/or protein extraction), and storage for IRB-approved protocols; and
    - Data and sample management including the FreezerPro laboratory management system of over 10,000 samples.

In addition to maintaining this resource, the CTSI-CN Biorepository leverages existing expertise and resources to include a state-of-the-art HIV-related biorepository.

The Pilot Translational and Clinical Studies Program (PTC) program is an essential underpinning of a strong CTR program. Without the support to develop methods, test concepts, or establish feasibility, the successful conduct of definitive evaluative research is virtually impossible.

The primary goal of the Regulatory Knowledge and Support (RKS) module is to assist CTR investigators and their teams by providing proactive, innovative regulatory and research ethics education and support services to assure that child health CTR research meets the highest standards of ethical conduct and regulatory compliance.

The overall objective of the Translational Workforce Development (TWD) module is to provide workforce members with a flexible and continuous learning environment that will lead to high quality, efficient, and effective CTR. The major TWD initiatives focus on:

- Expanding the portfolio of on-demand training opportunities targeted at faculty and trainees, as well as staff and community members;
- Integrating a team science curriculum into our training and educational initiatives; and
- Focusing on team and leadership development within translational research teams.