Program Announcement

for the

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Congressionally Directed Medical Research Programs

Gulf War Illness Research Program

New Investigator Award

Funding Opportunity Number: W81XWH-14-GWIRP-NIA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), September 11, 2014
- **Application Submission Deadline:** 11:59 p.m. ET, September 25, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, September 30, 2014
- **Peer Review:** November 2014
- **Programmatic Review:** January 2015

<u>*Change for Fiscal Year 2014*</u>*: The CDMRP eReceipt System has been replaced with the electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.*

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

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I.   FUNDING OPPORTUNITY DESCRIPTION

A.   Program Description

Applications to the Fiscal Year 2014 (FY14) Gulf War Illness Research Program (GWIRP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The GWIRP was initiated in 2006 to provide support for research of exceptional scientific merit to study the health effects of deployment to the 1990-1991 Persian Gulf War on U.S. warfighters. Appropriations for the GWIRP from FY06 through FY13 totaled $69 million (M). The FY14 appropriation is $20M.

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, sleep problems, 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 33% (or 175,000 to 210,000) of Gulf War veterans continue to experience symptoms associated with their deployment as described above.

The GWIRP will focus its FY14 funding on innovative projects that have the potential to make a significant impact on finding treatments for GWI. While such projects may include identification of objective indicators of pathology that distinguish ill from healthy Gulf War veterans or studies to understand the underlying pathobiology of GWI, the FY14 GWIRP intends to focus on supporting research projects that exhibit clear translational potential to lead to treatments for veterans with GWI. The GWIRP encourages high-risk/high-reward research; however, all projects must demonstrate solid judgment and sound rationale.

B.   Award Information

The New Investigator Award (NIA) mechanism is being offered by the GWIRP for the first time in FY14.

The intent of the GWIRP NIA is to support investigators new to the field of GWI research at different stages of career development. This award enables such investigators to compete for funding separately from investigators with established programs of GWI research. Previous experience in GWI research is allowed, but not required. However, Principal Investigators (PIs) with a limited background in GWI research are strongly encouraged to strengthen their applications through collaboration with investigators who are experienced in GWI research and/or possess other relevant expertise. It is the PI's responsibility to describe how the collaboration(s) will augment his or her ability to address the research question.

All applicants for the NIA must meet specific eligibility criteria under one of the following categories, as described in Section I.C., Eligibility Information.

- Transitioning Postdoctoral Fellow
- Early-Career Investigator
- New GWI Researcher

The NIA is designed to promote new ideas in GWI research and establish proof-of-principle for further development in future studies. Applications are not required to include preliminary data; however, preliminary data may be used to support the objectives of an application. These data are not required to have come from the GWI research field. Applications not supported by preliminary data should be based on sound scientific rationale and may reflect clinical observations or seek to evaluate discoveries made in relation to other chronic multi-symptom illnesses for their application in GWI. Regardless of the approach, the focus should be clearly on veterans with GWI. It is the responsibility of the PI to clearly and explicitly articulate the project's potential impact on GWI.

The NIA supports research focusing on the complex of symptoms known as GWI, improving the case definition and diagnosis of GWI, characterizing disease symptoms, and better understanding the pathobiology. The NIA encourages basic through clinical research aimed at identification of objective measures (e.g., biomarkers) to distinguish healthy veterans from those with GWI, or improve understanding of the pathobiology underlying symptoms associated with GWI. Particular topic areas of interest include biological processes or abnormalities in GWI associated with:

- Central nervous system structure and function, in particular, the role of glial cells, astrocytes, and microglia in GWI symptomatology
- Central neuroinflammatory processes
- Autonomic nervous system function
- Neuroendocrine measures
- Immune parameters/Indicators of chronic infection
- Gastrointestinal complaints/symptoms
- Genetic, genomic, proteomic, or metabolic characteristics
- Respiratory symptoms
- Sexual dysfunction
- Sleep problems

Applications may also address other topic areas that are directly relevant to GWI.

Studies that characterize chronic effects of neurotoxic exposures at dosages comparable to that encountered in-theatre during the Gulf War are of interest. Studies using animal models should focus on long-term and latent effects of toxic exposures to closely represent the current status of GWI patients. All studies using animal models should use an established model unless there is a

compelling scientific justification for the development or use of a new model. Development of new animal models is discouraged.

