Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Peer Reviewed Orthopaedic Research Program

Orthopaedic Care and Rehabilitation Consortium Award

Funding Opportunity Number: W81XWH-15-PRORP-OCRCA

Catalog of Federal Domestic Assistance Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), November 5, 2015
- **Application Submission Deadline:** 11:59 p.m. ET, December 8, 2015
- **End of Application Verification Period:** 5:00 p.m. ET, December 11, 2015
- **Peer Review:** February 2016
- **Programmatic Review:** April 2016
- **Kick-Off Meeting:** March 2017

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.

TABLE OF CONTENTS

I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2015 (FY15) Peer Reviewed Orthopaedic Research Program (PRORP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs [OASD(HA)], the DHA RDA Directorate manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The executing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The PRORP was initiated in 2009 to provide support for research of exceptional scientific merit focused on optimizing initial treatment, recovery, and restoration of function for military personnel with orthopaedic injuries sustained in combat or combat-related duties. Appropriations for the PRORP from FY09 through FY14 totaled $248.5 million (M). The FY15 appropriation is $30M.

The FY15 PRORP challenges the scientific community to design innovative, high-impact, clinically relevant research that will foster new directions for, and address neglected issues in, the field of combat-related orthopaedic injury research. Additionally, the research will address the most significant gaps in care for the leading burden of injury and loss of fitness for military duty and advance optimal patient-related outcomes including treatment and rehabilitation from injuries sustained during combat or combat-related activities. It is expected that any research findings would also provide benefit to the general population.

B. FY15 PRORP Focus Areas

The FY15 PRORP has established a set of acute care and rehabilitation Focus Areas, listed below. ***All applications for the PRORP Orthopaedic Care and Rehabilitation Consortium Award (OCRCA) must address at least four (minimum of two acute care and two rehabilitation) Focus Areas. Applications that do not meet this requirement will be administratively withdrawn and not considered. Studies that propose nominal or iterative advancements are discouraged.***

Acute Care Focus Areas (address at least two):

- Segmental Peripheral Nerve Defects: Treatment strategies to improve outcomes from segmental peripheral nerve defects.
- Prevention of Heterotopic Ossification: Techniques to retard or prevent the development of human post-traumatic heterotopic ossification in the upper extremity.
- Volumetric Muscle Loss: Techniques to regenerate functional, innervated muscle units in treatment of volumetric muscle loss.
- Lower Extremity Fractures: Optimal time to weight bearing for lower extremity fractures.
- Economic Impact: Economic impact of innovations in orthopaedic trauma research.

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

Rehabilitation Focus Areas (address at least two):

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

C. Award Information

The PRORP OCRCA mechanism is being offered for the first time in FY15. The PRORP OCRCA is intended to support the establishment of a Consortium that consists of multiple organizations and individuals collaboratively working on clinical studies that are focused on improving both acute care treatment outcomes and functional, long-term rehabilitation outcomes of severe musculoskeletal injuries commonly associated with military combat or combat-related activities. The Consortium will consist of a single Coordinating Center in collaboration with multiple military treatment facilities (MTFs) (required) and non-military Clinical Study Sites (encouraged). The Government anticipates that applicants will assemble an expert team from multiple institutions, including, but not limited to, academia, MTFs, other Government agencies, clinical research institutions, industry partners, and not-for-profit enterprises to satisfy the objectives of this Program Announcement/Funding Opportunity. It is expected that relevant clinical outcomes will require longitudinal evaluations to optimize recovery and restoration of

function. At the end of the performance period, it is anticipated that the awardee will establish a strong infrastructure for continuing clinical studies on combat-relevant musculoskeletal injuries and produce products (information, practice guidelines, validated techniques, or devices) that result in changes to, or validation of, current clinical practices that lead to better outcomes for injured Service members, U.S. Veterans, and civilians. All projects should develop a procurement cost estimate for successful treatments so that the military and civilian medical community can conduct a cost-benefit analysis with current practice alternatives, as well as distinguish the optimal cost-effective treatments.

Projects must be relevant to the military, have well-defined objectives, control for confounding variables, have a patient population that will allow for an appropriately robust sample size at each Site, be of high quality, and be capable of producing results that are likely to change practice. Studies involving non-military patient populations must describe how they simulate the targeted population (i.e., Armed Forces and/or the U.S. Veteran population). While large, randomized, controlled clinical studies are expected to be part of this multi-institutional Consortium effort, small randomized or pilot clinical trials and observational prospective studies to develop metrics or provide proof of principle to inform future clinical studies are also appropriate.

All projects shall be limited to clinical research and clinical trials. A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. 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. Clinical research encompasses studies in which individuals are observed or those where certain outcomes are measured. 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 ***Animal studies are excluded from consideration*.**

The Coordinating Center must apply to this Program Announcement/Funding Opportunity through a single application, and may also serve as a Study Site. The PRORP OCRCA resulting from this Program Announcement/Funding Opportunity will be issued as a cooperative agreement between the recipient (Coordinating Center) and the Government. The Government will have substantial involvement in the Consortium through a Government Steering Committee (GSC) and U.S. Army Medical Research and Materiel Command (USAMRMC) staff interactions with the Consortium. The GSC will review research priorities and make recommendations to the Grants Officer's Representative (GOR) for the GOR's consideration, with ultimate approval decisions made by the USAMRAA Grants Officer (GO). Award funds will be used to support the Coordinating Center's efforts as well as Consortium-associated studies at the Clinical Study Sites. The Coordinating Center will provide management and funding for the Clinical Study Sites through the appropriate subaward or other instrument.

1. **Required MTF Collaboration:** Military relevance is a key element of the PRORP OCRCA. Applicants should provide a plan to ensure that MTF Clinical Study Sites

have input and participate in all Consortium activities at levels equivalent with other Clinical Study Sites. The Coordinating Center must plan to provide resources to the MTFs for their role in Consortium-supported studies, including supplies and research personnel support as necessary. ***Funds provided through this award may not be used to support Government salaries, but may be used to support contract research personnel.*** **All applications must have a direct relevance to orthopaedic injuries sustained during military combat or combat-related activities. Clinical research and clinical trials that include military and/or Veteran populations are encouraged.**

2. **The Management Core:** The PRORP OCRCA supports the development of a Consortium whose framework will consist of a Coordinating Center that will provide leadership and infrastructure support to multiple Clinical Study Sites. The Coordinating Center Principal Investigator (PI) must be located at the Coordinating Center and will serve as the Director of the Consortium, Chair of the Consortium Committee, and the primary liaison with the GOR. The PI of the Coordinating Center should provide evidence of prior experience with the management and oversight of multi-institutional clinical studies. The PI must also demonstrate broad experience in orthopaedic injury research, including knowledge of the current state of clinical studies and clinical priorities related to the FY15 PRORP OCRCA Focus Areas, which address critical militarily relevant issues.

   The Coordinating Center will collaborate with multiple Study Sites, including a minimum of two MTF Sites. Coordinating Center applicants may collaborate with the MTFs of their choice. Successful applications will demonstrate evidence of strongly relevant collaborations between the Coordinating Center and the Clinical Study Sites. Strong academic, industry, Department of Veterans Affairs (VA), other military/Government, and nonprofit organization collaborations are also encouraged. Applicants are to provide the Consortium with a Clinical Research Manager who will be responsible for coordinating and facilitating clinical protocol approval, patient accrual, and study activities across all Sites. Applicants are strongly encouraged to leverage existing clinical programs to enhance collaboration and educational/training opportunities for clinical researchers.

