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

Translational Research Award

Funding Opportunity Number: W81XWH-14-PRORP-TRA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), June 27, 2014
- **Invitation to Submit an Application:** August 2014
- **Application Submission Deadline:** 11:59 p.m. ET, October 24, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, October 29, 2014
- **Peer Review:** December 2014
- **Programmatic Review:** February 2015

Change for Fiscal Year 2014: *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 2014 (FY14) 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 activities. Appropriations for the PRORP from FY09 through FY13 totaled $218.5 million (M). The FY14 appropriation is $30M.

The FY14 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. FY14 PRORP Focus Areas

All applications must address at least one of the following FY14 PRORP Translational Research Award Focus Areas:

- Identify and reduce the secondary health effects (e.g., joint contracture, obesity, metabolic syndrome, poor bone health) that follow reduced mobility from traumatic neuromusculoskeletal injury, excluding spinal cord injuries. The focus should be on injuries sustained prior to the age of 45 and secondary health effects that develop within 5 years of injury.

- Strategies to inhibit neuromas at surgical/amputation sites.

- The application of ***novel and/or innovative*** technologies and materials in prosthetic and orthotic device development toward the improvement or enhancement of:

    - Long-term socket performance, to include afferent and efferent user interface.

    - The fit of prosthetics, including the design and development of flexible socket suspension systems and incorporated interoperability of components to improve stability and usability.

    - Socket performance (comfort, fit, moisture management, residual limb skin integrity, and durability). Novel upper extremity prosthetic sockets, including the design and development of flexible socket suspension systems, are highly encouraged.

- Myoelectric prosthetic durability (e.g., water resistance, waterproof components) to enhance the use of myoelectric prostheses in all military environments.

Studies that propose nominal or iterative advancements are not encouraged.

- Research toward osseointegration of upper extremity prostheses, including optimization of the skin-implant interface, prevention of infection, control strategies, and sensory feedback.

- Research on treatment of non-battle orthopaedic injuries that impact unit readiness and reflect historical return to work rates less than 50% or longer than 6 months. Non-penetrating/non-ballistic injuries involving knee, shoulder, elbow, hip, or ankle will be considered, but funding will favor studies focusing on a single joint complex. Includes strategies for timing and effectiveness of treatment for multi-ligamentous knee injuries.

C. Award Information

The PRORP Translational Research Award is designed to support multidisciplinary translational research that will accelerate the movement of promising ideas in orthopaedic research into clinical applications to benefit Warfighters and Veterans recovering from traumatic orthopaedic injuries.

To encourage meaningful and productive multidisciplinary collaborations***, there must be at least one laboratory scientist and at least one clinician participating in the research.*** A clinician is defined as an individual who is credentialed (possesses the necessary degrees, licenses, and other certifications) and practicing as a care provider in a relevant capacity. In addition, ***at least one member of the research team must have significant experience in either orthopaedic or musculoskeletal research or medicine.*** Biographical sketches should include appropriate documentation of credentials. It is the responsibility of the Principal Investigator (PI) and the collaborating investigators to describe how their combined expertise will better address the research question, why the work should be performed through collaboration rather than through separate efforts, and how the research design will create a reciprocal flow of ideas and information between the multiple disciplines represented. The proposed collaboration should involve substantial contributions from each of the key collaborators identified, with evidence of significant intellectual input from each key collaborator into the design of the project.

Observations that drive a research hypothesis may be derived from a laboratory discovery, population-based studies, or a clinician's firsthand knowledge from providing care to patients. While the ultimate goal of translational research is to move an observation forward into clinical application, the PI should view translational research as a two-way continuum between bench and bedside. Developmental pathways for translational research that may be useful for designing translational research studies for support under this mechanism are described on the National Cancer Institute website http://www.cancer.gov/researchandfunding/trwg/pathways-to-clinical-goals. These pathways, while created for cancer research initiatives, have broad applicability to other areas of research, are comprehensive, and span the entire translational research continuum from discovery of a target to clinical trials.