The NIA can also be used for testing of GWI-targeted pharmacologic agents in Adsorption, Distribution, Metabolism, Excretion (ADME) studies, and toxicology testing, including Investigational New Drug (IND)-enabling pharmacology/toxicology testing. Preclinical development of non-pharmacological interventions is also acceptable.

All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in Landis, S.C. et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nature* 2012, 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies. Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at http://www.nc3rs.org.uk/page.asp?id=1357.

Use of Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local Institutional Review Board (IRB) of record. Local IRB approval at the time of submission is *not* required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for additional information. *Applications that include clinical research involving Gulf War veterans must clearly indicate how this population and/or data from Gulf War veterans will be accessed.* Applicants proposing clinical research are encouraged to collaborate with an investigator who has demonstrated access to Gulf War veterans, particularly investigators within the U.S. Department of Veterans Affairs, to ensure access to Gulf War veteran populations, as applicable to the proposed project.

Applicants proposing clinical research 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 2014 report of the Research Advisory Committee on Gulf War Veterans' Illnesses, *Gulf War Illness and the Health of Gulf War Veterans: Research Update and Recommendations, 2009-2013*, provides information on GWI, including case definitions and research on epidemiology, etiology, pathobiology, and treatment. The 2014 report can be found online at http://www.bu.edu/sph/files/2014/04/RAC2014.pdf. In addition, the pre-publication report (available online at http://www.iom.edu/Reports/2014/Chronic-Multisymptom-Illness-in-Gulf-War-Veterans-Case-Definitions-Reexamined.aspx) released by the Institute of Medicine includes recommendations for a consensus case definition.

Research involving human subjects is permitted under this funding opportunity but is restricted to studies <u>without</u> clinical trials. A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. For more information on clinical research, see Human Subject Resource Document at https://cdmrp.org/Program_Announcements_and_Forms/.

PIs interested in applying 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/gwirp). Retrospective studies or other non-interventional studies are acceptable under the NIA.

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, also called Lou Gehrig's disease) at twice the rate of veterans who did not serve in the Gulf War, the GWIRP will not accept applications focusing on ALS research. However, applications that focus on GWI symptomatology may include Gulf War veterans with ALS if the latter disorder is included in the study's GWI case definition. [For those interested in pursuing ALS-focused studies, the office of the Congressionally Directed Medical Research Programs (CDMRP) has a separate ALS Research Program (see http://cdmrp.army.mil/alsrp].

The Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section L.

C.   Eligibility Information

- PIs may apply under one of the following three eligibility categories:
  - Transitioning Postdoctoral Fellow: Current senior postdoctoral fellows who have completed at least 3 years of postdoctoral training;
  - Early Career Investigator: Independent investigators who are within 5 years of their last training position;
  - New GWI Researcher: Established independent investigators at all academic levels (or equivalent) who have received less than $300,000 in federally funded, non-mentored funding for GWI research.
- In addition, all PIs must:
  - Be able to demonstrate the freedom to pursue independent research goals without formal mentorship;

- ○ Not have received a New Investigator Award or similar career development award from any program within the CDMRP.

- Graduate students and junior postdoctoral fellows (i.e., with less than 3 years of postdoctoral training) are not eligible for this award.

- Cost sharing/matching is not an eligibility requirement.

- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations.

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

D.   Funding

- The maximum period of performance is **3** years.

- The maximum allowable direct costs for the entire period of performance are **$500,000** 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 request the entire maximum funding amount for a project that may have a period of performance less than the maximum **3** years.

- Regardless of the period of performance proposed, 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.4., for budget regulations and instructions for the Research & Related Budget. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

For this award mechanism, direct costs:

Must be requested for:

- Travel costs for the PI(s) to disseminate project results at one DoD military-relevant meeting. Costs associated with travel to this meeting, up to $1,800, should be included in Year 2 of the budget. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary

- Research-related subject costs

- Clinical research costs

- Publication costs
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings in addition to the required meeting described above

Intramural (DoD), other federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. *In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.*

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from federal agencies submit applications, they must submit through Grants.gov. Therefore, federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other federal agencies will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Direct transfer of funds from the recipient to a federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4. Research & Related Budget, for additional information on budget considerations for applications involving federal agencies.

