Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Tuberous Sclerosis Complex Research Program (TSCRP)

Idea Development Award

Funding Opportunity Number: W81XWH-08-TSCRP-IDA

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I. HELPFUL INFORMATION

A. Contacts

1. Program announcement, proposal format, or required documentation: To view all funding opportunities offered by the Congressionally Directed Medical Research Programs (CDMRP), perform a Grants.gov basic search using the CFDA Number 12.420. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079

Fax: 301-619-7792

Email: cdmrp.pa@amedd.army.mil

2. eReceipt system: Questions related to pre-application components through the CDMRP eReceipt system should be directed to the eReceipt help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time.

Phone: 301-682-5507

Website: https://cdmrp.org

Email: help@cdmrp.org

3. Grants.gov contacts: Questions related to submitting applications through the Grants.gov (http://www.grants.gov/) portal should be directed to Grants.gov help desk. Deadlines for proposal submission are 11:59 p.m. Eastern time on the deadline date. Therefore, there is an approximate 3-hour period during which the Grants.gov help desk will NOT be available. Please plan ahead accordingly, as the CDMRP help desk is not able to answer questions about Grants.gov submissions.

Phone: 800-518-4726, Monday to Friday, 7:00 a.m. to 9:00 p.m. Eastern time

Email: support@grants.gov

Grants.gov will notify Principal Investigators (PIs) of changes made to this Program Announcement and/or Application Package ONLY if the PI clicks on the "send me change notification emails" link and subscribes to the mailing list on the Opportunity Synopsis Page for this announcement. If the PI does not subscribe and the Application Package is updated or changed, the original version of the Application Package may not be accepted.

B. National Technical Information Service

The technical reference facilities of the National Technical Information Service (www.ntis.gov) are available for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. All other sources also should be consulted to the extent practical for the same purpose.

C. Commonly Made Mistakes

- Not obtaining or confirming the organization's DUNS number well before the proposal submission deadline.
- Not obtaining or confirming the organization's registration with the Central Contractor Registry (CCR) well before the proposal submission deadline.
- Failing to request "send me change notification emails" from Grants.gov.
- Not contacting HELP DESKS until just before or after deadlines.
- Not completing the pre-application submission before the mandatory pre-application deadline (pre-application remains in draft status).
- Using an incorrect Grants.gov application package to submit a proposal through Grants.gov. Each Program Announcement/Funding Opportunity requires a specific application package.
- Uploading attachments into incorrect Grants.gov forms.
- Attaching files in the wrong location on Grants.gov forms.
- Submitting attachments that are not PDF documents, except for the R&R Subaward Budget Attachment(s) Form.
- Exceeding page limitations.
- Failing to submit a proposal 48-72 hours before the deadline so that Grants.gov can provide notification of errors and allow for resubmission of application package.
- Failing to submit proposal by submission deadline.

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History and Objectives

The Tuberous Sclerosis Complex Research Program (TSCRP) was established in Fiscal Year 2002 (FY02) to promote innovative research focused on eradicating tuberous sclerosis complex (TSC). Appropriations for the TSCRP from FY02 through FY06 totaled $13.5 million (M). The FY08 appropriation is $4M.

The overall goal of the FY08 TSCRP is to lessen the impact of TSC. Within this context, the encouragement of established scientists in the field and the attraction of new scientific expertise from other fields are essential to the TSC community. Proposals that address the needs of

minority, low-income, rural, and other under-represented and/or medically underserved populations are encouraged and may be submitted from any eligible institution.

The TSCRP challenges the scientific community to design innovative research that will foster new directions for, address neglected issues in, and bring new investigators to the field of TSC research. Scientific ventures that represent under-investigated avenues of research or novel applications of existing technologies are highly sought. The TSCRP encourages risk-taking research, although such projects must demonstrate solid scientific judgment and rationale.

B. Award Description

The TSCRP Idea Development Award was created in FY02. Since then, 81 Idea Development Award proposals have been received and 21 have been recommended for funding**.**

The Tuberous Sclerosis Complex Research Program (TSCRP) Idea Development Award supports innovative research aimed at understanding the pathogenesis of TSC and improving its diagnosis and treatment.

Important aspects of the Idea Development Award are as follows:

1. The fiscal year 2008 TSCRP encourages proposals in the following areas:

   a. Development of clinical resources.

   b. Translational research.

