

Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Tuberous Sclerosis Complex Research Program

Pilot Clinical Trial Award

Funding Opportunity Number: W81XWH-15-TSCR-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, 2015
- **Application Submission Deadline:** 11:59 p.m. ET, July 27, 2015
- **End of Application Verification Period:** 5:00 p.m. ET, July 30, 2015
- **Peer Review:** September 2015
- **Programmatic Review:** November 2015

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 2015 (FY15) Tuberous Sclerosis Complex Research Program (TSCRCP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs, the DHA RDA Directorate manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The executing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). 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 FY14 totaled \$53 million (M). The FY15 appropriation is \$6M.

B. FY15 TSCRCP Mission and Focus Areas

The mission of the FY15 TSCRCP is to encourage innovative research aimed at understanding the pathogenesis and preventing and treating the manifestations of TSC. Within this context, the FY15 TSCRCP encourages applications to address one or more of the following Focus Areas:

- Mechanisms Underlying Clinical Manifestations
 - Epilepsy
 - Neurocognition and behavior
 - Tumor development and progression
 - Cell and animal models
 - Genetics and disease modifiers
- Novel Therapeutic Strategies
 - Dose, timing, and duration of mTOR inhibitors and other therapeutics
 - New targets and combination therapies
 - Preclinical and clinical studies
 - Biomarkers
 - Preventative therapies

If the proposed research project does not address one of the FY15 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 3, Section L.

C. Award Information

The TSCRCP Pilot Clinical Trial Award (PCTA) mechanism was offered for the first time in FY13. Since then, eight PCTA applications have been received and three have been recommended for funding.

The PCTA mechanism supports exploratory studies involving limited human exposure that produce diagnostic or therapeutic information, safety, and tolerability studies and studies to determine the mechanism of action. These studies should be aimed at obtaining preliminary data leading to the development of interventions, as well as clinical biomarkers, with the potential to improve TSC outcomes. ***Preclinical studies will not be supported by this mechanism.***

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

- Identification of an appropriate population for the proposed study.
- Identification of the dosage, duration, and/or delivery strategy of an intervention.
- Evaluation of the feasibility of the intervention in TSC.
- Development of clinical biomarkers or outcome measures for future clinical trials.
- 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) 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 or exemption 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 preliminary data relevant to TSC and the proposed study.
- Demonstrate documented availability of, and access to, the drug, compound, device, and/or other materials needed, as appropriate.

- Demonstrate documented availability of, and access to, a suitable patient population that will support a meaningful outcome for the study.
- Clearly describe the steps taken to advance the clinical biomarker, or intervention into the next stage of development following the conclusion of the work proposed in this award.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All Department of Defense (DoD)-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers 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 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 requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes.*** The HRPO reviews and approves the participation of each site in the clinical trial. Refer to the General Application Instructions, Appendix 5, and the Human Subject Resource Document available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information.

The CDMRP intends that information, 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 3, 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, nonprofit, 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 anticipated direct costs budgeted for the entire period of performance will not exceed **\$300,000**. Associated indirect costs can be budgeted in accordance with the organization’s negotiated rate. No budget will be approved by the Government

exceeding **\$300,000** direct costs or using an indirect rate exceeding the organization's negotiated rate.

- 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.

Refer to the General Application Instructions, Section II.C.5., 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.5. 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 to attend scientific/technical meetings

Shall not be requested for:

- Preclinical research costs

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 Section II.A. 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 may be executed through a direct fund transfer (e.g., 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.5. Research & Related Budget, for additional information on budget considerations for applications involving Federal agencies.

The CDMRP expects to allot approximately \$0.96M of the \$6M FY15 appropriation to fund approximately two 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 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.

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/>). Refer to the General Application Instructions, Section II.A. for registration and submission requirements for eBRAP and Grants.gov.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements, and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

PIs should ensure that their name and email address are the same as the name and email address that will be provided on the SF-424 Form of the Grants.gov application package submitted to Grants.gov. The organization, Business Officials, PI(s), and eBRAP log number named in the full application submitted to Grants.gov must match those named in the pre-application in eBRAP. ***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.***

A. Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-15-TSCR-PCTA in Grants.gov (<http://www.grants.gov/>).

B. Pre-Application Submission Content

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**
 - Enter contact information for the PI. Enter the organization’s Business Official responsible for sponsored program administration (the “person to be contacted on matters involving this application” in Block 5 of the Grants.gov SF-424 Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
 - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Collaborators and Key Personnel – Tab 3**
 - Enter the name, organization, and role of all collaborators and key personnel associated with the application.
 - FY15 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 Help Desk at help@eBRAP.org or 301-682-5507.
- **Conflicts of Interest (COIs) – Tab 4**
 - List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship).
- **Pre-Application Files – Tab 5**
 - **Letter of Intent (LOI) (one-page limit):** Provide a brief description of the research to be conducted. If applicable, include the Focus Area 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 6**

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

C. Full Application Submission Content

The CDMRP cannot make allowances/exceptions to its policies for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.

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

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline. If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a “Changed/Corrected Application” with the previous Grants.gov Tracking ID ***prior to the application submission deadline.***

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**

Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

- **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 may result in administrative withdrawal of the application.

Describe the proposed project in detail using the outline below.