   It is the responsibility of the applicant to describe clearly within the application how the proposed Consortium will have a significant impact on both acute care and rehabilitation of combat-related orthopaedic injuries. The application should include an overarching research strategy that adequately addresses the FY15 PRORP OCRCA Focus Areas. The application should also describe the Coordinating Center and infrastructure, core laboratory facilities, and any proposed Clinical Study Sites. It is anticipated that the Consortium will be comprised of existing high-volume and high-productivity Sites that have a clinical research track record to maximize enrollment within the available funding constraints.

   The Coordinating Center and associated Clinical Study Sites must apply to this Program Announcement/Funding Opportunity through a single application. A single award will be made to the Coordinating Center, and award funds will be used to

support the Coordinating Center's efforts as well as Consortium-associated studies at each of the Clinical Study Sites. The Coordinating Center will provide management and funding through the appropriate instruments for the non-MTF Clinical Study Sites to conduct medical research toward improving initial care and early treatment, reconstruction, and rehabilitation for combat and combat-related orthopaedic injuries. The Coordinating Center will provide management and support (research personnel, supplies, etc.) to the MTFs through various appropriate means.

The PRORP plans to allocate FY15 funding in support of the Orthopaedic Care and Rehabilitation Consortium. The PRORP concept for the Orthopaedic Care and Rehabilitation Consortium is that following the award period of 5 years, the Consortium will be an ongoing, financially self-sustaining entity.

3. **Consortium Structure:** The Consortium framework will consist of a Coordinating Center that will provide leadership and infrastructure support to competitively selected clinical research and/or clinical trial Sites. The Coordinating Center, which may also serve as a Clinical Study Site, will facilitate the rapid selection, design, and execution of clinical studies within the Consortium. The Coordinating Center will also provide the administrative support, protocol development coordination, regulatory coordination, and statistical resources necessary to facilitate Consortium studies.

   As appropriate, OCRCA applications should name and describe individual core facilities at member organizations that will serve as official Consortium core facilities (e.g., informatics, imaging, and statistical support). Establishment of Consortium-wide core facilities will enable more consistent, high-quality, standardized data to be collected across Sites for Consortium-supported studies. See Figure 1 for a proposed structure of the PRORP Orthopaedic Care and Rehabilitation Consortium.

4. **Clinical Study Sites/Proposed Studies:** The Consortium shall present a plan for incorporating clinical research and clinical trial Sites necessary to effectively support the Consortium goals. The plan should include criteria that will be used to evaluate and select new studies and Sites after award. Criteria should require all Sites to have experience and multidisciplinary expertise in supporting orthopaedic research.

   In addition to the proposed management structure and core facility organization, OCRCA applications must include an initial set of Clinical Study Sites. These Sites will support an initial set of proposed studies **(approximately three to seven studies)** reflective of the FY15 PRORP OCRCA Focus Areas that will be considered during the review and selection process. Some or all of the initial studies proposed may be carried out if recommended for funding and approved for funding by the USAMRAA GO. The initially proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium. Once the PRORP OCRCA awardee is selected, a separate post-award, kick-off meeting will be held with the GSC, GO, and GOR within 6 months of award date.

   During the performance period of the award, the Coordinating Center and all Study Sites, including the MTFs, will be responsible for working collaboratively to identify

new studies for implementation by the Consortium. It is preferred that some of the Sites have experience working with military and Veteran populations. Additional competencies of proposed Sites may be identified and justified as being essential to the success of the Consortium. Pursuit of funding by the Consortium from additional sources, including industry, private sector, and other Federal organizations is encouraged. Additional applications from new Study Sites after the initial award has been made may be considered by the GSC. Projects from new Sites may be solicited and funded as appropriate. Such projects may be targeted via new solicitation(s) or via existing Study Sites. All proposed studies and Study Sites utilizing funds from this award will be subject to selection through peer review, GSC review, and GO approval prior to implementation. Additionally, the investigators of these projects will be incorporated into the Consortium management structure.

Collectively, the Core Facility Directors, the Clinical Research Manager, and the Clinical Study Site PIs will constitute the Consortium Committee. The Consortium Committee will be responsible for proposing and conducting clinical studies focused on both acute care and rehabilitation for combat-related orthopaedic injuries and for determining which Consortium organizations will participate in each study. As the Chair of the Consortium Committee, the Coordinating Center PI will be responsible for facilitating this process, and the application should include a description of how the Coordinating Center plans to coordinate with the Clinical Study Sites to propose, design, externally peer review, and prioritize the most relevant clinical studies once the Consortium is established. Additional prioritized clinical studies will be presented to the GSC, the GO, and the GOR at the kick-off meeting and subsequent annual meetings for review and approval recommendations prior to implementation. See Section I.C.5., Oversight of the Consortium, for further information regarding the GSC.

5. **Oversight of the Consortium:** A GSC comprised of Government personnel will be established by USAMRMC. The GSC will review progress, and it will provide input on scientific and military relevance and on the coordination of proposed projects with other military-relevant initiatives. The GSC will provide approval recommendations to the GO and GOR regarding proposed Consortium studies prior to implementation. The Coordinating Center PI (and other key personnel, as applicable) must present written and oral briefings to the GSC and USAMRMC staff at annual, 1-day meetings to be held in a centralized location. Based on these reports and presentations, the GSC and USAMRMC staff will evaluate progress, provide feedback, and invoke modifications as needed to facilitate the success of the Consortium.

   The Consortium Committee, through the Coordinating Center PI, is expected to maintain monthly, or more frequent, contact with a Government-appointed GOR, who will maintain full documentation of interactions. The USAMRAA GO will issue the final approval of any proposed projects or award modifications, as well as issue approval to release funds for the initiation of approved studies.