2. All Idea Development Award proposals must include preliminary data relevant to TSC research and the proposed project.

Proposals including Clinical Trials: If a proposal requests support for a clinical trial, the PI is required to submit a clinical protocol in addition to the proposal by the proposal receipt deadline. Guidelines for protocol preparation are outlined in the Application Instructions (Appendix 8). The protocol will be reviewed separately.

Clinical trials must begin within 12 months of the award date. If an Investigational New Drug (IND) or Investigational Device Exemption (IDE) is required, additional time may be granted. However, preference will be given to proposals that have U.S. Food and Drug Administration (FDA) approval at the time the award is made.

It is the responsibility of the PI to clearly and explicitly articulate the project's innovation and the impact it may have on the field of TSC research.

C. Eligibility

Investigators at or above the Assistant Professor level (or equivalent) are eligible to submit proposals. Refer to Application Instructions, Appendix 1, for general eligibility information.

D. Funding

Funding for an Idea Development Award can be requested for up to $450,000 for direct costs for up to a 3-year performance period, plus indirect costs as appropriate.

Within the guidelines provided in the Application Instructions, funds can cover:

- Salary
- Research supplies
- Equipment
- Clinical costs
- Travel to scientific/technical meetings
- Travel between collaborating institutions

Proposals including Clinical Trials: PIs also should budget for travel to a pre-award meeting and protocol workshop at Fort Detrick, Maryland. At a minimum, it is expected that the PI and Clinical Research Coordinator will attend the pre-award meeting, although up to three individuals may attend. Justification must be provided if additional personnel are included in the travel budget.

The CDMRP expects to allot approximately $2.03M of the $4.0M FY08 TSCRP appropriation to fund approximately 3 Idea Development Award proposals, depending on the quality and number of proposals received. Funding of proposals received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

E. Award Administration

Transferring an award that includes a clinical trial will not be permitted. Refer to the Application Instructions, Appendix 5, for general award administration information.

III. TIMELINE FOR SUBMISSION AND REVIEW

Proposal submission is a two-step process consisting of (1) pre-application submission and (2) proposal submission. ***Pre-application submission is a required first step***.

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time, May 22, 2008**
- **Proposal Submission Deadline: 11:59 p.m. Eastern time, June 12, 2008**
- **Peer Review: July 2008**
- **Programmatic Review: September 2008**

Awards will be made approximately 4 to 6 months after receiving the funding notification letter, but no later than September 30, 2009.

IV. SUBMISSION PROCESS

Proposal submission is a two-step process consisting of (1) a pre-application submission through the CDMRP eReceipt system (https://cdmrp.org/) and (2) a proposal submission through Grants.gov (http://www.grants.gov/).

Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

A. Step 1: Pre-Application Components and Submission

The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the CDMRP eReceipt system by ***5:00 p.m. Eastern time on the deadline***. Refer to the Application Instructions for detailed information.

1. Proposal Information
2. Proposal Contacts
3. Collaborators and Conflicts of Interest (COI)
4. Letter of Intent (LOI) Narrative

B. Step 2: Proposal Components and Submission

Proposal submission will not be accepted unless a pre-application was submitted by the pre-application deadline. Proposals must be submitted electronically by the Authorized Organizational Representative (AOR) through Grants.gov (www.grants.gov). No paper copies will be accepted.

Each proposal submission must include the completed Grants.gov application package of forms and attachments identified in www.grants.gov for the US Army Medical Research Acquisition Activity (USAMRAA) program announcement. In addition to the specific instructions below, please refer to the Application Instructions for detailed requirements of each component.

The package includes:

1. **SF-424 (R&R) Application for Federal Assistance Form**
2. **Attachments Form**
   - Attachment 1: Project Narrative **(10-page limit.)**

     Describe the proposed project in detail using the outline below. ***Proposals must include preliminary data relevant to TSC research and the proposed project.***

     Background: Present the ideas and reasoning behind the proposed work. Cite relevant literature.

Hypothesis or Objective: State the hypothesis to be tested or the objective to be reached.

Preliminary Data: Provide pertinent TSC-relevant data to support the necessity, feasibility, and potentiality of the proposed project.

Specific Aims: Concisely explain the projects' specific aims to be funded by this proposal.

Research Strategy: Describe the experimental design, methods, and analyses including appropriate controls in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. A detailed plan for the recruitment of subjects or the acquisition of samples must be included.

