Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Gulf War Illness Research Program

Clinical Trial Award

Funding Opportunity Number: W81XWH-08-GWIRP-CTA

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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 the 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 through 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 should also 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 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 (i.e., 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 Gulf War Illness Research Program (GWIRP) was established in fiscal year 1994 (FY94) to study the health effects of warfighters deployed in the 1991 Persian Gulf War. Appropriations for the GWIRP from FY94 through FY07 totaled $217.2 million (M). The FY08 appropriation is $10.0M.

The GWIRP challenges the scientific community to design innovative research that will improve the health and lives of veterans who have Gulf War Illness (GWI), which refers to the complex of chronic symptoms that affect veterans of the 1990-1991 Gulf War at an excess rate. The illness is characterized by persistent symptoms such as chronic headache, widespread pain,

cognitive difficulties, unexplained fatigue, gastrointestinal problems, respiratory symptoms, and other abnormalities that are not explained by familiar medical or psychiatric diagnoses. The GWIRP focuses its funding on innovative projects that have the potential to make a significant impact on GWI.

B. Award Description

The GWIRP Clinical Trial Award mechanism is being offered for the first time in FY08. The Clinical Trial Award supports rapid execution of clinical trials with the potential to have a significant impact on the health and lives of veterans with GWI.

The GWIRP seeks proposals that will contribute to identification of effective treatments for GWI. This might include smaller-scale pilot trials of treatments that have not previously been studied for their effectiveness in treating GWI or larger, more definitive clinical trials of studies that preliminary evidence indicates may provide substantial benefit for veterans with GWI. Health outcomes of interest include effects of treatments on:

- Global health measures, functional status
- Symptom complexes (e.g. cognitive function, musculoskeletal/pain symptoms, gastrointestinal symptoms, fatigue, respiratory problems, skin abnormalities) individually and as they may interact with each other
- Measurable clinical outcomes, biomarkers
- GWI subgroups characterized by symptom or other clinical characteristics

Methods used to identify GWI cases and GWI patient subgroups of interest, health status, and treatment outcomes must be clearly described. Assessed treatment outcomes should include global changes in health status, specific objective measures where applicable, and changes in symptom domains of interest (e.g., pain, cognitive function, gastrointestinal problems, sleep difficulties, abnormalities, fatigue, respiratory function).

Proposals are required to include preliminary data, but it does not necessarily have to come from the GWI research field. Each proposal must include only one clinical trial. PIs are encouraged to pursue correlative studies that accompany their trials. PIs conducting correlative studies must describe in detail the study aims, procedures or methods, and plans for data management and analysis, including an appropriately powered statistical plan.

It is expected that the intervention, drug, or device to be used in the proposed trial will be available in sufficient quantities and ready for clinical trials at the time that the award is made. Further, it is expected that the clinical trial will be initiated within 12 months of the award date. Note that Investigational New Drug (IND)/Investigational Device Exemption (IDE) approvals, if applicable, should be in process or completed before submission of an application to this mechanism. ***If IND/IDE approval is not received by April 30, 2009, the Government reserves the right to not fund the award.*** Funding from this award mechanism cannot be used for preclinical research studies.

Important aspects of the Clinical Trial Award are:

- The protocol must include a named study coordinator who will guide the protocol through local institutional review board (IRB), US Army Medical Research and Materiel Command (USAMRMC), and other regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate volunteer accrual.
- IND or IDE approvals, if applicable, should be in process or completed before submission of the proposal to the Clinical Trial Award mechanism. If IND/IDE approval is not received by April 30, 2009, the Government reserves the right to not fund the award.
- The clinical trial should have a potentially high impact.
- The clinical trial must have clearly defined and appropriate endpoints.
- Proposals must clearly indicate how accrual goals will be achieved.

Please note that all DOD-funded research involving human subjects and human biological substances must be reviewed and approved by the USAMRMC's 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.

