Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Defense Health Program

Chiropractic Clinical Trial Award

Funding Opportunity Number: W81XWH-10-DHP-CCTA

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

The medical mission of the Department of Defense (DOD) Defense Health Program (DHP) is to enhance DOD and our Nation's security by providing health support for the full range of military operations and sustaining the health of all those entrusted to our care. As part of its mission, DHP directs research and development activities to achieve joint force health protection capabilities and modernization, including research funding to advance biomedical science to benefit the Warfighter, DOD beneficiaries, and the American public.

The DHP Chiropractic Clinical Trial Award, executed by the Office of the Congressionally Directed Medical Research Programs (CDMRP), has been created to provide for and report on clinical trials to assess chiropractic treatment on service member groups of the Armed Forces. This funding opportunity is to be supported with fiscal year 2010 (FY10) DHP funds.

B. Award Description

The Chiropractic Clinical Trial Award mechanism is being offered for the first time in FY10. This award is intended to support the rapid implementation of clinical trials that examine the effect of chiropractic clinical treatment, either exclusively or as an adjunct to other treatments, on health concerns relevant to the Warfighter, including non-surgical orthopaedic injury, pain management, smoking cessation, injury prevention, and enhancing fitness for duty. The proposed clinical trial(s) must fall under the following ***required topics***, provided by the 2010 National Defense Authorization Act (NDAA), Public Law 111-84, Section 725. See Appendix A for the complete language of Section 725 of the 2010 NDAA:

> (1) CONTROLLED TRIALS – The clinical trials shall include controlled trials that, at a minimum, compare the outcomes of chiropractic treatment, used either exclusively or as an adjunct to other treatments, with conventional treatment on the following topics:
>
> (A) Pain management.
>
> (B) Orthopedic injuries or disorders that do not require surgery.
>
> (C) Smoking cessation.
>
> (2) INTERVENTIONAL TRIALS – The clinical trials shall include interventional trials that, at a minimum, cover the following topics:
>
> (A) The effect of chiropractic treatment on the reflexes and reaction times of special operation forces.
>
> (B) The effect of chiropractic treatment on strength, balance, and injury prevention for members of the Armed Forces with combat specialties operating in a combat theater.

Applications must propose a clinical trial or multiple clinical trials to address ALL of the above required topics. A Research Plan must be provided as part of the application, to include a description of how all of the required topics will be addressed, through either one clinical trial with multiple measured outcomes, or multiple trials with distinct aims. In addition to the Research Plan, applicants must provide a fully developed Clinical Protocol, submitted as the

Project Narrative of the application. Only one Clinical Protocol may be submitted as the Project Narrative, even if the Research Plan includes multiple trials to satisfy coverage of the required topics. Additional clinical protocols, if applicable, will be submitted by the Principal Investigator (PI) and finalized during the execution of the award on a timeline to be agreed upon by the Government and the PI.

This award is intended to bring the chiropractic clinical research expertise of independent academic institutions or the National Institutes of Health to bear on non-surgical orthopaedic injury, pain management, smoking cessation, physical fitness, and injury prevention, all of which are issues highly relevant to military populations. To ensure maximum benefit to the Warfighter, ***clinical trial participants must be members of the Armed Forces on active duty*.** No trials shall be conducted with deployed service members in theater.

Funding from this award mechanism must support a clinical trial(s). In general, a clinical trial is defined as a prospective accrual of patients for a study where an intervention (e.g., device, drug, behavioral, surgical procedure, or other) is tested on human subjects for a measurable outcome. Refer to the General Application Instructions, Appendix 5, for additional information about studies involving human subjects. ***The proposed clinical trial submitted as the Project Narrative is expected to begin no later than 12 months after the award date.*** Additional clinical trials, if applicable, will begin on a schedule outlined in the Statement of Work and agreed upon by the Government. If the study is in support of an application to the U.S. Food and Drug Administration (FDA), Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications should be submitted prior to the grant application submission. The Government reserves the right to withdraw funding if an active exemption from marketing approval for the IND or investigational device has not been acquired within 6 months of the award date.

This award mechanism may not be used to conduct preclinical research studies.

The following are important aspects of applications to the Chiropractic Clinical Trial Award:

- Demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study or studies. **Clinical trial participants must be members of the Armed Forces on active duty.** No trials shall be conducted with deployed service members in theater.
- Include preliminary data to support the feasibility of the research hypotheses and research approaches.
- Describe clearly defined and appropriate endpoints for the proposed clinical trial(s). Endpoints should correspond to the trial design and sample size proposed.
- Within the Clinical Protocol/Project Narrative, clearly articulate the statistical analysis plan. Include a power analysis that supports the sample size proposed.
- Discuss the potential impact of the research results for patients with combat-relevant non-surgical orthopaedic injuries and pain management.
- Include a study coordinator(s) who will guide the clinical protocol(s) through Institutional Review Board (IRB), Human Subjects Research Review Board, and other

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

Multi-institutional clinical trials: If the proposed clinical trial(s) is/are multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the Clinical Protocol. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials.

Use of human subjects and human biological substances: All DOD-funded research involving human subjects and human biological substances must be reviewed and approved by the US Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to local IRBs. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed, and will require information in addition to that supplied to the local review board. Allow a minimum of 6 months for regulatory review and approval processes for studies involving human subjects.

