

Program Announcement

for the

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Congressionally Directed Medical Research Programs

Peer Reviewed Orthopaedic Research Program Clinical Trial Award

Funding Opportunity Number: W81XWH-13-PRORP-CTA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline: 5:00 p.m. Eastern time (ET), April 4, 2013**
- **Invitation to Submit an Application: mid-May 2013**
- **Application Submission Deadline: 11:59 p.m. ET, July 18, 2013**
- **Peer Review: To Be Determined**
- **Programmatic Review: To Be Determined**

This Program Announcement 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 2013 (FY13) Peer Reviewed Orthopaedic Research Program (PRORP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The PRORP was initiated in 2009 to support research 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 FY12 total \$188.5 million (M). The executing agent for the PRORP is the Congressionally Directed Medical Research Programs (CDMRP).

The FY13 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. Applications involving multidisciplinary collaborations among academia, industry, the military services, the Department of Veterans Affairs (VA), and other federal Government agencies are highly encouraged.

Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of FY13 federal funds for this program. As of the release of this Program Announcement/Funding Opportunity, the FY13 Defense Appropriations Bill has not been passed and there is no guarantee that any funds will be made available to support this Program Announcement/Funding Opportunity. Funding allotted for this Program Announcement/Funding Opportunity is approximate and subject to change.

B. Award Information

The PRORP Clinical Trial Award is intended to support the rapid implementation of clinical trials with the potential to have a significant impact on military combat-related orthopaedic injuries. The clinical trials may be designed to evaluate promising new products, pharmacologic agents (drugs or biologics), devices, clinical guidance, and/or emerging approaches and technologies. All applications are required to justify the relevance of the proposed project to military and/or Veteran populations affected by combat-related orthopaedic injury.

Collaboration with military researchers and clinicians is encouraged, and studies that include active duty military or Veteran participants as all or a portion of the study population will be given higher priority for funding during programmatic review.

Proposed projects may range from small proof-of-concept (i.e., pilot, first in human, or Phase 0) trials, to demonstrate feasibility or inform the design of more advanced trials, through large-scale trials, to determine efficacy in relevant patient populations. Proof-of-concept trials should not request the maximum funding amount allowed under this Program Announcement/Funding Opportunity. All funding amounts requested should be well-justified and appropriate to the scope of work proposed.

All applications must propose a clinical trial addressing at least one of the following FY13 PRORP Clinical Trial Award Focus Areas:

- Characteristics of and strategies for optimizing long-term (5 to 10 years) functional outcomes for traumatic military amputee and/or limb salvage patients.
- Strategies to prevent or mitigate post-traumatic osteoarthritis resulting from fracture and/or ligament injury, including novel surgical approaches and other interventions for treatment, the effect of weight bearing, and retrospective studies of the impact of prior surgical interventions on the occurrence of post-traumatic osteoarthritis.
- Surgical interventions for combat-related spine fractures and instability.
- Physical or occupational therapy (PT/OT) interventions, such as studies that establish optimal strategies for weight bearing progression or studies that examine the comparative effectiveness of different PT/OT regimens.
- Establishment of bone, joint, and soft tissue health guidelines based upon validated measures to aid clinicians in returning patients safely to high-impact activities, including, but not limited to, validation of markers of bone quality that can predict susceptibility to injury, and comparative effectiveness studies of training and therapeutic interventions to improve bone quality and muscle function that maximize performance while minimizing injury.
- Interventions to improve secondary health effects (e.g., joint contracture, obesity, cardiovascular disease, poor bone health) that follow reduced mobility from primary neuromusculoskeletal injury, excluding spinal cord injuries.
- Maintenance or enhancement of long-term socket performance and fit of prosthetics, including the design and development of flexible socket suspension systems, the evaluation of socket performance (comfort, fit, and durability), and the application of new technologies to improve existing prosthetic sockets.
- Studies to improve moisture management and residual limb skin care at the prosthetic socket interface.
- Clinical studies on the effectiveness of local strategies to minimize surgical site infections, including but not limited to local application of antibiotics, debridement techniques, and/or subatmospheric wound dressing.

Funding from this award mechanism must support a clinical trial and may not be used for preclinical research studies. 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. Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other funding opportunities being offered. The term “human subjects” is used in this Program Announcement/Funding Opportunity to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at [https://cdmrp.org/Program Announcements and Forms/](https://cdmrp.org/Program%20Announcements%20and%20Forms/).