Studies whose principal focus is on treatment of psychiatric conditions will not be funded under this Program Announcement/Funding Opportunity.

For further information about GWI and the intent of this award, see the Information Paper at http://cdmrp.army.mil/funding/pdf/08gwirpinfopaper.pdf

C. Eligibility

PIs at all academic levels (or equivalent) are eligible to submit proposals.

Refer to the Application Instructions, Appendix 1, for general eligibility information.

D. Funding

Funding for a Clinical Trial Award can be requested for up to $750,000 for direct costs for up to a 3-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

PIs should also budget for travel to a pre-award meeting/protocol workshop at Fort Detrick, Maryland. At a minimum, it is expected that the PI and Clinical Research Coordinator will attend the pre-award meeting, although up to three individuals may attend. Justification must be provided if additional personnel are included in the travel budget.

The CDMRP expects to allot approximately $2.59M of the $10.0M FY08 GWIRP appropriation to fund two 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.

E. Award Administration

Clinical Trial Awards cannot be transferred to another institution. A change in PI will not be allowed for the Clinical Trial Award except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer, provided that the intent of the award mechanism is met.

Refer to the 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, July 2, 2008**
- **Invitation to Submit a Proposal: August 8, 2008**
- **Proposal Submission Deadline: 11:59 p.m. Eastern time, October 15, 2008**
- **Peer Review: December 2008**
- **Programmatic Review: January 2009**

Awards will be made approximately 4 to 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 pre-application deadline***. In addition to award-specific information provided below, refer to the Application Instructions for detailed information.

- **Proposal Information:** The PI must enter the Proposal Information before continuing the pre-application.
- **Proposal Contacts:** The PI must enter his or her contact information.
- **Collaborators and Conflicts of Interest (COI):** The PI must enter the contact information for any collaborators.
- **Preproposal Narrative:** The Preproposal Narrative has a ***three-page limit*** inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the preproposal. The preproposal narrative should address the following:
  - **Research Idea:** State the ideas and reasoning on which proposed work is based.
  - **Research Strategy:** Concisely state the project's objective and specific aim.
  - **Impact:** State explicitly how the proposed work will have an impact on accelerating the movement of a promising idea in GWI research into clinical applications.
- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application are:
  - **References:** One-page limit.
  - **Biographical Sketches:** Include biographical sketches for the PI and other key collaborators.
  - **Use of Hazardous Chemical or Biological Agents (if applicable):** The applicant must submit a plan for acquiring, using, and maintaining hazardous agents if such agents are to be used in the study. The plan must contain all applicable information such as Centers for Disease Control and Prevention (CDC) registration, an approved institutional safety plan to use the agent(s), and letters of collaboration, agreement, or approval from government sites issuing any agent(s). Indicate also if agents used are purchased commercially, and if so, confirm that the amount is under regulated limits.

Include a statement addressing this requirement along with accompanying letters of collaboration, approvals, and certifications.

Pre-Application Screening: Pre-applications will be screened by the GWIRP Integration Panel (IP), composed of scientists, clinicians, and consumer advocates. The pre-application screening criteria are as follows:

- **Research Idea:** How the rationale and collaboration will advance the GWI research field.
- **Research Strategy:** How the specific aims support the research idea.
- **Impact:** How the study addresses an important problem related to GWI. If successful, how the aims of the application are likely to accelerate the movement of promising ideas in GWI research into clinical applications.