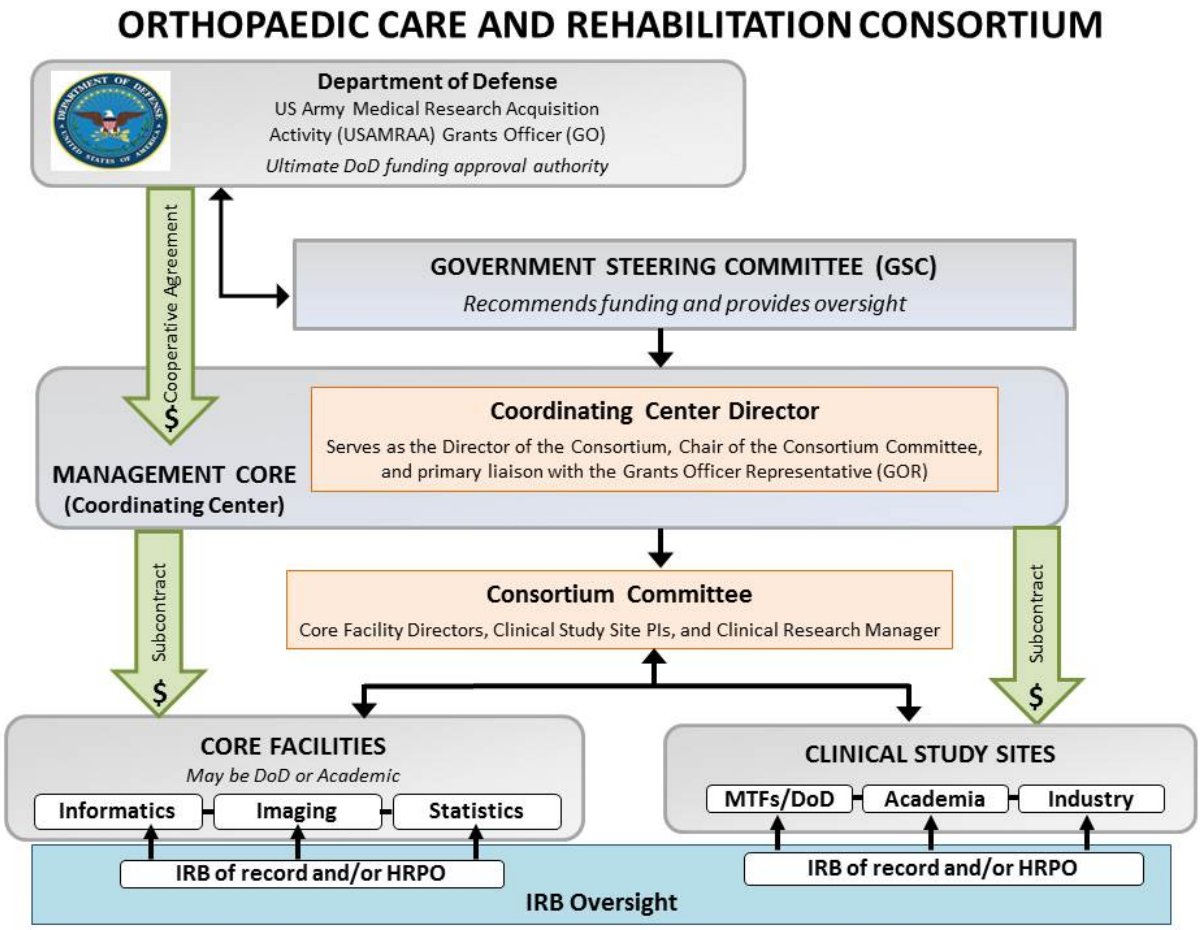

Figure 1: Proposed Consortium Structure. Applicants may propose an alternative organizational structure for the Consortium; however, in all configurations, a GSC will provide consultation to the Consortium governing body on research gaps, military priorities, and project selection.

6. Summary of Responsibilities:

- **Responsibilities of All Consortium Participants:** Procedures for the Consortium, while proposed by the Coordinating Center, will be fully developed and agreed upon by all participants working collaboratively after award via a process to be detailed in the OCRCA application. Among other items, the process should propose a means for project selection, evaluation, and termination to account for the addition or removal of projects as allowed under this award mechanism. The process shall be codified in a Standard Operating Procedure (SOP), for review by the GOR and GSC within 1 year of award date.
- **Consortium Coordinating Center Director:** The Coordinating Center PI will serve as the Director of the Consortium, Chair of the Consortium Committee, and the primary liaison with the GOR. This PI will:
    - Ensure that a minimum number of clinical studies, as agreed upon by the GOR, GSC, and GO, are initiated by the start of the second year of the award;
    - Ensure that the Consortium adheres to the planned timeline and milestones for overall study execution;

- Develop and maintain the Consortium organizational structure;
- Manage Consortium-developed procedures for study prioritization and implementation of clinical studies proposed by, or through, Consortium members;
- Establish a mechanism to provide MTFs with resources necessary for participation in the Consortium;
- Establish and manage procedures to ensure that all Sites maintain compliance with local Institutional Review Boards (IRBs) and the USAMRMC Office of Research Protections (ORP), Human Research Protection Office (HRPO) for the proper conduct of clinical studies and the protection of human subjects;
- Provide a Consortium Clinical Research Manager who will oversee the efforts of the Clinical Research Coordinators at the Clinical Study Sites. The Clinical Research Manager will manage Consortium-developed quality assurance and quality control mechanisms for study monitoring, including but not limited to:
  - Registration, tracking, and reporting of participant accrual
  - Timely medical review, rapid reporting, communication of adverse events, and data management/coordination among all Sites
  - Interim evaluation and consideration of measures of outcome
- Establish and manage procedures for ensuring compliance with U.S. Food and Drug Administration (FDA) requirements for investigational agents, devices, and procedures;
- Establish and manage a communications plan and a real-time communications system among the Coordinating Center, Core Facilities, and Clinical Study Sites, including the purchase of multi-Site licenses, if necessary;
- Ensure the standardized analyses of specimens, imaging products, and other data through the establishment of scientific core facilities;
- Manage Consortium-developed comprehensive data collection and data management systems that address the needs of all affiliated organizations in terms of access to data, data security, and data integrity measures;
- Coordinate statistical support, planning, and analyses for all Consortium clinical studies;
- Manage costs to support the Clinical Study Sites, including provision of personnel, equipment, and materials required to conduct approved clinical studies;
- Manage Consortium-developed intellectual and material property among organizations participating in the Consortium;
- Manage Consortium-developed procedures for the timely publication of major findings and other public dissemination of data;

- Attend a kick-off meeting to develop the operational features and direction of the Consortium, outline the requirements for progress and evaluation, and discuss new projects;
- Coordinate the preparation of written and oral briefings to the GSC and USAMRMC staff at annual, 1-day meetings to be held in a location to be determined by USAMRMC;
- Develop, organize, and submit quarterly written progress reports, annual reports, and a final written comprehensive report to the USAMRMC; and
- Prepare for a Site visit audit, if requested.

- **Clinical Study Sites**
  - Participate fully in the Consortium Committee;
  - Include a Clinical Study Site PI who will:
    - Attend a kick-off meeting to develop the operational features of the Consortium, outline the requirements for progress and evaluation, identify clinical studies for development and proposal to the GSC, and align selected studies with appropriate Clinical Study Sites;
    - Participate in the preparation of written and oral briefings to the GSC and USAMRMC staff at annual, 1-day meetings to be held in a location to be determined by USAMRMC; and
    - Assist with the preparation of quarterly written progress reports and the final written comprehensive report.
  - Provide a Clinical Research Coordinator, who will interact with the Clinical Research Coordinators of other Clinical Study Sites and the Consortium Clinical Research Manager at the Coordinating Center to expedite and guide clinical protocols through regulatory approval processes and to coordinate patient accrual and study activities across Sites;
  - During the performance period of the award, identify potential studies and develop proposals in accordance with the Consortium SOP for presentation to the GSC;
  - Integrate with clinical studies at other Clinical Study Sites;
  - In accordance with Consortium-developed guidelines, meet and maintain subject screening and enrollment goals in all Consortium-associated studies;
  - Implement the Consortium's core data collection methodology and strategies;
  - Comply with Consortium-developed quality assurance and quality control procedures, as appropriate, including:
    - Participate in an on-site monitoring program to be managed by the Coordinating Center;
    - Implement the Consortium-developed management plan for acquisition and aggregation of protocol-specified specimens, biological fluids, and relevant

clinical data to the appropriate laboratories for testing or storage necessary for the conduct and analyses of clinical studies during the performance period of the award;

- Submit appropriate data and materials to allow for verification and review of protocol-related procedures (e.g., pathology, imaging techniques, surgical methods, and therapeutic use);

- Implement procedures established by the Coordinating Center for ensuring compliance with FDA requirements for investigational agents, as appropriate;
- Implement procedures established by the Coordinating Center to meet the local IRB and the USAMRMC ORP HRPO requirements for the conduct of clinical studies and the protection of human subjects;
- Serve as a resource or core (e.g., data management, image processing, biostatistics, etc.), as appropriate;
- Participate in Consortium-developed procedures for the timely publication of major findings;
- Participate in Consortium-developed procedures for resolving intellectual and material property issues among organizations participating in the Consortium; and
- Prepare for a Site visit audit, if applicable.