Clinical trials selected for funding through this Program Announcement/Funding Opportunity are required to be initiated within 12 months of the date of award. Thus, it is expected that applicants will have already made significant progress on the administrative and logistical tasks necessary for starting a clinical trial at the time of full application submission to Grants.gov. Applicants needing time and resources to develop aspects of a study such as the study team, the clinical protocol, Institutional Review Board (IRB) and Food and Drug Administration (FDA) reviews, and management plans are strongly encouraged to apply to the FY13 PRORP Clinical Trial Development Award (W81XWH-13-PRORP-CTDA) instead of this Program Announcement/Funding Opportunity.

If the study proposed involves the use of a drug or biologic that has not been approved by the FDA for its investigational use, evidence that an Investigational New Drug (IND) exemption application has been submitted or will be submitted ***within 4 months of notification of funding status*** (i.e., release of funding notification letters) is required. If the investigational product is a device, evidence that an Investigational Device Exemption (IDE) has been submitted or will be submitted ***within 4 months of notification of funding status*** or that the device is exempt from an IDE, is required. ***The Government reserves the right to withdraw funding if documentation of IND or IDE application submission to the FDA has not been provided to the CDMRP within 4 months of the funding status notification date.***

The following are important aspects of submission for the Clinical Trial Award:

- The proposed clinical trial is expected to begin no later than 12 months after the award date.
- The proposed intervention to be tested should offer significant potential impact for military personnel with combat-related orthopaedic injuries.
- Inclusion of preliminary (published or unpublished) data relevant to the proposed clinical trial is required.
- The proposed clinical trial must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature.
- The application should demonstrate documented availability of and access to the drug/compound, device, and/or materials needed, as appropriate.
- The application should demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study. The PI should discuss how accrual goals will be achieved and how standards of care may impact the study population.
- The proposed clinical trial should include clearly defined and appropriate endpoints.
- The application should include a clearly articulated statistical analysis plan appropriate to the phase of the clinical trial, as well as appropriate statistical expertise and a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- The application should include a study coordinator(s) who will guide the clinical protocol through the local Institutional Review Board (IRB) of record and other regulatory

approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.

- The application should include a Transition Plan (including potential funding and resources) showing how the intervention will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the PRORP Clinical Trial Award.

NESTED CAREER DEVELOPMENT OPTION

A nested career development opportunity is being offered as a Clinical Trial Award option. The intent of the nested Career Development Option is to support research training opportunities for U.S. military investigators pursuing careers in orthopaedic research. This option supports individuals in the early stages of their careers by providing the experience necessary to pursue career opportunities at the forefront of orthopaedic trauma research and make significant contributions to combat-related orthopaedic research and clinical care.

- **Career Development Investigator:** The Career Development Investigator must be a U.S. *active-duty military* research- or physician-scientist at either the postdoctoral or early-career level as described in Section I.C., Eligibility Information. Only one Career Development Investigator may be included within a given Clinical Trial Award application. The Career Development Investigator must be a named individual (“To be named” Career Development Investigators are not allowed) and must submit all required supporting documents listed below. Recipients of prior PRORP Career Development Awards or Nested Career Development Option awards are not eligible to apply as a Career Development Investigator to this Program Announcement/Funding Opportunity.
- **Orthopaedic Research Mentorship:** A designated mentor is required. Multiple mentors may be proposed, if appropriate, but one must be identified as the primary mentor. The mentor may be the PI of the application, a member of the research team, or outside of the research team. This mentor must be an established orthopaedic researcher, have a history of orthopaedic research funding, and have a record of orthopaedic research publications in peer-reviewed journals. In addition, the mentor must demonstrate a commitment to developing and sustaining the Career Development Investigator’s research career in orthopaedic research. The mentor may request salary support, as appropriate to his/her level of effort. *To promote collaboration between military and non-military organizations, it is encouraged, but not required, that the mentor be from an academic, VA, or other non-military organization.*
- Applications that contain a nested Career Development Investigator will qualify for a higher level of funding as described in Section I.D., Funding).
- Supporting documentation must include a biographical sketch for the Career Development Investigator, a Career Development Statement, and a letter of support from the Career Development Investigator’s primary mentor. A biographical sketch must also be provided for the mentor(s) if it is not already included in the Clinical Trial Award application Key Personnel Biographical Sketches.

