Clinical & Translational Science Institute
of Southeast Wisconsin

CTSI Translational & Clinical Studies Program

2020 Request for Applications for Traditional Pilot Awards

The CTSI Translational and Clinical Studies Program Traditional Pilot Awards are supported by the Advancing a Healthier Wisconsin Research and Education Program (AHW REP) and the National Institutes of Health (NIH).

The total available funding CTSI is offering for the 2020 cycle is $50,000 each, funded by AHW REP, for up to 12 meritorious projects. Due to the importance of supporting research to address the opioid epidemic in alignment with the NIH HEAL Initiative the CTSI has set aside funding for up to 3 meritorious opioid-related pilot studies for the 2020 cycle. This does not preclude the funding of additional pilot proposals that are opioid-related and demonstrate merit.

These awards are intended to stimulate **inter-institutional** and **interdisciplinary** translational and clinical research among the CTSI partner institutions. By supporting collaboration, these awards will promote best practices in team science research.

KEY DATES

RFA for 2020 Pilot cycle release date: May 3, 2019
Intent to Apply due: June 1, 2019, 5:00 p.m. CDT
Application deadline via REDCap: August 1, 2019, 5:00 p.m. CDT
Notification of recommendation for award: Mid-November 2019
IRB Submission deadline: December 1, 2019*
Mandatory orientation: January 2020
Project start date: April 1, 2020
Project end date: March 31, 2021

** CTSI is supported by the National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS). As such:*

- *"NIH expects that all sites participating in multi-site studies, which involve non-exempt human subjects research funded by the NIH, will use a single Institutional Review Board (sIRB) to conduct the ethical review required for the protection of human subjects." (https://grants.nih.gov/policy/humansubjects/single-irb-policy-multi-site-research.htm) Please be sure to reach out to your respective IRB Reliance office at the time of application if needed.*
- *CTSI is required to submit documentation based on IRB approval for each applicable pilot project that has been recommended for funding. NCATS requires IRB approval and all related documentation at least 30 days before the project start date. To accommodate this timeline, IRB must be submitted no later than December 2, 2019 or the recommendation for funding may be withdrawn. Verifiable proof of submission is required.*

OVERVIEW & PURPOSE

ABOUT THE CTSI PILOT AWARD PROGRAM

This program is designed to advocate, facilitate, and foster the continuum of research from bench to bedside, and from bedside to community practice. In a sense, translational research focuses on discovery and the application of scientific findings into a real-world setting. It is the goal of the CTSI to diminish the barriers between institutions and disciplines while encouraging novel approaches to solving complex health related problems. Ultimately, we strive to improve health outcomes by creating new, bidirectional flows of information between our biomedical research enterprise and the community we serve.

GOALS OF THIS FUNDING OPPORTUNITY

The fundamental goal of this RFA is to stimulate clinical and translational research among the institutions that comprise the CTSI of Southeast Wisconsin through meaningful collaboration and high-quality team science. This award uses a multiple investigator model to encourage inter-institutional and interdisciplinary collaboration between clinical and basic biomedical scientists, social scientists, ethicists, engineers, biostatisticians, informatics specialists, and other members of the clinical health care delivery team with the appropriate training and expertise to make a substantive scientific contribution to the study.

FUNDS WILL BE PROVIDED TO:

- Support new and promising clinical and translational projects across all disciplines, including special emphasis categories of opioid-related research, community-engaged health disparities, and underserved and special populations;
- Garner preliminary data for projects poised to be competitive for new extramural grant submissions;
- Model best practices in team science research;
- Maximize scientific interactions between junior and senior investigators;
- Stimulate collaborative research between bench and clinical investigators from similar research areas;
- Foster interdisciplinary and inter-institutional collaborations;
- Support research in novel technologies and/or novel approaches and applications to clinical practice and community health

DEFINITIONS & REQUIREMENTS

CLINICAL & TRANSLATIONAL RESEARCH

This pilot award program funds clinical and translational research according to the NIH definitions described below:

CLINICAL RESEARCH

The NIH definition of clinical research[1] has three parts:

1. Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies.
2. Epidemiologic and behavioral studies
3. Outcomes research and health services research

[1] Glossary of NIH Terms

TRANSLATIONAL RESEARCH

Applications will be reviewed and considered for funding based on NIH-identified translational areas:

> Translational research includes two areas of translation. One is the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans. The second area of translation concerns research aimed at enhancing the adoption of best practices in the community. Cost-effectiveness of prevention and treatment strategies is also an important part of translational science.[2]

[2] National Institutes of Health. RFA-RM-07-007: Institutional Clinical and Translational Science Award (U54) Mar2007.

