

Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Gulf War Illness Research Program

Investigator-Initiated Research Award

Funding Opportunity Number: W81XWH-09-GWIRP-IIRA

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Objectives

The Gulf War Illness Research Program (GWIRP) was established in fiscal year 1994 (FY94) to study the health effects of deployment to the 1990-1991 Persian Gulf War on US warfighters.. Appropriations for the GWIRP from FY94 through FY08 totaled \$227.2 million (M). The FY09 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 1990-1991 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 or studies to understand the underlying pathobiology of GWI. The GWIRP encourages risk-taking research; however, all projects must demonstrate solid judgment and sound rationale.

B. Award Description

The GWIRP Investigator-Initiated Research Award (IIRA) mechanism was first offered in FY06. Since that time, 35 IIRA applications have been received, and 15 have been recommended for funding.

The Investigator-Initiated Research Award supports research focusing on the complex of symptoms known as Gulf War Illness, improving its diagnosis, and better understanding its pathobiology. It is intended to encourage basic or clinical developmental research aimed at identification of objective measures to distinguish ill from healthy veterans (e.g., biomarkers), or elucidate potential treatment targets for GWI. Studies that characterize chronic effects of neurotoxic exposures encountered during the Gulf War (and at comparable dosage) are also acceptable.

The GWIRP also seeks proposals that can contribute to improved diagnostic testing for GWI and/or improved understanding of its pathobiology. Particular areas of interest include research on objective indicators of biological processes or abnormalities in GWI associated with:

- Central nervous system structure and function
- Central neuroinflammatory processes
- Neuroendocrine measures
- Autonomic nervous system function
- Immune parameters
- Indicators of chronic infection
- Gastrointestinal complaints/symptoms
- Genetic, genomic, proteomic, or metabolic characteristics

The Investigator-Initiated Research Award is designed to promote new ideas in Gulf War Illness research. Proposals are not required to include preliminary data; however, preliminary data may be used to support the objectives of a proposal. This data does not necessarily have to come from the GWI research field. Proposals not supported by preliminary data should be based on a sound scientific rationale and may reflect clinical observations or seek to evaluate in GWI discoveries made in relation to other chronic multi-symptom illnesses. Using either approach, however, the focus should be clearly on ill Gulf War veterans.

It is the responsibility of the PI to clearly and explicitly articulate the project's potential impact on GWI.

Clinical trials are not allowed under this mechanism. Principal Investigators (PIs) wishing to apply for funding for a clinical trial should utilize either the Innovative Treatment Evaluation Award or the Clinical Trial Award mechanisms (for information about those mechanisms, see <http://cdmrp.army.mil>). Refer to the Application Instructions and General Information, Appendix 6, for helpful information about distinguishing clinical trials and clinical research. Retrospective studies or other non-interventional designs are acceptable under this IIRA award mechanism.

Studies whose principal focus is on psychiatric disease or psychological stress as the primary cause of GWI will not be funded under this Program Announcement/Funding Opportunity.

While Gulf War veterans are affected by Amyotrophic Lateral Sclerosis (ALS, or Lou Gehrig's disease), at twice the rate of veterans who did not serve in the Gulf War, the GWIRP will not accept proposals focusing on ALS research. The CDMRP is offering a separate ALS Research Program in FY 09 (see <http://cdmrp.army.mil>).

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 multisymptom conditions (pp. 285-287). The report can be found online at: <http://www1.va.gov/RAC-GWVI/>.

Use of Human Subjects and Human Biological Substances: All Department of Defense (DOD)-funded research involving human subjects and human biological substances must be reviewed and approved by the 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. Refer to Application Instructions and General Information, Appendix 6, for detailed information. **Proposals that include clinical research involving GW veterans must clearly indicate how this population and/or data from GW veterans will be accessed.**

C. Eligibility

Independent investigators at all academic levels (or equivalent) are eligible to submit proposals. Refer to the Application Instructions and General Information, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is 3 years.
- The maximum allowable funding for the entire period of performance is **\$600,000** in direct costs.
- More cost-effective studies that do not request the full available funding amount are encouraged. The applicant may also request the entire maximum direct cost amount for a project that may be less than the maximum 3-year period of performance.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum direct cost. In addition to the direct costs, indirect costs may be proposed in accordance with the institution's negotiated rate agreement.

