Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Peer Reviewed Medical Research Program (PRMRP)

Clinical Trial Award

Funding Opportunity Number: W81XWH-08-PRMRP-CTA

TABLE OF CONTENTS

I. Helpful Information 2
- A. Contacts 2
- B. National Technical Information Service 3
- C. Commonly Made Mistakes 3

II. Funding Opportunity Description 3
- A. Program History and Objectives 3
- B. Award Description 4
- C. FY08 PRMRP Congressionally Directed Topic Areas 5
- D. Eligibility 6
- E. Funding 6
- F. Award Administration 7

III. Timeline For Submission and Review 7

IV. Submission Process 7
- A. Step 1: Pre-Application Components and Submission 7
- B. Step 2: Proposal Components and Submission 8

V. Information For Proposal Review 9
- A. Proposal Review and Selection Overview 9
- B. Review Criteria 9

VI. Compliance Guidelines 12

I. HELPFUL INFORMATION

A. Contacts

1. Program Announcement, proposal format, or required documentation: To view all funding opportunities offered by the Congressionally Directed Medical Research Programs (CDMRP), perform a Grants.gov basic search using the CFDA Number 12.420. 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
Fax: 301-619-7792
Email: cdmrp.pa@amedd.army.mil

2. eReceipt system: Questions related to pre-application components through the CDMRP eReceipt system should be directed to the eReceipt help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time.

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

3. Grants.gov contacts: Questions related to submitting applications through the Grants.gov (http://www.grants.gov/) portal should be directed to Grants.gov help desk. Deadlines for proposal submission are 11:59 p.m. Eastern time on the deadline date. Therefore, there is an approximate 3-hour period during which the Grants.gov help desk will NOT be available. Please plan ahead accordingly, as the CDMRP help desk is not able to answer questions about Grants.gov submissions.

Phone: 800-518-4726, Monday to Friday, 7:00 a.m. to 9:00 p.m. Eastern time
Email: support@grants.gov

Grants.gov will notify Principal Investigators (PIs) of changes made to this Program Announcement and/or Application Package ONLY if the PI clicks on the "send me change notification emails" link and subscribes to the mailing list on the Opportunity Synopsis Page for this announcement. If the PI does not subscribe and the Application Package is updated or changed, the original version of the Application Package may not be accepted.

B. National Technical Information Service

The technical reference facilities of the National Technical Information Service (www.ntis.gov) are available for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. All other sources also should be consulted to the extent practical for the same purpose.

C. Commonly Made Mistakes

- Not obtaining or confirming the organization's DUNS number well before the proposal submission deadline.
- Not obtaining or confirming the organization's registration with the Central Contractor Registry (CCR) well before the proposal submission deadline.
- Failing to request "send me change notification emails" from Grants.gov.
- Not contacting HELP DESKS until just before or after deadlines.
- Not completing the pre-application submission before the mandatory pre-application deadline (pre-application remains in draft status).
- Using an incorrect Grants.gov application package to submit a proposal through Grants.gov. Each Program Announcement/Funding Opportunity requires a specific application package.
- Uploading attachments into incorrect Grants.gov forms.
- Attaching files in the wrong location on Grants.gov forms.
- Submitting attachments that are not PDF documents, except for the R&R Subaward Budget Attachment(s) Form.
- Exceeding page limitations.
- Failing to submit a proposal 48-72 hours before the deadline so that Grants.gov can provide notification of errors and allow for resubmission of application package.
- Failing to submit proposal by submission deadline.

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History and Objectives

The PRMRP was established in 1999 to provide support for military health-related research of clear scientific merit. Appropriations for the PRMRP from Fiscal Year 1999 (FY99) through FY06 totaled $344.5 million (M). The FY08 appropriation is $50M.

The vision of the FY08 PRMRP is to find and fund the best medical research to protect, support, and advance the health and welfare of military personnel and all beneficiaries. The PRMRP challenges the scientific and clinical communities to address one of the 21 FY08 topic areas with innovative ideas to foster new directions in basic science and translational research; novel product development leading to improved therapeutic or diagnostic tools, or improvements in

clinical policies/guidelines; or clinical trials that address an immediate clinical need. The PRMRP seeks proposals in laboratory, clinical, behavioral, and epidemiologic research as well as public health and policy, environmental sciences, nursing, occupational health, alternative therapies, ethics, and economics.

B. Award Description

The PRMRP Clinical Trial Award mechanism is being offered for the first time in FY08.

