

Program Announcement

for the

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Congressionally Directed Medical Research Programs

Tuberous Sclerosis Complex Research Program

Pilot Clinical Trial Award

Funding Opportunity Number: W81XWH-14-TSCRP-PCTA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), July 10, 2014
- **Application Submission Deadline:** 11:59 p.m. ET, July 24, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, July 29, 2014
- **Peer Review:** September 2014
- **Programmatic Review:** November 2014

Change for Fiscal Year 2014: *The CDMRP eReceipt System has been replaced with the electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.*

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2014 (FY14) Tuberous Sclerosis Complex Research Program (TSCRCP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The TSCRCP was initiated in 2002 to provide support for research of exceptional scientific merit and to promote innovative research focused on decreasing the clinical impact of tuberous sclerosis complex (TSC). Appropriations for the TSCRCP from FY02 through FY13 totaled \$47 million (M). The FY14 appropriation is \$6M.

B. FY14 TSCRCP Mission and Focus Areas

The mission of the FY14 TSCRCP is to encourage innovative research to improve the lives of individuals with TSC through understanding the pathogenesis and manifestations of TSC and developing improved diagnostic and treatment approaches. Within this context, the FY14 TSCRCP encourages applications that address one or more of these vital program Focus Areas:

- Clinical Aspects of TSC
 - Infantile spasms and epileptic encephalopathy, including biomarkers for early diagnosis and treatment
 - Neurocognitive, sleep, and behavioral issues, e.g., TAND (TSC-associated neuropsychiatric disorders)
 - Impact of TSC manifestations in adults, including LAM and angiomyolipomas
- Personalization of Care
 - Developmental origin of TSC manifestations
 - Phenotype/genotype studies and genetic modifiers
 - Gene dose and lesional genetics
 - Biomarkers for perinatal/newborn screening
- Optimization of Treatments
 - Pathogenesis-based biomarkers of disease progression and response to treatment
 - Development or validation of clinical endpoints in TSC
 - Identification or development of novel pathogenesis-based treatment targets
 - Continued refinement of cell-based and preclinical models
 - Dose, timing, and duration of treatment with mTORC-1 inhibitors

If the proposed research project does not address one of the FY14 Focus Areas, justification that the proposed research project addresses an important problem related to TSC research and/or patient care should be provided.

TSCRCP Research Resources Initiative: Resources developed through TSCRCP 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 proposed research project. For more guidance on data sharing, *refer to the General Application Instructions, Appendix 4, Section L.*

C. Award Information

The TSCRCP Pilot Clinical Trial Award mechanism was offered for the first time in FY13. Since then, four Pilot Clinical Trial Award applications have been received and one has been recommended for funding.

The TSCRCP Pilot Clinical Trial Award mechanism supports exploratory studies involving limited human exposure that produce diagnostic or therapeutic information (e.g., screening studies, microdose studies), toxicity studies of an intervention, and studies to determine the mechanism of action and side effects of an intervention. These studies should be aimed at obtaining preliminary data leading to the development of interventions, as well as clinical biomarkers, and endpoints, with the potential to improve TSC outcomes.

Examples of studies *include but are not limited to the following:*

- Identification of an appropriate population.
- Identification of the dosage, duration, and/or delivery strategy of an intervention.
- Evaluation of the feasibility of the intervention in TSC.
- Evaluation of efficacy and safety.

If the clinical trial involves the use of a drug that has not been approved by the U.S. Food and Drug Administration (FDA) for the proposed investigational use, then an Investigational New Drug (IND) application to the FDA that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312) may be required and must be submitted to the FDA *prior to the application submission deadline*. If the investigational product is a device, evidence that an Investigational Device Exemption (IDE) application that meets all requirements under 21 CFR 812 has been submitted to the FDA *prior to the application submission deadline*, or that the device is exempt from an IDE, is required. Documentation of *approval of the IND or IDE prior to Programmatic Review* must be obtained and submitted to the CDMRP Help Desk (help@eBRAP.org), otherwise the Government reserves the right to withdraw the application.

