Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Tuberous Sclerosis Complex Research Program

Exploration – Hypothesis Development Award

Funding Opportunity Number: W81XWH-16-TSCRP-EHDA

Catalog of Federal Domestic Assistance Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), July 1, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, July 18, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, July 21, 2016
- **Peer Review:** September 2016
- **Programmatic Review:** November 2016

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 2016 (FY16) Tuberous Sclerosis Complex Research Program (TSCRP) 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 (OASD[HA]), the DHA RDA Directorate manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The managing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The TSCRP 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 TSCRP from FY02 through FY15 totaled $59 million (M). The FY16 appropriation is $6M.

B. FY16 TSCRP Mission and Focus Areas

The mission of the FY16 TSCRP is to encourage innovative research aimed at understanding the pathogenesis, and preventing and treating the manifestations of TSC. Within this context, the FY16 TSCRP encourages applications to address one or more of the following Focus Areas:

- Understanding phenotypic heterogeneity in TSC
- Gaining a deeper knowledge of TSC signaling pathways and the cellular consequences of TSC deficiency
- Improving TSC disease models
- Developing clinical biomarkers for TSC
- Facilitating therapeutics and clinical trials research

If the proposed research project does not address one or more of the FY16 Focus Areas, justification that the proposed research project addresses an important problem or unmet need related to TSC research and/or patient care should be provided.

TSCRP Research Resources Initiative: Resources developed through TSCRP funding are available to the scientific community and can be found at http://cdmrp.army.mil/tscrp/resources/tscresources; investigators are urged to leverage these resources. Investigators are expected to share data and resources developed through TSCRP funding via the Research Resources. A Data and Resource Sharing Plan (Attachment 8) describing how data and resources generated during the performance of the proposed research project will be made available to the scientific community should be included in the application. For additional guidance on sharing data and research resources information, refer to the General Application Instructions, Appendix 4, Section K.

C. Award Information

The TSCRP Exploration – Hypothesis Development Award (EHDA) mechanism was first offered in FY02. Since then, 143 EHDA applications have been received, and 30 have been recommended for funding.

The EHDA supports the initial exploration of innovative, high-risk, high-gain, and potentially groundbreaking concepts in the TSC research field. The studies supported by this award mechanism are expected to lay the groundwork for future avenues of scientific investigation. The proposed research project should include a well-formulated, testable hypothesis based on strong scientific rationale and study design. ***Preliminary and/or published data are not required.***

The proposed research project must be innovative, feasible, and supported by strong rationale. Innovative research may introduce a novel paradigm, challenge existing paradigms, look at existing problems from novel perspectives, or exhibit other highly creative qualities. Research that is an incremental advance upon published data is not considered innovative and is not consistent with the intent of this award mechanism. It is the responsibility of the Principal Investigator (PI) to clearly and explicitly articulate how the proposed research project is innovative in the field of TSC.

Research involving human subjects and human anatomical substances is permitted; however, studies must be exempt under Title 32 of the Code of Regulations, Part 219.101(b) (32 CFR 219.101(b)) or eligible for expedited review (32 CFR 219.110 or 21 CFR 56.110). Exemption or expedited status is first determined by the Institutional Review Board (IRB) of record. Investigators must review their institutional requirements and guidelines for filing with the IRB for exempt or expedited status. Studies that do not qualify for exempt or expedited status will be administratively withdrawn. ***Clinical trials are not allowed under this Program Announcement/Funding Opportunity.*** For more information on clinical trials and clinical research overall, a Human Subject Resource Document is provided on the electronic Biomedical Research Application Portal (eBRAP) system at https://ebrap.org/eBRAP/public/Program PIs wishing to apply for funding for a pilot clinical trial should utilize the FY16 TSCRP Pilot Clinical Trial Award mechanism (Funding Opportunity Number: W81XWH-16-TSCRP-PCTA).

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) prior to research implementation. This administrative review requirement is in addition to the local Institutional Review Board (IRB) or Ethics Committee (EC) review. Local IRB/EC 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/EC. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. Refer to the General Application Instructions, Appendix 6, 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.