This award supports rapid implementation of clinical trials of interventions with the potential to have a significant impact on a disease or condition addressed in one of the FY08 PRMRP topic areas. All proposed clinical trials must be responsive to the health care needs of the Armed Forces and family members, the U.S. Veteran population, and the general public and may address prevention, detection, diagnosis, treatment, and/or quality of life. The clinical trial may be designed to evaluate a pharmacologic agent (drug or biologic), device, or behavioral intervention. Funding from this award mechanism cannot be used for preclinical research studies.

Each proposal should contain only one clinical trial with a distinct study design. Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications should be submitted or approved prior to proposal submission. The Government reserves the right to withdraw funding if IND/IDE approval is not received within 6 months of the award date. Principal Investigators (PIs) must clearly specify in the Clinical Protocol (main body of the proposal) which type of clinical trial is being proposed: Phase I, Phase I/II, Phase II, or Phase III. For descriptions of each type of clinical trial, please refer to www.fda.gov/cder/guidance/6384dft.htm and http://www.clinicaltrials.gov. The proposed clinical trial is expected to begin within 12 months of the award date.

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

- Demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study
- Describe clearly defined and appropriate endpoints for the proposed clinical trial
- Clearly articulate the statistical analysis plan
- Discuss the potential impact of the study results for patients with the specified disease/condition
- Include a named study coordinator who will guide the clinical protocol through Institutional Review Board (IRB), Human Subjects Research Review Board (HSRRB), and other regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual

Multi-institutional Clinical Trials: If the proposed clinical trial is 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.

Encouraged DOD alignment: Alignment with current DOD research is encouraged. The following websites may be useful in identifying information about ongoing DOD areas of research interest within the FY08 PRMRP topic areas:

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

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

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

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

Navy and Marine Corps Public Health Center
www-nmcphc.med.navy.mil/main.htm

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

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

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

U.S. Naval Research Laboratory
www.nrl.navy.mil

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

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

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

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

Use of military populations: Clinical trials involving military subjects will require a letter of approval for access to the population. A military collaborator is recommended for research involving military troops performed at non-military organizations.

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 USAMRMC Office of Research Protections, 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. Refer to Instructions For Regulatory Requirements, Appendix 6, for detailed information.

C. FY08 PRMRP Congressionally Directed Topic Areas

All applications for PRMRP funding must specifically and clearly address one of the topic areas. ***If the research has no relevance to currently advertised PRMRP topic areas, the Government reserves the right to administratively withdraw the proposal.*** The Government reserves the right to reassign the proposal's topic area if submitted under an inappropriate topic area. The FY08 topic areas are listed below.

Alcoholism Research
Amyotrophic Lateral Sclerosis
Blood Cancer
Drug Abuse
Epilepsy Research
Eye and Vision Research
Integrated Tissue Hypoxia Research
Interstitial Cystitis
Inflammatory Bowel Disease
Leishmaniasis
Lupus
Kidney Cancer
Mesothelioma
Multiple Sclerosis
Nutrition and Health Promotion
Paget's Disease
Polycystic Kidney Disease
Pulmonary Hypertension
Scleroderma
Social Work Research
Tinnitus

D. Eligibility

PIs must be independent investigators at any academic level (or equivalent). Refer to Application Instructions, Appendix 1, for general eligibility information.

E. Funding

Funding for a Clinical Trial Award can be requested for up to $2.5M for direct costs for up to a 4-year performance period, plus indirect costs as appropriate.

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

- Salary
- Research supplies
- Equipment
- Clinical costs
- Travel to scientific/technical meetings
- Travel between collaborating institutions

In addition, each investigator must request travel funds to attend one Military Health Research Forum (MHRH) during the award performance period. The MHRF is a CDMRP-sponsored meeting for PRMRP funded investigators that is typically held every 2-3 years.

The CDMRP expects to allot approximately $7.5M of the $50M FY08 PRMRP appropriation to fund approximately 2 Clinical Trial Award proposals, depending on the quality and number of proposals received. Funding of proposals received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

F. Award Administration

At the Government's discretion, the PI and Clinical Study Coordinator may be requested to participate in a pre-award meeting.

Transferring this award to another institution will not be permitted. Refer to Application Instructions, Appendix 5, for general award administration information.

III. TIMELINE FOR SUBMISSION AND REVIEW

Proposal submission is a two-step process consisting of (1) pre-application submission and (2) proposal submission. ***Pre-application submission is a required first step***.