7. **Performance Metrics:** Applicants should lay out a plan for the number and types of clinical studies the Consortium expects to execute. As a preliminary guideline, the Consortium should be prepared to complete between three to seven studies (clinical research and/or clinical trials) during the performance period of the award, depending upon the size and complexity of each study. By the start of the second year of the performance period, a minimum number of clinical studies, as agreed upon by the GSC, the GO, and the GOR shall be initiated. It is anticipated that within the first 2 years of the award, the Consortium will gain approval to initiate at least two studies and release a solicitation for projects that will begin in the future. A timeline outlining the overall plan for study initiation, performance, and analyses shall be developed, with clear milestones to which the Consortium will be held accountable. For individual clinical studies, the Coordinating Center should ensure the maintenance of overall patient accrual per year, as appropriate for the target population. The Consortium Committee will estimate the minimum and maximum accrual metrics for each Clinical Study Site, as appropriate to overall accrual goals and the size of each Site's pool of potential participants. The Coordinating Center will be required to submit quarterly written reports that outline accrual and retention statistics, any problems with study execution, and actions to disseminate study results. It is expected that the Consortium will submit to other agencies for additional funding in order to increase the breadth of research and create a self-sustaining entity that will continue functioning beyond the 5-year performance period of the award.

Research Involving 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 USAMRMC ORP HRPO, in addition to the local IRB of record. Local IRB approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. The HRPO reviews and approves the participation of each Site in a given clinical study or clinical trial. Refer to the General Application Instructions, Appendix 5, and the Human Subject Resource Document available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

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

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

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

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

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

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

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

Defense Health Agency
http://www.health.mil/dha

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

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

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

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

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

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

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

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

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

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

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

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

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

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 3, Section L.

D. Eligibility Information

- ***The Coordinating Center PI must be an independent investigator at or above the level of Associate Professor (or equivalent) at an eligible organization.***
- Cost sharing/matching is not an eligibility requirement.
- Organizations eligible to apply include national, international, for-profit, nonprofit, public, and private organizations.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, nonprofit, public and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

A single award will be made to support the FY15 PRORP Orthopaedic Care and Rehabilitation Consortium. This award will be made to the Coordinating Center applicant that is selected for funding. The Coordinating Center will provide funding support to the Clinical Study Sites through the appropriate subaward or other instrument.

All applicants are requested to propose a minimum of three studies. The proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium. The overall Consortium budget should detail costs and separate items for the following: the Management Core, the other Cores (as applicable), and estimated research costs (e.g., Clinical Study Sites) throughout the performance period of the award. Following award,

research budgets will be negotiated individually once clinical study selections are made and approved.

- The maximum period of performance is **5** years.
- The anticipated total costs (direct plus indirect) budgeted for the entire period of performance will not exceed **$18M.** Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$18M** total costs or using an indirect rate exceeding the organization's negotiated rate.
- The Coordinating Center is expected to provide a mechanism to transfer resources such as supplies and support necessary to the MTF Clinical Study Sites, DoD laboratories, or DoD activities embedded within a civilian medical center to support their participation in Consortium studies. Direct transfer of funds to a Government organization or agency is not allowed except under very limited circumstances and as subject to the prior GO approval. Details on exceptions to the prohibition of direct fund transfer to Government entities can be found in the General Application Instructions, Section II.C., Content and Form of Application Submission, Budget Instructions, Section K (Budget Justification).

Refer to the General Application Instructions, Section II.C.5., for budget regulations and instructions for the Research & Related Budget. ***For all Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.5. of the General Application Instructions***.

For this award mechanism, direct costs **may** be requested for (not all-inclusive):

- **Management Core Budget**
  - Salary
  - Implementation of Consortium-developed standardization plans, data management program, real-time communications system, and administration plans for the Consortium
  - Support of Consortium-related meetings, teleconferences, and travel among participating investigators
  - Costs associated with the external scientific peer review of future clinical studies/research
  - Purchase of computers, specialized software, and specialized software licenses for Clinical Study Sites when required to fulfill Coordinating Center-specific tasks
  - Costs associated with coordination of informed consent/assent form preparation and other IRB-required materials among different organizations
  - Costs associated with using Consortium core facilities
  - Costs associated with conducting the IRB review of the clinical protocols and informed consent/assent forms
  - Costs associated with management of intellectual property among organizations

- Other costs directly associated with planning and developing the Consortium
- Support for multidisciplinary collaborations

- **Consortium Core Facilities' Budgets**
  - Salary
  - Research Supplies
  - Purchase of minor equipment necessary for specimen collection, data storage and/or data transfer
- **Study-Specific Budgets**
  - Salary
  - Research supplies
  - Research-related subject costs
  - Clinical research costs
  - Support for multidisciplinary collaborations
- **Travel**
  - Travel between collaborating organizations
  - Travel costs to attend scientific/technical meetings in addition to the required meeting described below

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

- Travel costs for the Coordinating Center PI to disseminate project results annually during the period of performance at the Extremity War Injuries Symposium. For planning purposes, it should be assumed that these meetings will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.
- Travel costs for the Coordinating Center PI and each Clinical Study Site PI to attend one DoD military research-related meeting per year, to be determined by the Government during the award period of performance. These travel costs are in addition to those allowed for annual scientific/technical meetings.
- Travel costs for the Coordinating Center PI and each Clinical Study Site PI to attend the annual, 1-day briefings with the GSC and USAMRMC staff at a Government location (to be determined). For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

Intramural (DoD), other Federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds

through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. ***In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.***

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from Federal agencies submit applications, they must submit through Grants.gov. Therefore, Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Section II.A. of the General Application Instructions for further information regarding Grants.gov requirements.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other Federal agencies may be executed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR] or Funding Authorization Document [FAD] process). Direct transfer of funds from the recipient to a Federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.5. Research & Related Budget, for additional information on budget considerations for applications involving Federal agencies.

The CDMRP expects to allot approximately $18M of the $30M FY15 appropriation to fund approximately one Orthopaedic Care and Rehabilitation Consortium Award application, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission of applications that propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application.

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/). Refer to the General Application Instructions, Section II.A. for registration and submission requirements for eBRAP and Grants.gov.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's

responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

PIs should ensure that their name and email address are the same as the name and email address that will be provided on the SF-424 Form of the Grants.gov application package submitted to Grants.gov. The organization, Business Officials, PI(s), and eBRAP log number named in the full application submitted to Grants.gov must match those named in the pre-application in eBRAP.

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.

A. Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-15-PRORP-OCRCA in Grants.gov (http://www.grants.gov/).

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the Principal Investigator through eBRAP (https://eBRAP.org/).

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

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
    - Enter contact information for the PI. Enter the organization's Business Official responsible for sponsored program administration (the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF-424 Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Collaborators and Key Personnel – Tab 3**
    - Enter the name, organization, and role of all collaborators and key personnel associated with the application.

- FY15 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.

- **Conflicts of Interest (COIs) – Tab 4**
  - List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship).