Research Involving Animals: All DoD-funded research involving new and ongoing research with animals must be reviewed and approved by the USAMRMC ORP Animal Care and Use Review Office (ACURO), in addition to the local Institutional Animal Care and Use Committee (IACUC) of record. IACUC approval at the time of submission is not required. Specific documents relating to the use of animals in the proposed research will be requested **if the application is selected for funding**. The ACURO must review and approve all animal use prior to the start of working with animals, including amendments to ongoing projects. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." ***Allow at least 2 to 3 months for ACURO regulatory review and approval processes for animal studies.*** Refer to General Application Instructions, Appendix 6, 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 4, Section K.

D. Eligibility Information

- Investigators at all academic levels (or equivalent), including postdoctoral fellows, 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 Federal agencies, national, international, for-profit, nonprofit, public, and private organizations.
- 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. Submissions from intramural (DoD) organizations are allowed and encouraged for this Program Announcement/Funding Opportunity. Applicants submitting through their intramural organizations are reminded to coordinate receipt and commitment of funds through their respective resource managers. ***If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.***
- 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 **$200,000**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$200,000** 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.

For this award mechanism, direct costs may be requested for (not all-inclusive):

- Salary
- Research supplies
- Travel costs for up to one investigator to travel to one scientific/technical meeting per year

Shall not be requested for:

- Clinical trial costs

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural (DoD) agencies and other Federal agencies may be managed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR]; Funding Authorization Document [FAD] process; or DD Form 1144 Support Agreement). Direct transfer of funds from the recipient to a DoD agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

The CDMRP expects to allot approximately $1.6M of the $6M FY16 TSCRP appropriation to fund approximately five Exploration – Hypothesis Development Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission 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(s).

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.

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. 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.

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.

The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent for the entire pre-application and application submission process. Inconsistencies may delay application processing and limit the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application deadline.

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.*** Prior to the full application deadline, a corrected or modified full application package may be submitted. Other application components may be changed until the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

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-16-TSCRP-EHDA in Grants.gov (http://www.grants.gov/).

B. Pre-Application Submission Content

The pre-application process should be started early to avoid missing deadlines. There are no grace periods. **During the pre-application process, each submission is assigned a unique log**

number by eBRAP. This unique eBRAP log number will be needed during the application process on Grants.gov.

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 preapplication, 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):

- **Tab 1 – Application Information**
- **Tab 2 – Application Contacts**
  - 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 SF424 (R&R) Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
  - Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 (R&R) Form), and click on "*Add Organizations to this Pre-application.*" The organization(s) must either be selected from the eBRAP drop-down 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.
- **Tab 3 – Collaborators and Key Personnel**
  - Enter the name, organization, and role of all collaborators and key personnel associated with the application.
  - FY16 TSCRP Programmatic Panel members should not be involved in any preapplication or application. For questions related to Programmatic Panel 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.
  - To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in application preparation, research, or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Applications that include names of

withdrawn unless plans to manage conflicts of interest (COIs) are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- **Tab 4 – Conflicts of Interest**
  - 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). Refer to Appendix 1, Section C, of the General Application Instructions for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

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

- **Tab 6 – Submit Pre-Application**
  - This tab must be completed for the pre-application to be accepted and processed.

C. Full Application Submission Content

The application process should be started early on Grants.gov to avoid missing deadlines. There are no grace periods. Verify the status of the applicant's organization's Entity registration in the SAM well in advance of the application submission deadline. Allow 3 to 4 weeks to complete the entire SAM registration process. Refer to the General Application Instructions, Section II, for additional information.

All contributors and administrators to the application must use matching compatible versions of Adobe software when editing and preparing application components. The use of different software versions will result in corruption of the submitted file. See Section II.C. of the General Application Instructions for details on compatible Adobe software.

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

1. **SF424 (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 (four-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.

     - **Rationale:** Clearly articulate the rationale for the proposed research project, including a clear mechanistic underpinning. Include relevant literature citations. ***The presentation of preliminary and/or published data is not required.***
     - **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
     - **Specific Aims:** Concisely explain the proposed research project's specific aims to be funded by this award.
     - **Research Strategy:**
       - Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for scientific peer review. Address potential problem areas and present alternative methods and approaches.
       - Describe the statistical plan appropriate for the proposed research project.