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time, June 4, 2008**
- **Proposal Submission Deadline: 11:59 p.m. Eastern time, July 2, 2008**
- **Peer Review: September 2008**
- **Programmatic Review: December 2008**

Awards will be made approximately 4-6 months after receiving the funding notification letter, but no later than September 30, 2009.

IV. SUBMISSION PROCESS

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

Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

A. Step 1: Pre-Application Components and Submission

The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the CDMRP eReceipt system by ***5:00 p.m. Eastern time on the deadline***. Refer to the Application Instructions for detailed information.

1. Proposal Information
2. Proposal Contacts
3. Collaborators and Conflicts of Interest (COI)
4. Letter of Intent (LOI) Narrative

B. Step 2: Proposal Components and Submission

Proposal submission will not be accepted unless a pre-application was submitted by the pre-application deadline. Proposals must be submitted electronically by the Authorized Organizational Representative (AOR) through Grants.gov (www.grants.gov). No paper copies will be accepted.

Each proposal submission must include the completed Grants.gov application package of forms and attachments identified in www.grants.gov for the US Army Medical Research Acquisition Activity (USAMRAA) Program Announcement. In addition to the specific instructions below, please refer to the Application Instructions for detailed requirements of each component.

The package includes:

1. **SF-424 (R&R) Application for Federal Assistance Form**

2. **Attachments Form**

   - Attachment 1: Clinical Protocol: No-page limit.

   The Clinical Protocol is the main body of the proposal and must address the required components described in Application Instructions (Appendix 8).

   - Attachment 2: Supporting Documentation
     - References Cited
     - Acronyms and Symbol Definitions
     - Facilities & Other Resources
     - Description of Existing Equipment
     - Publications and/or Patent Abstracts: Five-document limit.
     - Letters of Institutional Support: Two-page limit per letter.
     - Letters of Collaboration (if applicable): Two-page limit per letter.
     - Intellectual and Material Property Plan (if applicable)
   - Attachment 3: Technical and Public Abstracts: One-page limit per abstract.
   - Attachment 4: Statement of Work (SOW): Two-page limit.
   - Attachment 5: Impact Statement: One-page limit.

   State explicitly how the proposed clinical trial will have an impact on the prevention, detection, diagnosis, or treatment of the specified disease/condition, if successful. Explain the potential clinical applications, benefits, and risks.

   - Attachment 6: Letter of approval for access to military populations (if applicable): One-page limit.

   If the proposed study involves military recruits or subjects, military-controlled study materials, databases, and restricted facilities (e.g., biological or chemical containment facilities), a letter of support signed by the responsible commander (Installation, Troop, or Institute Commander) confirming access to recruits/military subjects and military materials is required.

   - Attachment 7: Federal Agency Financial Plan (if applicable)

3. **Research & Related Senior/Key Person Profile (Expanded Form)**

- PI Biographical Sketch (four-page limit)
- PI Current/Pending Support
- Key Personnel Biographical Sketches (four-page limit each)
- Key Personnel Current/Pending Support

4. **Research & Related Budget Form**
   - Budget Justification
5. **Research & Related Project/Performance Site Location(s) Form**
6. **R&R Subaward Budget Attachment(s) Form (if applicable)**

V. INFORMATION FOR PROPOSAL REVIEW

A. Proposal Review and Selection Overview

All proposals are evaluated by scientists and clinicians using a two-tier review process. The first tier is a scientific peer review of proposals against established criteria for determining scientific merit. The second tier is a programmatic review that compares submissions to each other and recommends proposals for funding based on scientific merit and overall goals of the program. Additional information about the two-tier review process used by the CDMRP may be found at http://cdmrp.army.mil/fundingprocess.htm.

The peer review and program review processes are conducted confidentially and anonymously to maintain the integrity of the merit-based selection process. Each tier review requires panelists to sign a non-disclosure statement attesting that proposal 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 correcting actions. Correspondingly, institutional personnel and PIs are prohibited from contacting persons involved in the proposal review process to gain protected evaluation information or to influence the evaluation process. Violations of this prohibition will result in the administrative withdrawal of the institution's proposal. Violations by panelists or PIs that compromise the confidentiality or anonymity of the peer review and program review processes may also result in suspension or debarment of their employing institutions from Federal awards.

The Government reserves the right to review all proposals based on one or more of the required attachments or supporting documentation (e.g., Impact Statement, etc.).