Encouraged DOD alignment: Relevance to the health care needs of the Armed Forces and/or the U.S. veteran population is a key feature of this award. Therefore, PIs are strongly encouraged to collaborate, integrate, and/or align their research projects with military and/or VA research laboratories and programs. 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

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

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

Defense Technical Information Center
http://www.dtic.mil

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

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

Office of Naval Research
http://www.onr.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
http://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. Naval Research Laboratory
www.nrl.navy.mil

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

C. Eligibility

Independent investigators from the National Institutes of Health or an independent academic institution are eligible to apply**.** Chiropractic treatment must be provided by a doctor of chiropractic who is licensed as a doctor of chiropractic, chiropractic physician, or chiropractor by a State, the District of Columbia, or a territory or possession of the United States. Refer to General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **4** years.
- The maximum allowable funding for the entire period of performance is **$7.5M** in total (direct plus indirect) costs.
- The applicant may request the entire maximum direct cost amount for a project that may be less than the maximum **4**-year period of performance.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable funding. In addition to the direct costs, indirect costs may be proposed in accordance with the organization's negotiated rate agreement.

Within the guidelines provided in the General Application Instructions, funds can cover:

- Salary
- Research supplies
- Equipment
- Clinical research costs
- Research-related subject costs
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings
- Other direct costs as described in the General Application Instructions for the Detailed Budget and Justification

In addition, the PI must request travel funds, up to $1,800, to attend one DOD military research-related meeting to be determined by CDMRP during the award performance period.

The CDMRP expects to allot approximately $7.5M to fund approximately 1 Chiropractic Clinical Trial 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.

E. Award Administration

Quarterly technical progress reports will be required.

The transfer of an award to another institution is strongly discouraged. Approval of an institutional transfer request will be at the discretion of the Grants Officer.

Awards will be made approximately 2 to 3 months after receiving a funding notification letter. Refer to the General Application Instructions, Appendix 4, for general award administration information.

II. TIMELINE FOR SUBMISSION AND REVIEW

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time (ET), July 16, 2010**
- **Application Submission Deadline: 11:59 p.m. ET, August 3, 2010**
- **Scientific Peer Review: August 2010**
- **Programmatic Review: September 2010**

Application submissions will not be accepted unless the pre-application process is completed by the pre-application deadline.

III. SUBMISSION PROCESS

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

Submission of the same research project to different funding opportunities within the same program and fiscal year is discouraged. The Government reserves the right to reject duplicative applications.

PIs and organizations identified in the application should be the same as those identified in the pre-application. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the eReceipt help desk at help@cdmrp.org or 301-682-5507.

A. Step 1 – Pre-Application Components

All pre-application components must be submitted through the CDMRP eReceipt system by ***5:00 p.m. ET on the deadline***.

The pre-application consists of the following components, which are organized in the CDMRP eReceipt system by separate tabs (Refer to the General Application Instructions for additional information on pre-application submission):

- **Proposal Information – Tab 1**
- **Proposal Contacts – Tab 2**
- **Collaborators and Conflicts of Interest – Tab 3**
- **Required Files – Tab 4**

  Letter of Intent (LOI) Narrative (one-page limit): Provide a brief description of the research to be conducted. LOI Narratives are used for program planning purposes only (e.g., reviewer recruitment) and ***will not be reviewed*** during either the peer or programmatic review sessions.

- **Submit Pre-application – Tab 5**
- **Other Documents Tab**

  Not applicable.

B. Step 2 – Application Components

Applications are submitted by the Authorized Organizational Representative (AOR) through Grants.gov (http://www.grants.gov/). Applications must be submitted **by *11:59 p.m. ET on the deadline.***

Each application submission must include the completed application package of forms and attachments identified in Grants.gov for this Program Announcement/Funding Opportunity.

The Grants.gov application package consists of the following components (Refer to the General Application Instructions, Section II.B., for additional information on application submission):

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

2. Attachments Form

- **Attachment 1: Project Narrative (no-page limit):** Upload as "ProjectNarrative.pdf."

  For the Chiropractic Clinical Trial Award mechanism, the Project Narrative is a Clinical Protocol, which is the main body of the application. Only one Clinical Protocol may be submitted as the Project Narrative, even if the applicant is proposing multiple trials to address the required topics outlined in Public Law 111-84 Section 725 (See Section I. B, Award Description, and Appendix A). The Clinical Protocol must address the required components described in Section V, Clinical Protocol and Supporting Clinical Documentation. While there is no page

limit for the Clinical Trial Award Project Narrative, clinical protocols tend to range between 20 and 100 pages.

- **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. ***Each component has no page limit unless otherwise noted.***
    - References Cited: List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate). The inclusion of Internet URLs to references is encouraged.
    - List of Acronyms and Symbols: Provide a list of acronyms and symbols (e.g., PCR = polymerase chain reaction).
    - 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 USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present contract under which the facilities or equipment items are now accountable. There is no form for this information.
    - Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then they must be included. Extra items will not be reviewed.
    - Letters of Organizational Support (two-page limit per letter): Provide a letter (or letters if applicable), signed by the Department Chair or appropriate organization official, reflecting the laboratory space, equipment, and other resources available for the project. If the PI is a clinician, the institution must clearly demonstrate a commitment to the clinician's research.
    - Letters of Collaboration (if applicable) (two-page limit per letter): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
    - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.
- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Technical abstracts should be written using the outline below.
    - Background: Present the ideas and reasoning behind the proposed work.
    - Objective/Hypothesis: State the objectives/hypotheses to be tested. Provide evidence or rationale that supports the objectives/hypotheses.
    - Specific Aims: State the specific aims of the study.

- Study Design: Briefly describe the study design including appropriate controls.
- Military Relevance: Briefly describe how the proposed project(s) will have an impact on military-relevant orthopaedic injury, pain management, smoking cessation, injury prevention, and physical fitness.

- **Attachment 4: Public Abstract (one-page limit):** Upload as "PublicAbs.pdf."

  Public abstracts should be written using the outline below.

  - Clearly describe, in a manner readily understood by lay persons, the rationale and objective for the proposed work.
    - Do not duplicate the technical abstract.
  - Describe the ultimate applicability of the research.
    - What types of patients will it help, and how will it help them?
    - What are the potential clinical applications, benefits, and risks?
  - What are the likely contributions of these studies to advancing the field of research?

