Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Joint Program Committee 8 / Clinical and Rehabilitative Medicine Research Program

Reconstructive Transplant Research Translational Research Award

Funding Opportunity Number: W81XWH-15-RTR- TRA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), August 25, 2015
- **Invitation to Submit an Application:** September 2015
- **Application Submission Deadline:** 11:59 p.m. ET, December 1, 2015
- **End of Application Verification Period:** 5:00 p.m. ET, December 7, 2015
- **Peer Review:** January 2016
- **Programmatic Review:** March 2016

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) Reconstructive Transplant Research (RTR) program 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. This Program Announcement/Funding Opportunity and subsequent awards will be managed and executed by the Congressionally Directed Medical Research Programs (CDMRP) with strategic oversight from Joint Program Committee 8/Clinical and Rehabilitative Medicine Research Program (JPC-8/CRMRP).

The RTR program was initiated in 2012 to fund innovative projects that have the potential to make a significant impact on improving the function, wellness, and overall quality of life for injured military Service members and Veterans, their caregivers and family members, and the American public. Appropriations for the RTR from FY12 through FY14 totaled $30 million (M). The FY15 appropriation is $15M.

The JPC-8/CRMRP mission is to implement long-term strategies to develop knowledge and materiel products to reconstruct, rehabilitate, and provide definitive care for injured Service members. The ultimate goal is to return Service members to duty and restore their quality of life. Through the RTR program, the JPC-8/CRMRP challenges the scientific community to design innovative research that will foster new directions for, and address neglected issues in, the field of reconstructive transplantation (RT), specifically vascularized composite allotransplantation (VCA)-focused research, also known as composite tissue allotransplantation. VCA refers to the transplantation of multiple tissues such as muscle, bone, nerve, and skin, as a functional unit (e.g., a hand or face) from a deceased donor to a recipient with a severe injury. Psychosocial issues are associated with barriers to VCA outcomes and the characterization of appropriate strategies which address psychosocial issues are needed to improve outcomes.

Applications from investigators within the military Services and applications involving multidisciplinary collaborations among academia, industry, the military Services, the U.S. Department of Veterans Affairs (VA), and other Federal Government agencies are highly encouraged. Though the RTR award mechanisms support groundbreaking research, all projects must demonstrate solid scientific rationale with military-relevant utility.

B. FY15 RTR Focus Areas

To meet the intent of the FY15 RTR award mechanisms, applicants must address one or more of the Focus Areas listed below.

- Immune system regulation
    - Understanding mechanisms of immune rejection
    - Immunomodulation approaches and mechanisms (e.g., tolerance induction, chimerism)

- Optimizing immunosuppressive drug regimens
- Exploiting inflammatory processes, controlling and modulating a patient's immune response to improve existing therapies and maximize outcomes (e.g., immuno-engineering)

- Improved access to reconstructive transplantation
  - Improved tissue preservation techniques or technologies to extend radius of donor procurement
  - Development of educational programs for health care providers to improve referrals of potential reconstructive transplantation candidates
  - Identification of patient-driven barriers to transplantation (i.e., patient is suitable anatomically and immunologically, but declines opportunity for transplant)
  - Identification of barriers to donor offers for reconstructive transplantation, and strategies to address the same
- Reconstructive transplantation rehabilitation
  - Novel rehabilitation strategies that improve reconstructive transplant function
  - Development of Quality of Life outcome measures for VCA
- Graft surveillance – clinical monitoring
  - Non-invasive imaging technologies
  - Immune profiling (e.g., gene expression, graft rejection markers, cytokine screens)
- Psychosocial issues associated with VCA
  - Identification of strategies and behavioral interventions that optimize patient engagement and adherence

C. Award Information

The RTR Translational Research Award (RTR TRA) mechanism is being offered for the first time in FY15. A synopsis of all FY15 RTR Program Announcements/Funding Opportunities is available at http://cdmrp.army.mil/funding/pdf/15rtrpreftable.pdf

The intent of the FY15 RTR TRA mechanism is to support the development of data and model systems to complete the Food and Drug Administration (FDA) regulatory review process and position the product for a clinical trial. ***Applications must include preliminary and/or published data that is relevant to RTR and the proposed research project.*** Observations that drive a research idea may be derived from many sources, such as a laboratory discovery, population-based studies, or a clinician's firsthand knowledge of patients and anecdotal data. While the ultimate goal of translational research is to move an observation forward into clinical application, Principal Investigators (PIs) should not view translational research as a one-way continuum from bench to bedside. The research plan must involve reciprocal flow of ideas between basic and clinical science. Collaborations between laboratory scientists and clinicians are encouraged.

