

Program Announcement
for the
Department of Defense
Defense Health Program
Congressionally Directed Medical Research Programs

Peer Reviewed Orthopaedic Research Program
Applied Research Award

Funding Opportunity Number: W81XWH-16-PRORP-ARA
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), September 7, 2016
- **Invitation to Submit an Application:** October 20, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, December 7, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, December 12, 2016
- **Peer Review:** February 2017
- **Programmatic Review:** April 2017

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) Peer Reviewed Orthopaedic Research Program (PRORP) 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 PRORP was initiated in 2009 to provide support for research of exceptional scientific merit focused on optimizing recovery and restoration of function for military personnel with orthopaedic injuries sustained in combat or combat-related duties. Appropriations for the PRORP from FY09 through FY15 totaled \$278.5 million (M). The FY16 appropriation is \$30M.

The FY16 PRORP challenges the scientific community to address the most significant gaps in care for the leading burden of injury and loss of fitness for military duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from neuromusculoskeletal injuries (excluding spinal cord injuries) sustained during combat or combat-related activities. It is expected that research findings would also provide benefit to the general population. Applications involving multidisciplinary collaborations among academia, industry, the military Services, the Department of Veterans Affairs (VA), and other Federal agencies are highly encouraged.

B. FY16 PRORP Focus Areas

All applications must address one and only one of the following FY16 PRORP Focus Areas. The Focus Area addressed should be one from either the Surgical Care category or the Rehabilitation category. Studies that propose nominal or iterative advancements are not encouraged.

Surgical Care Focus Areas:

- Peripheral Nerve Injuries: Treatment strategies to improve outcomes from segmental peripheral nerve defects of motor and mixed (motor and sensory) peripheral nerve damage from crush or complete injury.
- Prevention of Heterotopic Ossification: Techniques to retard or prevent the development of human post-traumatic heterotopic ossification in the upper extremity.
- Volumetric Muscle Loss: Techniques to regenerate functional, innervated muscle units in treatment of volumetric muscle loss.
- Extremity Fractures: Strategies to optimize patient outcomes after extremity fracture (i.e., time to begin rehabilitation, weight-bearing strategy, etc.)
- Pelvic Ring Injuries: Treatment strategies to improve outcomes of complex pelvic ring injuries.

- Compartment Syndrome: Strategies to improve current diagnoses for compartment syndrome.
- Gaps in Clinical Practice Guidelines: Address gaps in current orthopaedic clinical practice guidelines (CPG) and recommendations (<http://www.usaisr.amedd.army.mil/cpgs.html>). Applications under this Focus Area **must** specify which orthopaedically relevant CPG their application is intended to support. Applicants should also highlight the expected impact of their research on orthopaedic clinical practice.
- Surgical Techniques to Optimize Gait: Validate surgical techniques to optimize gait efficiency and outcomes for patients with amputation or limb salvage.
- Soft Tissue Trauma: Strategies to develop and/or identify musculoskeletal extremity soft tissue trauma treatments optimizing return to duty, work, or reintegration.

Rehabilitation Focus Areas:

- Post-Operative Pain Management: Develop and/or validate strategies for post-operative pain management following orthopaedic trauma that minimize or eliminate opioid use. The primary outcome measures should relate to rehabilitation endpoints and not focus solely on pain scores.
- Prosthetic and/or Orthotic Device Function: Development and optimization of novel, innovative technologies to improve prosthetic and/or orthotic device function and durability, including intuitive efferent (motor) and afferent (sensory) user interfaces and considerations for interoperability.
- Secondary Physical Health Effects: Techniques or technologies that improve prediction, identification, and reduction of secondary physical health effects (e.g., obesity, arthritis, osteoporosis, cardiovascular disease) following severe/high-energy traumatic neuromusculoskeletal non-spinal cord injury. The focus should be on injuries sustained between the ages of 18-50 and secondary physical health effects that develop within 5 years of injury.
- Physical or Occupational Therapy: Development and/or validation of optimal physical or occupational therapy treatment strategies and sequence of progression throughout the rehabilitation continuum to maximize functional outcomes following severe neuromusculoskeletal injury, excluding central nervous system. Examples include optimal timing, frequency, duration, and intensity of rehabilitation interventions.
- Barriers to Successful Therapy Outcomes: Identify, quantify, and stratify confounding treatable factors (e.g., pain, sleep, nutrition, compliance, etc.) that inhibit or delay optimal orthopaedic rehabilitation outcomes.
- Rehabilitation Outcomes: Development and/or validation of, standardized measures to objectively assess and improve rehabilitation outcomes, including multi-extremity trauma and/or psychosocial resiliency and reintegration, following neuromusculoskeletal injury.

