Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Tuberous Sclerosis Complex Research Program

Exploration – Hypothesis Development Award

Funding Opportunity Number: W81XWH-11-TSCRP-EHDA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-application Submission Deadline:** 5:00 p.m. Eastern time (ET), July 18, 2011
- **Application Submission Deadline:** 11:59 p.m. ET, August 1, 2011
- **Scientific Peer Review:** October 2011
- **Programmatic Review:** December 2011

New for fiscal year 2011 (FY11): The Grants.gov Research & Related Budget form is a mandatory component of all Grants.gov application packages.

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I.   FUNDING OPPORTUNITY DESCRIPTION

A.   Program Description

The Tuberous Sclerosis Complex Research Program (TSCRP) was established in 2002 to promote innovative research focused on decreasing the clinical impact of tuberous sclerosis complex (TSC). Appropriations for the TSCRP from FY02 through FY10 totaled $29.5 million (M). The FY11 appropriation is $6.4M.

TSCRP Research Resources Initiative: Resources developed through TSCRP funding that are available to the scientific community can be found at http://cdmrp.army.mil/tscrp/resources/ tscresources.shtml. Investigators are urged to leverage and contribute to these resources and include a sharing and distribution plan in the application for data and resources generated during the performance of the project. For more guidance on data sharing, refer to the General Application Instructions, Appendix 4.

B.   FY11 TSCRP Mission and Focus Areas

The mission of the TSCRP is to encourage innovative research aimed at understanding the pathogenesis of TSC and to translate these findings to the care of individuals with TSC. Within this context, the FY11 TSCRP seeks applications that address these vital program focus areas:

- In vivo study of pathobiology of clinical manifestations of TSC (e.g., epilepsy, cognitive, renal)

- Long-term benefits and side effects of rapamycin and homologues in TSC patients

- Identification of novel strategies for treatment and prevention of TSC (e.g., cytotoxic drugs, epilepsy treatments, psychotropic agents)

- Understanding the cellular and molecular mechanisms of TSC (including cell origin, cell-type specificity, and developmental stage)

- Genetic and non-genetic modifiers of TSC

- Identifying biomarkers for prognosis and prediction of treatment outcomes (including imaging, electrophysiology, and pharmacogenetics)

C.   Award Information

The TSCRP Exploration – Hypothesis Development Award mechanism was first offered in FY09. Since then, 41 Exploration – Hypothesis Development Award applications have been received, and 11 have been recommended for funding.

The Exploration – Hypothesis Development Award supports the initial exploration of innovative, high-risk, high-gain, and potentially groundbreaking concepts in the TSC research field. Results of studies conducted through this award should provide the scientific rationale upon which a new hypothesis can be based, or they should provide initial principles of an innovative hypothesis. This award is designed to provide investigators with the opportunity to pursue serendipitous observations. ***The presentation of preliminary data is encouraged, but not required.***

It is the responsibility of the Principal Investigator (PI) to clearly and explicitly articulate how the proposed research is innovative and how the concept is novel.

Research involving human subjects and human anatomical substances is permitted; however, studies must be exempt under 32 CFR 219.101(b) or eligible for expedited review (32 CFR 219.110 or 21 CFR 56.110). Clinical trials are not allowed under this funding opportunity. A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. PIs wishing to apply for funding for a clinical trial should utilize the FY11 TSCRP Clinical Trial Award mechanism (Funding Opportunity Number: W81XWH-11-TSCRP-CTA).

Use of Human Subjects and Human Anatomical Substances: All Department of Defense (DOD)-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the US Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local Institutional Review Board (IRB) of record. Local IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DOD. These laws and directives are rigorous and detailed, and will require information in addition to that supplied to the local IRB. Allow a minimum of 4 months for HRPO regulatory review and approval processes. Refer to the General Application Instructions, Appendix 5, for more information.

D.   Eligibility Information

- Independent investigator (including junior faculty but excluding postdoctoral fellows) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E.   Funding

- The maximum period of performance is **2** years.
- The maximum allowable direct costs for the entire period of performance is **$100,000** plus indirect costs**.**
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **2** years.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.

- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C., for budget regulations and instructions for the Research & Related Budget form. In addition, for this award mechanism, direct costs:

May be requested for (not all-inclusive):

- Salary

- Research supplies

- Equipment

- Travel between collaborating organizations

- Travel costs of up to $1,800 per year to attend scientific/technical meetings

The Office of the Congressionally Directed Medical Research Programs (CDMRP) expects to allot approximately $0.9M of the $6.4M FY11 TSCRP appropriation to fund approximately 6 Exploration – Hypothesis Development Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a multi-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

Submission of the same research project to different funding opportunities within the same program and fiscal year is discouraged. The Government reserves the right to reject duplicative applications.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-11-TSCRP-EHDA.