The following are important aspects of submission for the Pilot Clinical Trial Award:

- The application must include scientific rationale and/or preliminary data relevant to TSC and the proposed study.
- The application must demonstrate documented availability of, and access to, the drug/compound, device, and/or other materials needed, as appropriate.
- The application should demonstrate documented availability of, and access to, a suitable patient population that will support a meaningful outcome for the study.
- The application should clearly describe the steps that will be taken to advance the clinical biomarker, endpoint, or intervention into the next stage of development following the conclusion of this award.
- Preclinical studies will not be supported by this mechanism.

Use of Human Subjects and Human Anatomical Substances: The term “human subjects” is used in this Program Announcement/Funding Opportunity to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at <https://ebrap.org/eBRAP/public/Program.htm>. 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 U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local 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 will require information in addition to that supplied to the IRB. Allow a minimum of 2-3 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for more information.

The Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section L.

D. Eligibility Information

- PIs *at or above* the level of Assistant Professor (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations.
- 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 are **\$200,000** plus indirect costs.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- 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.
- 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.4., for budget regulations and instructions for the Research & Related Budget. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions.***

For this award mechanism, direct costs:

May be requested for (not all-inclusive):

- Salary
- Research-related subject costs
- Clinical research costs
- Research supplies
- Equipment
- Travel between collaborating organizations
- Travel costs of up to \$1,800 per year to attend scientific/technical meetings

Shall not be requested for:

- Preclinical research studies

Intramural (DoD), other federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. ***In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.***

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from federal agencies submit applications, they must submit through Grants.gov. Therefore, federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other federal agencies will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Direct transfer of funds from the recipient to a federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4. Research & Related Budget, for additional information on budget considerations for applications involving federal agencies.

The CDMRP expects to allot approximately \$0.64M of the \$6.0M FY14 TSCRP appropriation to fund approximately 2 Pilot Clinical Trial 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 two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (<https://eBRAP.org/>) and (2) application submission through Grants.gov (<http://www.grants.gov/>).

New for FY14: *The CDMRP has replaced its eReceipt System with eBRAP.* Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at <https://ebrap.org/eBRAP/public/UserGuide.pdf>). Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. *Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.* If verification is not completed

by the end of the application verification period, the application will be reviewed as submitted through Grants.gov or may be subject to administrative rejection (see [Section IV.A., Rejection](#)).

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application.

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-14-TSCR-PCTA.

B. Pre-Application Submission and Content Form

All pre-application components must be submitted by the PI through eBRAP (<https://eBRAP.org/>).

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

The pre-application consists of the following components, which are organized in eBRAP 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**

- It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

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

FY14 TSCR Integration Panel (IP) members should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to [Section IV.C., Withdrawal](#), or contact the CDMRP at help@eBRAP.org or 301-682-5507.

- **Required Files – Tab 4**

Letter of Intent (LOI) (one-page limit): Provide a brief description of the research to be conducted. 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**

This tab must be completed for the pre-application to be accepted and processed.

C. Application Submission Content and Forms

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 through the Grants.gov portal (<http://www.grants.gov/>).

New for FY14: Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification. The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in [Section IV.A., Rejection](#)), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Proposal Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a “Changed/Corrected Application” with the Previous Grants.gov Tracking ID **prior to the application submission deadline (which occurs earlier than the end of the application verification period).**

Grants.gov application package components: For the Pilot Clinical Trial 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 (10-page limit):** Upload as “ProjectNarrative.pdf.” The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and will result in administrative withdrawal of the application.

Describe the proposed project in detail using the outline below.

- **Background:** Describe in detail the clinical biomarker, endpoint, or intervention and rationale for the proposed pilot clinical trial and include a literature review, preliminary studies, and/or preclinical data that led to the development of the proposed study. Establish the relevance of the study and explain the applicability of the proposed findings. ***The Project Narrative must include scientific rationale and/or preliminary data relevant to TSC and the proposed pilot clinical trial.***