C. Award Information

The PRORP Applied Research Award (ARA) mechanism was first offered in FY15. Since then, 44 ARA applications have been received, and 6 have been recommended for funding.

The PRORP ARA seeks applied research applications focused on advancing optimal treatment and restoration of function for military personnel with musculoskeletal injuries sustained during combat or combat-related activities. It is expected that any research findings would also provide benefit to the general population. To meet the intent of the award mechanism, applications **must** specifically address one and only one of the FY16 PRORP Focus Areas listed in Section I.B. above.

Awards may not be used to support fundamental basic research. Basic research is defined as research directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications toward process or products in mind.

The FY16 PRORP ARA is focused on **applied research**, defined as work that refines concepts and ideas into potential solutions with a view toward evaluating technical feasibility of promising new knowledge products, pharmacologic agents, behavioral and rehabilitation interventions, diagnostic and therapeutic techniques, clinical guidance, and/or emerging approaches and technologies.

Research Scope: Research proposed under the FY16 PRORP ARA may include small- to large-scale projects. These awards are expected to yield potential health products, approaches, or technologies positioned for human testing. Upon successful completion, the proposed research is expected to yield knowledge products, approaches, or technologies that have the potential to advance toward clinical translation.

Presentation of preliminary data is required: Inclusion of preliminary and/or published data relevant to the research question is required. In addition, investigators must demonstrate logical reasoning. To be competitive, the application must include a sound scientific rationale and a well formulated, testable hypothesis established through a critical review and analysis of the literature.

Studies allowed under the FY16 PRORP ARA may include, but are not limited to:

- Refinement of concepts and ideas into potential solutions with a view toward evaluating technical feasibility of emerging approaches, technologies, and promising new knowledge products.
- Evaluation, maturation, and/or down-selection of potential product candidates (drugs, biologic constructs, or devices/systems) in vitro and/or in vivo.
- Preparation activities needed to support a future clinical trial or regulatory submission.

Awards may not be used to support clinical trials: A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or

efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. For more information on how to distinguish clinical research from clinical trials, see the Human Subject Resource Document at <https://ebrap.org/eBRAP/public/Program>. Investigators seeking support to conduct a clinical trial should apply to the FY16 PRORP Clinical Trial Award (W81XWH-16-PRORP-CTA) mechanism, which can be accessed at <http://cdmrp.army.mil/funding/default>.

Guidelines for Animal Research: All projects should adhere to a core set of 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 (<http://www.nature.com/nature/journal/v490/n7419/nature11556/>). 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 7, 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 Department of Defense (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, including amendments to ongoing projects. Principal Investigators (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.

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) 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.

Use of Military and VA Populations or Resources: If the proposed research plan involves access to active duty military and/or VA patient populations or resources, the Principal Investigator (PI) is responsible for establishing such access. If possible, access to target active duty military and/or VA patient populations/resources should be confirmed at the time of application submission by inclusion of a letter of support, signed by the lowest ranking person with approval authority, for studies involving active duty military Service members, Veterans, military- and/or VA-controlled study materials, and military and/or VA databases. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources. Note that access to a Veteran population for clinical studies may only be obtained by either collaboration with a VA investigator, where the VA investigator has a substantial role in the research, or by advertising to the general public. Use Attachment 2 to provide this documentation (see [Section II.C., Full Application Submission Content, Supporting Documentation](#)).

