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-15-PRORP-ARA

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 13, 2015
- **Invitation to Submit an Application:** October 2015
- **Application Submission Deadline:** 11:59 p.m. ET, November 19, 2015
- **End of Application Verification Period:** 5:00 p.m. ET, November 24, 2015
- **Peer Review:** February 2016
- **Programmatic Review:** March/April 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) 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, the DHA RDA Directorate manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The executing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The 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 FY14 totaled $248.5 million (M). The FY15 appropriation is $30M.

The FY15 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 musculoskeletal injuries sustained during combat or combat-related activities. It is expected that any 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 Government agencies are highly encouraged.

B. FY15 PRORP Focus Areas

All applications must address at least one of the following FY15 PRORP Focus Areas. The area addressed can be either an Acute Care or Rehabilitation Focus Area. Applications proposing research outside of the Focus Areas listed below will be administratively withdrawn and not considered. Studies that propose nominal or iterative advancements are not encouraged.

Acute Care Focus Areas:

- Segmental Peripheral Nerve Defects: Treatment strategies to improve outcomes from segmental peripheral nerve defects.
- 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.
- Lower Extremity Fractures: Optimal time to weight bearing for lower extremity fractures.
- Economic Impact: Economic impact of innovations in orthopaedic trauma research.

- Biomarkers and Clinical Parameters: Biomarkers and clinical parameters to guide the decision to perform early total care (definitive) versus damage control orthopaedics.
- Pelvic Ring Injuries: Outcomes of complex pelvic ring injuries requiring advanced resuscitation.

Rehabilitation Focus Areas:

- Post-Operative Pain Management: Development of post-operative pain management strategies for optimal fracture rehabilitation. The primary outcome measure should relate to rehabilitation endpoints and not focus solely on pain scores or opioid use.
- Prosthetic and/or Orthotic Device Function: Development and optimization of novel and/or innovative technologies to improve prosthetic and/or orthotic device function and durability, including intuitive efferent and afferent user interfaces and considerations to interoperability.
- Secondary Physical Health Effects: Techniques or technologies that improve prediction, identification, and reduction of secondary physical health effects (e.g., obesity, arthrosis, osteoporosis, cardiovascular disease) following severe/high-energy traumatic neuromusculoskeletal 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 and Occupational Therapy: Development and/or validation of optimal physical and 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 dose, timing, frequency, duration, and intensity of rehabilitation interventions.
- Rehabilitation Outcomes: Development of validated, standardized measures to objectively assess and improve rehabilitation outcomes, including multi-extremity trauma and/or psychosocial resiliency and reintegration, following severe neuromusculoskeletal injury.

C. Award Information

The PRORP Applied Research Award (ARA) mechanism is being offered for the first time in FY15. 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 of the FY15 PRORP ARA Focus Areas listed 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 FY15 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 products, pharmacologic agents, behavioral and rehabilitation interventions, diagnostic and therapeutic techniques, clinical guidance, and/or emerging approaches and technologies. Upon successful completion, these studies are expected to yield potential health products, approaches, or technologies positioned for human testing.

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. In order 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 FY15 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 products.
- Evaluation, maturation, and/or down-selection of potential product candidates (drugs, biologic constructs, or devices/systems) in vitro and/or in vivo.
- Conducting preclinical safety and/or toxicity studies sufficient to support Investigational New Drug/Investigational Device Exemption (IND/IDE) applications.
- 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 PRORP Clinical Trial Award (W81XWH-15-PRORP-CTA) mechanism, which can be accessed at http:cdmrp/army.mil/funding.

Research Scope: Research proposed under the FY15 PRORP ARA may include small- to large-scale projects such as nonclinical efficacy studies, effective comparison studies, human use and/or observational studies. Two different funding levels, based on the scope of the research, are available under this Program Announcement/Funding Opportunity. ***It is the responsibility of the Principal Investigator (PI) to select the funding level that is most appropriate for the proposed research project.***

The following are general descriptions, although not all-inclusive, of the scope of research projects that would be appropriate to propose under each funding level:

- **Funding Level 1:** Research that is already supported by preliminary data and has the potential to make significant advancements toward clinical translation. Demonstration of efficacy in in vivo models, as applicable.

- **Funding Level 2:** Advanced translational studies that have the potential for near-term clinical investigation.

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 (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 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) 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 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 Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local Institutional Review Board (IRB) of record. Local IRB approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. 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 plan involves access to active duty military and/or VA patient populations or resources, the 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 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 areas of research interest:

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

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://dmrdp.fhpr.osd.mil/home.aspx

Military Infectious Disease 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/

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. Naval Research Laboratory
https://www.nrl.navy.mil/

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

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 requested budget level should be appropriate for the scope of the research proposed.