- **Attachment 5: Statement of Work (SOW) (four-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.B., for detailed information.

  The SOW should be inclusive of all work to be conducted under this award, including the Clinical Protocol submitted as the Project Narrative, as well as pertinent milestones of additional clinical studies to be conducted to meet the topic requirements of the mechanism, as applicable.

- **Attachment 6: Detailed Budget and Justification (no page limit):** Upload as "Budget.pdf." Use the Detailed Budget and Justification form (available for download on the Full Announcement page in Grants.gov). Refer to the General Application Instructions, Section II.B., for detailed information.

- **Attachment 7: Subaward Detailed Budget and Justification (if applicable) (no page limit):** Use a separate Detailed Budget and Justification form for each subaward budget. Combine into a single file and upload as "SubBudgets.pdf." Refer to the General Application Instructions, Section II.B., for detailed information.

- **Attachment 8: Research Plan (six-page limit):** Upload as "Research.pdf."

  Provide a description of each clinical trial proposed to ensure coverage of all the required topic areas described in Section I.B, Award Description. For each clinical trial, address the following:

  Background: Describe the ideas, reasoning and relevant preliminary data on which the proposed work is based, and how it addresses a central problem in military-relevant orthopaedic injuries or other health concerns (i.e. pain management, smoking cessation, injury prevention, enhancing physical fitness for duty).

Study Design: Concisely state the project's objectives and specific aims. Provide a brief description of the intervention, the target patient population(s), and the outcomes to be measured. Include a brief discussion of pertinent inclusion, exclusion, and randomization criteria, as well as sample size projections.

Timeline: Discuss the projected timeline for initiation and execution of all planned trials within the 4-year performance period of the award.

- **Attachment 9: Military Relevance Statement (two-page limit):** Upload as "MilRel.pdf."

  State explicitly how the proposed clinical study or studies, if successful, will accelerate the movement of chiropractic clinical care into practice for military-relevant orthopaedic injuries, pain management, smoking, injury prevention, and fitness for duty. Describe the potential impact of the proposal clinical trial(s) on patient care and/or quality of life.

  Describe the short-term impact: Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial(s).

  Describe the long-term impact: Explain the long-range vision for implementation of the intervention(s) in the clinic or field, and describe the anticipated long-term benefits for the targeted population(s). Compare the proposed intervention(s) to pharmacologic agents, devices, and/or clinical guidance currently available, if applicable, and describe how the proposed intervention(s) represents an improvement on these.

  The following are examples of ways in which proposed studies, if successful, may have an impact. ***Although not all-inclusive***, these examples are intended to help PIs frame the impact of the proposed research:

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

  For the active duty military population(s) to be used in the proposed work, describe the population(s), the appropriateness of the population(s) for the proposed study or studies, and the feasibility of using the population(s). Describe how the proposed study complements ongoing DOD areas of research interest.

- **Attachment 10: Human Subject Plan (two-page limit):** Upload as "HumSub.pdf."

  Describe the availability of the proposed study population(s), whether the PI and/or key personnel of the proposal currently have access to this population, and how access to potential clinical trial participants will be coordinated. Outline the recruitment strategy and past successes for recruiting similar populations.

- **Attachment 11: Approval for Access to Military Populations (one-page limit):** Upload as "MilPop.pdf."

  A letter of support, signed by the lowest ranking person with approval authority, should be included for studies involving active duty military, military families, or veterans; military-controlled study materials; databases; and/or restricted facilities (e.g., biological or chemical containment facilities).

- **Attachment 12: Data/Research Resources Sharing Plan:** Upload as "DatShar.pdf."

  The Data/Research Resources Sharing Plan will not be reviewed during the peer or programmatic review processes. It will be used for administrative purposes only.

  Describe how unique and/or final research data and resources will be shared with the research community and general public, including cases where pre-existing data or research resources will be utilized and/or modified during the proposed study. Clearly explain any limitations associated with a pre-existing agreement that preclude subsequent data/research resources sharing.

  The content of the data/research resource sharing plan may depend on the data being collected or the resources being developed. PIs should describe briefly the expected schedule for sharing, format of the final dataset, documentation to be provided, analytic tools to be provided, data sharing or material transfer agreement (or other documentation) including criteria for deciding who can receive the data/research resource, and whether or not any conditions will be placed on their use, and mode of data/research resource sharing (e.g., posting data on an institutional or personal website). If research involves human subjects and the data and/or research resource(s) are intended to be shared, the application should discuss how the rights and confidentiality of participants would be protected. PIs should follow their institution's technology transfer policies and provide links to model technology transfer agreement used by the institution, as appropriate. Refer to the General Application Instructions, Appendix 4, for more information on Data and Research Resources Sharing.

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

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

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

IV. INFORMATION FOR APPLICATION REVIEW

A. Application Review and Selection Overview

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review of applications against established criteria for determining scientific merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General, USAMRMC, based on scientific merit, the overall goals of the program, and specific intent of the award mechanism. The highest scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP may be found at http://cdmrp.army.mil/fundingprocess.htm.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each level of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Organizational personnel and PIs 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 panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations from Federal awards. Furthermore, it is a crime for Federal officials to disclose confidential information of one party to another third party (Title 18 United States Code 1905).

B. Review Criteria

1. Peer Review: All applications will be evaluated according to the following criteria, which are of equal importance:

- **Environment**
  - How the evidence indicates an appropriate scientific environment, clinical setting, and the accessibility of institutional resources to support the research effort at each participating center or institution (including collaborative arrangements).
  - The evidence for appropriate institutional commitment from each participating institution.
- **Military Relevance**
  - How well the patient population(s) that will participate in the proposed intervention(s) are identified.
  - How the anticipated short-term outcomes will impact patient care and/or quality of life.
  - How the anticipated long-term vision for implementation of the intervention(s) in the clinic or field will impact patient care and/or quality of life.