Encouraged DoD and/or VA Collaboration and Alignment: Military relevance is a key feature of this award. Therefore, PIs are strongly encouraged to collaborate, integrate, and/or align their projects with military and/or VA research laboratories and programs. Although not a comprehensive list, the following websites may be useful in identifying information about ongoing DoD and VA areas of research interest, ongoing research, or potential opportunities for collaboration:

Air Force Office of Scientific Research
<http://www.wpafb.af.mil/afri/afosr/>

Air Force Research Laboratory
<http://www.wpafb.af.mil/afri/>

Armed Forces Radiobiology Research Institute
<http://www.usuhs.edu/afri/>

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 Technical Information Center
<http://www.dtic.mil>

Defense Threat Reduction Agency
<http://www.dtra.mil/>

Military Health System Research Symposium
<https://mhsrs.amedd.army.mil/SitePages/Home.aspx>

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

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

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

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

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/>

Telemedicine and Advanced Technology Research Center
<http://www.tatrc.org/>

Uniformed Services University of the Health Sciences
<http://www.usuhs.edu/research>

U.S. Army Institute of Surgical Research
<http://www.usaisr.amedd.army.mil/>

U.S. Army Research Institute of Environmental Medicine
<http://www.usariem.army.mil/>

U.S. Army Medical Research Institute of Infectious Diseases
<http://www.usamriid.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 4, Section K.

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 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 **3** years.
- The anticipated total costs budgeted for the entire period of performance will not exceed **\$500,000**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **\$500,000** total 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 **3** years.

For this award mechanism, direct costs must be requested for:

- Travel costs for the PI(s) to disseminate project results at one DoD PRORP In-Progress Review meeting in Year 3. 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
- Research supplies and equipment
- Support for multidisciplinary collaborations, including travel
- Travel costs for up to two investigators to travel to one scientific/technical meeting per year in addition to the required IPR meeting described above.

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 \$2.5M of the \$30M FY16 PRORP appropriation to fund approximately five Applied 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(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-PRORP-ARA 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/>). 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 need to be made after submission of the pre-application, the applicant should contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507 prior to the pre-application deadline.

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 PRORP 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 personnel from either of these companies will be administratively 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**

Note: Upload documents 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 (three-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:

- **Alignment with Focus Areas:** Explain how the proposed work addresses one, and only one, of the FY16 PRORP Focus Areas.
- **Research Idea:** State the hypothesis to be tested or the objective to be reached. State how this project addresses an important problem relevant to combat-related orthopaedic injuries. State the ideas and reasoning on which the proposed work is based.

- **Research Strategy:** Clearly describe the research strategy for the proposed project. Concisely state the specific aims and ultimate endpoints of the project. Describe the proposed methods and how they will accomplish the project’s aims.
- **Impact:** State explicitly how the proposed work may have an immediate and long-term impact on patient care and/or restoration of function for those who have sustained traumatic orthopaedic injuries.
- **Military Benefit:** Describe how the proposed work would impact the healthcare needs of Service members and/or Veterans who have sustained combat-related orthopaedic injuries, as well as their families, caregivers, and the general public.
- **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the described research (*detailed key personnel biographical sketches [six pages per individual] are allowed as part of pre-application supporting documentation, as described below*). Note any DoD or VA collaborations.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application *must be uploaded as individual files* 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.
- **Key Personnel Biographical Sketches (six-page limit per individual).** *All biographical sketches should be uploaded as a single combined file.* Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.
- **Quad Chart: Upload as “QuadChart.ppt”:** the Quad Chart template is a one-page PowerPoint file that must be downloaded from eBRAP at <https://ebrap.org/eBRAP/public/Program.htm> in the “Generic Forms for Application Submission” section, then completed and saved as a PPT or PPTX file.

- **Tab 6 – Submit Pre-Application**

- 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 and the PRORP, pre-applications will be screened based on the following criteria:

- **Alignment with Focus Areas:** How well the project addresses one, and only one, FY16 PRORP Focus Area. To what degree the proposed project addresses the

intent of the award mechanism and addresses an important problem relevant to the PRORP.

- **Research Idea and Strategy:** How well the rationale, objectives, and specific aims support the research idea. Whether the proposed methodology is appropriate to the specific aims. How the endpoints are appropriate for the proposed study.
- **Impact:** To what extent the potential immediate and long-range outcome(s) of the proposed study, if successful, will produce results that are likely to translate into improved patient care and/or restoration of function for those who have sustained traumatic orthopaedic injuries.
- **Military Benefit:** How well the proposed study will directly or indirectly impact the healthcare needs of Service members and/or Veterans, who have sustained combat-related orthopaedic injuries, as well as their families, caregivers and the general public.
- **Personnel:** How the qualifications and expertise of the PI and key personnel are appropriate to perform the proposed research.
- **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. Invitations to submit a full application are based on the Pre-Application Screening Criteria as published above.