T-LEVELS

Applications must provide a T-level designation for the proposed research according to the CTSI translational continuum described below, based on NIH guidelines.

Proposals for T1-T2 studies will be grouped and reviewed together; likewise, proposals for T3-T4 studies will be grouped and reviewed together.

- Proposals that are only T-0 are ***not*** eligible to apply. T-0 research can be described as:
  - Pre-clinical approaches designed to inform an investigator about a pathway, pathophysiology, or treatment approach. Examples include:
    - animal models of human disease, human blood or cell lines
    - development of questionnaires, computational models, and human physiological studies
  - "Bench" research which may or may not require approvals from human or animal use committees.

- T-1 Translation to Humans
  - Studies with human participants that yield knowledge about human behavior, physiology, pathophysiology and the potential for intervention (i.e. diagnoses, therapies, etc.)
  - Findings from basic research are tested for clinical effect and/or applicability.[3]

- T-2 Translation to Patients
  - Test new interventions under controlled environments to form the basis for clinical application and evidence-based guidelines.[3]
  - Yield knowledge about the efficacy of the interventions in optimal settings.[3]

NOTE: Pilot studies in T-3 and T-4 levels would provide preliminary evidence to bolster competitiveness for larger studies in the following areas:

- T-3 Translation to Practice
  - Study health services and community-based participatory research (dissemination, communication, implementation)
  - Explore ways of applying recommendations or guidelines in general practice.[3]
  - Yield knowledge about how interventions work in real-world settings.[3]

- T-4 Translation to Communities/Population Health
  - Study factors and interventions that influence the health of populations.[3]
  - Obtain results to benefit society & improve global health in areas such as improving disease prevention and reducing medical costs.

- T-5 Policy-level Research
  Proposals that incorporate T5 in addition to one of T1 through T4 are eligible to apply.

[3] T-levels of translational research

SPECIAL EMPHASIS CATEGORIES

Research in these areas is not a requirement for the award; however, additional review weight will be applied to these studies as being in alignment with a focus of the CTSI.

- **OPIOID SPECIAL EMPHASIS CATEGORY**
  The Clinical and Translational Science Institute of Southeast Wisconsin announced in 2018 a special emphasis category for pilot funding focused on factors contributing to opioid misuse and abuse and strategies to address the opioid epidemic.

  Proposals should describe a clear link to future funding opportunities, such as specific NIH program announcements or other federal or private funding opportunities (e.g., NIDA, CDC). Applications in this area may include but are not limited to:
  - Prevention modalities for patients around opioid misuse and abuse
  - Personal and social factors impacting risk for opioid addiction
  - Provider practices and structure of the healthcare system as contributing to opioid misuse and abuse
  - The intersection between pain conditions and opioid use disorder
  - The neurobiology of pain as related to efficacy of opioids vs. non-addictive analgesics
  - Innovative treatment modalities, including non-addictive analgesics and non-pharmacologic approaches

- **Under-served & Special Populations Research**.
  Examples include:

  - **Underserved Populations:** Blacks/African Americans; Hispanics/Latinos; American Indians/Alaska Natives; Asian Americans; Native Hawaiians and other Pacific Islanders; socioeconomically disadvantaged populations (low-income communities); rural populations; health disparity populations
  - **Special populations**: specific age groups (infants; children; geriatric); survivors of formerly lethal childhood diseases; adults with chronic health conditions that originated in childhood

PRINCIPAL INVESTIGATOR & STUDY TEAM ROLES

Note that for the purposes of this award and in the language of this RFA, the roles of Principal Investigator (PI) and Co-Principal Investigator (Co-PI) are equivalent. These are distinct and have different requirements from the roles of the Co-Investigator (Co-I).

