Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Gulf War Illness Research Program

Clinical Trial Development Award

Funding Opportunity Number: W81XWH-11-GWIRP-CTDA
Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time (ET), May 25, 2011**
- **Application Submission Deadline: 11:59 p.m. ET, August 24, 2011**
- **Scientific Peer Review: November 2011**
- **Programmatic Review: January 2012**

New for fiscal year 2011 (FY11): The Grants.gov Research & Related Budget form is a mandatory component of all Grants.gov application packages.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

The Gulf War Illness Research Program (GWIRP) was established in FY94 to study the health effects of deployment to the 1990-91 Persian Gulf War on U.S. warfighters. Appropriations for the GWIRP from FY94 through FY10 have totaled $243 million (M). The FY11 appropriation is $8.0M.

The GWIRP challenges the scientific community to design high-impact research that will improve the health and lives of veterans who have Gulf War Illness (GWI). GWI is characterized by multiple diverse symptoms that typically include chronic headache, widespread pain, cognitive difficulties, debilitating fatigue, gastrointestinal problems, respiratory symptoms, and other abnormalities that are not explained by established medical diagnoses or standard laboratory tests.

The population of veterans affected by GWI is a subset of the nearly 700,000 who served during the Gulf War. Specifically, these Gulf War veterans were deployed to the theatre of operations in Southwest Asia, including Iraq, Kuwait, and Saudi Arabia. Studies indicate that approximately 25 to 32 percent (or 175,000 to 210,000) of Gulf War veterans continue to experience symptoms associated with their deployment as described above.

The GWIRP focuses its funding on innovative projects that have the potential to make a significant impact on GWI. These may take the form of identification of objective indicators of pathology that distinguish ill from healthy veterans, studies to understand the underlying pathobiology of GWI, or new treatments for ill Gulf War veterans. The GWIRP encourages risk-taking research; however, all projects must demonstrate solid judgment and sound rationale.

B. Award Information

The GWIRP Clinical Trial Development Award (CTDA) mechanism is offered for the first time in FY11. The CTDA is intended to support planning activities necessary for the conduct of a Phase II or Phase III clinical trial (or a trial of devices in FDA classes I-III), since these activities usually represent a significant expenditure of time and effort. The CTDA is a one-year grant intended to allow investigators time to undertake preparatory activities and have the study rationale for a future clinical trial scientifically reviewed. The CTDA is not intended for the collection of preliminary data or the conduct of pilot studies to support the rationale for a future clinical trial.

Clinical trial developmental activities allowed under a CTDA may include, but are not limited to:

- Developing the clinical protocol and experimental design
- Composing the research team and initiating collaborations necessary for the future clinical trial, and developing training procedures, as applicable
- Investigating potential intellectual or material property issues, as applicable

- Initiating access to an ill Gulf War veteran population and planning a recruitment strategy
- Developing quality control/assurance procedures
- Developing data collection/data management procedures
- Developing a data analysis/statistical plan
- Assessing potential issues regarding test article purity and formulation
- Developing a safety monitoring plan
- Determining a process for finalizing a U.S. Food and Drug Administration (FDA) Investigational New Drug (IND) / Investigational Device Exemption (IDE) application, if applicable
- Conducting other preparatory activities needed to support the future clinical trial

These activities do not involve the collection of data supported by traditional investigator initiated research awards. Investigators interested in generating proof of principle data should consider the GWIRP's Investigator-Initiated Research Award, aimed at basic research for Gulf War Illness, or the Innovative Treatment Evaluation Award, which supports the initial evaluation of a treatment or intervention in small, early phase or pilot clinical trials (Phase II or I/II). For information about these award mechanisms, see http://cdmrp.army.mil/funding/gwirp

Clinical trials supported by the GWIRP must recruit appropriately-defined ill Gulf War veteran cohorts. ***Therefore, PIs applying to the CTDA must provide a published case definition they intend to use to define their GWI population.*** Any case definition must recognize the multi-symptom nature of GWI. NOTE: The 2008 report of the Research Advisory Committee on Gulf War Veterans' Illnesses, *Gulf War Illness and the Health of Gulf War Veterans*, provides information on GWI case definitions (pp. 29-30, p. 57), previous treatment research in Gulf War veterans (pp. 36-39), and treatment research related to other multi-symptom conditions (pp. 285-287). The report can be found online at http://www1.va.gov/RAC-GWVI**.**

Investigators awarded a CTDA are expected to apply to the GWIRP's Clinical Trial Award in the program year following completion of the CTDA (i.e. FY11 CTDA awardees would apply for an FY13 or FY14 Clinical Trial Award, if that award is offered). The FY13 (or FY14) CTA application would include the results of the completed CTDA. Applications for an FY13 (or FY14) Clinical Trial Award, if offered, will only be accepted from investigators awarded an FY11 CTDA. However, award of an FY11 CTDA is in no way an assurance of funding for a future Clinical Trial Award. The funding of FY13 (or FY14) Clinical Trial Awards will be contingent upon the availability of federal funds for the program.