Preclinical animal studies are encouraged under the FY15 RTR TRA mechanism. All projects involving animals should adhere to accepted standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in Landis, S.C., et al. A call for transparent reporting to optimize the predictive value of preclinical research, *Nature* 2012, 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies. Projects that include research on animal models are required to submit Attachment 9, Animal Research Plan, as part of the application package to describe how these standards will be addressed. Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at http://www.elsevier.com/__data/promis_misc/622936arrive_guidelines.pdf.

Research Involving Animals: All DoD-funded research involving new and ongoing research with animals must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (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. 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 3 to 4 months for regulatory review and approval processes for animal studies.*** Refer to General Application Instructions, Appendix 5, for additional information.

Research involving human subjects and human anatomical substances is permitted; however, clinical trials are not allowed under this funding opportunity. A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, etc.) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction.

PIs wishing to apply for funding for a clinical trial should utilize the FY15 RTR Clinical Trial Award mechanism (Funding Opportunity Number: W81XWH-15-RTR-CTA).

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRMC 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***. 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.

Use of Military and VA Populations: If the proposed research involves access to military and/or VA population(s) and/or resource(s), the PI is responsible for establishing access. If possible, access to target military and/or VA patient population(s) should be confirmed at the time of application submission. A letter of support, signed by the lowest ranking person with approval authority, should be included for studies involving military Service members, Veterans, military and/or VA-controlled study materials, and military and/or VA databases. Use Attachment 2 to provide this documentation (see Section II.C., Application Submission Content and Form, Supporting Documentation).

DoD Collaboration and Alignment Encouraged: Relevance to the health care needs of the Armed Forces, their family members, and/or the U.S. Veteran population is a key feature of this award. Therefore, Principal Investigators (PIs) are strongly encouraged to collaborate, integrate, and/or align their research projects with military and/or VA research laboratories and programs. The following websites may be useful in identifying information about ongoing DoD areas of research interest:

Air Force Research Laboratory http://www.wpafb.af.mil/afrl

Armed Forces Institute of Regenerative Medicine http://www.afirm.mil

Center for Neuroscience and Regenerative Medicine http://www.usuhs.mil/cnrm/

Clinical and Rehabilitative Medicine Research Program https://crmrp.amedd.army.mil

Combat Casualty Care Research Program https://ccc.amedd.army.mil

Congressionally Directed Medical Research Programs http://cdmrp.army.mil

Defense Advanced Research Projects Agency http://www.darpa.mil

Defense Medical Research and Development Program http://cdmrp.army.mil/dmrdp/default

Defense Technical Information Center http://www.dtic.mil

Military Infectious Diseases Research Program https://midrp.amedd.army.mil

Military Operational Medicine Research Program https://momrp.amedd.army.mil

National Center for Telehealth and Technology http://t2health.org/

National Museum of Health and Medicine http://www.medicalmuseum.mil/index.cfm

Naval Health Research Center http://www.med.navy.mil/sites/nhrc

Navy and Marine Corps Public Health Center http://www.med.navy.mil/sites/nmcphc

Office of Naval Research http://www.med.navy.mil

Office of the Under Secretary of Defense for Acquisition, Technology and Logistics http://www.acq.osd.mil/

U.S. Army Medical Research Acquisition Activity https://www.usamraa.army.mil/

U.S. Army Medical Research and Materiel Command https://mrmc.amedd.army.mil

U.S. Army Research Laboratory http://www.arl.army.mil

U.S. Department of Defense Blast Injury Research Program
https://blastinjuryresearch.amedd.army.mil/

U.S. Department of Veterans Affairs, Office of Research and Development
http://www.research.va.gov

U.S. Naval Research Laboratory
http://www.nrl.navy.mil

Walter Reed Army Institute of Research
http://wrair-www.army.mil

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

- Independent investigators at all academic levels (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 total costs (direct and indirect) budgeted for the entire period of performance will not exceed **$1,000,000**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$1,000,000** total costs or using an indirect rate exceeding the organization's negotiated rate.
- 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 must be requested for:

- Travel costs for the PI(s) to disseminate project results at one DoD CRMRP RTR meeting. For planning purposes, it should be assumed that the meeting will be held in

the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary of non-Governmental personnel (includes contract research personnel at Government facilities)
- Research supplies
- Equipment
- Research-related subject costs (clinical trials are NOT allowed)
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs to attend scientific/technical meetings in addition to the required meeting described above

Shall not be requested for:

- Clinical trial 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 $3.0M of the $15M FY15 RTR appropriation to fund approximately 3 FY15 RTR Translational Research 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.

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- RTR-TRA 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/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

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 JPC-8 Regenerative Medicine Working Group** members should not be involved in any pre-application or application. For questions related to the FY15 JPC-8 Regenerative Medicine Working Group 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**

  Note: Upload document(s) as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

  Preproposal Narrative (two-page limit): The Preproposal Narrative page limit 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 Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

The Preproposal Narrative should include the following:

- **Background/Research Problem/Rationale:** State the ideas and reasoning on which the proposed research is based. Clearly demonstrate that there is sufficient scientific evidence and/or rationale to support the proposed stage of research. Describe how the preliminary data and rationale support the research idea. State how this project meets the intent of the award mechanism.
- **Hypothesis or Objective:** State the hypothesis to be tested or the objectives to be reached.
- **Specific Aims and Study Design:** Concisely state the project's specific aims and ultimate endpoints, and describe the scientific approach and how it will accomplish the study aims. Include a description of controls, as appropriate, and demonstrate that the work has appropriate statistical power.
- **Impact and Focus Area:** Describe the impact of this study on the field of reconstructive transplantation research, patient care, and/or quality of life, including the impact on one or more of the FY15 RTR Focus Areas.
- **Translational Potential:** Describe how the proposed research will allow for a reciprocal flow of ideas between basic and clinical science. Explain how the project will accelerate promising laboratory research findings into clinical applications.
- **Military Benefit:** Describe how the proposed work would impact the health care needs of military Service members and/or U.S. Veterans recovery from traumatic injury as well as their families, caregivers, and/or communities.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application ***must be uploaded as individual documents*** and are limited to:

- **References Cited (one-page limit):** List the references cited (including URLs if available) in the Preproposal 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 used in the Preproposal Narrative.
- **PI Biographical Sketch (two-page limit):** Include a biographical sketch for the PI only.

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

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP, JPC-8/CRMRP, and RTR program, pre-applications will be screened based on the following criteria:

  - **Background/Research Problem/Rationale:** How well the background and scientific rationale demonstrate sufficient evidence to support the proposed research project.
  - **Specific Aims and Study Design:** How well the specific aims are stated and supported through scientific rationale and referenced literature and how well the proposed study's approach will address these aims. Whether the proposed methodology is appropriate.
  - **Impact and Alignment with Focus Areas:** How well the proposed project addresses at least one of the FY15 RTR Focus Area(s) and will make important contributions toward the goal of resetting our wounded warriors, both in terms of duty performance and quality of life.
  - **Translational Potential:** How well the project will accelerate promising, well-founded research findings into clinical applications.
  - **Military Benefit:** How the proposed work would benefit the health care needs of military Service members and/or U.S. Veterans recovering from traumatic injury as well as their families, caregivers, and/or communities.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity.

C. Full Application Submission Content

Applications will not be accepted unless the PI has received notification of invitation.

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 FY15 RTR Translational Research 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.

     The Project Narrative must include preliminary or published data that is relevant to reconstructive transplantation and the proposed research project.

     Describe the proposed project in detail using the outline below.