Due to the requirement of the funding source for the Traditional Pilot Awards, only MCW faculty can be PIs. An MCW PI can submit more than one application but only one project can be funded, with one exception. The CTSI allows for a multiple PI model such that the Co-PI can be from a partner institution. Therefore, a second award to an MCW PI will be considered if the following are clearly explicated and justified:

1) the study proposed is part of the program of research of the Co-PI from the partner institution;
2) the MCW PI has meaningful contribution to the science (cannot be an administrative PI only);
3) the study protocols are distinctly different; and,
4) the scientific research teams are substantially different.

For questions, please contact the CTSI Pilot Award Program Manager, Renee McCoy, at 414-955-2524 or rmccoy@mcw.edu.

PI REQUIREMENTS

- All projects must have an MCW PI. This condition is a requirement of the funding source of these awards: Advancing a Healthier Wisconsin Research and Education Program (AHW REP).
- This award allows for, but does not mandate, a multiple PI model. In cases where a project has multiple PIs, **the primary PI** must be from MCW.
- The role of PI/Co-PI must remain as originally submitted.
- According to MCW corporate policy, the MCW PI has overall responsibility for the conduct of a research project, including all technical, programmatic, financial, compliance, and administrative aspects. The PI is responsible for controlling the technical direction and academic quality of the project and will ensure that the project is carried out in compliance with the terms, conditions, and policies of the institution and sponsor, when applicable.[4]
- The MCW PI will have the additional expectation of managing the award through the MCW *eBridge* system and through her/his department.
- All PIs must have a minimum of 5% effort and be fully vested in the project in both spirit and practice and contribute actively on the project. It is encouraged that PIs seek institutional/department cost-sharing to support all or a portion of personnel effort, thereby leaving more funds available for other research expenses. Note: cost-sharing commitment documentation is *not* required at the time of application and is only required for projects which have received recommendation for funding.
- All PIs must have full-time or full professional effort status. Adjunct and part-time faculty are not eligible to apply as a PI.[5]
- PIs are responsible for fulfilling reporting requirements as a condition of receipt and continuation of funds. Non-compliance of final and/or annual reporting could result in the rescission of funds by CTSI.
- All PIs must be CTSI Members. To become a member, please complete the CTSI Membership Form.

[4] MCW Human-Research-Protection-Program SOP
[5] Principal Investigator Eligibility

CO-INVESTIGATOR / OTHER PERSONNEL

- A co-investigator must have the requisite research training/credentials/expertise to make a substantive contribution to the science of the study.
- Study personnel such as research assistant, study coordinator or other staff needed for the conduct of the study may not serve as a Co-Investigator
- All personnel must be identified prior to the start date to replace any "to be named" positions proposed in the application.

INTER-INSTITUTIONAL REQUIREMENT

- Projects must be inter-institutional: the research team must include investigators from at least two different CTSI partner institutions: Versiti, CHW, Froedtert, MCW, MSOE, MU, UWM, Milwaukee VA (Zablocki). Please note, this condition is based on the investigator's institution of primary employment.
- Community partners or investigators from other academic institutions would be welcome additions to projects as Co-PIs or Co-Is, but alone do not meet the inter-institutional requirement. Please note, primary employment is used to determine institutional affiliation.
- Faculty from the MU/MCW joint department of biomedical engineering should use their employment platform to determine institutional affiliation.
- All investigators must be CTSI Members. To become a member, please complete the CTSI Membership Form.
- Investigators that are interested in forming new collaborative relationships are encouraged to contact the CTSI Pilot Award Program Manager, Renee McCoy at 414-955-2524 or rmccoy@mcw.edu.