- *To qualify for the nested Career Development option, all requirements described above must be included in the application. If these requirements are not met, the Government reserves the right to review the application as a standard Clinical Trial Award.*

Use of Human Subjects and Human Anatomical Substances: All Department of Defense (DoD)-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the Institutional Review Board (IRB) of record. IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DoD. These laws and directives will require information in addition to that supplied to the IRB of record. Allow a minimum of 4 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 5, for more information.

Use of Military and VA Populations: If applicable, access to target military or VA patient population(s) should be confirmed at the time of application submission. A letter of support, signed by the lowest ranking person with approval authority, should be included for studies involving active duty military, Veterans, military and/or VA-controlled study materials, and military and/or VA databases.

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. While 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>

Defense Technical Information Center

<http://www.dtic.mil>

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

<http://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 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.

C. Eligibility Information

- PIs must be at or above the level of Assistant Professor (or equivalent).
- Nested Career Development Option: The Career Development Investigator must be U.S. active-duty military and must have at the time of the application submission deadline:
 - Completed a doctoral-level degree,
 - A total of less than 8 years of postdoctoral clinical or research experience (excluding clinical residency or fellowship training),
 - Been awarded less than \$500,000 in direct costs in aggregate as a PI of federal or private, non-mentored, peer reviewed awards, and
 - Not been the recipient of a prior PRORP Career Development Award or Nested Career Development Option award.
- Cost sharing/matching is not an eligibility requirement.
- Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations. Both intramural (i.e., DoD) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **4** years.
- The maximum allowable direct costs for the entire period of performance are **\$2.5M** plus indirect costs. If requesting the Nested Career Development Option, the maximum allowable direct costs for the entire period of performance are **\$2.725M** plus indirect costs.

- The applicant is encouraged to request less than the maximum allowable direct cost limit, as appropriate to the scope of work proposed. Proof-of-concept trials should not request the maximum funding amount allowed under this Program Announcement/Funding Opportunity.
- 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 4 years.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.
- Any application that requests the higher level of funding and does not include an eligible Nested Career Development Investigator will have its budget reduced as appropriate.

Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget.

In addition, for this award mechanism, direct costs:

Must be requested for:

- Travel funds of up to \$1,800 for the PI to attend one DoD-sponsored meeting to be specified by the CDMRP during the award performance period. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary of non-Government personnel (includes contract research personnel at Government facilities)
- Research supplies
- Equipment
- Clinical research costs
- Training-related costs for Nested Career Development Investigator
- Travel between collaborating organizations
- Support for multidisciplinary collaborations
- Travel costs of up to \$1,800 per year to attend scientific/technical meetings in addition to the required meeting described above

Shall not be requested for:

- Preclinical research studies
- Salary of Government personnel

Intramural (DoD) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. ***For all federal agencies or organizations collaborating with agencies, budget restrictions apply and are so noted in Section II.C.4. of the General Application Instructions.*** As required of all applicants to this Program Announcement, if PIs from federal agencies submit full applications, they must submit through Grants.gov. Therefore, federal applicants must be familiar with Grants.gov requirements, including the need for System for Award Management (SAM) and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

The PRORP expects to allot approximately \$11.25M of the FY13 PRORP appropriation to fund approximately 3 PRORP Clinical Trial Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (<https://cdmrp.org/>) and (2) application submission through Grants.gov (<http://www.grants.gov/>).

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.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (<http://www.grants.gov/>) basic search using the Funding Opportunity Number: W81XWH-13-PRORP-CTA.

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the PI through the CDMRP eReceipt System (<https://cdmrp.org/>). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

The pre-application consists of the following components, which are organized in the CDMRP eReceipt System 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**
- **Collaborators and Conflicts of Interest – Tab 3**

FY13 PRORP Steering Committee (SC) members should not be involved in any pre-application or application. For questions related to SC members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP [Help Desk](#) (301-682-5507).

- **Required Files – Tab 4**

Preproposal Narrative (three-page limit): The Preproposal Narrative page limit applies to text and any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons.