- **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 (five-citation limit): List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
    - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
    - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate 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 Patents: 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: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
    - Intellectual Property
        - Intangible property acquired, created or developed under this award will be subject to all rights and responsibilities established at 2 CFR 200.315. Should the applicant intend to use, in the performance of this program, pre-existing, legally protected and perfected intangible property and for which no Federal funds had been used in the development of said property, the applicant must:
            - Clearly identify all such property;

        - Identify the cost to the Federal government for use or license of such property, if applicable; or
        - Provide a statement that no property meeting this definition will be used on this project.
    - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf."** Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** 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 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.

  Describe the proposed research project including the following points:

  - Background: Present the ideas and rationale behind the proposed research project.
  - Hypothesis/Objective: State the hypothesis to be tested or the objective to be reached. Provide evidence or rationale that supports the objective/hypothesis.
  - Specific Aims: State the specific aims of the proposed research project.
  - Study Design: Briefly describe the study design including appropriate controls.
  - Innovation: Briefly describe how the proposed research project is innovative in the field of TSC.
  - Impact: Briefly describe how the proposed research project will have a short- and long-term impact on TSC research and/or patient care.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf."** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Lay abstracts should be written using the outline below. ***Do not duplicate the technical abstract.*** Minimize use of acronyms and abbreviations, where appropriate. The lay abstract is an important component of the application review process because it addresses issues of particular interest to the consumer community**.**

- Describe the scientific objective and rationale for the proposed project in a manner that will be ***readily understood by readers without a background in science or medicine***.
- 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 proposed research is too basic for-clinical applicability, describe the interim outcomes.
- What are the likely contributions of this proposed research project to advancing the field of TSC research and/or 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 Exploration – Hypothesis Development Award mechanism, use the SOW format example titled "SOW (Statement of Work) Generic Format." The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

- **Attachment 6: Innovation Statement (one-page limit): Upload as "Innovation.pdf."** Describe how the proposed research project is innovative in the field of TSC. Research deemed innovative may represent a new paradigm, challenge current paradigms, look at existing problems from new perspectives, or exhibit other highly creative qualities. Innovative research may include high-risk approaches. Research that is an incremental advance upon published data is not considered innovative.

  Although not all-inclusive, the following examples are ways in which the proposed research project may be innovative. The proposed research project will:

  - Explore a novel idea and/or research question in TSC.
  - Use or develop novel methods or technologies to address a question in TSC research and/or patient care.
  - Apply or adapt existing methods or technologies for novel TSC research or clinical purposes that differ fundamentally from those originally intended.

- **Attachment 7: Impact Statement (one-page limit): Upload as "Impact.pdf."** State explicitly how the proposed research project addresses one or more of the FY16 Focus Areas, or, if the project does not address a Focus Area, provide justification that the proposed research project addresses an important problem or unmet need in TSC research and/or patient care. Describe the anticipated outcomes (short-term gains) from the proposed research and how they will be used as a foundation for future research projects. Explain the anticipated long-term gains

from the proposed research project, including how the new understanding may ultimately contribute to the goal of advancing TSC research and/or patient care.

- **Attachment 8: Data and Research Resources Sharing Plan: Upload as "ResourceSharing.pdf."** Describe how data and resources generated during the performance of the proposed research project will be shared with the research community. Specifically describe a plan to make animal models, tissue samples, and other resources developed as part of the proposed research project available to the scientific community. Refer to the General Application Instructions, Appendix 4, Section K for more information about the CDMRP expectations for making data and research resources publicly available.

- **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 (https://ebrap.org/eBRAP/public/Program.htm), including a budget justification, for each Military Facility as instructed. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information.

   - 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. All biographical sketches should be submitted in the portable document format (pdf) that is not editable.

     Biographical Sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

   - 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.4., 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.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.