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.

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

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*.

The Grants.gov application package must be submitted using the unique eBRAP log number to avoid delays in application processing.

Grants.gov application package components: For the Applied 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. 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 (12-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, noting potential challenges and alternative solutions where appropriate.

- **Background:** Explain how the proposed work addresses one, and only one, of the FY16 PRORP Focus Areas. Establish the relevance of the study to the one FY16 PRORP Focus Area and explain the applicability of the proposed findings. Describe in detail the rationale for the study questions and/or study hypotheses. Cite relevant literature. Include pilot or preliminary data that led to the development of the proposed project.

- **Hypotheses/Objectives/Specific Aims:** State the hypotheses to be tested or the objectives to be reached. Concisely explain the specific aims of the project to be funded by this award.
- **Research Strategy:** Describe the study design, methods, and models, including appropriate controls, in sufficient detail for assessment of the application. Explain how this research strategy will meet the research goals and milestones. Provide a well-developed, well-integrated, and detailed research plan that supports the translational feasibility and promise of the approach.
- **Technical Risks:** Identify and describe potential problem areas in the proposed approach and alternative methods and approaches that will be employed to mitigate any risks that are identified.
- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives as appropriate to the type of study. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study.
- If any biological material will be used in the proposed studies, the name, definition, pathological classification, and source of the material must be provided.
- If human anatomical samples will be used, include a detailed plan for the acquisition of samples.
- This award may not be used to conduct clinical trials.
- **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 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.
- Current Quad Chart: Provide a current Quad Chart in the same format as the pre-application. If no changes have been made to the project, the same Quad Chart submitted with the pre-application may be used.
- 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.
- Letter(s) of Support for Use of Military and VA Populations or Resources (if applicable): If the proposed research plan involves access to active duty military and/or VA patient populations or resources, include a letter(s) of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.
- 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.
 - 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 4, Section K for more information about the CDMRP expectations for making data and research resources publicly available.
- **Attachment 3: Technical Abstract (one-page limit): Upload as “TechAbs.pdf.”** The technical 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.

Technical abstracts should be written using the outline below.

- Background: State the one FY16 PRORP Focus Area addressed by the proposed research. State how the proposed research addresses the intent of the award mechanism. Present the ideas and reasoning behind the proposed work.
- Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
- Specific Aims: State the specific aims of the study.
- Study Design: Briefly describe the study design, including appropriate controls.
- Military Benefit: Briefly explain how the proposed project, if successful, will have an immediate and/or long-term impact on optimizing recovery and restoration of function for Service members and/or Veterans with orthopaedic injuries sustained in combat or combat-related activities, as well as their families, caregivers, and the general public.
- **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. Do not duplicate the technical abstract.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.
 - Describe the objectives and rationale for the application in a manner that will be readily understood by readers without a background in science or medicine.
 - Describe the ultimate applicability of the research.
 - Which FY16 PRORP Focus Area will be addressed?
 - How will the proposed research impact the one Focus Area addressed?