B. Review Criteria

1. Peer Review: All proposals will be evaluated according to the following criteria, which are listed in order of decreasing importance:

- **Study Design**
  - How the scientific rationale and preliminary data, including critical review and analysis of the literature, and laboratory and preclinical evidence support the proposed clinical trial and its feasibility.

- How the aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are developed.
- 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 recruitment, informed consent, and screening processes for volunteers will be conducted to meet the needs of the proposed clinical trial.
- How the inclusion, exclusion, and randomization criteria meet the needs of the proposed clinical trial.

- **Impact**
  - How the results of the proposed clinical trial will affect the magnitude and scope of potential clinical applications (e.g., prevention, detection, diagnosis, treatment, management, and/or quality of life).
  - How the proposed clinical trial addresses one of the FY08 PRMRP topic areas.
- **Intervention, Drug, or Device**
  - How the intervention, drug, or device to be tested is appropriate for the proposed clinical trial.
  - How the availability and purity of the substance to be used in the clinical trial is appropriate for the proposed clinical trial.
  - Whether there is documentation that an IND/IDE application has been submitted.
- **Feasibility**
  - The evidence that the proposed clinical trial is feasible.
  - How the plan for addressing unanticipated delays (e.g., slow accrual) 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.
  - The evidence that the PI will have access to any military populations required for the clinical study, if applicable.
- **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.
  - How the data analysis plan is consistent with the study objectives.
- **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 clinical studies).
- How the levels of effort of the clinical team are appropriate for successful conduct of the proposed trial.

- **Environment**
  - How the evidence indicates an appropriate scientific environment, clinical setting, and the accessibility of institutional resources to support the clinical trial at each participating center (including collaborative arrangements).
  - The evidence for appropriate institutional commitment from each participating institution.
  - How the intellectual and material property plan that is agreed upon by each participating institution is appropriate for the proposed clinical trial.
- **Ethics and/or Regulatory Issues**
  - How the ethical considerations, information privacy, and assessment of risks and benefits of participation in the clinical trial will be addressed.
  - Evidence that an appropriate plan for dealing with adverse events, which should include named agencies or offices to be notified in this event, and point of contact information has been prepared.
  - How plans for data disposition during and after the clinical trial are appropriate for the proposed clinical trial.
  - How the procedures for protocol modifications during the course of the clinical trial have been addressed.
  - How the plans for data and safety monitoring are appropriate for the proposed clinical trial.
- **Budget**
  - How the budget is appropriate for the proposed research.

2. Programmatic Review: Criteria used by the Joint Programmatic Review Panel (JPRP) members to make funding recommendations that maintain the program's broad portfolio include:

- Responsiveness to FY08 PRMRP topic areas,
- Ratings and evaluations of the peer reviewers,
- Programmatic relevance,
- Relative impact,
- Military relevance,
- Program portfolio balance, and
- Adherence to the intent of the award mechanism.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by JPRP members and recommended for funding to the Commanding General, USAMRMC.

VI. COMPLIANCE GUIDELINES

Compliance guidelines have been designed to ensure the presentation of all pre-applications and proposals in an organized and easy-to-follow manner. Peer reviewers expect to see a consistent, prescribed format. Failure to adhere to formatting guidelines makes documents difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in pre-application or proposal rejection. **Pre-applications or proposals missing required components as specified in the Program Announcement/Funding Opportunity may be administratively rejected.**

If the research has no relevance to currently advertised PRMRP topic areas, the Government reserves the right to administratively withdraw the proposal.

The following will result in administrative rejection of the entire proposal:

- Clinical Protocol is missing.
- Margins are less than specified in the formatting guidelines.
- Print area exceeds that specified in the formatting guidelines.
- Spacing is less than specified in the formatting guidelines.
- Budget and/or budget justification are missing.
- FY08 JPRP members are included in any capacity in the pre-application process, the proposal, budgets, and any supporting document. A list of the FY08 JPRP members may be found at http://cdmrp.army.mil.

For any other sections of the proposal with a defined page limit, pages exceeding the specified limit will be removed and not forwarded for peer review.

Material submitted after the submission deadline, unless specifically requested by the Government, will not be forwarded for peer review.

Proposals that appear to involve any allegation of research misconduct will be withheld from further consideration pending institutional investigation. The institution will be requested to perform an investigation and provide those findings to the Grants Officer for a determination of the final disposition of the application.