REGULATORY REQUIREMENTS

- PIs must provide verifiable proof that **all regulatory applications** (IRB/IACUC, etc.) are in pre-submission or have been submitted or approved by time of application. If applicable, proof of any exempt status must be provided.
- **Please note that all applicable projects that receive recommendation for funding must provide proof that the IRB application/amendment has been submitted by December 1, 2019; this is a firm deadline.** This requirement is to accommodate necessary timelines for submitting NCATS Prior Approval documentation (see section below on NCATS Prior Approval).
- If your project involves human subject research, all study team members must obtain CITI training or equivalent training in human research protections.
- If your project involves FDA regulated research or NIH-funded clinical trials, all study team members must obtain training in Good Clinical Practice (GCP).
- Clinical research and clinical trials that utilize any Froedtert Hospital (FH) resources – medical records, staff, facilities, equipment, etc. – must be reviewed via the Office of Clinical Research and Innovative Care Compliance (OCRICC) to ensure that FH has the staff, equipment, and

other resources to successfully support the study. Visit the OCRICC website for a list of services that require OCRICC approval.

To help expedite OCRICC approval:

- Submit your project's OCRICC application at the same time as your IRB submission
- Add "CTSI PILOT" in the title of your OCRICC application
- Notify OCRICC when you receive IRB approval

- Applicants are encouraged to contact CTSI IRB Navigator, Jo Bergholte for assistance with any IRB-related issues: jbergholte@mcw.edu
- This program has an accelerated nature and only a 12-month funding period. If your project requires working with federal agencies such as NIDA, FDA (e.g., IND, IDE applications) or pharmacological agreements (e.g., clinical trial agreements, material transfer agreements), you must contact the CTSI Pilot Award Program Manager, Renee McCoy, at rmccoy@mcw.edu or 414-955-2524 prior to applying.

BUDGET REQUIREMENTS

- Projects will be funded at a level of up to $50,000
- Project duration will be 12 months (no extensions are permitted)
- All funds must be EXPENDED within the 12-month period.
- Funding under this RFA cannot be used as "bridge funding" for lapsed grants from any extramural source and is intended to be used for new projects.
- Advancing a Healthier Wisconsin Research and Education Program (AHW REP)
  - funds cannot be used to supplant funds or resources that are available from other sources. However, matching funding and opportunities to leverage AHW funds to obtain other sources of financial support are encouraged.
  - no "indirect costs" may be charged.
  - For more information on AHW REP processes, please view the AHW Partner Portal and the Advancing a Healthier Wisconsin Research and Education Program Award Administration Manual (PDF).
- All salaries are subject to the FY14 Executive Level II salary cap of $181,500.
- Effort must be specified for all personnel, even when cost-sharing. Indicate any cost-sharing within the budget justification and/or within a Letter of Support; cost-sharing commitment forms are no longer required at the time of application and need only be provided from MCW departments upon notification of recommendation for funding.
- One budget form is required for each institution/agency providing personnel effort on the study that is not considered consultative or fee-for-service. Consultant and/or service fees sourced from another institution or agency such as CHW or Froedtert Hospital can be included on the MCW budget and need not be paid via a subcontract. Use the appropriate budget template provided on the CTSI Traditional Pilot Award website.

PROCEDURE

HOW TO APPLY

FIRST STEP: THE ONLINE INTENT TO APPLY FORM MUST BE COMPLETED AND SUBMITTED BY JUNE 1, 2019 5:00 P.M. CDT.

REQUIRED APPLICATION MATERIALS

Once the Intent to Apply Form is reviewed and approved, applicants will be sent a link to an online application form which must be submitted along with the following documents (forms and templates are available from our 2020 Traditional Pilot Award website):

1. 2020 CTSI Pilot Award Proposal Form
2. Budget and Budget Justification Forms, one form is required for each institution providing personnel effort on the project that is not considered consultative or fee-for-service.
3. NIH Biosketch in the most current NIH format is required for all PIs; Co-PIs; Co-Investigators (limit 5 pages per individual)
4. AHW Goals Alignment Form
5. Letters of Support / Intent
    a. From Co-Investigators to PI(s)
        a.i. A Letter of Support is required from each co-Investigator to the PI(s) explaining her/his intention and commitment to this project.
        a.ii. Letters of Support should be addressed to ***all*** PIs/Co-PIs.
        a.iii. A Letter of Support is *not required* from a Co-PI to the other PI(s).
    b. From Department Chair(s) to the project PI(s)
        b.i. To acknowledge awareness and support of the project.
    c. From other institutions - Letters of Intent
        c.i. Please also include a Letter of Intent from any non-MCW institution indicating a willingness to negotiate a project-specific subaward and validation that the institution is on-board with the project and is aware of the effort commitments being made.