The Preproposal Narrative should include the following:

- **Focus Area:** Explain how the proposed work addresses at least one of the FY13 PRORP Clinical Trial Award Focus Areas.
- **Research Idea:** Describe the ideas and reasoning on which the proposed clinical trial is based; include relevant literature citations. Briefly describe the level of scientific evidence that supports the progression of this research to a clinical trial. Clearly specify which type (e.g., drug, device, behavioral) of clinical trial is being proposed and indicate the phase of trial and/or class of device and regulatory status, as appropriate.
- **Research Strategy:** Concisely state the project’s objectives and specific aims. Briefly describe the patient population(s) to be recruited for the clinical trial and the experimental approach.
- **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the clinical trial. If applicable, describe the roles of the Career Development Investigator and designated mentor(s) in the project.
- **Military Benefit:** Describe how the proposed work will have an impact on accelerating the movement of a promising treatment for combat-related orthopaedic injury into a military clinical application.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application are limited to:

- **References Cited (one-page limit):** List relevant references 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). The inclusion of Internet URLs to references is encouraged.
- **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
- **Key Personnel Biographical Sketches (four-page limit per individual)**

- **Submit Pre-Application – Tab 5**

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

- **Other Documents Tab**

No additional documents are required.

Pre-Application Screening

- **Pre-Application Screening Criteria**

To determine the technical merits of the pre-application and the relevance to the mission of the DoD and the PRORP, pre-applications will be screened based on the following criteria:

- **Research Idea:** The degree to which the proposed clinical trial addresses the intent of the award mechanism and aligns with FY13 PRORP Clinical Trial Award Focus Areas. How well the rationale is supported, and how well the background provided indicates the research is ready to move into a clinical trial.
- **Research Strategy:** How well the specific aims, patient population, and proposed methodology will address the hypothesis and achieve the desired outcomes.
- **Personnel:** How the background and experience of the PI and other key personnel are appropriate to successfully complete the clinical trial.
- **Military Benefit:** The degree to which the proposed clinical trial, if successful, will improve and/or innovate clinical care for Warfighters who have sustained combat-related orthopaedic injuries. Whether the proposed study includes active duty military personnel and/or Veterans in the targeted study population.

- **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. Application Submission Content and Form

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

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

Grants.gov application package components: For the Clinical Trial Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

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

Describe the proposed project in detail using the outline below. Include potential problems and associated alternative strategies wherever possible:

- **Background:** Describe in detail the rationale for the study and include a literature review, preliminary studies, and/or preclinical data that led to the development of the proposed clinical trial. Provide a summary of relevant clinical trials and distinguish how the proposed study differs from other relevant or recently completed clinical trials. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses.
- **Study Design:** Describe the type of study to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action.
 - Identify the intervention to be tested and describe the projected outcomes.

- Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
- Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
- Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
- Describe the reliability and validity of psychometric measures, if applicable.
- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects that will be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study.
- **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 may result in the removal of those items or administrative withdrawal of the application.***
 - **References Cited:** List the references cited (including URLs if available) in the project narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
 - **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols.
 - **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
 - **Publications and/or Patent Abstracts (five-document limit):** Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.

- Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. ***If a Career Development Investigator is included in the application, letters from the Career Development Investigator's immediate supervisor and Commander must be provided that demonstrate a commitment to allow the Career Development Investigator to participate in the project.***
- Mentor Letter of Support for Optional Nested Career Development Investigator (if applicable): Provide a letter signed by the designated primary mentor in support of the nested Career Development Investigator. Describe the following:
 - How the Career Development Investigator's achievements indicate a potential for a successful career in orthopaedic research.
 - How the training environment will promote the development of the Career Development Investigator as an orthopaedic researcher.
 - The mentor's qualifications, including how the research being performed under the mentor's direction is relevant to combat-related orthopaedic injury.
 - The mentor's proposed interactions with the Career Development Investigator, and the degree to which the Career Development Investigator will participate in the execution of the application if funded.
- 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.
- Intellectual Property
 - 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 4, 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."

Technical abstracts should be written using the following outline:

 - Background: State the FY13 PRORP Clinical Trial Award Focus Area(s) addressed by the proposed research. Present the ideas and reasoning behind the proposed work.
 - Objective/Hypothesis: State the objective/hypothesis to be tested. Describe the overall research goals for the study.
 - Specific Aims: State the specific aims of the study.

- Study Design: Briefly describe the clinical study design including appropriate controls.
- Military Benefit: State briefly how the proposed project, if successful, will have an impact on combat-related orthopaedic injury research and/or patient care.
- **Attachment 4: Lay Abstract (one-page limit):** Upload as “LayAbs.pdf.”

Lay abstracts should be written using the following outline.