The CDMRP expects to allot approximately $1.5M of the $20M FY14 GWIRP appropriation to fund approximately two New Investigator 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 two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

New for FY14: *The CDMRP has replaced its eReceipt System with eBRAP.* Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at *https://ebrap.org/eBRAP/public/UserGuide.pdf*). Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. *Application viewing, modification, and verification in eBRAP is **strongly** recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.* If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov, provided there is no cause for administrative rejection of the application (see Section IV.A., Rejection).

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application.

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-14-GWIRP-NIA.

B. Pre-Application Submission and Content Form

All pre-application components must be submitted by the PI through eBRAP (https://eBRAP.org/).

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

The pre-application consists of the following components, which are organized in eBRAP 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**
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Collaborators and Conflicts of Interest – Tab 3**

  FY14 GWIRP Integration Panel (IP) members should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP at help@eBRAP.org or 301-682-5507.

- **Required Files – Tab 4**

  Letter of Intent (LOI) (one-page limit): Provide a brief description of the research to be conducted. State which topic area directly relevant to GWI will be addressed. 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**

  This tab must be completed for the pre-application to be accepted and processed.

C. Application Submission Content and Forms

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 through the Grants.gov portal (http://www.grants.gov/).

New for FY14: *Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification.* The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a "Changed/Corrected Application" with the Previous Grants.gov Tracking ID *prior to the application submission deadline (which occurs earlier than the end of the application verification period).*

Grants.gov application package components: For the New Investigator 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 (10-page limit):** Upload as "ProjectNarrative.pdf." The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical

structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and will result in administrative withdrawal of the application.

Describe the proposed project in detail using the outline below. The Project Narrative may include preliminary data relevant to GWI and the proposed project, but these data are not required to have come from GWI research. Applications not supported by preliminary data should be based on sound scientific rationale and may reflect clinical observations or seek to evaluate discoveries made in relation to other chronic multi-symptom illnesses for their application in GWI.

- ○ **Background:** State which topic area directly relevant to GWI will be addressed. Present the ideas and reasoning behind the proposed work. Cite relevant literature. Describe previous research findings most pertinent to this project. Preliminary data are allowed, but not required.

- ○ **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 this award will 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 applicable, state which established GWI animal model will be used. If development of a new GWI animal model is proposed, present a clear justification for how it is necessary to support the proposed research. If clinical research is proposed, explain which published case definition of GWI will be used and how GWI cases, including any targeted illness subgroups, will be defined for the study. Include a detailed plan for the recruitment of subjects or the acquisition of samples and/or data. Specifically demonstrate plans to access veterans and or obtain personal data on veterans. Describe the statistical analysis plan in detail as appropriate for the proposed research. Address potential problem areas and present alternative methods and approaches.

- ○ **Collaboration(s) (encouraged but not required):** Describe the specific contributions of the established GWI researcher collaborator(s) to the research project.

This award may not be used to conduct clinical trials, research focused on ALS, or studies whose principal focus is on psychiatric disease or psychological stress as the primary cause of GWI.

- • **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. *There are no page limits for any of these components unless otherwise noted. Include only*

***those components described below; inclusion of items not requested may result in
the removal of those items or administrative withdrawal of the application.***

- ○ References Cited: 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 award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award 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 a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.

- ○ Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project.

- ○ Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.

  - – ***For Transitioning Postdoctoral Fellows:*** If the PI is likely to change organizations during the award period of performance (e.g., investigators transitioning into their first independent faculty position), describe how any proposed collaborations will be maintained.

- ○ Intellectual Property

  - – Background and Proprietary Information: All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.

  - – Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- *For Transitioning Postdoctoral Fellows only:* Provide transcripts from all graduate institutions attended. All foreign-language transcripts must be accompanied by a certified English translation. The Government reserves the right to request official transcripts during award negotiations. Diplomas are not acceptable in lieu of academic transcripts. If an institution does not provide academic transcripts (i.e., a record of courses completed, grades and credit hours earned, and indication of completion of degree), complete and include the Academic Statement (available for download on the Full Announcement page in Grants.gov) in place of the transcript.

- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section L for more information about the CDMRP expectations for making data and research resources publicly available.