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 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 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 the 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
     - Letters of Institutional Support

    - Letters of Collaboration (if applicable)
    - Intellectual and Material Property Plan (if applicable)
- Attachment 3: Technical and Public Abstracts
- Attachment 4: Statement of Work
- Attachment 5: Impact Statement

  State explicitly how the proposed work will, if successful, have an impact on GWI, and how the expected results of the proposal will contribute to the goal of improving the health and lives of veterans who have GWI.
- Attachment 6: Use of Hazardous Chemical or Biological Agents (if applicable) (no page limit)

  The applicant must submit a plan for acquiring, using, and maintaining hazardous agents if such agents are to be used in the study. The plan must contain all applicable information such as CDC registration, an approved institutional safety plan to use the agent(s), and letters of collaboration, agreement, or approval from government sites issuing any agent(s). Indicate also if agents used are purchased commercially, and if so, confirm that the amount is under regulated limits. Include a statement addressing this requirement along with accompanying letters of collaboration, approvals, and certifications.
- Attachment 7: Federal Agency Financial Plan (if applicable)

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

- 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, clinicians, and consumer advocates 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

The peer review and program review processes are conducted confidentially and anonymously to maintain the integrity of the merit-based selection process. Each tier of 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).

B. Review Criteria

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

- **Trial Design**
  - How the scientific rationale and preliminary data, including critical review and analysis of the literature and laboratory and preclinical evidence, support the proposed trial and its feasibility.
  - How well the aims, hypothesis(es) 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) are adequate.
  - How the recruitment, informed consent, and screening processes for volunteers will be conducted.
  - Whether the inclusion, exclusion, and randomization criteria are adequate.
- **Clinical Impact**
  - How this study, if successful, will affect the treatment and/or management of the disease.
  - How this study, if successful, will affect the magnitude and scope of potential clinical applications.

- **Intervention, Drug, or Device**
  - The appropriateness of the intervention, drug, or device to be tested in the clinical trial.
  - The availability and purity of the substance to be used in the clinical trial (if applicable).
  - Documentation that an IND/IDE has been submitted (if applicable).
- **Feasibility**
  - The feasibility of the proposed clinical study.
  - The plans for addressing potential delays (e.g., slow accrual) and completing the proposed study within the performance period.
  - The availability of volunteers for the clinical trial, the prospect of their participation, and the likelihood of volunteer attrition.
  - The progress toward obtaining local IRB approval of the clinical protocol and informed consent form.
- **Statistical Plan (as appropriate for phase of study)**
  - How the statistical plan, including sample size projections and power analysis, is adequate for the trial and all proposed correlative studies.
  - The consistency of the data analysis plan with the study objectives.
- **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.
  - The plan for dealing with adverse events, which should include named agencies or offices to be notified in this event and point of contact information.
  - The plans for data disposition during and after the clinical trial.
  - The procedures for protocol modifications during the course of the study.
  - The plans for data and safety monitoring.
- **Personnel**
  - How the clinical trial team's background and expertise are appropriate to accomplish the proposed work (i.e., statistical expertise, expertise in the disease, and clinical trials).
  - The appropriateness of the levels of effort for successful conduct of the proposed work.

- **Environment**
  - The evidence of an appropriate scientific environment, clinical setting, and the accessibility of institutional resources to support the clinical trial at each participating center.
  - Whether the clinical trial requirements are supported adequately by the accessibility to facilities and resources (including collaborative arrangements).
  - The institutional commitment from each participating institution.
- **Budget**
  - How the budget is appropriate for the proposed research.

2. Programmatic Review: Criteria used by programmatic reviewers to make funding recommendations that maintain the program's broad portfolio include:

- Ratings and evaluations of the peer reviewers,
- Programmatic relevance,
- Relative impact,
- 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 IP 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.**

The following will result in administrative rejection of the entire pre-application:

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative 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.

- FY08 IP members are included in any capacity in the pre-application process (excluding references). A list of the FY08 IP members may be found at http://cdmrp.army.mil.

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 IP members are included in any capacity in the pre-application process, the proposal, budgets, and any supporting document. A list of the FY08 IP members may be found at http://cdmrp.army.mil/research

For any other sections of the pre-application or 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 administratively withheld from further consideration pending institutional investigation. The institution will be requested to perform the investigation and provide those findings to the Grants Officer for a determination of the final disposition of the application.