- **Background:** Describe in detail the clinical biomarker or intervention, and the rationale for the proposed pilot clinical trial. Include review of literature, preliminary studies, and 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 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 studies:* Describe how the validation or qualification of the proposed candidate biomarker(s) will address critical problems in TSC clinical care and to what degree the biomarker(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 study 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 the following:
 - Intervention to be tested, as applicable.
 - Variables, projected outcomes, as applicable.
 - Method that will be used to recruit human subjects from the accessible population, including the inclusion and exclusion criteria.
 - Data or statistical analyses that will be performed.
 - Methods used for sample and data collection, including controls, as appropriate.
 - 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) or intervention into the next stage following the conclusion of this award.
- **Ethical Considerations:** Describe the process for seeking informed consent, clearly identify all study risks, and describe the safety measures that will be utilized 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 will result in the removal of those items or may result in 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: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may 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 support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.
- 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. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the 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 (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 3, 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.”** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

The technical abstract is used by all reviewers. Of particular importance, programmatic reviewers may not have access to the full application and therefore rely on the technical abstract for appropriate description of the project’s key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

Technical abstracts should be structured to include the following points:

- Background: Present the ideas and rationale behind the proposed pilot clinical trial.
- Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence and rationale that support the objective/hypothesis.
- Specific Aims: List the specific aims.
- 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.”** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

The lay abstract is an important component of the application review process because it addresses issues of particular interest to the advocate community. The lay abstract 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 and impact 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?
- 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.”** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP “Funding Opportunities & 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. Refer to the General Application Instructions, Section II.C.3., for detailed guidance on creating the SOW.
- **Attachment 6: 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 study.
- **Attachment 7: Impact Statement (one-page limit). Upload as “Impact.pdf.”**
 - Explain how the proposed pilot clinical trial addresses one or more of the FY15 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: Indicate 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 8: IND/IDE Documentation:** 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 an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the Agency, on clinical hold). Provide a summary of previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.
 - If an IND or IDE is not required for the proposed study, provide evidence in the form of communication from the FDA or the IRB of record to that effect.
 - **Attachment 9: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as “MFBudget.pdf.”** If a Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form (available for download on the eBRAP “Funding Opportunities & Forms” web page), including a budget justification, for each Military Facility as instructed. Refer to the General Application Instructions, Section II.C.8., for detailed information.
- 3. Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information. Note: Some of the items in this attachment may be made available for programmatic review.
- **PI Biographical Sketch (five-page limit):** Upload as “Biosketch_LastName.pdf.” The suggested biographical sketch format is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP. The five-page National Institutes of Health Biographical Sketch may also be used.
 - **PI Previous/Current/Pending Support (no page limit):** Upload as “Support_LastName.pdf.”
 - **Key Personnel Biographical Sketches (five-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.5., for detailed information.
 - Budget Justification (no page limit): Upload as “BudgetJustification.pdf.” The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.
5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.6., for detailed information.
6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.7., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the Grants.gov application submission. eBRAP will validate retrieved files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content. It is the applicant’s responsibility to review all application components and ensure proper ordering as specified in the Program Announcement/Funding Opportunity. *If either the Project Narrative or the budget fails eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov as a “Changed/Corrected Application” with the previous Grants.gov Tracking ID prior to the application submission deadline.* The Project Narrative and Budget Form cannot be changed after the application submission deadline.

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, Section II.A., for information on Grants.gov registration 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 DHA RDA Directorate and the Office of the Assistant Secretary of Defense for Health Affairs, 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 nondisclosure 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 of equal importance:
 - **Clinical Impact**
 - How well the application addresses one or more of the FY15 TSCRCP 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 short-term and long-term benefits for individuals with TSC.
 - **Rationale**
 - How well the scientific rationale, including a well-formulated, testable hypothesis, supports the proposed pilot clinical trial.
 - To what extent the provided preliminary data support the proposed pilot clinical trial.

- **Research Strategy and Feasibility**
 - 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., expertise in disease, statistics, and clinical studies).

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

- **Ethical Considerations**
 - How well the application 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 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 influence the review.

2. Programmatic Review: To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, 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 FY15 TSCRP, as evidenced by the following:**

- Adherence to the intent of the award mechanism
- Program portfolio composition, with consideration of the FY15 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.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- A FY15 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 FY15 TSCRP IP members can be found at <http://cdmrp.army.mil/tscrp/panels/panels15.shtml>.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- 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.
- An application submitted by a PI who does not meet the eligibility criteria will be withdrawn.
- 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, 2016. Refer to the General Application Instructions, Appendix 3, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms

and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, “Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards” (2 CFR part 200).

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 3, for general information regarding administrative requirements.

C. National Policy Requirements

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

D. Reporting

Refer to the General Application Instructions, Appendix 3, Section I, for general information on reporting requirements.

E. Award Transfers

The institution transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

Refer to the General Application Instructions, Appendix 3, 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 Grants.gov application package. If the Grants.gov 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	Upload Order	Action	Completed
SF-424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Surveys, Questionnaires, and Other Data Collection Instructions: Upload as Attachment 6 with file name "Surveys.pdf."	
	7	Impact Statement: Upload as Attachment 7 with file name "Impact.pdf."	
	8	IND/IDE Documentation: Upload as Attachment 8 with file name "IND-IDE.pdf."	
	9	Collaborating DoD Military Facility Budget Form(s): Upload Attachment 9 with file name "MFBudget.pdf," if applicable.	
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.	