   Collaborating DoD Military Facilities Form: A Military Facility collaborating in the performance of the project should be treated as a subaward for budget purposes. However, do not complete the Grants.Gov R & R Subaward Budget Attachment Form; instead, complete the Collaborating DoD Military Facility Budget Form (use Attachment 9, Collaborating DoD Military Facility Budget Form) to show all direct and indirect costs. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. 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 or 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.*** 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 submission rejection.

F. Other Submission Requirements

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

All extramural 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 applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the OASD(HA), based on technical merit, the relevance to the mission of the DHP and TSCRP, the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement/Funding Opportunity. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in Section III.B.2., Programmatic Review.*** Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a 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:

- **Innovation**
  - To what extent the proposed research project is innovative to the field of TSC in one or more of the following ways: research concept or question, development of novel research methods or technologies, adaptations of existing methods or technologies.
  - To what extent the proposed research project represents more than an incremental advance upon published data and/or may be considered high risk.
- **Rationale**
  - How well the scientific rationale, including a well-formulated, testable hypothesis and clear mechanistic underpinning, supports the proposed research project.
  - To what extent the PI supports the proposed research project through critical review and analysis of published literature and/or unpublished data, if applicable.
- **Research Strategy and Feasibility**
  - To what extent the aims, experimental design, methods, and analyses are appropriate to test the hypothesis.
  - To what extent the statistical plan is appropriate to the proposed research.
  - To what extent the proposed research project is feasible as described.
  - How well the PI identifies potential problems and addresses alternative approaches.
- **Impact**
  - ***Assuming the objectives/goals of the research project are realized:***
    - To what extent the anticipated outcomes (short-term) could be used as the foundation for future research projects.
    - To what extent the anticipated long-term gains will contribute to the goal of advancing TSC research and/or patient care.
  - How well the proposed research project addresses one or more of the FY16 TSCRP Focus Areas or a critical problem or unmet need in TSC research and/or patient care.

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

- **Personnel**
  - To what degree the PI's experience, expertise, and record of accomplishment demonstrate his/her ability to successfully complete the proposed research project.
  - To what extent the levels of effort by the PI and other key personnel are appropriate to ensure success of the proposed research project.

- **Environment**
  - To what degree the scientific environment is appropriate for the proposed research project.
  - 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 research project.
  - 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 criteria are used by programmatic reviewers:

   a. **Ratings and evaluations of the peer reviewers**

   b. **Relevance to the mission of the DHP and FY16 TSCRP, as evidenced by the following:**
      - Adherence to the intent of the award mechanism
      - Program portfolio composition
      - Relative impact and innovation

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.

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:

- An FY16 TSCRP Programmatic Panel 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 FY16 TSCRP Programmatic Panel members can be found at http://cdmrp.army.mil/tscrp/panels/panels16***.
- 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).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, 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.
- If the proposed research project does not qualify for exempt status under 32 CFR 219.101(b) or is not eligible for expedited review (32 CFR 219.110 or 21 CFR 56.110), the application will be withdrawn.
- If a clinical trial is proposed, the application will be withdrawn.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization 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, 2017. Refer to the General Application Instructions, Appendix 4, 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 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 H, for general information on reporting requirements.

E. Award Transfers

Approval of a transfer request will be made on a case-by-case basis at the discretion of the Grants Officer. An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

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

VI. VERSION CODES AND AGENCY CONTACTS

A. Program Announcement/Funding Opportunity and General Application Instructions Version

Questions related to this Program Announcement/Funding Opportunity should refer to the Program name, the Program Announcement/Funding Opportunity name, and the Program Announcement/Funding Opportunity version code 20160210i. The Program Announcement/ Funding Opportunity numeric version code will match the General Applications Instructions version code 20160210.

B. 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

C. 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; International 1-606-545-5035

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
SF424 (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	Innovation Statement: Upload as Attachment 6 with file name "Innovation.pdf."	
	7	Impact Statement: Upload as Attachment 7 with file name "Impact.pdf."	
	8	Data and Research Resources Sharing Plan: Upload as Attachment 8 with file name "ResourceSharing.pdf."	
	9	Collaborating DoD Military Facility Budget Form(s): Upload as 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.	