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

- Salary
- Research supplies
- Equipment
- Clinical costs (No clinical trials allowed)
- Travel between collaborating institutions
- Travel to scientific/technical meetings, including travel to the next CDMRP Military Health Research Forum (MHRF)

The Office of the Congressionally Directed Medical Research Programs (CDMRP) expects to allot approximately \$2.88M of the \$8M FY09 GWIRP appropriation to fund approximately three IIRA applications, depending on the quality and number received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent on the availability of Federal funds for this program.

E. Award Administration

Refer to the Application Instructions and General Information, Appendix 5, for general award administration information.

II. TIMELINE FOR SUBMISSION AND REVIEW

Proposal submission is a two-step process consisting of (1) pre-application submission and (2) application submission.

Pre-application Submission Deadline:	June 17, 2009, 5:00 p.m. Eastern Time
Invitations to Submit Full Proposals Sent:	July 29, 2009
Application Submission Deadline:	September 9, 2009, 11:59 p.m. Eastern Time
Scientific Peer Review:	October 2009
Programmatic Review:	January 2010

Awards will be made approximately 4 to 6 months after receiving a funding notification letter, but no later than September 30, 2010.

III. SUBMISSION PROCESS

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

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

The Government reserves the right to reject duplicative applications submitted to different award mechanisms within the same program or to other CDMRP programs.

A. Step 1 – Pre-Application Components and Submission

Pre-application submission is the required first step. The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the [CDMRP eReceipt system](https://cdmrp.org/) by **5:00 p.m. Eastern time (ET) on the deadline date**. Refer to the Application Instructions and General Information for detailed information.

- Proposal Information
- Proposal Contacts
- Collaborators and Conflicts of Interest (COI)

- **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 objectives and specific aims.
 - **Impact:** State explicitly how the proposed work will have an impact on accelerating the movement of a promising discovery for GWI into clinical application.

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.

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 described research focuses specifically on ill Gulf War veterans. How the rationale will advance GWI research.
- **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 study will improve the diagnosis of GWI or help the research community better understand its pathobiology.

B. Step 2 – Application Components and Submission

Application submissions will not be accepted unless the PI has been invited. Do not submit an application unless a letter of invitation has been received. Applications must be submitted electronically by the Authorized Organizational Representative (AOR) through Grants.gov (www.grants.gov).

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

The package includes:

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

2. Attachments Form

- **Attachment 1: Project Narrative (12-page limit)**

Describe the proposed project in detail using the outline below. The project narrative must include preliminary data that is relevant to Gulf War Illness and the proposed project.

- **Background:** Present the ideas and reasoning behind the proposed work. Cite relevant literature. Describe previous experience most pertinent to this project.
- **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
- **Specific Aims:** Concisely explain the project's specific aims to be funded by this application. If the proposed work is part of a larger study, present only tasks that the Department of Defense award would fund.
- **Research Strategy:** Describe the study design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. If human subjects or human biological samples will be used, include a description of the method by which Gulf War Illness cases (and targeted subgroups, if applicable) will be defined. Also include a detailed plan for the recruitment of subjects or the acquisition of samples. Specifically demonstrate plans to access veterans and/or obtain personal data on veterans. Describe the statistical plan if appropriate for the research proposed. *This award may not be used to conduct clinical trials.*

- **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)

If the PI is a practicing clinician, the institution must clearly demonstrate a commitment to the clinician's research.

- Letters of Collaboration (if applicable, two-page limit per letter)

If applying for the higher level of funding, the collaborator(s) must provide a letter of collaboration describing his/her involvement in the proposed work. It

should be clear that the success of the project depends on the unique skills and contributions of each collaborator.

- Intellectual and Material Property Plan (if applicable)
- Show approved access to GW veterans, if proposing to access the veteran population or use data from veterans (e.g., Defense Manpower Data Center Data Request System, collaborating investigators from the Veterans Administration, etc.) (if applicable).
- **Attachment 3: Technical Abstract (one-page limit)**
- **Attachment 4: Public Abstract (one-page limit)**
- **Attachment 5: Statement of Work (SOW, three-page limit)**
- **Attachment 6: Detailed Budget and Justification**
- **Attachment 7: Impact Statement (one-page limit)**

Explain how the expected results of the study will make an original and important contribution to the goal of advancing Gulf War Illness research and its impact on patient care. Describe the potential clinical applications, benefits, and risks.