The Translational Research Award is not intended to support definitive clinical trials, but may support correlative studies that are associated with an existing clinical trial and projects that optimize the design of future definitive clinical trials. Some limited clinical testing of a novel intervention or device is permissible if the clinical testing is necessary to inform the next step in the continuum of translational research. Such clinical pilot studies should be small, represent only a portion of the proposed Statement of Work, and be utilized to establish feasibility of a potential approach or to aid in device or intervention refinement. Research projects may also include preclinical studies in animal models, human subjects, and human anatomical substances.

Investigators seeking support for a definitive clinical trial should utilize the FY14 PRORP Clinical Trial Award (for conduct of the trial; W81XWH-14-PRORP-CTA) or Clinical Trial Development Award (for planning of the trial; W81XWH-14-PRORP-CTDA) mechanisms. 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

Use of Human Anatomical Substances, Human Subjects, or Human Cadavers: All Department of Defense (DoD)-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), 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. Funded applications that include clinical pilot studies may be required to obtain an independent, external scientific review of the clinical protocol prior to HRPO review. Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for additional information.

New for FY14: **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 8, Animal Research Plan, as part of the applications 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.nc3rs.org.uk/page.asp?id=1357.

Use of Active Duty 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.

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

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 Congressionally Directed Medical Research Programs (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 L.

D. Eligibility Information

- Independent investigators at all academic levels (or equivalent) are eligible to submit applications.
    - A collaborative research team is required. There must be at least one laboratory scientist and at least one clinician participating in the collaboration.
    - At least one investigator must have significant experience either in orthopaedic or musculoskeletal research or medicine.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations. .
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **3** years.
- The maximum allowable total costs for the entire period of performance are **$1.125M.**
- 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 applicant 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.4., 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.4. of the General Application Instructions***.

For this award mechanism, direct costs:

Must be requested for:

- Travel costs of up to $1,800 for the PI(s) to disseminate project results at one DoD 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
- Research supplies
- Equipment
- Clinical research costs
- Independent scientific review of clinical protocol
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings in addition to the required meeting described above

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 Appendix 3 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 will be executed through 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.4. Research & Related Budget, for additional information on budget considerations for applications involving federal agencies.

The CDMRP expects to allot approximately $2.25M of the $30M FY14 PRORP appropriation to fund approximately two Translational Research Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of federal funds for this program.

II. SUBMISSION INFORMATION

Submission 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/).

New for FY14: ***The CDMRP has replaced its eReceipt System with eBRAP.*** Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at *https://ebrap.org/eBRAP/public/UserGuide.pdf)*. Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. ***Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*** If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov, provided there is no cause for administrative rejection of the application (see Section IV.A., Rejection).

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-14-PRORP-TRA.

B. Pre-Application Submission and Content Form

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

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

A change in PI or organization after submission of the pre-application will be allowed only at the discretion of the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/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**
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  FY14 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 at help@eBRAP.org or 301-682-5507.
- **Required Files – Tab 4**

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

  Preproposal Narrative (two-page limit): The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

  The Preproposal Narrative should include the following:

    - **Focus Area:** Explain how the proposed work addresses at least one of the FY14 PRORP Translational Research Award Focus Areas.
    - **Research Idea:** Describe the ideas and reasoning on which the proposed research is based; include relevant literature citations. Show how the perspectives of the PI and each collaborator contributed to the development of the hypothesis.

- **Research Strategy:** Concisely state the project's hypothesis/objectives and specific aims. Briefly describe the experimental approach.
- **Collaboration:** Describe how the project depends on the unique skills of each team member. Describe how the proposed multidisciplinary collaboration involves a substantial contribution by each investigator and the reciprocal flow of ideas and information.
- **Translational Potential:** Describe how the proposed research will allow for a reciprocal flow of ideas between basic and clinical science. Explain how the project will accelerate promising laboratory research findings into clinical applications.
- **Military Benefit:** Describe how the proposed research will provide a significant benefit in the near-term and/or long-term to individuals who have sustained combat or combat-related orthopaedic injuries, and/or how the research has the potential to impact unit readiness and return-to-duty/work rates.

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 (four-page limit per individual).