- How the proposed intervention(s) represents an improvement to the standard of care currently available.
- The degree to which the results of the proposed clinical trial(s) will affect the patterns of clinical practice (e.g., treatment, management, and/or quality of life) for military relevant, non-surgical orthopaedic injuries, pain management, smoking cessation, injury prevention, and physical fitness for duty.

- **Personnel**
  - How the clinical study team's background and expertise are appropriate to accomplish the proposed work (i.e. statistical expertise, expertise in the disease, and in clinical studies).
  - How the levels of effort of the clinical team are appropriate for successful conduct of the proposed trial(s).
  - Evidence that a study coordinator with appropriate expertise is or will be identified at an appropriate level of effort.
- **Research Strategy**
  - How well the proposed trial(s) address all required topics outlined in Public Law 111-84, Section 725 (Section I.B, Award Description, and Appendix A).
  - The degree to which the proposed trial(s) is/are based on sound scientific rationale and preliminary data.
  - How the target patient population, intervention, endpoints and outcome measures for the study or studies described in the Research Plan are appropriate and feasible.
  - How the overall timeline proposed for execution of the proposed trial(s) is appropriate and feasible.

Criteria Specific to the Clinical Protocol/Project Narrative

- **Ethics**
  - How the risks to subjects are minimized, with evidence of a monitoring plan that is appropriate with the level of risk.
  - Evidence that procedures are consistent with sound research design and, when appropriate, procedures used are already in use for diagnostic or treatment purposes.
  - Selection of subjects is equitable, informed consent is sought and appropriately documented, and appropriate safeguards are in place for vulnerable populations.
- **Intervention, Drug, or Device**
  - Whether the intervention to be tested is appropriate for the proposed clinical trial.

- Whether there is documentation that an IND/IDE application has been submitted (if applicable).

- **Patient Recruitment and Accrual**
  - How the recruitment, informed consent, screening, and retention processes for volunteers will be conducted to meet the needs of the proposed clinical trial.
  - How the plan for addressing unanticipated delays (e.g., slow accrual, patient dropout) is likely to lead to success in completing the proposed clinical trial within the performance period.
  - How the proposal addresses the availability of volunteers for the clinical trial, the prospect of their participation, and the consideration of likelihood of volunteer attrition.
  - Evidence that the PI will have access to any military populations required for the clinical study.
- **Statistical Plan (as appropriate to phase of study)**
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
- **Study Design**
  - How the scientific rationale and preliminary data, including critical review and analysis of the literature, and laboratory and preclinical evidence support the rationale for testing the intervention.
  - How the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer an important clinical objective.
  - How the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, and standardization of procedures) meet the needs of the proposed clinical trial.
  - How the inclusion, exclusion, and randomization criteria meet the needs of the proposed clinical trial.

The following will not be individually scored, but may impact the overall evaluation of the application:

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - How the writing and components of the application influenced the review.

2. Programmatic Review: The following criteria are used by programmatic reviewers to make funding recommendations.

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

Scientifically sound applications that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by a programmatic review panel and recommended for funding to the Commanding General, USAMRMC.

V. CLINICAL PROTOCOL AND SUPPORTING CLINICAL DOCUMENTATION

A. Required Elements of the Clinical Protocol (uploaded as the Project Narrative on the Attachments Form)

Please note that the protocol should address the following elements:

- Trial design
- Intervention, drug, or device to be tested
- Feasibility of the study
- The statistical plan
- The personnel involved in the study
- Ethics and/or regulatory issues

Protocol elements:

1. **Protocol Title.**

2. **Phase or Class:** Designate the phase of the trial (i.e. Phase I, II, III, or a combination of phases), or class of device, if applicable. For descriptions of each type of clinical trial, please refer to http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm and http://www.clinicaltrials.gov.

3. **PI/Study Staff:** List the complete name, address, telephone and fax number, and email address of the PI. List the names of all key study personnel who will have significant involvement in the study; include their professional credentials (e.g., M.D. or R.N.), highest degree(s), job title, and employing institution.

4. **Study Location(s):** List all centers, clinics, or laboratories where the study is to be conducted. Provide the Federal-wide or DOD Assurance number for each institution engaged in study. Include the name, degree(s), title, employing institution, and complete address of the investigator(s) for each study site.

5. Time Required to Complete the Study: State the month and year of the expected start and completion times.

6. Background (suggested limit: 10 pages): Include a literature review that describes in detail the rationale for conduct of the study. Include descriptions of any preliminary studies and findings that led to the development of the protocol. The background section should clearly support the choice of study variables and explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

Note: If the protocol was initiated using other funding prior to obtaining the DOD funding, explain the history and evolution of the protocol and declare the source of prior funding. Specifically identify the portions of the study that will be supported with DOD funds. For ongoing protocols, HRPO approval is required prior to initiation of any human subjects research activities supported by the USAMRMC.

7. Objectives/Specific Aims/Study Questions: Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses.

8. Study Design: Describe the type of study to be performed (e.g., prospective, randomized, controlled, etc.), and outline the proposed methodology in sufficient detail to show a clear course of action.

- Define the study variables and describe how they will be measured.
- Describe the methods that will be used to obtain a sample of volunteers from the accessible population (i.e., convenience, simple random, stratified random).
- If applicable, describe the subject to group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures).
- Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
- Describe the reliability and validity of psychometric measures, if applicable.

9. 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 which the sample will be recruited/drawn). Demonstrate that the research team has access to the proposed study population. Furthermore, discuss past efforts in recruiting volunteers from the target population for previous clinical trials (if applicable), any potential barriers to accrual, such as a change in the target population demographics, a change in medical practices, or competing clinical trials; and plans for addressing unanticipated delays (e.g., slow accrual). Volunteer selection should be equitable. The protocol should include justification of any age, race, ethnicity, or sex limitations provided.