- Access to Gulf War veterans or veteran data (if applicable): Provide a letter showing approved access to Gulf War veterans if proposing to access the veteran population or use data from veterans (e.g., collaborating investigators from the Department of Veterans Affairs, Defense Manpower Data Center Data Request System, etc.). PIs whose applications will require obtaining and/or using veterans data from VA or military databases should confirm the ability to meet database requirements prior to application submission. A letter of support, signed by the lowest ranking person with approval authority, should be included for studies involving veterans, VA- or military-controlled study materials, and/or VA or military databases.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

The technical abstract is used by all reviewers. Of particular importance, programmatic reviewers typically do not have access to the full application and therefore rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

Use the outline below.

- **Background:** State which topic area directly relevant to GWI will be addressed. Present the ideas and reasoning behind the proposed work.

- **Objective/Hypothesis:** State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.

- **Specific Aims:** State the specific aims of the study.

- **Study Design:** Briefly describe the study design including appropriate controls.

- **Impact:** Summarize briefly how the proposed project will have an impact on GWI research and/or veterans with GWI.

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

  Lay abstracts should be written using the outline below. ***Do not duplicate the technical abstract.*** Minimize use of acronyms and abbreviations, where appropriate. The lay abstract is an important component of the application review process because it addresses issues of particular interest to the consumer advocate community.

  - Describe the scientific objective and rationale for the proposed project 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 the field of GWI research?

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

  The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Program Announcement and Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the NIA mechanism, use the SOW format example titled "SOW for Basic Research." The SOW must be in PDF format prior to attaching.

  The GWIRP strongly encourages timely dissemination of the results of GWIRP-sponsored research as a product of the research program. Timely dissemination is critical to improvement of the lives of veterans with GWI, the advancement of the field, and the continued success of the program. Therefore, SOWs submitted to the GWIRP must include at least one Task or Aim focused on preparation and submission of publications. This Task or Aim must be scheduled to commence at least six months prior to the end of the performance period of the award.

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

  Explain how the project addresses a critical problem in GWI. Describe how the outcomes of the project will advance the GWI field, such as improving the definition and diagnosis of GWI, elucidating potential targets for treatments, or increasing the understanding of GWI pathobiology. Describe how the project has the potential to lead to improved health or quality of life for veterans with GWI.

- **Attachment 7: Animal Research Plan (if applicable, one page limit per animal study):** Upload as "Animal.pdf."

  When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should

not submit a verbatim replica of the protocol(s) to be submitted to the Institutional Animal Care and Use Committee (IACUC) as the Animal Research Plan. The Animal Research Plan should address the following points for each proposed animal study:

- ○ Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.

- ○ Summarize the procedures to be conducted. Describe how the study will be controlled.

- ○ Describe the randomization and blinding procedures for the study, and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.

- ○ Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.

- ○ Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, statistical methods for data analysis, and identification of the primary endpoint(s).

- **Attachment 8: Use of Hazardous Chemical or Biological Agents (if applicable) (no page limit):** Upload as "Hazardous.pdf."

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 registration, an approved organizational safety plan to use the agent(s), and letters of collaboration, agreement, or approval from government sites issuing any agent(s). Indicate 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: Eligibility Statement (one-page limit):** Upload as "Eligibility.pdf."

Use the Eligibility Statement template (available for download on the Full Announcement page at www.Grants.gov) signed by the Department Chair, Dean, or equivalent official to verify that the eligibility requirements will be met at the application submission deadline.

- **Attachment 10: *(Required only for investigators not yet in an independent faculty position)*: Statement of Independence (one-page limit*): Upload as "Independence.pdf."

For investigators not yet in an independent faculty position, complete and sign the Statement of Independence template (available for download on the Full

Announcement page at www.Grants.gov). The Statement of Independence must also be signed by the investigator's current mentor/supervisor

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information. Note: Some of the items in this attachment may be made available for programmatic review.

- PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."

- PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

- Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
  - Include biographical sketches of collaborators experienced in GWI research if applicable.

- Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
  - Include information for collaborators experienced in GWI research if applicable.

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., 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.5., for detailed information.

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

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP

validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. ***The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.***

E.   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 either of these deadlines will result in application rejection.