Funding Level 1:

- The maximum period of performance is **3** years.
- The anticipated total costs (direct and indirect) 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.

Funding Level 2:

- The maximum period of performance is **3** years.
- The anticipated total costs (direct and indirect) budgeted for the entire period of performance will not exceed **$1M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$1M** total costs or using an indirect rate exceeding the organization's negotiated rate.

For both funding levels:

- The applicant must submit a comprehensive budget, broken down by year, that details the projected funding needed for the entire period of performance.
- 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.
- Regardless of the period of performance proposed, the award may not exceed the maximum allowable total costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

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 to disseminate project results at the annual Extremity War Injuries Symposium. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area for approximately 2 days. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Research-related subject costs (clinical trials are ***not*** allowed)
- Clinical research costs
- 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 $3M of the $30M FY15 PRORP appropriation to fund approximately two Level 1 and two Level 2 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 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-PRORP-ARA 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. A change in PI or organization after submission of the pre-application may be allowed after review of a submitted written appeal (contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507) and at the discretion of the USAMRAA Grants Officer.

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 PRORP Steering Committee (SC) members should not be involved in any pre-application or application. A list of the FY15 PRORP SC members can be found at http://cdmrp.army.mil/prorp/panels/panel15h. For questions related to SC 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 (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 at least one of the FY15 PRORP ARA Focus Areas.
  - **Rationale:** State how this project addresses an important problem relevant to combat-related musculoskeletal and orthopaedic injuries. State the ideas and reasoning on which the proposed work is based.
  - **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
  - **Research Strategy:** Clearly describe the research being proposed. Concisely state the project's objectives, specific aims, and ultimate endpoints. Describe the proposed methods and how they will accomplish the project's aims.
  - **Impact:** State explicitly how the proposed work may ultimately have an immediate and long-term effect on patient care and/or restoration of function for those who have sustained combat-related orthopaedic injuries.
  - **Military Benefit:** Describe how the proposed work would impact the health care needs of Service members and/or U.S. 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.

  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.
- **Key Personnel Biographical Sketches** (five-page limit per individual). The five-page National Institutes of Health Biographical Sketch may also be used.
- **Quad Chart:** The Quad Chart template is a one-page PowerPoint file that must be downloaded from eBRAP at https://cdmrp.org/Program_Announcements_and_Forms/, completed, and saved as a PDF file using Adobe Acrobat Reader.

- **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 missions of the DHP and the PRORP, pre-applications will be screened based on the following criteria:

  - **Research Plan:** How well the rationale, objectives, and specific aims support the research idea. To what degree the proposed project addresses the intent of the award mechanism and addresses an important problem relevant to the PRORP. How the endpoints are appropriate for the proposed study.
  - **Alignment with Focus Areas:** How well the project addresses at least one FY15 PRORP ARA Focus Area.
  - **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 orthopaedic injuries.
  - **Military Benefit:** How well the proposed study will directly or indirectly provide a significant benefit to military Service members and/or the U.S. Veterans who have sustained combat-related orthopaedic injuries that impact unit readiness and return-to-duty/work.
  - **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.

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 PRORP 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. **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 (20-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:** State the FY15 PRORP ARA Focus Area(s) being addressed. Establish the relevance of the study to at least one of the FY15 PRORP ARA Focus Areas 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.
- **Objectives/Specific Aims/Hypotheses:** State the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses.
- **Research Strategy:** Describe the experimental design, methods, and analyses including appropriate controls and statistical power needed in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches.
- **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. For research involving human subjects, specify the approximate number of human subjects that will be enrolled. 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 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.***

- **Attachment 2: Supporting Documentation. Start each document on a new page. Combine and upload as a single file named "Support.pdf."** If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.***
  - References Cited: List the references cited (including URLs if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
- Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
- Publications and/or Patent Abstracts: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.
- 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.
- Intellectual Property
  - Background and Proprietary Information: All software and data first produced under the award are subject to a Federal purpose license. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the Federal purpose license.
  - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.
- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 3, Section L for more information about the CDMRP expectations for making data and research resources publicly available.
- 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, to include:

- Availability of and access to research resources, and/or
- Availability of and access to appropriate populations (and/or access to available samples/data or databases), if applicable

○ 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.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf."** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  The technical abstract is used by all reviewers. Therefore, clarity and completeness within the space limits of the technical abstract are highly important. Use the outline below. Proprietary or confidential information ***should not*** be included.

  ○ Background: State the FY15 PRORP ARA Focus Area(s) addressed by the proposed research. State how the proposed research addresses the intent of the 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 military personnel with orthopaedic injuries sustained in combat or combat-related activities, as well as their family members, caregivers, and the general public.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf."** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  The lay abstract is used by all reviewers. It is an important component of the application because it addresses issues of particular interest to the advocate community. Therefore, clarity and completeness within the space limits of the lay abstract are highly important. **Do not duplicate the technical abstract.** Use the outline below. Proprietary or confidential information ***should not*** be included.