The GWIRP Clinical Trial Award supports Phase II or Phase III (or FDA device class I-III) clinical trials of treatments with the potential to have a significant impact on the health and lives of veterans with GWI. The Clinical Trial Award requires that an IND or IDE application, if applicable, must be submitted prior to Clinical Trial Award application submission. Thus, investigators would be expected to use the CTDA period to initiate the IND/IDE application process. Please note that all Department of Defense (DOD)-funded research involving human subjects and human anatomical substances must be reviewed and approved by the US Army

Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protections Office (HRPO), in addition to the local IRB of record. For more information about clinical trials and human subject research requirements, refer to the General Application Instructions, Appendix 5, D.

The GWIRP Clinical Trial Award application requires extensive descriptions of clinical trial components. CTDA applicants are encouraged to reference the GWIRP FY11 Clinical Trial Award Program Announcement to become familiar with these requirements and to help direct activities during the CTDA period. The GWIRP FY11 Clinical Trial Award Program Announcement can be accessed at http:/cdmrp.army.mil/funding.

Each CTDA application can only request support for preparations for a single clinical trial. However, investigators may submit more than one CTDA application supporting preparations for different clinical trials.

C. Eligibility Information

- Independent investigators at all academic levels (or equivalent) are eligible to apply.
- Cost sharing/matching is not an eligibility requirement.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **1** year.
- The maximum allowable direct costs for the entire period of performance are **$100,000** plus indirect costs**.**
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- The applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C., for budget regulations and instructions for the Research & Related Budget form. In addition, for this award mechanism, direct costs:

May be requested for (not all-inclusive):

- Salary
- Administrative costs
- Support for establishing collaborations
- Travel between collaborating organizations

Must not be requested for:

- Equipment
- Research supplies

The Office of the Congressionally Directed Medical Research Programs (CDMRP) expects to allot approximately $640,000 of the $8M FY11 GWIRP appropriation to fund approximately 4 Clinical Trial Development Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a multi-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.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-11-GWIRP-CTDA.

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the PI through the CDMRP eReceipt System (https://cdmrp.org/).

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 CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

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, Section II.B., for additional information on pre-application submission):

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

  Letter of Intent (LOI) (one-page limit): Provide a brief description of the proposed intervention, the future clinical trial and the supporting rationale.

  LOIs are used for program planning purposes only (e.g., reviewer recruitment) and ***will not be reviewed*** during either the peer or programmatic review sessions.
- **Submit Pre-application – Tab 5**

- **Other Documents Tab**

  No additional documents are required**.**

C. Application Submission Content and Form

Applications will only be accepted from PIs who have submitted an LOI.

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

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

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.
2. **Attachments Form**
   - **Attachment 1: Project Narrative (six-page limit):** Upload as "ProjectNarrative.pdf."
     - Describe the background, rationale and objectives behind the future clinical trial and the intervention, drug, or device to be tested.
     - Describe plans to develop the clinical protocol and finalize the experimental design.
     - Describe the published case definition of Gulf War Illness that will be used in the future clinical trial.
     - Describe plans for developing the research team and any proposed research resource or professional collaborations that will be established, and plans for training team members, as applicable.
     - Describe plans to investigate potential intellectual or material property issues, as applicable.
     - Describe the PI's background and expertise in conducting large-scale clinical trials.
     - Describe the preliminary management plan for the clinical trial, including key participants and their contributions (additional information on collaborators can be included in the Biographical Sketch section, C.3., below).
     - Provide a preliminary estimate of sample size for the future clinical trial, a preliminary recruitment/accrual plan
     - Provide evidence of access to an appropriate ill Gulf War veteran patient population.

- Describe plans to develop data collection/monitoring plans, a data analysis plan, and other data collection tools.
- If applicable, provide evidence that drug product is available in sufficient quantity under current Good Manufacturing Practice production. Describe plans for carrying out the FDA IND application process, including tentative milestones, if applicable.
- Describe how other preparatory activities will be accomplished.

- **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 (five-citation limit): List the references cited (including URLs if available) in the project narrative using a standard reference format that includes the full citation (i.e. author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
  - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project, and any additional facilities or equipment proposed for acquisition at no cost to the US Army Medical Research and Materiel Command (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 to the PI for the future clinical trial.
- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  The technical abstract is used by all reviewers; however, programmatic reviewers do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects.