Applications for this award are **not** required to be submitted in eBridge. Instead of starting a funding proposal in eBridge, please simply submit the online REDCap application form to CTSI by 5:00 p.m. on August 1, 2019. If your application is selected for funding, a funding proposal will be initiated at that time.

ADDITIONAL REQUIREMENTS BY INSTITUTION

For Marquette University (MU) investigators, the application must be registered via the routine Proposal Registration process with the Office of Research and Sponsored Programs prior to submission. This process is required for proposals in which MU is the prime applicant and those for which MU is the collaborating applicant receiving funds. Marquette requires that a signed institutional letter of intent is in hand from all sub-awardees or collaborating institutions who will be receiving funds (i.e. MCW, UWM, MSOE, etc.) from a grant in which MU is the prime applicant prior to submission. Please contact an ORSP staff member early in your application preparation process as we can assist with forms, budget formulation, proofreading, securing sub-award letters of intent, etc.

For UWM investigators, full applications must be routed using the WISPER system and approved by the Office of Sponsored Programs prior to submission to MCW. UWM applicants with new collaborators must process the sub-award within the MCW timeline. Letters of intent do not require a WISPER record.

For MSOE investigators, please contact Sheku Kamara, Dean of Applied Research, 277-7416, kamara@msoe.edu

REVIEW PROCESS

To ensure that the results of scientific research will be used to directly benefit human health, proposals in all disciplines relevant to biomedical investigation will be considered for funding. Criteria that must be met for funding of any proposal include:

- the clear potential to directly translate anticipated results into improved preventative health, diagnostics, therapeutics or health outcomes for our southeast Wisconsin community; and
- the potential for proposed studies, when completed, to generate extramural funding.

Each Intent to Apply that has been received by deadline will be reviewed; for those that meet eligibility criteria and are approved, the submitting PI will be notified and sent a personalized link to proceed with the full application.

CTSI and the CTSI Pilot Award Committee (PAC) will initially review all applications for technical feasibility and compliance with above requirements. CTSI PAC is comprised of members from partner institutions Marquette University (MU), Medical College of Wisconsin (MCW), Milwaukee School of Engineering (MSOE), and University of Wisconsin-Milwaukee (UWM).

All applications will undergo peer-review. To assist you in developing a strong proposal, specific review criteria will be available within the online application form for your reference.

CTSI participates in a national CTSA External Reviewer Exchange Consortium (CEREC) to improve fairness in the scientific review process and better match applicants with feedback from experts in their respective fields. Applications for this cycle may be reviewed externally through our association with CEREC and we require that you acknowledge within the online application form that your proposal may undergo external review.

Maintaining confidentiality throughout the peer review process is essential to allow for the candid exchange of scientific opinions and evaluations; and to protect trade secrets, commercial or financial information, and information that is privileged or confidential. Similar to the NIH peer review process, the CTSI is committed to protect the integrity of and to maintain confidentiality in peer review. See Guide Notice NOT-OD-14-073 and NOT-OD-15-106.

Projects will be reviewed based on their selected Translational T-level according to specific review criteria for each T-level grouping: T-1 and T2 will be grouped and reviewed together and T-3 and T-4 will be grouped and reviewed together.

TERMS & CONDITIONS

National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS) Terms and Conditions for CTSI Pilot Award Projects

RESTRICTION OF CLINICAL ACTIVITY BEYOND THE END OF PHASE IIB:
In accordance with section 479(b) of the Public Health Service Act (as amended by the Consolidated Appropriations Act, 2012, Public Law 112-74 and by the 21st Century Cures Act, 2016, Public Law 114-255), NCATS is authorized to use fiscal year 2018 funds to provide infrastructure and resources for all phases of clinical trials research, but can only support clinical trials through the end of Phase IIB (with the exception of certain clinical trial activities involving treatment of a rare disease or condition; consult NCATS program staff for additional information).