- Describe the objectives and rationale for the application in a manner that will be readily understood by lay readers, as well as those without a background in science or medicine.
- Describe the ultimate applicability of the research.
  - Which FY15 PRORP ARA Focus Area(s) will be addressed?
  - How will the proposed research impact the Focus Area(s) addressed?
  - What are the potential clinical applications, benefits, and risks?
  - What is the projected timeline it may take to achieve the expected patient-related outcome?
- Describe how the proposed project will benefit Service members and/or U.S. 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 General Format" or "SOW for Collaborative PI project," as appropriate for the proposed project. 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 "MilBen.pdf."**
  - Describe the potential immediate or long-term effect on the lives of individuals recovering from combat-related orthopaedic injuries, including but not limited to, how the expected results of the proposed work will contribute to the goals of decreasing the clinical impact of these injuries.
  - Describe how the proposed study is responsive to the health care needs of military Service members and the U.S. Veteran population that sustained orthopaedic injuries. Provide information about the incidence and/or prevalence of orthopaedic injuries in military Service members and/or U.S. Veterans, if appropriate and available. Show how the proposed study complements ongoing DoD and VA areas of research interest.
  - 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 a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Services and/or the

U.S. Veteran population). Show how the proposed study complements ongoing DoD areas of orthopaedic research interest. Describe how the study design will replicate field conditions, if applicable.

- Describe the short-term impact, as well as the anticipated long-term benefits of the proposed research. 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.

- **Attachment 7: Animal Research Plan (five-page limit): Upload as "AnimalPlan.pdf,"** if applicable.
  - 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 Institutional Animal Care and Use Committee (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 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 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 5, 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.
  - **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.

○ **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 within a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form (available for download on the eBRAP "Funding Opportunities & Forms" web page), including a budget justification, for each Military Facility as instructed. Refer to the General Application Instructions, Section II.C.8., for detailed information.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information. Note: Some of the items in this attachment may be made available for programmatic review.

    - PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The five-page National Institutes of Health Biographical Sketch may also be used.
    - PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
    - Key Personnel Biographical Sketches (five-page limit each): Upload as "Biosketch_LastName.pdf."
    - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

    - Budget Justification (no page limit): Upload as "BudgetJustification.pdf." The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.6., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.7., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

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

E. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in application rejection.

F. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Section II.A., for information on Grants.gov registration requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the Office of the Assistant Secretary of Defense for Health Affairs, based on (a) technical merit and (b) the relevance to the mission of the DHP and PRORP, 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:

   - **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 the proposed alternative methods and approaches address those areas.
     - The degree to which the plan to study military populations, if applicable, is appropriate and feasible.
   - **Impact and Military Benefit**
     - How the proposed study addresses the FY15 PRORP ARA Focus Area(s).
     - How relevant the anticipated research outcomes are with regard to the FY15 PRORP ARA Focus Area(s).
     - How well the PI describes the potential immediate and long-term effect 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 usability of the proposed research on the health and well-being of Service members, Veterans, and/or their families or communities.
     - How well the study addresses a critical issue in the treatment of 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 well the composition of the research or study team is appropriate to accomplishing the proposed work (e.g., statistical expertise, expertise in orthopaedic injury, etc.).
    - How well the levels of effort by the PI and other key personnel are appropriate to ensure success of this project.
    - How well the 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:

- **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
    - To what extent the application components reflect knowledge and respect for the needs of the general community and the affected individuals.
- **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 accessibility to facilities and resources (including collaborative arrangements).
    - How the quality and extent of institutional support are appropriate for the proposed project.
    - If applicable, whether there is evidence for appropriate institutional commitment from each collaborating institution.
    - If applicable, how the intellectual and material property plan that is agreed upon by each participating institution is appropriate for the proposed research project.
    - If applicable, to what degree the intellectual and material property plan is appropriate.

2. **Programmatic Review:** To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following equally considered criteria are used by programmatic reviewers:

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

   b. **Relevance to the mission of the DHP and FY15 PRORP, as evidenced by the following:**

      - Adherence to the intent of the award mechanism
      - Relative Impact and Military Relevance
      - Programmatic relevance
      - Program portfolio composition

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 Funding Opportunities within the same program and fiscal year.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the 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 PRORP SC 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 PRORP SC members can be found at http://cdmrp.army.mil/prorp/panels/panel15h.
- 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.
- The application does not address one of the FY15 PRORP ARA Focus Areas.

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.

E. Award Transfers

Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer. Changes in PI will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

Refer to the General Application Instructions, Appendix 3, Section M, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. Federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the Grants.gov application package. If the Grants.gov application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF-424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	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 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.	