- **For interventional studies:** Include a discussion of any current clinical use of the intervention under investigation and/or details of its study in clinical trials for other indications (as applicable).
- **For clinical biomarker and clinical endpoint studies:** Describe how the validation or qualification of the proposed candidate biomarker(s) or endpoint(s) will address critical problems in TSC clinical care and to what degree the biomarker(s) or endpoint(s) will be assessed through noninvasive or minimally invasive means, if applicable.
- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the proposed pilot clinical trial with detailed specific aims and/or study questions/hypotheses.
- **Research Strategy and Feasibility:** Describe the type of proposed pilot clinical trial to be performed and outline the proposed methodology in sufficient detail to show a clear course of action.
 - Describe variables, projected outcomes, and endpoints to be studied, as applicable.
 - Describe the method that will be used to recruit human subjects from the accessible population, including the inclusion and exclusion criteria.
 - Describe the data or statistical analyses that will be performed.
 - Describe methods used for sample and data collection, including controls as appropriate.
 - Describe the availability of, and access to, the drug, compound, device, and/or other materials needed, as appropriate.
- **Transition Plan:** Describe the steps that will be taken to advance the clinical biomarker(s), endpoint(s), or intervention into the next stage of development following the conclusion of this award.
- **Ethical Considerations:** Describe the process for seeking informed consent and clearly identify all study risks and describe safety measures to minimize risks to human subjects and study personnel.
- **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. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested may result in the removal of those items or administrative withdrawal of the application.***
 - **References Cited:** 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 whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award 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 a copy/copies of the published manuscript(s) must be included in Attachment 2. 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, confirming 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.
- Availability of Intervention (if applicable): If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
- Intellectual Property
 - Background and Proprietary Information: All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. Provide a list of all background intellectual property to be used in the project. Identify any proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.
 - Intellectual and Material Property Plan: Provide a plan for resolving intellectual and material property issues among participating organizations.
- Data and Research Resources Sharing Plan (if applicable): Describe how data and resources generated during the performance of the proposed pilot clinical trial will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section L for more information about the CDMRP expectations for making data and research resources publicly available.

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

Technical abstracts should be written using the outline below. The technical abstract is used by all reviewers. Of particular importance, programmatic reviewers do not have access to the full application and therefore rely on the technical abstract for appropriate description of the project’s key aspects.

- Background: Present the ideas and reasoning behind the proposed pilot clinical trial.
- 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 proposed pilot clinical trial.
- Study Design: Briefly describe the study design including appropriate controls and endpoints, as appropriate.
- Clinical Impact: Briefly describe how the proposed pilot clinical trial will have an impact on TSC patient care.

- **Attachment 4: Lay Abstract (one-page limit):** Upload as “LayAbs.pdf.”

Lay abstracts should be written using the outline below. The lay abstract is used by consumer reviewers along with other components of the application package.

- Clearly describe, in a manner readily understood by lay persons, the rationale and objective for the proposed research project.
 - 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 the proposed study to advancing TSC patient care?

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as “SOW.pdf.” Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

The suggested SOW format and examples specific to different types of research projects are available on the eBRAP “Program Announcement and Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>). For the Pilot Clinical Trial Award mechanism, use the SOW format example titled “SOW for Clinical Research (Including Trials, Special Populations).” The SOW must be in PDF format prior to attaching.

- **Attachment 6: Impact Statement (one-page limit):** Upload as “Impact.pdf.”
 - Explain how the proposed pilot clinical trial addresses one or more of the FY14 TSCRP Focus Areas, or, if the project does not address a Focus Area, provide justification that the proposed pilot clinical trial addresses an important problem in TSC patient care.
 - Identify the volunteer population(s) that will participate in the proposed pilot clinical trial.
 - Describe the short-term impact: Detail the anticipated outcome(s) that will be directly attributed to the results of the proposed study.
 - Describe the long-term impact: Explain the anticipated long-term gains from the proposed study, including how the new understanding may ultimately contribute to the goal of advancing TSC patient care.
 - Describe any relevant controversies or treatment issues that will be addressed by the proposed pilot clinical trial and any potential issues that may limit its impact.
 - Compare the proposed intervention to other interventions currently available or standard of care, if applicable.

- **Attachment 7: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit):** Upload as “Surveys.pdf.” The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the proposed pilot clinical trial. Describe the psychometrics of each instrument and discuss whether any modifications will be made to the instrument.