     - **Background/** Present the ideas and scientific rationale behind the proposed research project, and clearly demonstrate that there is sufficient evidence to support the proposed stage of research. Cite relevant literature. Describe previous experience most pertinent to this project.
     - **Hypothesis or Objective:** State the hypothesis to be tested or the objective(s) to be reached.
     - **Specific Aims:** Concisely explain the project's specific aims. If the proposed research project is part of a larger study, present only tasks that would be funded under the RTR TRA.
     - **Study Design and Feasibility:** Describe the research strategy, methods, and analyses, including appropriate controls, in sufficient detail for analysis of

appropriateness and feasibility. Describe the statistical plan and power analysis as appropriate for the proposed research. Address potential problem areas and present alternative methods and approaches. If animal studies are proposed, briefly describe the key elements of the study/studies as they relate to the overall project; detailed information is required in Attachment 9, Animal Research Plan. If human subjects or human anatomical samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples. ***This award may not be used to conduct clinical trials,*** though limited clinical research in human subjects as a portion of the Statement of work is permissible.

- **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 (five-document limit): 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.

- Letters of Commitment (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 project for the duration of the study, support for the proposed phase of research, and support for the indication being tested.
- Letter(s) of Support for Use of Military and VA Populations or Resources (if applicable): Provide a letter(s) signed by the lowest ranking person with approval authority for studies involving military Service members, Veterans, military and/or VA-controlled study materials, databases, or restricted facilities.
- 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.
  - Commercialization Strategy (if applicable): Describe the commercialization plan. The plan should include intellectual property, market size, financial analysis, strengths and weaknesses, barriers to the market, competitors, and management team. Discuss the significance of this development effort, when it can be anticipated, and the potential commercial use for the technology being developed.
- 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.
- Quad Chart: The Quad Chart template is a one-page PowerPoint file that must be downloaded from eBRAP (https://ebrap.org/eBRAP/public/Program.htm).

- **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.

  Technical abstracts should be written using the outline below. The technical abstract is used by all reviewers. Proprietary or confidential information should not be included.

- Background: Present the ideas and scientific rationale behind the proposed research project, including sufficient scientific evidence to support the proposed stage of research.
- Hypothesis/Objective: State the hypothesis/objective to be tested. Provide evidence or rationale that supports the hypothesis/objective.
- Specific Aims: State the specific aims of the proposed research project.
- Study Design: Briefly describe the study design, including appropriate controls.
- Impact: Briefly describe the impact of this study on the field of reconstructive transplantation research, patient care, and/or quality of life, including the impact on one or more of the FY15 RTR Focus Areas.
- Translational Potential: Briefly describe how the proposed research project will translate promising, well-founded research findings into clinical applications in reconstructive transplantation.
- Military Benefit: Briefly explain how the proposed project will have immediate or potential long-term benefit for the health care needs of military Service members and/or U.S. Veterans recovering from traumatic injury as well as their families, caregivers, and/or communities.

- **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.

  Lay abstracts should be written using the outline below. Proprietary or confidential information should not be included. Minimize the use of acronyms and abbreviations, where appropriate. The lay abstract is an important component of the application review process because it addressed issues of particular interest to the consumer advocate community.

  - Clearly describe the objectives and rationale for the application in a manner readily understood by readers without a background in science or medicine.
    - 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? Include the current available statistics to the related injury/condition.
    - What are the potential clinical applications, benefits, and risks?
    - What is the projected time it may take to achieve a patient-related outcome?
    - Briefly describe how the proposed project will benefit Service members, Veterans, and/or their family members.
  - What are the likely contributions of the proposed research to advancing the field of VCA research?

- **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 RTR Translational Research Award mechanism, use the SOW format example titled "SOW for Advanced Tech Development Research." 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: Impact and Military Benefit Statement (two-page limit): Upload as "ImpactMilBen.pdf.**" Describe the short- and long-term impact of this study on the field of reconstructive transplantation research, patient care, and/or quality of life, including an assessment of the likelihood that a successful outcome of the proposed research project will lead to a practical application in individuals recovering from traumatic injury. Address the impact on one or more FY15 RTR Focus Areas. Although not all-inclusive, the following are examples of ways in which research projects may have an impact, if successful:
    - Has the potential to advance the field of reconstructive transplantation research.
    - Has the potential to change the standard of care.
    - Contributes to the development or validation of evidence-based policy or guidelines for patient evaluation and care.

  In addition, demonstrate how the proposed research is responsive to the health care needs and quality of life of military Service members and Veterans recovering from traumatic injury. If the active duty military, Veteran, or military family member population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed research, and the feasibility of using the population. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population.