10. Inclusion/Exclusion Criteria. List the inclusion and exclusion criteria in the protocol. 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. Ensure that exclusions are justified. Clearly state the exclusion criteria for volunteers with disease, taking medications, or from certain groups.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report and recent congressional legislation, special attention is given to inclusion of women and 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. If women and/or minorities will be excluded from the protocol, an appropriate justification must be included.

11. Description of the Recruitment Process: Explain methods for identification of potential volunteers (e.g., medical record review, obtaining sampling lists, health care provider identification, etc.).

- Describe the recruitment process ***in detail***. Address who will identify potential volunteers, who will recruit them, and what methods will be used to recruit them.
- If volunteers will be compensated for participation in the study, a detailed description of the compensation plan should be included in the protocol. Ensure that the compensation plan is fair and does not provide undue inducement. If the study requires multiple visits, a plan for pro-rating payments in the event of volunteer withdrawal should be considered.
- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements, and should accurately reflect the study. An ombudsman should be considered for use with particularly vulnerable populations.
- Some important considerations for recruitment materials include:
    - Recruitment materials should not promise a cure or benefit beyond what is mentioned in the protocol or consent form.
    - If the volunteers will be paid, the amount of payment should not be presented in bold type, larger than other text, or otherwise overemphasized.
    - Recruitment materials should not promise “free medical treatment” when treatment is not the true intent of the study.

12. Sample Size Justification. A complete power analysis must be included in the protocol to ensure that the sample size is appropriate to meet the objectives of the study. The protocol should specify the approximate number of volunteers that will be enrolled. If the protocol involves multiple sites, the number enrolled at each site should be stated in the master protocol.

13. Description of the Informed Consent Process. Specifically describe the plan for obtaining informed consent from volunteers. Provide the informed consent form.

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent.

- Include information regarding the timing and location of the consent process.
- If applicable, address issues relevant to the mental capacity of the potential volunteer (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 volunteer age).
- Address how privacy and time for decision making will be provided, and whether or not the potential volunteer will be allowed to discuss the study with anyone before making a decision.
- As consent is an ongoing process, 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.
- If volunteers who cannot give their own consent to participate will be included in the study, there must be a plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the volunteer's participation in the study. State law defines who may act as the LAR. The IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site.
- If illiterate volunteers are anticipated, the consent process to be followed for illiterate volunteers should be outlined in the protocol. The consent form should be verbally read/explained to the volunteer in the presence of a witness. The volunteers must sign or make a mark (such as a thumbprint) to indicate agreement to participate, and the witness must sign to attest that the content of the written consent form was accurately conveyed to the volunteer.
- If it is anticipated that volunteers who do not speak the primary language of the host country will be enrolled in a trial, all documentation provided to volunteers (consent form, information sheets, etc.) should be translated, with a copy provided to the HRPO for review at a later date. A plan should be included for ensuring that volunteers' questions will be addressed during the consent process and throughout the trial.

  NOTE: When consent will be obtained in a language other than English, documentation that the foreign language version of the consent form is an accurate translation of the English version of the consent form must be provided to the HRPO at a later date. Documentation must be provided from a qualified translator certifying the translation, along with the English and foreign language version of the consent forms. The documentation of translation should include the following statement: "I certify that this is an accurate and true translation." The signature, name, address, phone number, and, if available, fax number of the translator should also be included.

- If a waiver of all or part of the consent process is being sought, or a waiver of documentation of consent is desired, include justification of why the waiver should be considered. This justification should include how the protocol meets the criteria set forth in 32 CFR 219 (Title 32 of the Code of Federal Register, Section 219). If

consent to use existing samples or data in a future study was provided as part of another study protocol, this should be clearly explained. If the institution is a covered entity, justification for Health Insurance Portability and Accountability Act (HIPAA) waiver requests should also be provided.

Assent. When minors are included in a study, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. Age-appropriate assent forms should be developed for use with minors when assent is obtained. Capacity to provide assent should also be considered for other populations that cannot provide informed consent, and assent should be obtained whenever possible.

14. Volunteer 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.

15. Study Procedures/Study Interventions: Describe the study intervention or activity that the volunteer will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the volunteer will experience and when it will occur. Provide a schedule of study evaluations and follow-up procedures. Provide all case report forms, data collection forms, questionnaires, rating scales, and interview guides, etc., that will be used in the study.

16. Description of Protocol Drugs or Devices: If the protocol uses a drug, biologic, device, or dietary supplement, provide the following information:

- For medical products regulated by the Food, Drug, and Cosmetic Act, designate the protocol as Phase 0, I, II, or III research.
- If the study is in support of an application to the FDA or other appropriate agency, provide the IND/IDE number and name of the sponsor.
- Provide complete names and composition of all medications, devices, or placebos.
- Identify the source of medications, devices, or placebos.
- Describe the location of storage for study medications.
- Describe the dose range, schedule, and administration route of test articles.
- Describe washout period, if used, in detail.
- Describe the duration of drug or device treatment.
- Declare concomitant medications allowed.
- Identify any antidotes and treatments available for potential side-effects.
- Describe the plan for disposition of unused drug.

- For FDA-regulated studies, describe the procedure by which the IND sponsor will monitor the protocol in accordance with 21 CFR 312.