- Attachment 2: Supporting Documentation
  - References Cited
  - Acronyms and Symbol Definitions
  - Facilities & Other Resources
  - Description of Existing Equipment
  - Publication and/or Patent Abstracts **(Five-document limit.)**
  - Letters of Institutional Support **(Two-page limit per letter.)**
  - Letters of Collaboration (if applicable) (**Two-page limit per letter.)**
  - Intellectual and Material Property Plan (if applicable)
- Attachment 3: Technical and Public Abstracts **(One-page limit for each abstract.)**
- Attachment 4: Statement of Work (SOW) **(Two-page limit.)**
- Attachment 5: Impact Statement **(One-page limit.)**

  Describe the impact of this study on research or patient care. Describe how the expected results of the proposal will contribute to the goals of eradicating the disease and advancing methods, concepts, diagnosis, or treatment of the disease or quality of life for patients.
- Attachment 6: Innovation Statement **(One-page limit.)**

  Summarize how the proposal is innovative. The following examples of ways in which proposals may be innovative, ***although not all-inclusive***, are intended to help PIs frame the innovative features of their proposals:

  - Study concept – Investigation of a novel idea and/or research question.
  - Research method or technology – Use of novel research methods or new technologies, including technology development, to address a research question.
  - Existing methods or technologies – Application or adaptation of existing methods or technologies for novel research or clinical purposes, or for research or clinical purposes that differ fundamentally from those originally intended.

Investigating the next logical step or incremental advancement on published data is not considered innovative.

- Attachment 7: Clinical Protocol (if applicable)

  The Clinical Protocol must address the required components described in Application Instructions Appendix 8.

- Attachment 8: Federal Agency Financial Plan (if applicable)

3. **Research & Related Senior/Key Person Profile (Expanded Form)**

   - PI Biographical Sketch **(Four-page limit.)**
   - PI Current/Pending Support
   - Key Personnel Biographical Sketches **(Four-page limit each.)**
   - Key Personnel Current/Pending Support

4. **Research & Related Budget Form**

   - Budget Justification

5. **Research & Related Project/Performance Site Location(s) Form**

6. **R&R Subaward Budget Attachment(s) Form (if applicable)**

V. INFORMATION FOR PROPOSAL REVIEW

A. Proposal Review and Selection Overview

All proposals are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review of proposals against established criteria for determining scientific merit. The second tier is a programmatic review that compares submissions to each other and recommends proposals for funding based on scientific merit and overall goals of the program. Additional information about the two-tier review process used by the CDMRP may be found at http://cdmrp.army.mil/fundingprocess

The peer review and program review processes are conducted confidentially and anonymously to maintain the integrity of the merit-based selection process. Each tier review requires panelists to sign a non-disclosure statement attesting that proposal and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other correcting actions. Correspondingly, institutional personnel and PIs are prohibited from contacting persons involved in the proposal review process to gain protected evaluation information or to influence the evaluation process. Violations of this prohibition will result in the administrative withdrawal of the institution's proposal. Violations by panelists or PIs that compromise the confidentiality or anonymity of the peer review and program review processes may also result in suspension or debarment of their employing institutions from Federal awards.

The Government reserves the right to review all proposals based on one or more of the required attachments or supporting documentation (e.g., Impact Statement, Innovation Statement, etc.).

B. Review Criteria

1. Peer Review: All proposals will be evaluated according to the following criteria, which are listed in order of decreasing importance:

- **Innovation**
  - How the proposed research is innovative in one or more of the following ways: Concept or question, research methods or technologies, adaptations of existing methods or technologies, and clinical interventions.
  - How the project proposes new paradigms or challenges existing paradigms.
  - How the proposed research represents more than an incremental advance upon published data.
  - How the potential gain warrants the perceived risk.
- **Impact**
  - How the project addresses a critical problem in TSC research or patient care.
  - How the project makes an original and important contribution to advancing basic, clinical, and translational research that will improve outcomes for TSC.
  - The difference the proposed project will make on TSC research or patient care, if successful.
- **Research Strategy and Feasibility (Preliminary data are required.)**
  - How the scientific rationale supports the project and its feasibility as demonstrated by a critical review and analysis of the literature, preliminary data and logical reasoning.
  - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed.
  - How well the PI acknowledges potential problems and addresses alternative approaches.
- **Personnel**
  - Whether the applicant meets the eligibility requirements.
  - How the research team's background and expertise are appropriate to accomplish the proposed work.
  - Appropriateness of the levels of effort for successful conduct of the proposed work.
- **Environment**
  - The appropriateness of the scientific environment for the proposed research.

- How the research requirements are supported adequately by the availability of and accessibility to facilities and resources (including collaborative arrangements).