- **Attachment 8: IND/IDE Documentation (if applicable):** If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “IND-IDE.pdf.”
 - Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov.
 - For studies requiring an IND or IDE, provide the status of the FDA application (e.g., past the critical 30-day period, pending response to questions raised, on clinical hold). Inclusion of a copy of the FDA meeting minutes is encouraged but not required. If an IND or IDE is not required for the proposed pilot clinical trial, provide evidence in the form of communication from the FDA or the IRB of record to that effect.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information. *Note: Some of the items in this attachment may be made available for programmatic review.*
 - PI Biographical Sketch (four-page limit): Upload as “Biosketch_LastName.pdf.”
 - PI Previous/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 Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”
4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., 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.5., for detailed information.
6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. *The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*

E. 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 either of these deadlines will result in application rejection.

F. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an “Active” status 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 applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, U.S. Army Medical Research and Materiel Command (USAMRMC), based on (a) technical merit and (b) the relevance to the mission of the DHP and TSCRCP and to 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 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. Panel members sign a non-disclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations 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 panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

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

- **Clinical Impact**
 - How well the applicant addresses one or more of the TSCRP Focus Areas and/or a critical problem in TSC patient care.
 - To what extent the anticipated outcomes of the proposed pilot clinical trial are relevant to individuals with TSC.
 - How the potential outcomes of the proposed clinical trial will significantly provide/improve short-term and long-term benefits for individuals with TSC.
- **Research Strategy and Feasibility**
 - How well the scientific rationale and/or preliminary data support the proposed pilot clinical trial.
 - How well the study design supports the objective of the proposed pilot clinical trial.
 - To what extent the proposed pilot clinical trial is feasible as described.
- **Personnel:**
 - To what extent the levels of effort by the PI and other key personnel are appropriate to ensure success of the proposed pilot clinical trial.
 - To what degree the study team's experience, expertise, and records of accomplishment are appropriate to successfully complete the proposed pilot clinical trial (e.g., statistical expertise, expertise in the disease, and clinical studies).

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

- **Ethical Considerations**
 - How well the applicant identifies potential study risks and outlines safety steps to protect study subjects and staff.
- **Environment**
 - To what degree the scientific environment is appropriate for the proposed study.
 - How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
 - To what degree the quality and extent of institutional support/commitment are appropriate for the proposed study.
 - If applicable, to what degree the intellectual and material property plan is appropriate.

- **Budget**
 - Whether the budget is appropriate for the proposed study and within the limitations of this Program Announcement/Funding Opportunity.
 - **Application Presentation**
 - To what extent the writing, clarity, and presentation of the application components influence the review.
- 2. Programmatic Review:** To make funding recommendations, the following equally considered criteria are used by programmatic reviewers:
- a. Ratings and evaluations of the peer reviewers**
 - b. Relevance to the mission of the DHP and FY14 TSCRP, as evidenced by the following:**
 - Adherence to the intent of the award mechanism
 - Program portfolio composition, with consideration of the FY14 TSCRP Focus Areas
 - Programmatic relevance
 - Relative impact

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

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 email notification of posting of the funding recommendation in eBRAP. Each PI will receive a 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:

- Pre-application was not submitted.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- For studies requiring an IND or IDE (Attachment 8), documentation of IND/IDE application to the FDA is missing.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in [Section IV.A., Rejection](#)), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- A FY14 TSCRP IP member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. A list of the FY14 TSCRP IP members can be found at <http://cdmnp.army.mil/tscrp/panels/panels14.shtml>.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.

- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The proposed research is not a clinical trial.
- The PI does not meet the eligibility criteria.
- For studies requiring an IND or IDE, documentation of IND/IDE approval is not submitted to the CDMRP Help Desk (help@eBRAP.org) prior to Programmatic Review.

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 USAMRAA 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, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 5 for general information regarding national policy requirements.

D. Reporting

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

E. Award Transfers

Changes in PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

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

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP 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: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

Questions related to application submission through 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: 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 or by responding to the prompt provided by Grants.gov when first downloading the application package. 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	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	Surveys, Questionnaires, and Other Data Collection Instructions: Upload as Attachment 7 with file name "Surveys.pdf."	
	IND/IDE Documentation: Upload as Attachment 8 with file name "IND-IDE.pdf."	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Previous/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 Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete 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.	