- What are the potential clinical applications, benefits, and risks?
- What is the projected timeline to achieve the expected patient-related outcome?
- Describe how the proposed project will benefit Service members and/or Veterans who sustained combat-related orthopaedic injuries, as well as their families, caregivers, and the general public.
- **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 Applied Research Award mechanism, use the SOW format example titled “SOW 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: Impact and Military Benefit Statement (two-page limit): Upload as “MilBen.pdf.”**
 - Describe the short-term impact, as well as the anticipated long-term benefits, of the proposed research on the lives of individuals recovering from traumatic orthopaedic injuries. Include details about the anticipated patient care and/or restoration of function outcomes that will be directly attributed to the results of the proposed research.
 - Describe how the proposed study is responsive to the healthcare needs of military Service members and the Veteran population that sustained orthopaedic injuries. Provide information about the incidence and/or prevalence of orthopaedic injuries in military Service members and/or Veterans, if appropriate and available.
 - If active duty military and/or Veteran population(s) or dataset(s) will be used in the proposed research, describe the population(s)/dataset(s), the appropriateness of the population(s)/dataset(s) for the proposed study, and the feasibility of using the population(s)/dataset(s). If a non-military population will be used for the proposed research, explain how the population simulates the targeted population (i.e., military Service members or Veterans). If applicable, show how the proposed study complements ongoing DoD and/or VA areas of orthopaedic research interest. Describe how the study design will replicate field conditions, if applicable.
- **Attachment 7: Animal Research Plan (if applicable, 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 proposed animal species, strain, and model(s) are appropriate for addressing 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 handled, statistical methods for data analysis, and identification of the primary endpoint(s).
- **Attachment 8: Human Sample Acquisition and Safety Procedures (if applicable; required for all studies recruiting human subjects; no page limit): Upload as “HumSamAcq.pdf.”** The Human Sample Acquisition and Safety Procedures attachment should include the components listed below.
 - a. **Study Population and Design:** Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site (population from whom the samples were obtained). *Use of military or Veteran populations is preferable but not required.* If a military population is not used, describe how the identified population serves as a surrogate to the military experience.
 - Demonstrate that the research team has access to the proposed study population.
 - If applicable, discuss past effort(s) in recruiting human subjects from the target population from previous interventional or observational studies. Address any potential barriers to accrual and plan for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided.
 - For some in vitro diagnostics, the link between analytical performance and clinical performance is not well defined. In these circumstances, clinical information may be required.
 - The FDA rarely requires prospective clinical studies for in vitro diagnostics, but regularly requests clinical samples with sufficient laboratory and/or

clinical characterization to allow an assessment of the clinical validity of a new device. This is usually expressed in terms of clinical sensitivity and clinical specificity or agreement.

- Note that the study design may include identification of surrogate endpoints to establish the device performance (clinical sensitivity and specificity or agreement) with relation to the identified endpoints in corollary studies using randomly collected clinical studies. Use of laboratory samples from military populations is preferable but not required. If a military population is not used, describe how the identified population serves as a surrogate to the military experience. Demonstrate that the research team has access to the proposed study population
- b. Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, “Ethical Principles and Guidelines for the Protection of Human Subjects,” and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the study.

- c. Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study inclusion and the diagnostic criteria for entry. Please note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.
- d. Description of the Informed Consent Process:** In certain cases, Federal regulations allow the IRB to approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent, or to waive the requirement to obtain any informed consent. Most complete waivers of consent involve studies in which there are minimal risks to subjects. Specifically describe the plan for obtaining informed consent from human subjects.
 - ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***
 - Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects’ questions will be addressed during the consent process and throughout the trial.
 - Include information regarding the timing and location of the consent process.

- Describe the biological origin of the samples to be tested (e.g., primary fibroblast cells from adults with and without disease).
 - The narrative should also describe the sample source(s), such as purchased human samples obtained from a clinical repository, or previously collected as part of a research effort. If samples will be or have been collected as part of a research activity, the application should state whether donors provided consent for use of their samples in future research consistent with this proposed effort.
 - Describe the plan, if appropriate, for obtaining waivers of informed consent or the informed consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study.
 - **Waiver of Informed Consent**, described in Federal Regulation 45 CFR 46.116(d), establishes four criteria for waiving consent or altering the elements of consent in minimal risk studies. These four criteria must be addressed.
 - **Waiver of Documentation of Consent**, described in Federal Regulation 45 CFR 46.117(c), allows the IRB to waive the requirement for obtaining signed consent if it finds that either:
 - The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (these criteria cannot be used for FDA-regulated studies), or
 - The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. This paragraph only also applies to FDA-regulated studies per 21 CFR 56.109(c)(1).
 - State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed research to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (<http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf>). If applicable, please refer to the General Application Instructions, Appendix 6, Regulatory Requirements, for more information.
- e. Risks/Benefits Assessment:**
- **Foreseeable risks:** Clearly identify all study risks. Study risks include any risks that the human subject is subjected to (including retroactively, as identified by the ORP and IRB) as a result of participation in the research. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:** Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel, or to manage unpreventable risks.
 - **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.
- **Attachment 9: Data Management (if applicable; required for all studies recruiting human subjects; no page limit): Upload as “Data_Manage.pdf.”** The Data Management attachment should include the components listed below.
 - a. **Data Management:** Describe all methods used for data collection to include the following:
 - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
 - **Confidentiality**
 - Explain measures taken to protect the privacy of study human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
 - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of USAMRMC are eligible to review study records.
 - Address requirements for reporting sensitive information to state or local authorities.
 - **Data capture, verification and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, and the length of time data will be stored.
 - **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.
 - b. **Laboratory Evaluations**
 - **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
 - **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).