- **Pre-Application Files – Tab 5**

  Letter of Intent (LOI) (two-page limit): LOIs are used for program planning purposes only (e.g., reviewer recruitment) and will not be reviewed during either the peer or programmatic review sessions.
  - Provide a description of the overall Consortium vision and research strategy, as well as a brief description of the goals of each proposed study.
  - Include a list of all of the FY15 PRORP OCRCA Focus Areas under which the application will be submitted. As noted above, all applications must address at least four (minimum of two Acute Care and two Rehabilitation) FY15 PRORP OCRCA Focus Areas.
  - Provide the name of each proposed Clinical Study Site (including the required minimum of two MTFs).
  - Provide the name and contact information for the lead PI of each proposed Clinical Study Site.
  - Provide the names and contact information of the senior MTF representatives from each MTF that will be providing an official letter of collaboration at the time of application.

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

C. Full Application Submission Content

The CDMRP cannot make allowances/exceptions to its policies for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.

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

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline. If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application

package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID ***prior to the application submission deadline***.

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

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

2. **Attachments Form**

   Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

   - **Attachment 1: Project Narrative (no page limit, except 10-page limit for the Research Plan of each Proposed Clinical Study):** Upload as "ProjectNarrative.pdf." The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

     Describe the key features of the Consortium using the outline below.

     - **Overarching Research Strategy:** Describe the overall plan, aims and objectives of the proposed Consortium. Include the rationale for inclusion of the initial studies (approximately three to seven) selected, as well as the process for adding additional studies. Describe how these studies will address at least four of the FY15 PRORP OCRCA Focus Areas (minimum of two acute care and two rehabilitation) and generate outcomes responsive to each of these areas. Be sure to explain how the studies will answer critical research questions and close significant gaps in the field of combat-related orthopaedic injury. The overarching research strategy should also outline a feasible timeline that aligns milestones and deliverables with the Consortium aims and objectives. It is expected that within the first 2 years of the award date, the applicant will gain approval to initiate at least two studies and release a solicitation for additional projects.

       – Describe how each study will address an overarching challenge in a unique but complementary way. Explain how the combined efforts of the proposed

studies (approximately three to seven) will address this challenge more effectively than if the studies were done independently. Describe how the proposed Consortium will be organized to meet the overall Consortium goals, including a description on how the key components (Coordinating Center, Clinical Study Sites, and Core leadership) will be integrated to meet the overarching objectives of the Consortium.

- In a separate section of this narrative, titled "Research Plan," applicants must provide detailed descriptions of the initially proposed studies (approximately three to seven studies). The number, type, size, and scope for each study that the applicant expects to execute within the Consortium during the award's performance period will be presented in the Research Plan section of the Project Narrative. The critical research questions that will address at least four of the FY15 PRORP OCRCA Focus Areas (minimum of two acute care and two rehabilitation) and generate outcomes responsive to each of these areas should be described in detail in the Research Plan section of the Project Narrative.

- **Consortium Expertise and Resources**
  - Identify key personnel.
  - Describe the current multidisciplinary expertise and previous experience of the Coordinating Center Director (PI) and other key personnel (within the Coordinating Center) with respect to their role(s) in the Consortium. Include previous experience with the design, implementation, and administration of relevant orthopaedic research studies and collaborative experience in multi-site efforts. Likewise, include previous experience with intellectual property management and oversight of regulatory strategies of multi-institutional studies. In Attachment 2, reference relevant publications and submit reprints or citations with the application supporting documentation (see Attachment 2: Supporting Documentation).
  - Describe the available Consortium resources for the establishment and management of multi-institutional collaborative partnerships.
  - Describe previous experience and expertise in fiscal administration of multi-site studies, including the distribution and management of funds.
  - Describe any experience working with military and Veteran populations and access to appropriate populations.
  - Describe any plans to leverage existing clinical or translational funding programs and infrastructure for the proposed Consortium.
  - Describe ongoing and previous collaborations between Study Site entities related to the current effort(s).
- **Coordination of Consortium Components:** Outline the organizational structure of the proposed Consortium. Identify the knowledge, unique expertise, and technical innovations that the team from the Coordinating Center will utilize to make decisions, allocate resources, and accomplish the

milestones. Describe the administrative organization/oversight, including decision-making procedures and coordination of all Clinical Study Sites as an integrated unit.

- ***Site Coordination and Communication*:** Present an overall management plan to facilitate consistent and intensive interactions by all Consortium members, including aspects such as adherence to regulatory requirements, administrative support, and oversight to accelerate translation of the studies' outcomes to patients and/or for clinical use.
- Describe the fiscal organization necessary for the proper distribution of funds between Clinical Study Sites for performance of clinical studies.
- ***Government Coordination:*** Describe plans to communicate and partner with the MTFs. Explain how the MTF Clinical Study Sites will provide input on all Consortium procedures and studies to a level commensurate with all other Clinical Study Sites. Outline a plan for providing resources to the MTFs and supporting the research capabilities needed at the MTFs for full Consortium participation.
- ***Information Technology (IT) Resources*:** Because the Consortium will rely heavily on IT, provide the name of the individual(s) who will be responsible for database and information infrastructure. Describe relevant personnel and organizational experience with implementing multi-institutional real-time communications.
- In Attachment 2, provide evidence of organizational commitment for the Coordinating Center, core laboratory facilities, and each participating Study Site for the use of facilities and resources in the conduct of Consortium (see Attachment 2: Supporting Documentation). Describe the organizational commitment of each participating Clinical Study Site to work collaboratively with all Consortium Sites.

- **New Study Proposal Procedures:** Outline a plan for the solicitation, design, evaluation, and prioritization of potential future Consortium studies that are to be funded by the PRORP and presented to the GSC (including independent, external scientific peer review processes and progress reviews) following initial study implementation. Include a mechanism for determining Clinical Study Site participation and approval for new study ideas. Describe how funding sources (both internal and external) for Consortium studies will be identified and approved.
- **Study Project Management and Monitoring:** Describe the plans for real-time communication among all organizations participating in the Consortium, including complete and timely reporting of adverse events, as well as research results.
  - Include a named Consortium Clinical Research Manager who will interact with other individual Site Clinical Coordinators to guide clinical protocols through the regulatory approval process, coordinate participant accrual, and

coordinate study activities across Sites, as well as describe his/her expertise with these activities.

  - Outline procedures for quality assurance, quality control, patient safety, and study monitoring.
  - Describe how individual project performance will be assessed during the course of the award, including progression toward defined milestones and realization of study objectives and the overarching challenge. If an External Advisory Board is to be utilized, describe the role of the board and the expertise to be sought in its members, including any individuals representing the advocacy community. Do not contact, recruit, or name potential members at this time to avoid potential COIs during review of the application.