- 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*.
 - Do not duplicate the technical abstract.
- Describe the ultimate applicability of the clinical research.
 - What types of patients will it help, and how will it help them?
 - What are the potential clinical applications, benefits, and risks?
 - What is the projected timeline it may take to achieve the expected patient-related outcome?
 - Briefly describe how the proposed project will benefit military populations and impact combat-related orthopaedic research and patient care.
- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as “SOW.pdf.” Refer to the General Application Instructions, Section II.C., for detailed information, including guidance on appropriate SOW formats.
- **Attachment 6: Human Subject Recruitment and Safety Procedures (no page limit):** Upload as “HumSubProc.pdf.” The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.
 - a. **Study Population:** 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 sample will be recruited/drawn). Demonstrate that the research team has access to the proposed study population. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual including those specific to recruitment from military and/or Veteran populations (if applicable). Provide plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided.
 - 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 clinical trial.

- c. **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification). *Include a description of any considerations unique to recruitment from military or Veterans medical treatment facilities, if applicable.*
- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
 - Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.
 - Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.
- d. **Description of the Informed Consent Process:** 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.
 - Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
 - Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
 - Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
 - Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. 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 clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980)

(http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=browse_usc&docid=Cite:+10USC980.) If applicable, please refer to the General Application Instructions, Appendix 5, for more information.

- **Assent.** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.
- e. **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation 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.

f. **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks. Study risks include any risks that the human subject is subjected to as a result of participation in the clinical trial. 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. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
 - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
 - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
 - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

- **Attachment 7: Intervention (no page limit):** Upload as “Intervention.pdf.” The Intervention attachment should include the components listed below.
 - a. **Description of the Intervention:** As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed.

Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety of the intervention. Description of devices should include detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described.
 - b. **Study Procedures:** Describe the interaction with the human subject to include the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Discuss how compliance with Good Clinical Practices, Good Manufacturing Practices, and other regulatory considerations will be established, monitored, and maintained, as applicable.
- **Attachment 8: Data Management (no page limit):** Upload as “DataManage.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.
 - **Disposition of data:** 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 9: Study Personnel and Organization (no page limit):** Upload as “Personnel.pdf.” The Study Personnel and Organization attachment should include the components listed below.
 - a. **Principal Investigator/Study Staff:** Provide an organizational chart identifying key members of the study team including institution/center/department. Briefly describe their roles on the project. A medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included.
 - b. **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included. Provide a plan for real-time communication among collaborating institutions (if applicable).
- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit):** Upload as “Surveys.pdf.” The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study.

- **Attachment 11: Military Benefit Statement (one-page limit):** Upload as “MilBen.pdf.”

State explicitly how the proposed clinical trial, if successful, will accelerate the movement of the product, pharmacologic agent, device, clinical guidance, and/or emerging technology into clinical practice for combat-related orthopaedic injuries. Further, describe the impact of this study 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 goal of decreasing the clinical impact of these injuries. The following are examples of ways in which proposed studies, if successful, may have an impact. *Although not all-inclusive*, these examples are intended to help PIs frame the impact of the proposed research:

- Has the potential to change the standard of care for military orthopaedic injuries
- Proposes new paradigms or challenges existing paradigms in patient care of military orthopaedic injuries
- Contributes to development or validation of evidence-based policy or guidelines for patient evaluation and care

Demonstrate how the proposed study is responsive to the health care needs of the military services and/or the U.S. Veteran population. If active duty military or Veteran population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of using the population(s). 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.

- **Attachment 12: Transition Plan (one-page limit):** Upload as “Transition.pdf.” Provide information on the methods and strategies proposed to move the product to the next phase of clinical trials and/or delivery to the military or civilian market after successful completion of the award. The transition plan should include the components listed below.
 - Details of the funding strategy that will be used to bring the outcomes to the next level of clinical trials and/or delivery to the military or civilian market (e.g., specific potential industry partners, specific funding opportunities to be applied for).
 - A description of collaborations and other resources that will be used to provide continuity of development. For any industry partner(s), include a description of prior product development and/or marketing experience.
 - A brief schedule and milestones for bringing the outcome(s) to the next phase of clinical trials and/or delivery to the military or civilian market.
 - A risk analysis for cost, schedule, manufacturability, and sustainability.

- A description of relevant product patents and intellectual property ownership, and their potential impact on product development and the Government’s ability to access any technology or products supported with this award.