Therefore, unless specifically authorized via Revised Notice of Award, with attendant specific Terms of Award, no clinical trial activity beyond phase IIB using fiscal year 2018 funds may be supported by this grant through the pilot project, K or T programs. However, all phases of clinical trials may utilize infrastructure and resources provided through the CTSA.

NCATS PRIOR APPROVAL FOR STUDIES INVOLVING HUMAN SUBJECTS

For every applicable pilot project that receives a recommendation for funding (scheduled to be sent mid-November), CTSI will request from the PIs documentation for NCATS Prior Approval in accordance with federal requirements. The following conditions must then be met:

- NCATS requires IRB approval at the time of submission for Prior Approval
- NCATS requires receipt of documents at least 30 days before the project start date
- PIs will utilize the REDCap repository to upload the required NCATS documents.

To accommodate this time restriction, CTSI requires that all IRB applications be submitted to each respective IRB by December 1, 2019. If the complete IRB application has not been submitted by December 1, 2019 the recommendation for funding may be rescinded.

STEM CELLS

- No funds in this award may be used for any research involving human embryonic stem cells (hESCs) until the grantee has submitted to NIH information on the specific, approved hESC line(s) that will be used from the NIH Human Embryonic Stem Cell Registry. While the Registry will include lines pending review; only those hESCs listed on the Registry as eligible for NIH funding may be used in this award. Information should be submitted from an Authorized Organizational Representative to the assigned Grants Management Specialist.
- The grantee may use only those hESCs that appear on the NIH Human Embryonic Stem Cell Registry as eligible for NIH funding and in accord with any restrictions placed on the use of those lines. For more information, view the NIH Guidelines on Human Stem Cell Research

HUMAN/ANIMAL SUBJECTS RESTRICTION

- It is understood that no clinical research study member will be permitted to work on any project involving live vertebrate animals or human subjects that has not been approved by the IACUC and/or IRB, as appropriate.
- No funds may be drawn down from the payment system and no obligations may be made against Federal funds for research involving human subjects by any site engaged in such research for any period not covered by both an OHRP-approved Assurance and an IRB approval consistent with 45 CFR Part 46. See " Human Subjects Protections" Part II, Chapter 4 (NIH Grants Policy Statement (PDF)) for specific requirements and grantee responsibilities related to the protection of human subjects.

HUMAN SUBJECTS EDUCATION CERTIFICATION REQUIREMENT

- This award reflects the NCATS' acceptance of the certification that all key personnel have completed education on the protection of human subjects, in accordance with NIH policy, "Required Education in the Protection of Human Research Participants," found here: (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html). Any individual involved in the design and conduct of the study that is not included in the certification must satisfy this requirement prior to participating in the project. Failure to comply can result in the suspension and/or termination of this award, withholding of support of the continuation award, audit disallowances, and/or other appropriate action.

CLINICAL AND TRANSLATIONAL SCIENCE INSTITUTE

CTSI seeks to promote the highest quality of human subjects research, therefore as part of the post award process, pilot projects that were ranked 4.5 or higher on the NIH Likert scale, will be analyzed for trends in deficiencies. The purpose of this analysis will result in generalizable knowledge, as required by NCATS, and be used for educational training opportunities to enhance translational science and investigator knowledge. Note, this quality improvement initiative will have no impact on the CTSI Pilot Review process. All information shared as educational material will be de-identified. For any questions or concerns, please contact the project lead, Amit Gode, MD, MCW, CTO Director, at agode@mcw.edu.

FUNDING ACKNOWLEDGMENT

AHW REP and NIH Funding Acknowledgment: *Important Reminder* – Please acknowledge the AHW REP and NIH when publishing or presenting any outcomes resulting from your study by including the CTSI Funding Acknowledgement. *Please also refer to the* AHW REP Award Administration Manual (PDF) *for the AHW Acknowledgement Policy*.

RESOURCES FOR APPLICANTS

Please see our website for guidance documents for our investigators and applicants.