- **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
 - **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.
 - **Attachment 10: 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 (six-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 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 (six-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 10, 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 the PRORP, 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 listed in decreasing order of importance:
 - **Research Strategy and Feasibility**
 - How well the scientific rationale supports the project and its feasibility, as demonstrated by a critical review and analysis of the literature, logical reasoning, and the presentation of preliminary data or published data.

- How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed and integrated into the project and how well they address the need(s) described.
- How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, power analysis, blinding, randomization, and data handling.
- How consistent the methods and procedures are with sound research design.
- If applicable, to what degree the statistical plan and power analysis are appropriate for the proposed project.
- How well the potential problem and risk areas in the experimental approach were identified and the extent to which the proposed alternative methods and approaches address those areas.
- **Impact and Military Benefit**
 - How the proposed study addresses one FY16 PRORP Focus Area.
 - How relevant the anticipated research outcomes are to the one FY16 PRORP Focus Area addressed in the application.
 - How well the PI describes the potential immediate and long-term impact of the proposed research on patient care and restoration of function from orthopaedic injuries sustained during combat or combat-related activities.
 - The potential immediate or long-term benefit and applicability of the proposed research on the health and well-being of Service members and/or Veterans, as well as their families, caregivers, and the general public.
 - How well the study addresses a critical issue in the treatment of combat-related injuries, as well as non-battle orthopaedic injuries that impact unit readiness and the ability to return to work/duty, if applicable.
- **Personnel**
 - How well the background and expertise of the PI and other key personnel demonstrate their ability to successfully complete the proposed research.
 - How appropriate the composition of the research or study team is to accomplishing the proposed work (e.g., statistical expertise, expertise in orthopaedic research, etc.).
 - How appropriate the levels of effort by the PI and other key personnel are to ensuring success of this project.
 - How well each investigator's record(s) of accomplishment demonstrates his/her ability to accomplish the proposed work.

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

- **Ethical Considerations**

- If applicable, how the level of risk to human subjects is minimized, and how the safety monitoring and reporting plan is appropriate for the level of risk.
- If applicable, how well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
- If applicable, to what degree privacy issues are appropriately considered.
- If applicable, to what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Environment**

- To what degree the scientific environment and the accessibility of institutional resources support the proposed research project.
- How well the research requirements are supported by the availability of and the accessibility to facilities and resources (including collaborative arrangements).
- How the quality and extent of institutional support are appropriate for the proposed 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 criteria are used by programmatic reviewers:

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

- b. **Relevance to the mission of the DHP and FY16 PRORP, as evidenced by the following:**

- Adherence to the intent of the award mechanism
- Program portfolio composition
- Relative impact and military Relevance

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 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.

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:

- An FY16 PRORP 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 PRORP Programmatic Panel members can be found at <http://cdmrp.army.mil/prorp/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.
- Submission of the same research project to different Funding Opportunities within the same program and fiscal year.
- The application proposes a clinical trial

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.

Quarterly technical progress, quad charts, and in-person presentations will be required.

E. Award Transfers

Approval of an organizational or PI transfer request will be 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 20160210j. 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	Impact and Military Benefit Statement: Upload as Attachment 6 with file name "MilBen.pdf."	
	7	Animal Research Plan: Upload as Attachment 7 with file name "AnimalPlan.pdf," if applicable.	
	8	Human Sample Acquisition and Safety Procedures: Upload as Attachment 8 with file name "HumSamAcq.pdf," if applicable.	
	9	Data Management: Upload as Attachment 9 with file name "Data_Manage.pdf," if applicable.	
	10	Collaborating DoD Military Facility Budget Form(s): Upload as Attachment 10 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.	