- **Attachment 13: Letters Confirming Access to Target Military or VA Patient Population(s), if applicable (no page limit):** Upload as “Access.pdf.”

If applicable, provide a letter(s) signed by the lowest ranking person with approval authority for studies involving active duty military, Veterans, military and/or VA-controlled study materials, and military and/or VA databases.

- **Attachment 14: Career Development Statement, if applicable (three-page limit):** Upload as “CareerDev.pdf.”

The required Career Development Statement from the proposed Career Development Investigator should:

- Identify the designated primary mentor. Multiple mentors may be proposed, if appropriate, but one must be identified as primary.
- Describe a Career Development Plan, which may include coursework, hands-on laboratory and clinical techniques, conferences, seminars, teaching responsibilities, and/or clinical responsibilities.
- Describe the research that will be performed by the Career Development Investigator in the context of the proposed clinical trial.
- Articulate career goals and how the proposed research training will promote a career in orthopaedic trauma research.

- **Attachment 15: IND/IDE Documentation (no page limit):** If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “IND-IDE.pdf.”

Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov. If an IND or IDE has been submitted, an explanation of the status of the IND or IDE should be provided (e.g., past the critical 30-day period, pending response to questions raised by the Agency, on clinical hold). Inclusion of a copy of the Agency meeting minutes is encouraged but not required. If the IND or IDE application is not yet submitted, provide evidence that an IND or IDE will be submitted *within 4 months of notification of funding status* (i.e., release of funding notification letters). Examples include a pre-IND or pre-IDE meeting with the FDA, a pre-IND/pre-IDE meeting request to the FDA, or other communication with the FDA. Provide the anticipated date of IND/IDE submission. If an IND or IDE is not required for the proposed study, provide evidence in the form of communication from the FDA or the IRB of record to that effect.

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

- PI Biographical Sketch (four-page limit): Upload as “Biosketch_LastName.pdf.”

- PI Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”
 - Key Personnel Biographical Sketches (four-page limit each): Upload as “Biosketch_LastName.pdf.”
 - If applying under the Nested Career Development Option, include biographical sketches for the Career Development Investigator and mentor(s).
 - Key Personnel Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”
 - If applying under the Nested Career Development Option, include the current/pending support of the Career Development Investigator and mentor(s).
- 4. Research & Related Budget:** Refer to the General Application Instructions, Section II.C., for detailed information.
- Budget Justification (no page limit): Upload as “BudgetJustification.pdf.”
- 5. Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C., for detailed information.
- 6. R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C., for detailed information.

D. 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 any one of the deadlines will result in application rejection.

E. 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 Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an “Active” status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov 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 a 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 Office of the Assistant Secretary of Defense, Health Affairs,

based on technical merit, the relevance to the mission of the DHP and the PRORP and 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 twotier review 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 non-disclosure 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 Criteria

1. Peer Review: To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of equal importance:

- **Military Benefit and Clinical Impact**
 - How relevant the anticipated outcomes of the proposed clinical trial are to individuals with combat-related orthopaedic injuries.
 - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
 - How the potential outcomes of the proposed clinical trial will provide/improve the short-term benefits for individuals with combat or combat-related orthopaedic injuries.
 - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
 - The degree to which the results of the proposed clinical trial will affect clinical practice for military combat-related orthopaedic injuries.
- **Research Strategy**
 - How well the scientific rationale for testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.
 - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer an important clinical objective.

- How well the inclusion and randomization criteria meet the needs of the proposed clinical trial.
- How well the exclusion criteria are justified.
- **Statistical Plan**
 - To what degree the statistical model and data analysis plan are suitable for the planned study.
 - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
- **Intervention**
 - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
 - To what degree the intervention addresses a defined clinical need(s).
 - To what degree the PI has provided preclinical and/or clinical evidence to support the safety of the intervention.
 - How the intervention compares with currently available interventions and/or standards of care.
 - Whether a member of the study team holds the IND/IDE or whether the timeline proposed for IND/IDE application is appropriate (if applicable).
 - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including the capability to provide the monitoring required by the FDA.
 - To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.
 - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **Recruitment, Accrual, and Feasibility**
 - How well the PI addresses the availability of human subjects for the clinical trial, and the prospect of their participation.
 - Whether the PI has demonstrated access to the proposed human subjects population.
 - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
 - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
 - To what extent the proposed clinical trial affects the daily lives of the individual human subjects participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?).