F.   Other Submission Requirements

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

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an "Active" status 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 applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Office of the Assistant Secretary of Defense, Health Affairs, based on (a) technical merit and (b) the relevance to the mission of the DHP and GWIRP and to 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 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. Panel members sign a non-disclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations 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 panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

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

- **Research Strategy and Feasibility**
  - How well the hypotheses or objectives, aims, study design, methods, analyses and statistical plan are developed and integrated into the project.
  - How well the preliminary data, if provided, and/or scientific rationale support(s) the research project.
  - How well the PI identifies potential problems and addresses alternative approaches.
  - For clinical research, whether a published case definition for GWI was included in the application.
  - For studies involving animal models:
    - How clearly the study (or studies) is representative of the current status of ill Gulf War veterans in terms of choice of model and the endpoints/outcome measures to be used
    - How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.
  - For studies proposing a new animal model, to what extent the unique features of this model are required in order to conduct the proposed research.
  - For studies involving hazardous agents, whether the application includes an appropriate plan for acquiring, using, and maintaining the hazardous agents.

- **Impact**
  - How well the project addresses a critical problem in GWI.
  - To what extent the anticipated outcomes of the project will make an original and important contribution to the goal of advancing the GWI field, improving the definition and diagnosis of GWI, elucidating potential targets for treatments, or increasing the understanding of GWI pathobiology.
  - To what extent the proposed project has the potential to lead to an improved health or quality of life for veterans with GWI.

- **Personnel**
  - How well the PI's record of accomplishment demonstrates his/her potential for contributing to the field of Gulf War Illness research and completing the proposed work.
  - If applicable, how well the proposed contributions of collaborators will complement the New Investigator's ability to perform the proposed work.

- ○ Whether the levels of effort by the PI and other key personnel are appropriate to ensure success of the project.

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

- **Environment**
  - ○ If applicable, to what degree the intellectual and material property plan is appropriate.
  - ○ To what extent the scientific environment is appropriate for the proposed research.
  - ○ How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
  - ○ Whether the quality and extent of organizational support are appropriate for the proposed research.
- **Budget**
  - ○ Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - ○ To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations, the following equally considered criteria are used by programmatic reviewers:

a. **Ratings and evaluations of the peer reviewers**

b. **Relevance to the mission of the DHP and FY14 GWIRP, as evidenced by the following:**
   - Adherence to the intent of the award mechanism
   - Program portfolio composition
   - Programmatic relevance
   - Relative impact and innovation

C.   Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

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 email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the application:

- Pre-application was not submitted.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- A FY14 GWIRP Integration Panel (IP) member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. A list of the FY14 GWIRP IP members can be found at http://cdmrp.army.mil/gwirp/panels/panels14.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.

- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.

- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.

- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.

- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.

- The proposed research is or includes a clinical trial.

- The application describes research focusing on ALS. (Applications that focus on GWI symptomatology may include Gulf War veterans with ALS if the latter disorder is included in the study's GWI case definition.)

- The application describes research whose principal focus is on psychiatric disease or psychological stress as the primary cause of GWI.

- The PI does not meet the eligibility criteria as described in this Program Announcement/Funding Opportunity.

D.   Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the USAMRAA 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, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B.   Administrative Requirements

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

C.   National Policy Requirements

Refer to the General Application Instructions, Appendix 5 for general information regarding national policy requirements.

D. Reporting

Refer to the General Application Instructions, Appendix 4, Section J, for general information on reporting requirements.

E. Award Transfers

Changes in PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

To assist New Investigators who are transitioning into their first independent faculty position, the submitting organization must agree to relinquish the award when the PI obtains an independent faculty position, or equivalent, at another institution so that it can be transferred to the new institution.

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

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP 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: 301-682-5507
>
> Email: help@eBRAP.org

B. Grants.gov Contact Center

Questions related to application submission through 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: 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 or by responding to the prompt provided by Grants.gov when first downloading the application package. 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	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	Animal Research Plan (if applicable): Upload as Attachment 7 with file name "Animal.pdf."	
	Use of Hazardous Chemical or Biological Agents (if applicable): Upload as Attachment 8 with file name "Hazardous.pdf."	
	Eligibility Statement: Upload as Attachment 9 with file name "Eligibility.pdf."	
	Statement of Independence (for Transitioning Postdoctoral Fellows only): Upload as Attachment 10 with file name "Independence.pdf."	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Previous/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 Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete 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.	