- **Core Facilities:** Include a plan for the establishment and maintenance of core infrastructure that will effectively support Consortium activities and Study Sites. Outline essential cores and other facilities to be shared that will be necessary for facilitation of Consortium success. Describe functions and responsibilities of each core facility and how the core facilities will be utilized and integrated across all Study Sites.
- **Clinical Protocol Development and Human Subject Protections:** Describe plans for coordinating the development of clinical protocols and associated clinical documents that address HRPO (and VA IRB, if applicable) requirements. Outline a plan for the external peer review of all Consortium clinical protocols and the coordination of IRB submissions and approvals. Describe the development of a plan for addressing human subject protection requirements as outlined by HRPO at http://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo. Outline plans for developing procedures to ensure compliance with FDA regulations for investigational agents, as appropriate.
- **Data Management:** Describe plans for communication, data transfer among the collaborating institutions, and how data, specimens, and/or imaging products obtained during the study will be handled.
  - Describe methods for the collecting, handling, distribution, analysis, banking and security of any specimen and/or imaging products generated from Consortium-sponsored studies (if applicable). If applicable, describe how SOPs will be created, reviewed, implemented, and modified during the course of the award.
  - Describe the resources and expertise in each participating Clinical Study Site for data management and maintenance of data security/confidentiality.
  - Describe plans for ensuring rapid publication and other public dissemination of data while maintaining participant privacy. Include a plan to provide for open architecture of any prosthetic or orthotic development that results from Consortium studies.

- **Research Plan (10-page limit for *each* Proposed Clinical Study):** The Research Plan must include an initial set of proposed studies (approximately three to seven) agreed upon by the Consortium participants, which are reflective of Consortium Objectives and the FY15 PRORP OCRCA Focus Areas. Applicants must provide a description of three to seven studies in sufficient detail to allow for evaluation of the scientific merit alone and in relation to meeting the overall objectives of the Consortium. Details about each proposed project must include the following:
  - **Title:** Provide a title for each project.
  - **Background:** Present the theoretical background and rationale supporting the proposed work. Provide sufficient preliminary data to support the feasibility of work proposed. Each project must demonstrate logical reasoning and include sound scientific rationale as established through a critical review and analysis of published literature. It is important to describe the project showing proof of concept and, if applicable, efficacy in an in vivo system(s) to support the translational feasibility and promise of the approach. Describe previous experience most pertinent to this project.
  - **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses. Provide a clear description of what the study deliverables will be and the timeline for each study.
  - **Research Strategy:** Identify the FY15 PRORP OCRCA Focus Area(s) addressed by each study. Describe the study design, methods, and analyses, including appropriate controls and/or comparison groups, in sufficient detail for analysis. Explain how the research strategy will address the overarching challenge and meet appropriate milestones. Address potential problem areas and present alternative methods and approaches.
    - Describe the traumatic orthopaedic injury patient populations at each Clinical Study Site and provide evidence of the ability to enroll adequate patient numbers into Consortium-sponsored studies. Include a detailed plan for the recruitment of human subjects. Provide an estimate of case enrollment/patient load and the track record of research in this area for each Clinical Study Site and each Clinical Study Site PI.
    - Describe the resources and facilities available within each Clinical Study Site for both the acute care and rehabilitation of orthopaedic trauma patients.
    - If human biological samples will be used, include a detailed plan for the acquisition of samples.
    - Provide sufficient information on the methods, metrics, and statistical power for each study to allow for an evaluation of the proposed design and study budget.

- ***For clinical trials:***
  - State the intervention to be tested.
  - Clearly define the primary clinical outcome measure and describe the projected outcomes.
- ***For clinical trials and clinical research involving human subjects:***
  - Provide detailed plans for initiating and conducting the clinical trial during the course of this award. As appropriate, outline a plan for applying for and obtaining Investigational New Drug/Investigational Device Exemption (IND/IDE) status (or other FDA approvals) in a timely manner. Describe the rationale for the trial and summarize the previous work that led to the development of the proposed clinical trial. Describe the type of clinical trial to be performed (e.g., prospective, randomized, controlled) and indicate the phase of trial and/or class of device, as appropriate. Outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.
  - 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). Provide information on the inclusion and exclusion criteria, the availability of and access to the appropriate patient population(s), as well as the ability to accrue a sufficient number of subjects.
  - 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 statistical model and data analysis plan with respect to the study objectives. Specify the 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.
  - Provide evidence of documented availability of and access to all critical reagents, and describe how quality control will be addressed. Include a description of how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and Good Clinical Practices (GCP) will be established, monitored, and maintained, as applicable.

- **Study Personnel:** Identify the Clinical Study Site PI and any key personnel as appropriate, describing each person's qualifications and specific contributions to the project. Describe the background and expertise of investigators. Briefly describe their roles on the project. Provide details on how the entire team possesses the appropriate expertise in conducting clinical trials and/or clinical research.

- **Attachment 2: Supporting Documentation. Start each document on a new page. Combine and upload as a single file named "Support.pdf."** If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.***
  - References Cited: List the references cited (including URLs if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
  - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
  - Publications and/or Patent Abstracts: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.
  - Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. (Letters of support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.)
  - Letters of Collaboration: Provide a signed letter from each collaborating individual or organization (including each Clinical Study Site) that will demonstrate that the PI (Coordinating Center Director), as well as the lead PI of each proposed Clinical Study Site both have the support or resources necessary for the proposed Consortium effort, including but not limited to the availability of and access to appropriate orthopaedic injury patient populations. If any of the proposed research plans involve access to active duty military and/or VA

patient populations or resources, include a letter(s) of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.

- Intellectual Property
  - Background and Proprietary Information: All software and data first produced under the award are subject to a Federal purpose license. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the Federal purpose license.
  - Intellectual and Material Property Plan (if applicable): Describe how the Consortium will implement intellectual property and contractual plans, as well as resolve conflicts and issues among participating organizations.
- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 3, Section L for more information about the CDMRP expectations for making data and research resources publicly available.

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

  The technical abstract is used by all reviewers 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 outline below:

  - **Background:** Describe the general management and organizational structure of the Consortium. Outline the management and clinical expertise of Consortium personnel at the Coordinating Center and Clinical Study Sites.
  - **Objectives:** Describe the Consortium's overall clinical research goals and agenda.
  - **Proposed Clinical Studies:** Identify the clinical studies that the Consortium plans to pursue during the period of performance. State the FY15 PRORP OCRCA Focus Areas that will be addressed by these studies, and briefly describe how the collaborative effort addresses these Focus Areas.
  - **Clinical Impact:** Briefly describe how the proposed effort will have an immediate and long-term impact on patient care and/or restoration of function for those who have sustained combat-related orthopaedic injuries.

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

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

  - Describe the clinical objectives and rationale for the proposal in a manner readily understandable by those without a background in science or medicine.
  - Describe the ultimate applicability and impact of the Consortium's clinical research.
    - Which FY15 PRORP OCRCA Focus Areas will be addressed?
    - What patient needs will be addressed, and how will it help them?
    - What are the potential clinical applications, benefits, and risks?
    - What is the projected time it may take to achieve clinically relevant outcomes?
  - Describe how the overall effort will benefit military populations and impact patient care and/or restoration of function for those who have sustained combat-related orthopaedic injuries.
  - What contributions will this effort make to advance the field of orthopaedic research and patient-related outcomes?

- **Attachment 5: Statement of Work (SOW) (10-page limit): Upload as "SOW.pdf."** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the OCRCA mechanism, use the SOW format example titled "SOW for Clinical Research (Including Trials, Special Populations)." The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.3., for detailed guidance on creating the SOW.

- **Attachment 6: Impact Statement (two-page limit): Upload as "Impact.pdf.**"
  - State explicitly how the proposed work, if successful, will have an impact on accelerating the evaluation and movement of promising acute care and rehabilitation treatments for orthopaedic injuries into clinical practice. Further, describe the impact of the Consortium studies on the lives of individuals recovering from combat-relevant orthopaedic injuries, including but not limited to, how the expected results of the proposed work will contribute to the goals of decreasing the clinical impact of these injuries.
  - Describe the short-term impact, as well as the anticipated long-term benefits of the proposed studies. Be sure to describe how this collaborative effort will

benefit civilian populations. Include details about the anticipated patient care and/or restoration of function outcomes that will be directly attributed to the results of the proposed research.