17. Laboratory Evaluations:

- **Specimens to be collected, schedule, and amount.** All specimens that will be collected for study purposes must be clearly stated in the protocol. The collection schedule and amount of material collected must also be clearly described. This may be represented using a table or schematic for more involved protocols.
- **Evaluations to be made.** All evaluations that will be made for study purposes should be stated in the protocol. Copies of all data collection forms must be provided. The protocol should explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of volunteers).
- **Storage.** Specimen storage must be described in the protocol, to include where, how long, any special conditions required, labeling, and disposition. If there is a plan to store specimens for future use (either by the investigator or through an established repository) this should be outlined in the protocol. If samples will be collected for future use in other studies (and if this is not the sole purpose of the protocol), volunteers should be given the chance to opt out. Potential future uses of samples should be addressed to the degree possible. If volunteers are given a menu of options regarding sample donation for future research, procedures should be in place to ensure that volunteers' wishes for use of the samples are honored. Procedures for withdrawal of samples at the request of the volunteer should be described if samples will remain coded or identified.
- **Labs performing evaluations and special precautions.** The laboratory performing each evaluation should be clearly identified in the protocol, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the volunteer before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, provisions for ensuring proper storage during transport should be included in the protocol.

18. Data Analysis: Describe the data analysis plan. The data analysis plan should be consistent with the study objectives.

19. Data Management:

- **Methods used for data collection.** All methods used for data collection should be described in the protocol. Copies of data collection forms and any test instruments administered should be provided. Data collection forms should be adequate and accurate according to the data collection plan described in the protocol. Whenever possible, identifiers should be removed from data collection forms. Critical measurements used as endpoints should be identified.
- **Volunteer identifiers.** If unique identifiers or a specific code system will be used to identify volunteers, this process should be described in the protocol.

- **Confidentiality:**
    - Explain measures taken to protect the privacy of study volunteers and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed. Investigators collecting particularly sensitive information should consider obtaining a Certificate of Confidentiality.
    - Address who will have access to study records, data, and specimens. The protocol should acknowledge that representatives of USAMRMC are eligible to review study records.
    - Requirements for reporting sensitive information to state or local authorities should be addressed in the protocol. Examples of sensitive information that may require reporting include positive HIV, hepatitis, or tuberculosis test results, illegal residency, child or spouse abuse, or participation in other illegal activities. These requirements will vary from state to state. Investigators should consult his/her IRB for assistance with state requirements.
- **Disposition of data.** Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, and the length of time data will be stored. Note that records of IND studies must be kept for 2 years after a New Drug Application is approved/issued, or for 2 years after the IND is withdrawn. Records required for IDE studies should be retained for 2 years following the date that the investigation is terminated or completed, or the date that the records are no longer required for support of the pre-market approval application, whichever is sooner.
- **Sharing study results.** In cases where the volunteer could possibly benefit medically or otherwise from the information, the protocol should explain whether or not the results of screening and/or study participation will be shared with volunteers or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study. The potential benefits of providing volunteers with the information should be weighed against the potential risks. It is generally not advisable to use experimental assays or techniques to guide clinical care.

20. Risks/Benefits Assessment:

- **Foreseeable risks.** Clearly identify all study risks. Study risks include any risks that the volunteer is subjected to as a result of participation in the protocol. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated in the protocol. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response.**
    - Clearly list all measures to be taken to minimize and/or eliminate risks to volunteers and study personnel, or to manage unpreventable risks. All safety measures in place to mitigate risk (e.g., core temperature monitoring, electrocardiogram monitoring, observation periods, special procedures to avoid disclosure of potentially damaging information) should be described.
    - Planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values, and other safeguards should be detailed in the protocol.
    - If there is a chance a volunteer may require emergency care or treatment for an adverse event, the protocol should discuss the overall plan for provision of care for study-related injuries, to include who will be responsible for the cost of such care. For example, if a study sponsor or institution has committed to providing care for study-related injury at no cost to volunteers, this provision should be explained in the protocol. The clinical site must have adequate personnel and equipment to respond to expected adverse events, and the nearest medical treatment facility should be identified in the emergency response plan.
    - Any special precautions to be taken by the volunteers before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention, etc.) must be addressed. If pregnant volunteers will be excluded from participation in the study, the method used to determine pregnancy status in women of childbearing potential must be specified. Also, the time that will elapse between the pregnancy test and exposure to study procedures or medical products must be stated, as well as how long the non-pregnant volunteer should use effective contraceptive practices after participating in the study. Please note that contraceptive practices may be necessary for male volunteers participating in certain types of studies. For IND studies, pregnancy testing is recommended within 48-72 hours before the start of the study. Consideration should be given to repeating testing prior to administration of test articles.
    - 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 volunteers enrolled in the study must be described in the protocol.
- **Potential benefits.** Describe real and potential benefits of the study to the volunteer, a specific community, or society. Ensure that the benefits are not overstated. ***NOTE: Payment and/or other compensation for participation are not considered to be benefits and must be addressed in a separate section.***
- **Intent to benefit.** If volunteers cannot give their own consent to participate in an experimental study, and Title 10 United States Code Section 980 (10 USC 980), http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=browse_usc&docid=Cite:+10USC980, applies, a clear intent to benefit each volunteer must be described in the protocol.

21. Study Personnel:

- **Roles and responsibilities of key study personnel.** Briefly describe the duties of key study personnel. Describe their roles in the study effort. A study coordinator is required at an appropriate level of effort whose duties may include the following: Recruit and consent volunteers, maintain study records, administer study drug, take and record vital signs, and enter data into computer database. A key person must be identified who will be responsible for guiding the protocol through the IRB, HRPO, and other regulatory approval processes, coordinating activities from all sites participating in the trial and coordinating participant accrual.
- **Conflicts of interest.** Investigators and key study staff must disclose any real or apparent conflicts of interest (financial or other). This information may be provided in the protocol or by submission of a conflict of interest declaration form. Many institutions have a form for this purpose, as does the FDA. A Financial Disclosure Form for Investigators is also available on the HRPO website at https://mrmc-www.army.mil/rodorphrpo.asp that will meet this requirement. Measures taken to mitigate the impact of conflicts of interest must be provided. Information regarding conflicts of interest should be disclosed to volunteers in the consent form. All protocols that support development of a drug, device, or other intellectual property require completion of a conflict of interest declaration by all investigators on the protocol. Other protocols may require conflict of interest statements on a case-by-case basis.