  Use the outline below.
  - Present the background and rationale behind the future clinical trial.
  - Describe the intervention and state the objectives of the future clinical trial.
  - Provide an overview of activities to be undertaken during the award period as described in the Project Narrative.

- Summarize briefly how the proposed project will have an impact on ill Gulf War veterans.

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

  Do not duplicate the technical abstract. The public abstract is used by consumer peer reviewers along with other components of the application package.

  - Describe the rationale and objectives of the future clinical trial in a manner that will be readily understood by readers without scientific or medical backgrounds.
  - 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 is the projected time it may take to achieve a patient-related outcome?
    - What are the likely contributions of this study in advancing treatment for Gulf War Illness?

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

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

  State how the future clinical trial will, if successful, impact the goal of improving the health and lives of veterans with GWI.

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

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

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

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

D. Submission Dates and Times

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

E. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Organizations are required to provide a Data Universal Number System (DUNS) number and register with the Central Contractor Registry (CCR) to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General, US Army Medical Research and Materiel Command (USAMRMC), based on technical merit, the relevance to the mission of the Department of Defense (DOD) and CDMRP, and the specific intent of the award mechanism. The highest scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. 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. Application Review Criteria

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

- **Potential Clinical Impact**
    - How the anticipated results of the future clinical trial, if successful, will impact the goal of improving the health and lives of veterans with GWI.
- **Scientific Rationale and Feasibility**
    - How appropriate are the background, rationale and objectives behind the future clinical trial and the intervention, drug, or device to be tested.
    - How appropriate are plans to develop the clinical protocol and finalize the experimental design.
    - How appropriate is the preliminary management plan for the future clinical trial.
    - How appropriate are plans to develop data collection/monitoring plans, the data analysis plan and other data collection tools.
    - How appropriate are plans to accomplish other preparatory activities, including investigation of potential intellectual and material property issues, as applicable.
- **Intervention**
    - If applicable, how appropriate is evidence of the availability of drug product in sufficient quantity under current Good Manufacturing Practice production.
    - If applicable, how appropriate are plans for carrying out the FDA IND/IDE application process.
- **Patient Recruitment and Accrual**
    - Whether a published case definition of Gulf War Illness is provided for use in the future clinical trial.
    - How appropriate are the estimated sample size and proposed recruitment/ accrual plan.
    - Whether the PI provided evidence of access to an appropriate ill Gulf War veteran patient population.
- **Personnel**
    - How the PI's background and expertise are appropriate to accomplish the current work and future trial.
    - How appropriate are plans for developing the research team and any proposed research resource or professional collaborations, and plans for training team members, as applicable.

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

- **Environment**
    - Whether there is evidence of institutional support demonstrated for the future clinical trial.
- **Budget**

- Whether the budget is appropriate for the proposed activities and is within the limitations of this Program Announcement/Funding Opportunity.

- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

2. **Programmatic Review:** To determine the application's relevance to the mission of the DOD and CDMRP, as well as to make funding recommendations, the following equally considered criteria are used by programmatic:

- Ratings and evaluations of the peer reviewers
- Programmatic relevance
- Relative impact
- Program portfolio balance
- Adherence to the intent of the award mechanism

C. Recipient Qualification

Refer to the General Application Instructions, Appendix 1, for additional information on organization and Government agency requirements.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive notification of the funding recommendation. PIs will receive a scientific peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from CDMRP eReceipt or 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.

- Pre-application was not submitted.

B. Modification

- 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 IV.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:

- FY11 GWIRP Integration Panel (IP) member is found to be involved in the preapplication or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY11 GWIRP IP members may be found at http://cdmrp.army.mil/gwirp/panels/panels11.
- 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 Research and Related Budget form exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs with the exception of links to published references.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- PI does not meet the eligibility criteria
- The proposed study is or contains a clinical trial or preclinical research.

D. Withhold

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

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2012. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

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

C. Reporting

Refer to the General Application Instructions, Appendix 4, Section D, for general information on reporting requirements. Technical progress reports will be required every six months.

D. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section E, for general information on organization or PI changes.

Transfer of a CTDA to a different PI or institution is discouraged. A change in PI or institution will only be allowed under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the USAMRAA Contracting/Grants Officer.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

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

Phone: 1-301-682-5507

Email: help@cdmrp.org

B. Grants.gov Contact Center

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

Phone: 1-800-518-4726

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.

VII. 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.	
	Leave Attachment 3 blank.	
	Leave Attachment 4 blank.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Impact Statement (Impact.pdf) as Attachment 6.	
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.	
Research & Related Budget	Complete form as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.	