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the PI through the CDMRP eReceipt System (https://cdmrp.org/).

PIs and organizations identified in the application should be the same as those identified in the pre-application. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

The pre-application consists of the following components, which are organized in the CDMRP eReceipt System by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Application Information – Tab 1**

- **Application Contacts – Tab 2**

- **Collaborators and Conflicts of Interest – Tab 3**

- **Required Files – Tab 4**

  Letter of Intent (LOI) (one-page limit): Provide a brief description of the research to be conducted. Include the focus area(s) under which the application will be submitted. LOIs are used for program planning purposes only (e.g., reviewer recruitment) and will not be reviewed during either the peer or programmatic review sessions.

- **Submit Pre-application – Tab 5**

- **Other Documents Tab**

  No additional documents are required

C.   Application Submission Content and Form

Each application submission must include the completed application package of forms and attachments provided in Grants.gov for this Program Announcement/Funding Opportunity. The application package is submitted by the Authorized Organizational Representative (AOR) through the Grants.gov portal (http://www.grants.gov/).

Grants.gov application package components: For the Exploration – Hypothesis Development Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

   - **Attachment 1: Project Narrative (four-page limit):** Upload as "ProjectNarrative.pdf."

     Describe the proposed project in detail using the outline below. ***The presentation of preliminary data is encouraged, but not required.***

     ○ **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.

- ○ **Specific Aims:** Concisely explain the project's specific aims to be funded by this application. If this proposed work is part of a larger study, present only tasks that this award would fund.

- ○ **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail. Address potential problem areas and present alternative methods and approaches. Describe the statistical plan if appropriate for the research proposed. ***This award may not be used to conduct studies that are not exempt under 32 CFR 219.101(b) or eligible for expedited review (32 CFR 219.110 or 21 CFR 56.110).***

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***Each component has no page limit unless otherwise noted.***

  - ○ References Cited (five-citation limit): List the references cited (including URLs if available) in the project narrative using a standard reference format that includes the full citation (i.e. author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

  - ○ List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.

  - ○ Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project, and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present contract/assistance agreement under which the facilities or equipment items are now accountable. There is no form for this information.

  - ○ Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then they must be included. Extra items will not be reviewed.

  - ○ Letters of Organizational Support: Provide a letter (or letters if applicable), signed by the Department Chair or appropriate organization official, reflecting the laboratory space, equipment, and other resources available for the project.

  - ○ Letters of Collaboration (if applicable): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.

  - ○ Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

  - ○ Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, for more information about the expectations for making data and research resources publically available.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Technical abstracts should be written using the outline below.

  - Background: Present the ideas and reasoning behind the proposed work.

  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.

  - Specific Aims: State the specific aims of the study.

  - Study Design: Briefly describe the study design including appropriate controls.

  - Innovation: Briefly describe how the proposed project is innovative and advances the detection, diagnosis, and/or treatment of TSC.

  - Impact: Briefly describe how the proposed project will have an impact on TSC research or patient care.

- **Attachment 4: Public Abstract (one-page limit):** Upload as "PublicAbs.pdf."

  Public abstracts should be written using the outline below.

  - Clearly describe, in a manner readily understood by lay persons, the rationale and objective for the proposed work.

    – Do not duplicate the technical abstract.

  - Describe the ultimate applicability of the research.

    – What types of patients will it help, and how will it help them?

    – What are the potential clinical applications, benefits, and risks?

    – What is the projected time it may take to achieve a patient-related outcome?

  - If the research is too basic for clinical applicability, describe the interim outcomes.

  - What are the likely contributions of this study to advancing the field of TSC research or patient care?

- **Attachment 5: Statement of Work (SOW) (two-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C., for detailed information.

- **Attachment 6: Impact Statement (one-page limit):** Upload as "Impact.pdf." Explain how the expected results of the study will make an original and important contribution to the goal of advancing TSC research and its impact on patient care. Describe the potential for translation to clinical applications, benefits, and risks.

- **Attachment 7: Innovation Statement (one-page limit):** Upload as "Innovation.pdf." Summarize how the proposed work is innovative. Investigating the next logical step or incremental advancement on published data is not considered innovative.

  Although not all-inclusive, the following examples are ways in which the proposed work may be innovative, and are intended to help PIs frame the innovative features:

- 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.