- **Budget**
  - How the budget is appropriate for the proposed research.

2. Programmatic Review: Criteria used by the Integration Panel (IP) members to make funding recommendations that maintain the program's broad portfolio include:

- Ratings and evaluations of the peer reviewers,
- Programmatic relevance,
- Relative innovation and impact,
- Program portfolio balance, and
- Adherence to the intent of the award mechanism.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by Integration Panel members and recommended for funding to the Commanding General, USAMRMC.

VI. CLINICAL PROTOCOL REVIEW (IF APPLICABLE)

A. Required Elements of a Clinical Protocol

Refer to Appendix 8 of the Application Instructions for information.

B. Review Criteria

All clinical trials will be scientifically reviewed according to the following criteria as applicable. The reviewers will evaluate:

- **Study Design**
  - How the scientific rationale and preliminary data, including critical review and analysis of the literature and laboratory and preclinical evidence support the proposed study and its feasibility.
  - How well the aims, hypothesis or objectives, experimental design, methods, data collection procedures, and analyses are developed.
  - How the logistical aspects of the proposed clinical study (e.g., communication plan, data transfer and management, and standardization of procedures) meet the needs of the proposed study.
  - How the recruitment, informed consent, and screening processes for volunteers will be conducted.
  - How the inclusion, exclusion, and randomization criteria meet the needs of the proposed study.

- **Clinical Impact**
  - How this study will affect the magnitude and scope of potential clinical applications (e.g., detection, diagnosis, treatment, management, and/or quality of life).
  - How this study will affect the magnitude and scope of potential clinical applications.
- **Intervention, Drug, or Device**
  - The appropriateness of the intervention, drug, or device to be tested in the clinical study.
  - The availability and purity of the substance to be used in the clinical study.
  - Documentation that an IND/IDE has been submitted.
- **Feasibility**
  - The feasibility of the proposed clinical study.
  - The plans for addressing unanticipated delays (e.g., slow accrual) and completing the proposed study within the performance period.
  - The availability of volunteers for the clinical study, the prospect of their participation, and the likelihood of volunteer attrition.
- **Statistical Plan (as appropriate for phase of study)**
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - The consistency of the data analysis plan with the study objectives.
- **Personnel**
  - How the clinical study team's background and expertise are appropriate to accomplish the proposed work (i.e., statistical expertise, expertise in the disease, and clinical studies).
  - The appropriateness of the levels of effort for successful conduct of the proposed work.
- **Environment**
  - The evidence of an appropriate scientific environment, clinical setting, and the accessibility of institutional resources to support the clinical study at each participating center (including collaborative arrangements).
  - Whether the clinical study requirements are supported adequately by the accessibility to facilities and resources (including collaborative arrangements).
  - The institutional commitment from each participating institution.
  - The intellectual and material property plan that is agreed upon by each participating institution.

- **Ethics and/or Regulatory Issues**
  - How the ethical considerations, information privacy, and assessment of risks and benefits of participation in the clinical study will be addressed.
  - The plan for dealing with adverse events, which should include named agencies or offices to be notified in this event and point of contact information.
  - The plans for data disposition during and after the clinical study.
  - The procedures for protocol modifications during the course of the study.
  - The plans for data and safety monitoring.
- **Budget**
  - How the budget is appropriate for the proposed clinical study.

VII. COMPLIANCE GUIDELINES

Compliance guidelines have been designed to ensure the presentation of all pre-applications and proposals in an organized and easy-to-follow manner. Peer reviewers expect to see a consistent, prescribed format. Failure to adhere to formatting guidelines makes documents difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in pre-application or proposal rejection. **Pre-applications or proposals missing required components as specified in the Program Announcement/Funding Opportunity may be administratively rejected.**

The following will result in administrative rejection of the entire proposal:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Margins are less than specified in the formatting guidelines.
- Print Area exceeds that specified in the formatting guidelines.
- Spacing is less than specified in the formatting guidelines.
- Budget and/or budget justification are missing.
- FY08 IP members are included in any capacity in the pre-application process, the proposal, budgets, and any supporting document. A list of the FY08 IP members may be found at http://cdmrp.army.mil.

For any other sections of the pre-application or proposal with a defined page limit, pages exceeding the specified limit will be removed and not forwarded for peer review.

Material submitted after the submission deadline, unless specifically requested by the Government, will not be forwarded for peer review.

Proposals that appear to involve any allegation of research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be

requested to perform the investigation and provide those findings to the Grants Officer for a determination of the final disposition of the application.