- **Submit Pre-Application – Tab 5**

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

Pre-Application Screening

- **Pre-Application Screening Criteria**

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

  - **Research Idea:** The degree to which the proposed research addresses the intent of the award mechanism and aligns with one or more FY14 PRORP Translational Research Award Focus Areas. How well the rationale supports the research idea.
  - **Research Strategy:** How well the specific aims and proposed methodology support the research idea and objectives.
  - **Collaboration:** Whether the collaboration includes at least one laboratory scientist and one clinician. Whether the collaboration includes at least one investigator with significant experience in orthopaedic or musculoskeletal research or medicine.

How the background and expertise of the proposed research team is appropriate to accomplish the research in a way that could not be accomplished through separate efforts. How the disciplines represented on the research team are appropriate for the proposed work.

- **Translational Potential:** How the project will accelerate promising, well-founded research findings into clinical applications.
- **Military Benefit:** How the proposed work, if successful, would provide a significant benefit to military service members and Veterans who have sustained combat-related orthopaedic injuries or traumatic orthopaedic injuries that impact unit readiness and return-to-duty/work.

- **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 Forms

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/).

New for FY14: ***Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification.*** The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a "Changed/Corrected Application" with the Previous Grants.gov Tracking ID ***prior to the application submission deadline (which occurs earlier than the end of the application verification period).***

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

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

2. Attachments Form

- **Attachment 1: Project Narrative (12-page limit):** Upload as "ProjectNarrative.pdf." The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and will result in administrative withdrawal of the application.

  The Project Narrative must include preliminary or published data to support the feasibility of the project; however, these data may come from fields other than orthopaedic research.

  Describe the proposed project in detail using the outline below.

  - **Background:** Present the ideas and reasoning behind the proposed work, to include relevant literature citations. Describe previous experiences most pertinent to this application.
  - **Hypothesis or Objective:** State the hypothesis to be tested or the objective(s) to be reached.
  - **Specific Aims:** Concisely explain the project's specific aims. If the proposed research is part of a larger study, present only tasks that this PRORP award would fund.
  - **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. Clearly describe the statistical plan and the rationale for the statistical methodology as well as an appropriate power analysis, if applicable. If animal studies are proposed, briefly describe the key elements of the study/studies as they relate to the overall project; detailed information is required in Attachment 8, Animal Research Plan. If human subjects or human anatomical substances will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples. ***This award must not be used to conduct definitive clinical trials,*** though limited feasibility testing in human subjects as a portion of the Statement of Work is permissible.
  - **Collaboration:** Describe how the research project depends on the unique skills of each member of the research team. Provide the time commitment of each key collaborator toward the proposed research project. Describe how the proposed collaboration involves a substantial contribution by each member, with a reciprocal flow of ideas and information. Demonstrate how the collaboration will maximize the use of existing resources and minimize unnecessary duplication. Describe the communication plan and provide evidence of institutional support for resolving potential intellectual and material property issues and removing institutional barriers to achieve high levels of cooperation.

- **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.
    - Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
    - Letters Confirming Access to Military or VA Patient 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 of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.
    - Intellectual Property
        - Background and Proprietary Information: All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. 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 4, Section L for more information about the CDMRP expectations for making data and research resources publicly available.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  The technical abstract is used by all reviewers as a description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

  Technical abstracts should be written using the following outline.

  - Background: State the FY14 PRORP Translational Research 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 study design including appropriate controls.
  - Translation: Describe how the proposed collaboration and research will accelerate promising, well-founded research findings into clinical application.
  - Military Benefit: State briefly how the proposed project, if successful, will have an impact on combat-related orthopaedic injury research, unit readiness, return-to-duty/work, 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 research.
    - What types of patients will it help, and how will it help them?
    - What are the potential research and clinical applications, benefits, and risks?
    - What is the projected time it may take to achieve a clinically relevant outcome?
    - If the research is too basic for clinical applicability, describe the interim outcomes.

- Briefly describe how the proposed project will benefit military populations and impact combat-related orthopaedic research and/or patient care.

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

  The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Program Announcement and Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Translational Research Award mechanism, use the SOW format example titled "SOW (Statement of Work) Generic Format." The SOW must be in PDF format prior to attaching.