- **Attachment 8: 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 9: Federal Agency Financial Plan (if applicable)**
- **Attachments 10-15: Subaward Detailed Budget and Justification (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 Project/Performance Site Location(s) Form

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 submissions to each other and recommends proposals for funding based on scientific merit, overall goals of the program, and the specific intent of the award mechanism. 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 programmatic review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each tier 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. Institutional personnel and PIs are prohibited from contacting persons involved in the application 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 institution's application. Violations by panelists or PIs that compromise the confidentiality of the peer review and programmatic review processes may also result in suspension or debarment of their employing institutions 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).

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

B. Review Criteria

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

- **Research Strategy and Feasibility**
 - How well the preliminary data, if provided, and/or scientific rationale supports the research project.
 - How well the hypotheses or objectives, aims, study design, methods, and analyses are developed and integrated into the project.
 - In studies involving human subjects or biological samples, how clearly and appropriately GWI cases (and any targeted illness subgroups) are defined.
 - How well the PI acknowledges potential problems and addresses alternative approaches.

- **Impact**
 - How the project addresses a critical problem in Gulf War Illness research.
 - How the project makes an original and important contribution to the goal of advancing research, diagnosis, pathobiology of or identifying potential treatment targets for Gulf War Illness or on the quality of life of veterans affected by the disease.
- **Personnel**
 - The appropriateness of the levels of effort by the PI and other key personnel to ensure success of the project.
 - How the PI's record of accomplishment demonstrates his/her ability to accomplish the proposed work.

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

- **Environment**
 - How the scientific environment is appropriate for the proposed research.
 - How the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
 - How the quality and extent of institutional support are appropriate for the proposed research.
- **Budget**
 - Whether the budget is appropriate for the proposed research and within the limitations of the award mechanism.
- **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 that maintain the program's broad portfolio:

- Ratings and evaluations of the peer reviewers,
- Program portfolio balance,
- Programmatic relevance,
- Relative impact, 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 Integration Panel (IP) members and recommended for funding to the Commanding General, US Army Medical Research and Materiel Command. The highest scoring applications from the first tier of review are not automatically recommended for funding. All applications are

carefully considered to ensure that the funds available are allocated to those proposals that best fulfill the goals, objectives, and areas of encouragement of the program.

V. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eReceipt or applications from Grants.gov, the following administrative actions may occur.

A. Rejection

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

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

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 for all documents other than the Project Narrative.
- Documents not requested will be removed.
- **NEW for FY09:** Following the application deadline, the applicant may be contacted by email from CDMRP with a request to provide certain missing supporting documents (excluding those listed directly above in Section A, Rejection). The missing documents must be provided by 5:00pm Eastern Time on the second full business day following the date the e-mail was sent. Otherwise, the application will be peer reviewed without the missing documents.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- FY09 IP member(s) is found to be involved in the pre-application 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 FY09 IP members may be found at <http://cdmrp.army.mil/gwirp/panel09.htm>.
- Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs.
- The application does not conform to this funding opportunity description to an extent that precludes appropriate scientific peer and programmatic review.

- Direct costs as shown on the detailed budget form exceed the maximum allowed by the award mechanism.
- Inclusion of URLs, with the exception of links to published references.

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 USAMRAA Contracting/Grants Officer for a determination of the final disposition of the application.

VI. CONTACT INFORMATION

A. Program Announcement/Funding Opportunity, application format, or required documentation: To view all funding opportunities offered by the 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

B. 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. ET.

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

C. Grants.gov contacts: Questions related to application submission through the [Grants.gov](http://www.grants.gov/) (<http://www.grants.gov/>) portal should be directed to the Grants.gov help desk, which is available Monday through Friday, 7:00 a.m. to 9:00 p.m. ET. Deadlines for application submission are 11:59 p.m. ET on the deadline date. Please note that the CDMRP help desk is unable to answer questions about Grants.gov submissions.

Phone: 800-518-4726
Email: support@grants.gov

Grants.gov will notify PIs of changes made to this Program Announcement/Funding Opportunity and/or application package ONLY if the PI subscribes to the mailing list by clicking on the “send me change notification emails” link 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.