- **Attachment 7: Military Benefit Statement (two-page limit): Upload as "MilBen.pdf"**
  - Describe how the proposed effort is responsive to the health care needs of the Armed Forces and the U.S. Veteran population that sustained orthopaedic injuries. Provide information about the incidence and/or prevalence of orthopaedic injuries in military Service members and/or U.S. Veterans, if appropriate and available. Show how the proposed effort complements ongoing DoD and VA areas of research interest.
  - If active duty military and/or Veteran population(s) or dataset(s) will be used in the proposed research, describe the population(s)/dataset(s), the appropriateness of the population(s)/dataset(s) for the proposed study, and the feasibility of using the population(s)/dataset(s). If a non-military population will be used for the proposed research, explain how the population simulates the targeted population (i.e., military Service members or U.S. Veterans). If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Services and/or the U.S. Veteran population). Describe how the study design will replicate field conditions, if applicable.
  - Describe how the proposed effort will improve patient-related outcomes.
  - Describe how the Consortium studies build upon research initiatives ongoing at the MTF Clinical Study Sites.
  - Provide a description of how the knowledge, information, products, or technologies gained from the clinical studies could be implemented in a dual-use capacity to address a military need that also benefits the civilian population.

- **Attachment 8: Transition Plan (two-page limit). Upload as "Transition.pdf."** Provide information on the methods and strategies proposed to move the project to the next phase of research 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 (e.g., specific potential industry partners, specific funding opportunities to be pursued).
  - 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 their product development and/or marketing experience.
  - A brief schedule and milestones for bringing the outcome(s) to the next level.
  - A description of relevant patents and intellectual property ownership, and their potential impact on product development and the Government's ability to access any technology supported with this award.

- **Attachment 9: IND/IDE Documentation (if applicable):** 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. State whether the trial requires regulation by the FDA. If FDA regulation is required, describe the planned indication for the proposed product and whether an IND/IDE is necessary.
    - If an IND or IDE has been submitted, indicate when it was submitted to the FDA and provide an explanation of the status of the IND or IDE application (e.g., past the critical 30-day period, pending response to questions raised by the Agency, on clinical hold). Provide a summary of previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.
    - 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.

- **Attachment 10: Human Subject Recruitment and Safety Procedures (if applicable; required for all studies recruiting human subjects; no page limit): Upload as "HumSubProc.pdf."** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.
    - **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 and plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided.
    - **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.

- **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, and health care provider identification).
  - 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.
- **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://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf). If applicable, please refer to the General Application Instructions, Appendix 5, for more information.

- ***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.

- **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.

- **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 11: Intervention (if applicable; 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. Description of devices should include detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described.

- Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety of the intervention.

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 Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.

c. Clinical Monitoring Plan: Describe how the study will be conducted by and monitored for ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Good Clinical Practices (GCP) compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial Site/PI.

- **Attachment 12: Data Management (if applicable; required for all studies recruiting human subjects; no page limit): Upload as "Data_Manage.pdf."** The Data Management attachment should include the components listed below.

a. Data Management: Describe all methods used for data collection to include the following:

- **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
- **Confidentiality**
  - Explain measures taken to protect the privacy of study human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
  - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of USAMRMC are eligible to review study records.
  - Address requirements for reporting sensitive information to state or local authorities.

- **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time data will be stored. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. For FDA-regulated studies, compliance with 21 CFR 11 (the Code of Federal Regulations, Title 21, Part 11) is required.
- **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 13: Collaborating DoD Military Facility Budget Form(s): Upload as "MFBudget.pdf."** For each Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) that will be a collaborator in the performance of the project, complete the Collaborating DoD Military Facility Budget Form (available for download on the eBRAP "Funding Opportunities & Forms" web page), including a budget justification, as instructed. Refer to the General Application Instructions, Section II.C.8., for detailed information.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information.

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

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

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

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

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

D. Applicant Verification of Grants.gov Submission in eBRAP

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

E. Submission Dates and Times

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

F. Other Submission Requirements

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

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

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the OASD(HA), 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 twotier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a nondisclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from Federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

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

   Criteria for Evaluation of Consortium Effort:

   - **Overarching Research Strategy**
     - How the overall research plan (aims and objectives) and the types of Consortium studies address the goals of the Consortium, as well as the goals of the PRORP.
     - How well the Consortium Structure and Coordinating Center are organized to meet the goals and objectives of the Consortium.
     - The feasibility of the timeline that aligns milestones and deliverables with objectives for the Consortium.
     - How well the key components (core leadership and Clinical Study Sites) are integrated to meet the overarching objectives of the Consortium and address the goals of the PRORP.
     - How the scientific rationale of the Consortium research plan specifically addresses the FY15 PRORP OCRCA Focus Areas (minimum of two acute care and two rehabilitation).
     - How feasible the plan is to initiate at least two studies within the first 2 years of the award (number, types, and scope of clinical studies).
   - **Consortium Expertise and Resources**
     - To what extent the expertise, track record, and experience of the proposed Coordinating Center PI, Consortium Clinical Research Manager, and key personnel are appropriate with respect to the ability to manage and oversee multi-institutional orthopaedic clinical studies.
     - To what extent the background, track record, and expertise of key personnel within each Clinical Study Site are appropriate with respect to the successful conduct of orthopaedic injury-related studies and participation in multi-center clinical studies.
     - The appropriateness of each proposed Clinical Study Site to successfully achieve the goals of the Consortium.
     - To what extent each proposed Clinical Study Site provides non-duplicative and unique capabilities to the Consortium.
     - To what extent the variety of Clinical Study Sites includes high-volume and high-productivity Sites with the clinical research track record to maximize enrollment within the available funding constraints.
     - To what extent the Consortium has the experience to provide financial and intellectual property management and oversight of regulatory strategies of multi-institutional research.

- To what extent the levels of effort of key personnel are appropriate for successful conduct and communication of the proposed work.
- To what extent ongoing and previous collaborations between Study Site entities and the Coordinating Center promote success and relate to the currently proposed effort.
- To what extent the Consortium plans to leverage existing clinical or translational programs and infrastructure.
- The degree of experience the Consortium has in working with military and Veteran populations and access to appropriate populations.
- Evidence of experience with establishing and managing collaborative, multi-institutional relationships.

- **Coordination of Consortium Components**
  - To what extent the proposed overall organizational structure of the Consortium is appropriate.
  - How well the Coordinating Center addresses a plan to oversee and coordinate all Consortium Sites.
  - How well the plan for the establishment and maintenance of core facilities will effectively support Consortium activities.
  - How well each Clinical Study Site will function as part of an integrated unit.
  - How well the proposed Consortium structure and clinical studies support the Study Sites and their stated research goals.
  - To what degree the appropriate resources are provided for full participation at each Consortium Site.
- **Study Project Management and Monitoring**
  - How the plans for real-time communication among all organizations participating in the Consortium, including complete and timely reporting of adverse events, are appropriate in facilitating Consortium activities.
  - The extent of the named Consortium Clinical Research Manager's experience in guiding clinical protocols through the regulatory approval processes, coordinating participant accrual, and coordinating study activities across Sites.
  - How the outlined procedures for quality assurance, quality control, patient safety, and study monitoring are adequate for conducting multi-institutional clinical studies.
  - How the plans for specimen handling, distribution, analysis, banking, and security are appropriate to facilitate Consortium activities.
  - How well the procedures for soliciting, designing, evaluating, funding, and prioritizing potential future Consortium studies that are to be funded by the PRORP OCRCA are adequate to achieve the outlined performance metrics.