22. Roles and Responsibilities of Medical Monitor: The DOD requires that a medical monitor be assigned to greater-than-minimal-risk protocols. The specific roles the medical monitor will fulfill should be outlined in the protocol.

NOTE: The HRPO requires that the medical monitor review all unanticipated problems involving risk to volunteers or others, serious adverse events, and all volunteer deaths associated with the protocol, and provide an unbiased written report of the event within 10 calendar days. At a minimum, the medical monitor should comment on the outcomes of the adverse event and relationship of the event to the protocol or test article. The medical monitor should also indicate whether he/she concurs with the details of the report provided by the PI. Reports for events determined by either the investigator or medical monitor to be possibly or definitely related to participation, and reports of events resulting in death should be promptly forwarded to the HRPO.

23. Study Organization and Management Plan: Provide an organizational chart and a timetable for completion for the clinical trial and publication. Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). Provide a plan for real-time communication among collaborating institutions (if applicable).

24. Withdrawal from the Protocol: Volunteers may discontinue participation in the study at any time without penalty or loss of benefits to which the volunteer is otherwise entitled. If appropriate, the protocol should describe the procedure in place to support an orderly end of the volunteer's participation (e.g., exit exam or follow-up safety visits outside of the

context of the research study, information regarding prorated payment for partial participation, etc.) and the consequences of a volunteer's decision to withdraw from the study. The anticipated circumstances under which the volunteer's participation may be terminated by the investigator or others should also be addressed (e.g., noncompliance, safety issues, loss of funding, etc.).

25. Modifications to the Protocol: Describe the procedures to be followed if the protocol is to be modified, amended, or terminated before completion. Note that any modification to the protocol, consent form, and/or questionnaires, including a change to the PI, must be submitted to the local IRB for review and approval. Major modifications to the study protocol and any modifications that could increase risk to volunteers must be submitted to the HRPO for approval ***prior to implementation.*** Some examples of major modifications include a change in PI, addition of a study site, changes in study design, and addition or widening of a study population. All other amendments will be submitted with the continuing review report to the HRPO for acceptance. Address the procedure for submitting amendments even if modifications to the protocol are not anticipated.

- **Protocol Deviations.** Describe procedures and notifications to be made in the event of deviations from the approved protocol to include both the local IRB and the HRPO. ***NOTE: Any deviation to the protocol that may have an effect on the safety or rights of the volunteer, or the integrity of the study must be promptly reported to the HRPO.***

26. Reporting of Serious Adverse Events and Unanticipated Problems:

- Reporting procedures will differ from institution to institution, so it is important for investigators to identify the reporting requirements for all entities involved in review of the protocol, and to clearly define this procedure within the protocol.
- Serious adverse events and unanticipated problems can occur in any and all types of studies, not just experimental interventions or clinical trials.
- Include a definition of what constitutes an adverse event in the study. For IND or IDE studies, include definitions as described in 21 CFR 312.32 and the ICH (International Conference on Harmonization) E2A Guidelines (http://www.ich.org/cache/compo/475-272-1.html).
- Describe agencies or offices to be notified with point of contact information in the event of an unanticipated problem or serious adverse event.

All protocols should contain the following language regarding the HRPO reporting requirements for adverse events and unanticipated problems: "Unanticipated problems involving risk to volunteers or others, serious adverse events related to participation in the study, and all volunteer deaths related to participation in the study should be promptly reported by phone (301-619-2165), by email (hsrrb@amedd.army.mil), or by facsimile (301-619-7803) to the USAMRMC ORP, HRPO. A complete written report should follow the initial notification. In addition to the methods above, the complete report can be sent to the US Army Medical Research and Materiel Command, ATTN: MCMR-ZB-P, 504 Scott Street, Fort Detrick, Maryland 21702-5012."

For protocols that have a medical monitor assigned, the following language should also be included:

"The medical monitor is required to review all unanticipated problems involving risk to volunteers or others, serious adverse events, and all volunteer deaths associated with the protocol, and provide an unbiased written report of the event to the USAMRMC Office of Research Protections (ORP) Human Research Protections Office (HRPO). At a minimum, the medical monitor should comment on the outcomes of the event or problem, and in the case of a serious adverse event or death, comment on the relationship to participation in the study. The medical monitor should also indicate whether he/she concurs with the details of the report provided by the study investigator. Reports for events determined by either the investigator or medical monitor to be possibly or definitely related to participation, and reports of events resulting in death should be promptly forwarded to the HRPO."

27. Continuing Review and Final Report: The protocol should acknowledge that a copy of the approved continuing review report and the local IRB approval notification will be submitted to the HRPO as soon as these documents become available. A copy of the approved final study report and local IRB approval notification will be submitted to the HRPO as soon as these documents become available.

B. Surveys, Questionnaires, and Other Data Collection Instruments

If the study involves surveys, questionnaires, case report forms, data collection forms, rating scales, interview guides, or other instruments, include a copy of the most recent version of each of these documents with the protocol submission. For each instrument that is used, the following information at a minimum should be addressed.

- Information collected with study instrument must be related to the objectives of the study.
- Procedures for use of study instruments should be clear in the protocol. Study instruments should be coded to protect confidentiality whenever possible.
- For study instruments provided to and/or completed by volunteers, the study instrument should be legible and presented at a reading level appropriate to the population. Copies of instruments submitted for review must also be legible.

C. Additional Protocol Language Requirements

The following are reporting requirements and responsibilities of the PI to the USAMRMC ORP, HRPO, and should be reflected in the protocol:

- The protocol will be conducted in accordance with the protocol submitted to and approved by the USAMRMC ORP, HRPO and will not be initiated until written notification of approval of the research project is issued by the USAMRMC ORP, HRPO.
- Accurate and complete study records will be maintained and made available to representatives of the USAMRMC as a part of their responsibility to protect human

subjects in research. Research records will be stored in a confidential manner so as to protect the confidentiality of subject information.