- Novel method or technology: Development of a novel method or technology for preventing, detecting, diagnosing, or treatment.

- 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.

3. **Research & Related Senior/Key Person Profile (Expanded) Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."

   - PI Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."

   - Key Personnel Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C., for detailed information.

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C., for detailed information.

D.   Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet any one of the deadlines shall result in application rejection.

E.   Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All applications must be submitted through Grants.gov. Organizations are required to provide a Data Universal Number System (DUNS) number and register with the Central Contractor Registry (CCR) to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General, USAMRMC, based on technical merit, the relevance to the mission of the DOD and CDMRP, and the specific intent of the award mechanism. The highest scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.shtml.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each level of review requires panelists to sign a non-disclosure statement attesting that application 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 corrective actions. Organizational personnel and PIs are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations from Federal awards. Furthermore, it is a crime for Federal officials to disclose confidential information of one party to another third party (Title 18 United States Code 1905).

B. Application Review Criteria

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of decreasing importance:

   - **Innovation**
     - To what extent 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, or other ways.
     - How well the proposed research represents more than an incremental advance upon published data.

   - **Impact**
     - How well the project addresses a critical problem in TSC research or patient care.
     - How the project will, if successful, make an original and important contribution to the goal of advancing research on the treatment of TSC, or on the quality of life of patients.

- **Research Strategy and Feasibility**
  - How the scientific rationale supports the project and its feasibility as demonstrated by a critical review and analysis of the literature and logical reasoning.
  - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed and integrated into the project.
  - How well the PI identifies potential problems and addresses alternative approaches.
  - How the expected results should give rise to a testable hypothesis.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Personnel**
  - The PI's potential for contributing to the TSC research field.
  - How the PI's record of accomplishment demonstrates his/her ability to accomplish the proposed work.
  - Appropriateness of the levels of effort for successful conduct of the proposed work.

- **Environment**
  - How the scientific environment is appropriate for the proposed research.
  - How the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
  - How the quality and extent of institutional support are appropriate for the proposed research.

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.

- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

2. **Programmatic Review:** To determine the application's relevance to the mission of the DOD and CDMRP, as well as to make funding recommendations, the following equally considered criteria are used by programmatic reviewers:

- Adherence to the intent of the award mechanism
- Program portfolio composition
- Programmatic relevance
- Ratings and evaluations of the peer reviewers
- Relative impact and/or innovation

C. Recipient Qualification

Refer to the General Application Instructions, Appendix 1, for additional information on organization and Government agency requirements.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive notification of the funding recommendation. PIs will receive a scientific peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Pre-application is not submitted.

B. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative
- Documents not requested will be removed.
- Following the application deadline, you may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed in Section IV.A., Rejection). The missing documents must be provided by 5:00 p.m. ET on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- FY11 TSCRP Integration Panel (IP) member is found to be involved in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting

document. A list of the FY11 TSCRP IP members may be found at
http://cdmrp.army.mil/tscrp/panels/panels11.shtml.

- Submission of the same research project to different funding opportunities within the same program and fiscal year.

- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.

- Direct costs as shown on the Research and Related Budget form exceed the maximum allowed by this Program Announcement/Funding Opportunity.

- Inclusion of URLs with the exception of links to published references.

- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

- Studies not exempt under 32 CFR 219.101(b) or eligible for expedited review (32 CFR 219.110 or 21 CFR 56.110).

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2012. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

Refer to the General Application Instructions, Appendix 4, Section C, for general information regarding administrative and national policy requirements.

C. Reporting

Refer to the General Application Instructions, Appendix 4, Section D, for general information on reporting requirements.

D. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section E, for general information on PI changes.

Changes in organization are not allowed once the application has been awarded except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

VI. AGENCY CONTACTS

A.   CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements and questions related to the submission of the pre-application through the CDMRP eReceipt System should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 1-301-682-5507

Email: help@cdmrp.org

B.   Grants.gov Contact Center

Questions related to application submission through the Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. Federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 1-800-518-4726

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed.	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.	
	Upload Supporting Documentation (Support.pdf) as Attachment 2.	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.	
	Upload Public Abstract (PublicAbs.pdf) as Attachment 4.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Impact Statement (Impact.pdf) as Attachment 6.	
	Upload Innovation Statement (Innovation.pdf) as Attachment 7.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Current & Pending Support (Support_LastName.pdf) to the appropriate field.	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
	Attach Current & Pending Support (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete form as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.	