- **Data Management**
  - The degree to which the overall approach to data collection, management, analysis, and security measures is appropriate.
  - How clearly the effective application of methods to monitor quality and consistency of data collection and methods to measure outcomes in previous trials conducted have been demonstrated by the PI and key personnel.
  - How the plan for real-time data transfer is adequate for supporting the Consortium-associated activities.
  - The degree to which plans for the publication and other dissemination of data are appropriate.
- **Clinical Protocol Development and Human Subjects Protection**
  - The degree to which plans to submit the proposed clinical protocols and associated clinical documents within the period of performance are appropriate.
  - To what extent the plans for addressing human subject protection requirements, as described by HRPO and coordinating IRB submissions and approvals at participating Sites, are appropriate.
  - How well appropriate plans are considered for developing procedures to ensure compliance with FDA regulations for investigational agents.
- **Organizational Resources and Commitment**
  - The degree of organizational commitment for the use of facilities and resources in the conduct of Consortium operations.
  - Whether the organizations have demonstrated access to appropriate patient populations for conduct of Consortium studies.
  - How the facilities and resources within each Clinical Study Site are appropriate for the acute care and/or rehabilitative care of orthopaedic trauma patients.
  - How the resources and expertise at each organization are appropriate for coordinating specimen collection and processing.
  - How the resources and expertise at each organization are appropriate for data management and maintaining security/confidentiality.
  - The extent to which the intellectual and material property plan is developed and appropriate.
  - How well the commitment of the organizations to work with all Consortium Sites is demonstrated.
- **Impact and Military Benefit**
  - The degree to which the Overarching Research Strategy included efforts to develop and increase research capabilities, as well as educational and training opportunities at the MTFs.

- The degree to which Consortium activities, if successful, will have a significant impact on both the acute and rehabilitative care of individuals who have sustained combat-related orthopaedic injuries.
- How the proposed research will make original and important contributions toward the goal of advancing treatment and/or recovery from musculoskeletal injuries sustained during combat or combat-relevant activities.
- How well appropriate studies were proposed to resolve gaps related to the FY15 PRORP OCRCA Focus Areas (minimum of two acute care and two rehabilitation).

- **Transition Plan**
  - Whether the funding strategy described to bring the outcome(s) to the next level of development (e.g., higher-phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice) is appropriate.
  - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
  - How the schedule and milestones for bringing the proposed outcome(s) to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice) are appropriate.
  - How well the application identifies intellectual property ownership, describes any 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.
  - For knowledge products, to what degree the transition includes appropriate strategies for further knowledge development, dissemination, and incorporation into clinical care and/or improved patient-related outcomes.

Criteria for Evaluation of Each of the Proposed Clinical Study:

- **Clinical Impact**
  - How the proposed study addresses overarching and specific Consortium goals.
  - How relevant the anticipated outcomes of the proposed clinical trial or clinical research are to individuals with combat-related orthopaedic injuries, as well as to individuals within the general population.
  - How well the study 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.
  - 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 or clinical research will provide/improve short-term benefits for all individuals who have sustained orthopaedic injuries.

- How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
- To what degree the intervention represents an improvement over currently available interventions, patient-related outcomes, and/or standards of care.

- **Research Strategy**
  - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective.
  - 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 scientific rationale and preliminary data support each proposed initial study's design and objectives.
  - The degree to which the patient populations and sample size are appropriate for each proposed initial study.
  - The degree to which proposed methods and outcome measures are appropriate for the purposes of each proposed initial study.
  - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed and integrated into the project.
  - How the statistical plan, including sample size projections and power analysis, is adequate to achieve the study objectives and is appropriate to type and phase of study.
  - Description of the population(s) of interest, demonstration of access to these populations, and identification of sampling methods to gain a representative sample from the population(s) of interest.
  - How well the proposed study utilizes the Consortium resources.
  - To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.
- **Feasibility**
  - Whether there is sufficient evidence that the PI has the experience and resources to conduct the research successfully. Whether the described study population is feasible, with respect to access, recruitment strategies, inclusion/exclusion criteria, etc.
  - 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 subject 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.
- Acknowledgement of potential problems and alternative approaches.

- **Ethical Considerations**
  - How the level of risk to human subjects is minimized and communicated through informed consent.
  - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
  - How well safeguards are in place for vulnerable populations.
- **Personnel**
  - How the background and expertise of the Clinical Study Site PI(s) demonstrate his/her ability to perform the proposed work.
  - How the levels of effort by the Clinical Study Site PI(s) and key personnel are appropriate to ensure success of this study.
  - Whether the composition of the study team is appropriate.

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

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
  - Whether the division of funds between the Coordinating Center, Core Facilities, and each Clinical Study Site is appropriate.
  - Whether the monies allotted for travel are adequate and aligned with proposed Consortium activities.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.
  - To what extent the application components reflect knowledge and respect for the needs of the general community of affected individuals.

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

a. Ratings and evaluations of the peer reviewers

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

- Adherence to the intent of the award mechanism
- Program portfolio balance and composition
- Programmatic relevance
- Military benefit
- Relative 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 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 applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the application:

- Pre-application (LOI) was not submitted.
- 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 Project Narrative.

- Documents not requested will be removed. 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.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- A FY15 PRORP SC member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. **A list of the FY15 PRORP SC members can be found at http://cdmrp.army.mil/prorp/panels/panel15h.**
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- The PI does not meet the eligibility criteria.
- 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 application does not address at least four (minimum of two acute care and two rehabilitation) of the FY15 PRORP OCRCA Focus Areas.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2016. Refer to the General Application Instructions, Appendix 3, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms

and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards" (2 CFR part 200).

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 3 for general information regarding administrative requirements.

C. National Policy Requirements

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

D. Reporting

Refer to the General Application Instructions, Appendix 3, Section I, for general information on reporting requirements.

Quarterly technical progress reports and quad charts will be required.

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

E. Award Transfers

Changes in PI and/or organizations will be evaluated on a case-by-case basis and at the discretion of the GO.

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

VI. AGENCY CONTACTS

A. CDMRP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

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

Phone: 800-518-4726

Email: support@grants.gov

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

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF-424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	7	Military Benefit Statement: Upload as Attachment 7 with file name "MilBen.pdf."	
	8	Transition Plan: Upload as Attachment 8 with file name Transition.pdf."	
	9	IND/IDE Documentation: Upload as Attachment 9 with file name "IND-IDE.pdf," if applicable.	
	10	Human Subject Recruitment and Safety Procedures: Upload as Attachment 10 with file name "HumSubProc.pdf," if applicable.	
	11	Intervention: Upload as Attachment 11 with file name "Intervention.pdf," if applicable.	
	12	Data Management: Upload as Attachment 12 with file name "Data_Manage.pdf," if applicable; required for all studies recruiting human subjects.	
	13	Collaborating DoD Military Facility Budget Form(s): Upload as Attachment 13 with file name "MFBudget.pdf."	
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.	