- The knowledge of any pending compliance inspection/visit by the FDA, Office for Human Research Protections, or other government agency concerning clinical investigation or research, the issuance of Inspection Reports, FDA Form 483, warning letters, or actions taken by any Regulatory Agencies, including legal or medical actions, and any instances of serious or continuing noncompliance with the regulations or requirements will be reported immediately to the USAMRMC ORP, HRPO.

VI. 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:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

B. Modifications

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

C. Withdrawal

The following may result in administrative withdrawal of the application:

- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Direct costs as shown on the detailed budget form exceed maximum allowed by this Program Announcement/Funding Opportunity.

- Inclusion of URLs with the exception of links to published references.
- The proposed research is not a clinical trial.
- The PI does not meet the eligibility criteria as described in this Program Announcement/Funding Opportunity.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be requested to provide the findings of the investigation to the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer for a determination of the final disposition of the application.

VII. CONTACT INFORMATION

A. CDMRP Program Announcement Help Desk: Questions related to Program Announcement/Funding Opportunity content or submission requirements should be directed to the CDMRP Program Announcement help desk, which is available Monday through Friday from 7:30 a.m. to 4:00 p.m. ET. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079
Email: cdmrp.pa@amedd.army.mil

B. CDMRP eReceipt System Help Desk: Questions related to the submission of the pre-application through the eReceipt system should be directed to the CDMRP eReceipt system help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET.

Phone: 301-682-5507
Email: help@cdmrp.org

C. Grants.gov Contact Center: Questions related to application submission through the Grants.gov portal should be directed to Grants.gov help desk, which is available 24 hours a day, 7 days a week. Please note that the CDMRP Program Announcement and eReceipt system help desks are unable to provide technical assistance regarding Grants.gov submissions.

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. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VIII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1	
	Upload Supporting Documentation (Support.pdf) as Attachment 2	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3	
	Upload Public Abstract (PublicAbs.pdf) as Attachment 4	
	Upload Statement of Work (SOW.pdf) as Attachment 5	
	Upload Detailed Budget and Justification (Budget.pdf) as Attachment 6	
	Upload Subaward Detailed Budget and Justification (SubBudgets.pdf) as Attachment 7	
	Upload Research Plan (Research.pdf) as Attachment 8	
	Upload Military Relevance Statement (MilRel.pdf) as Attachment 9	
	Upload Human Subject Plan (HumSub.pdf) as Attachment 10	
	Upload Approval for Access to Military Populations Plan (MilPop.pdf) as Attachment 11	
	Upload Data/Research Resources Sharing Plan (DatShar.pdf) as Attachment 12	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field	
	Attach PI Current & Pending Support (Support_LastName.pdf) to the appropriate field	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field	
	Attach Current & Pending Support (Support_LastName.pdf) for each senior/key person to the appropriate field	
Project/Performance Site Location(s) Form	Complete form as instructed	
Additional Application Components	**Action**	**Completed**
Confidential Letters of Recommendation	Confirm upload to CDMRP eReceipt System	

APPENDIX A

PUBLIC LAW 111-84

FISCAL YEAR 2010 NATIONAL DEFENSE AUTHORIZATION ACT

SEC. 725. CHIROPRACTIC CLINICAL TRIALS.

(a) CLINICAL TRIALS REQUIRED.—The Secretary of Defense shall provide for the clinical trials described under subsection (b) to be conducted by the National Institutes of Health or an independent academic institution as the Secretary shall select for the purposes of conducting each trial.

(b) CLINICAL TRIALS DESCRIBED.—

(1) CONTROLLED TRIALS.—The clinical trials required by subsection (a) shall include controlled trials that, at a minimum, compare the outcomes of chiropractic treatment, used either exclusively or as an adjunct to other treatments, with conventional treatment on the following topics:

(A) Pain management.

(B) Orthopedic injuries or disorders that do not require surgery.

(C) Smoking cessation.

(2) INTERVENTIONAL TRIALS.—The clinical trials required by subsection (a) shall include interventional trials that, at a minimum, cover the following topics:

(A) The effect of chiropractic treatment on the reflexes and reaction times of special operation forces.

(B) The effect of chiropractic treatment on strength, balance, and injury prevention for members of the Armed Forces with combat specialties operating in a combat theater.

(c) SCHEDULE.—

(1) FIRST TRIAL.—The first clinical trial required by subsection

(a) shall begin not later than one year after the date of the enactment of this Act.

(2) FINAL TRIAL.—The final clinical trial required by subsection

(a) shall begin not later than two years after the date of the enactment of this Act.

(d) TRIAL PARTICIPANTS.—A participant of a clinical trial required by subsection (a) shall be a member of the Armed Forces on active duty.

(e) CHIROPRACTIC PROVIDERS.—Chiropractic treatment provided during a clinical trial required by subsection (a) shall be provided by a doctor of chiropractic who is licensed as a doctor of chiropractic, chiropractic physician, or chiropractor by a State, the District of Columbia, or a territory or possession of the United States, subject to credentialing requirements prescribed by the Secretary.

(f) REPORTS.—

(1) TRIAL PROTOCOL REPORTS.—Not later than 30 days before each clinical trial required by subsection (a) is scheduled to begin, the Secretary shall submit to the congressional defense committees a report on the protocol of such clinical trial.

(2) FINAL REPORTS.—Not later than one year after the completion of each clinical trial required by subsection (a), the Secretary shall submit to the congressional defense committees a report on such clinical trial, including any recommendations regarding chiropractic treatment for covered beneficiaries (as such term is defined in section 1072(5) of title 10, United States Code).