- **Ethical Considerations**
 - How the level of risk to human subjects is minimized, and whether there is sufficient evidence of a monitoring plan that is appropriate for the level of risk.
 - How well the evidence shows that the procedures are consistent with clinical research practices and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
 - To what degree privacy issues are appropriately considered.
 - To what degree the process for seeking informed consent is appropriate, and whether safeguards are in place for vulnerable populations.
- **Transition Plan**
 - Whether the funding strategy described to bring the outcome(s) to the next level of clinical trials and/or delivery to the military or civilian market is appropriate.
 - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
 - How the schedule of milestones for bringing the outcome(s) to clinical trial and/or delivery to the military or civilian market is appropriate.
 - How well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.
 - How well the application identifies intellectual property ownership, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent Government access to products supported by this Program Announcement/Funding Opportunity.
- **Personnel and Communication**
 - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
 - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in orthopaedic injury, and clinical studies).
 - How the levels of effort of the study team members are appropriate for the successful conduct of the proposed trial.
 - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, and standardization of procedures) meet the needs of the proposed clinical trial.
 - ***Nested Career Development applicants (if applicable):***
 - How the qualifications of the Career Development Investigator will augment the project and study team.
 - How the Career Development Investigator will benefit from participation in this project.

- How well the mentor, training environment, and career development plan are suited to providing the Career Development Investigator with a training experience that will further his/her career at the forefront of orthopaedic research.

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

- **Environment**

- To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
- Whether there is evidence for appropriate institutional commitment from each participating institution.

- **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 influenced the review.

2. Programmatic Review: To determine the application's relevance to the mission of the DoD and the PRORP, as well as to make funding recommendations, the following criteria are used by programmatic reviewers:

- Adherence to the intent of the award mechanism
- Programmatic relevance
- Program portfolio composition
- Ratings and evaluations of the peer reviewers
- Relative military benefit and clinical impact

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

All application review dates and times are indicated on the [title page](#) of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive notification of the funding recommendation. 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 the CDMRP eReceipt System 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 is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- Human Subject Recruitment and Safety Procedures (Attachment 6) are missing.
- Intervention (Attachment 7) is missing.
- Data Management (Attachment 8) is missing.

B. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative and Preproposal Narrative.
- Documents not requested will be removed.
- Following the application deadline, the PI may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed in Section IV.A., Rejection). The missing documents must be provided by 5:00 p.m. ET on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- A FY13 PRORP Steering Committee (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 document. A list of the FY13 PRORP SC members can be found at <http://cdmrp.army.mil/prorp/panels/panel13>.

- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The proposed research is not a clinical trial.
- The PI does not meet the eligibility criteria.
- The proposed project is not relevant to at least one of the FY13 PRORP Clinical Trial Award Focus Areas.
- An IND/IDE application has not been submitted, or will not be submitted within 4 months of notification of funding status, if applicable.

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, 2014. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

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

C. Reporting

Refer to the General Application Instructions, Appendix 4, Section E, for general information on reporting requirements.

Quarterly technical progress reports will be required.

In addition to written progress reports, oral presentations may be requested.

D. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section F, 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 the CDMRP eReceipt System 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@cdmrp.org

B. Grants.gov Contact Center

Questions related to application submission through the 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 application package. If the 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	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed.	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.	
	Upload Supporting Documentation (Support.pdf) as Attachment 2.	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.	
	Upload Lay Abstract (LayAbs.pdf) as Attachment 4.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Human Subject Recruitment and Safety Procedures (HumSubProc.pdf) as Attachment 6.	
	Upload Intervention (Intervention.pdf) as Attachment 7.	
	Upload Data Management (DataManage.pdf) as Attachment 8.	
	Upload Study Personnel and Organization (Personnel.pdf) as Attachment 9.	
	Upload Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (Surveys.pdf), as Attachment 10.	
	Upload Military Benefit (MilBen.pdf) as Attachment 11.	
	Upload Transition Plan (Transition.pdf) as Attachment 12.	
	Upload Letters Confirming Access to Target Military or VA Patient Population(s) (Access.pdf), if applicable, as Attachment 13.	
	Upload Career Development Plan (CareerDev.pdf), if applicable, as Attachment 14.	
	Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.
Attach PI 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 Current & Pending Support (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.	