- **Attachment 7: Translation Statement (one-page limit): Upload as "Translation.pdf."** Describe the translational research that will be performed through this award. State explicitly how the proposed research project is translational in nature, allowing for the reciprocal transfer of ideas between basic and clinical science.

  Provide information on the methods and strategies proposed to move the product or knowledge outcomes to the next phase of development such as clinical trials, commercialization, and/or delivery to the civilian or military market after successful completion of the award.

- **Attachment 8: Animal Research Plan (five-page limit): Upload as "AnimalPlan.pdf."** When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be

submitted to the IACUC as the Animal Research Plan. The Animal Research Plan should address the following points for each proposed animal study:

- Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.
- Summarize the procedures to be conducted. Describe how the study will be controlled.
- Describe the randomization and blinding procedures for the study, and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.
- Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.
- Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handles, statistical methods for data analysis, and identification of the primary endpoint(s).

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. .

- 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, JPC-8/CRMRP, and the RTR program, 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.

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 listed in decreasing order of importance:
    - **Translational Potential**
        - How well the PI provides sufficient evidence that the research is ready to move into the proposed stage of research.
        - How well the project will translate promising, well-founded basic or clinical research findings into clinical applications for individuals recovering from traumatic injury.
        - How well the project allows for the reciprocal transfer of ideas between basic and clinical science.
        - If applicable, to what degree the intellectual and material property plan is appropriate.

- **Study Design and Feasibility**
    - How well the preliminary data and scientific rationale support the proposed research project. How well the hypothesis or objectives, specific aims, research strategy, methods, and analyses are developed and integrated into the project.
    - To what extent the proposed research project is feasible as described.
    - How well the PI acknowledges potential problems and addresses alternative approaches.
    - The degree to which the plan to study military populations, if applicable, is appropriate and feasible.

  For applications involving animal research:

    - How well the animal study (or studies) is designed to achieve the objectives, including the choice of model and endpoints/outcome measures to be used.
- **Impact**
    - How well the proposed research project addresses one or more of the FY15 RTR Focus Areas.
    - How effective the proposed research project will be in making important contributions toward the goal of advancing reconstructive transplantation research and/or patient care.
    - How well the proposed research project addresses a critical problem in reconstructive transplantation research, patient care, and/or quality of life.
- **Military Benefit**
    - How relevant the anticipated outcomes of the proposed research are to military Service members and Veterans recovering from traumatic injury.
    - The potential immediate and/or long-term benefits of the proposed research on the health and well-being of Service members, Veterans, and/or their families or communities.
- **Statistical Plan**
    - If applicable, to what degree the statistical plan and power analysis are appropriate for the proposed project.
    - How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.
- **Personnel**
    - To what extent the background and expertise of the key personnel are appropriate to accomplish the proposed research project.
    - To what extent the levels of effort by the key personnel are appropriate to ensure the success of this project.

- How well the PI's record of accomplishment demonstrates his/her ability to accomplish the proposed research project.

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

- **Environment**
  - To what extent 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 extent the quality and level of institutional support are appropriate for the proposed research project.
- **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, JPC-8/CRMRP, and FY15 RTR, as evidenced by the following:

   - Adherence to the intent of the award mechanism
   - Relative impact and military relevance
   - Programmatic relevance
   - Program portfolio balance

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 pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the pre-application:

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different Program Announcements/Funding Opportunities within the same program and fiscal year.
- Translation Statement (Attachment 7) is missing.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and Project Narrative.
- Documents not requested will be removed.

C. Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- A FY15 JPC-8 Regenerative Medicine Working Group 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 JPC-8 Regenerative Medicine Working Group members can be found at** http://cdmrp.army.mil/rtrp/panels/panels15

- 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 invited application does not propose the same research project described in the pre-application.
- A clinical trial is proposed.
- The PI does not meet the eligibility criteria.
- Preliminary data are not included.

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.

Quarterly technical progress reports and quad charts will be required.

In addition to written progress reports, in-person presentations may be requested.

E. Award Transfers

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	Impact and Military Benefit Statement: Upload as Attachment 6 with file name "ImpactMilRel.pdf."	
	7	Translation Statement: Upload as Attachment 7 with file name "Translation.pdf."	
	8	Animal Research Plan: Upload as Attachment 8 with file name "AnimalPlan.pdf", if applicable.	
	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.	