- **Attachment 6: Translation Statement (one-page limit):** Upload as "Translation.pdf."

  State explicitly how the proposed research is translational in nature, allowing for the reciprocal transfer of information and ideas between basic and clinical science. Explain how the experience and expertise of the research team is complementary, multidisciplinary, and will accelerate the movement of the results to clinical application. Provide information on the methods and strategies proposed to move the product to the next phase of development, clinical trials, and/or delivery to the military or civilian market after successful completion of the award.

- **Attachment 7: Military Benefit Statement (one-page limit):** Upload as "MilBen.pdf."

  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 goals of decreasing the clinical impact of these injuries. For applicants addressing the Focus Area on non-battle orthopaedic injuries, describe the impact of the study on unit readiness and return-to-duty/work capabilities.

  Demonstrate how the proposed study is responsive to the health care needs of the military services and/or the U.S. Veteran population. If an active duty military or Veteran population(s) or dataset(s) will be used in the proposed research project, 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 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 8: 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).

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

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

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

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

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

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

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the

application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. ***The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.***

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, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the 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 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 Process

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of equal 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 or published data.
     - How well the hypotheses or objectives and aims are developed, and how the experimental design, methods, and analyses support completion of the aims.
     - If applicable, to what degree the statistical plan and power analysis are appropriate for the proposed project.
     - How well the PI acknowledges potential problems and addresses alternative approaches.
     - The degree to which the plan to study military populations, if applicable, is appropriate and feasible.

   For applications involving animal research:

     - How well the animal study (or studies) is designed to achieve the objectives, including the choice of model and endpoints/outcome measures to be used.
     - How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.

   - **Military Benefit**
     - To what degree the proposed project could, either in the short-term or long-term, make a significant impact on the lives of military service members and Veterans affected by orthopaedic injuries.
     - The degree to which the proposed project, if successful, will advance the research methods, understanding, and/or treatment of combat-related orthopaedic injuries, if applicable.

- How well the project addresses a critical issue in treatment of non-battle orthopaedic injuries that impact unit readiness and the ability to return to work/duty, if applicable.

- **Translational Potential**
  - The degree to which the project, if successful, will accelerate the translation of promising, well-founded laboratory or clinical research findings into clinical applications for traumatic orthopaedic injuries.
  - How well the proposed research plan will utilize the multiple disciplines represented in the collaboration to create a reciprocal flow of ideas and information between basic and clinical science.
- **Personnel**
  - How the background and expertise of the PI, collaborators, and other research team members are appropriate to accomplish the proposed work.
  - How well the project represents a meaningful collaboration with significant contributions from the proposed collaborators.
  - How the levels of effort by the PI, the collaborators, and other key personnel are appropriate to ensure the successful conduct of the project.

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

- **Environment**
  - The degree to which the scientific environment is appropriate for the proposed research.
  - How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
  - To what degree the quality and extent of institutional support are appropriate.
  - If applicable, to what degree the intellectual and material property plans are appropriate.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations, the following criteria are used by programmatic reviewers:

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

   b. **Relevance to the mission of the DHP and FY14 PRORP, as evidenced by the following:**

      - Adherence to the intent of the award mechanism
      - Program portfolio composition
      - Programmatic relevance
      - Relative military benefit

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.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- A FY14 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 FY14 PRORP SC members can be found at http://cdmrp.army.mil/prorp/panels/panel14.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Total 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 project is not relevant to at least one of the FY14 PRORP Translational Research Award Focus Areas.
- The PI does not meet eligibility criteria.
- The proposed collaboration does not meet the eligibility criteria.
- The proposed research is a definitive clinical trial.

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, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 5 for general information regarding national policy requirements.

D. Reporting

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

Quarterly technical progress reports with quad charts will be required.

E. Award Transfers

Refer to the General Application Instructions, Appendix 4, 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 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	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Translation Statement: Upload as Attachment 6 with the file name "Translation.pdf."	
	Military Benefit Statement: Upload as Attachment 7 with the file name "MilBen.pdf.")	
	Animal Research Plan: Upload as Attachment 8 with the file name "AnimalPlan.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.	