

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 Clinical Trial Award

Funding Opportunity Number: W81XWH-14-GWIRP-CTA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), July 1, 2014
- **Invitation to Submit an Application:** August 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

Change for Fiscal Year 2014: *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 30% (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 these may take the form of 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 FY14 GWIRP is offering two award mechanisms to evaluate potential interventions for GWI: the Clinical Trial Award (CTA) and the Innovative Treatment Evaluation Award (ITEA).

The CTA, described in this Program Announcement/Funding Opportunity, is intended to support larger, more definitive (Phase II-III, FDA device class I-III) clinical trials. In contrast, the ITEA supports the initial evaluation of a treatment or intervention in smaller, early phase or pilot clinical trials (Phase 0, I, or I/II), and does not require preliminary data. (For information about the ITEA, see <http://cdmrp.army.mil/funding/gwirp.shtml>.)

The CTA mechanism was first offered in FY08. Since then, 14 Clinical Trial Award applications have been received, and four have been recommended for funding.

The CTA supports execution of clinical trials with the potential to have a significant impact on the health and lives of veterans with GWI. Comparative studies of GWI treatments are allowed.

Health outcomes of interest should include effects of interventions on:

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

Proposed studies may be single-center or multi-center clinical trials. Applications may be submitted by a single PI or by a team of investigators led by an Initiating Principal Investigator (PI) with up to three Partnering PIs.

Multiple PI Option: The FY14 GWIRP supports collaborative projects to bring a new perspective to GWI research and/or facilitate advancement of GWI treatments through synergistic partnerships. Therefore, the FY14 GWIRP is offering a Multiple PI Option for this award mechanism. The Multiple PI Option is structured so that up to four investigators, each of whom will be designated “PI” and receive a separate award, will work synergistically on a single project. One member of the team will be identified as the Initiating PI and will be responsible for the majority of the administrative tasks associated with the application. The other member(s) will be referred to as the Partnering PI(s) (maximum of three). ***All the investigators must collaborate to submit a single project examining one or more treatment modalities or comparing untested or novel treatments for GWI symptoms.*** It should be clear that all investigators have an equal level of intellectual input and effort. The Initiating PI should have demonstrated expertise in GWI research, while the Partnering PIs may contribute expertise from a different field that can be applied to GWI. Multidisciplinary and multi-organizational projects are encouraged. If the project is multi-organizational, applications should include plans for communication between investigators at each organization. Additionally, participating organizations must be willing to resolve potential intellectual and material property issues and to remove any barriers that might interfere with achieving high levels of cooperation to ensure successful completion of the project. Application responsibilities unique to Partnering PIs will be identified in the supporting sections of this Program Announcement.

Applications proposing studies whose principal focus is on the treatment of psychiatric conditions, including post-traumatic stress disorder (PTSD), will be administratively withdrawn and 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 GW 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) offers a separate ALS research program (see <http://cdmrp.army.mil/alsrp>)].

Applications must clearly indicate how GWI cases, including any targeted illness subgroups, will be defined for purposes of the study. ***Applicants 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.

Applications are required to include preliminary data, which does not necessarily have to come from the GWI research field. The proposed research project should also be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature.

If there are no preliminary and/or preclinical data reflecting considerable development of a treatment, the application would not be deemed in keeping with the intent of the CTA. In this case, investigators are encouraged to apply to the GWIRP Innovative Treatment Evaluation Award (<http://cdmrp.army.mil/gwirp/default.shtml>).

Funding from this award mechanism must support a clinical trial and may not be used for preclinical research studies. 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. Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other award mechanisms/funding opportunities being offered. The term "human subjects" is used in this Program Announcement/Funding Opportunity to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at <https://ebrap.org/eBRAP/public/Program.htm>.

If the clinical trial involves the use of a drug that has not been approved by the U.S. Food and Drug Administration (FDA) for the proposed investigational use, evidence that an Investigational New Drug (IND) exemption application that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312) has been submitted or will be submitted to the FDA ***within 60 days of award*** is required. If the investigational product is a device, evidence that an Investigational Device Exemption (IDE) application that meets all requirements under 21 CFR 812 has been submitted or will be submitted to the FDA ***within 60 days of award***, or that the device is exempt from an IDE, is required. The Government reserves the right to withdraw funding if the IND or IDE application has not been submitted to the FDA within 60 days of the Department of Defense (DoD) award date or if the documented status of the IND or IDE has not been obtained within 6 months of the award date.

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

- The proposed clinical trial is expected to begin no later than 12 months after the award date or 18 months for FDA-regulated studies.
- The proposed intervention to be tested should offer significant potential impact for veterans with GWI.
- The application should demonstrate documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate. The quality of the product should be commensurate with FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practices).
- PIs must demonstrate availability of and access to a suitable Gulf War veteran population that will support a meaningful outcome for the study. Discuss how accrual goals will be achieved and how standards of care may impact the study population. PIs are encouraged to collaborate with an investigator who has demonstrated access to a population of Gulf War veterans, particularly investigators within the U.S. Department of Veterans Affairs.
- The proposed research project must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature and ***the application must identify the pathobiological mechanism being targeted.***
- Inclusion of preliminary data relevant to the proposed research project is required.
- The application should describe the planned indication for the product label, if appropriate, and include an outline of the development plan required to support that indication.
- The application should demonstrate documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate. The quality of the product should be commensurate with FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practices).
- The proposed clinical trial design should include clearly defined and appropriate endpoints, and follow Good Clinical Practice (GCP) guidelines, if applicable.
- The application should include a clearly articulated statistical analysis plan, appropriate statistical expertise, and a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- The application should include a clearly articulated data management plan, and use of an appropriate database to safeguard and maintain the integrity of the data.
- The application should include a clearly articulated safety management plan.
- The application should include a clearly articulated clinical monitoring plan, outlining how the study will be monitored for GCP compliance.
- The application should include a study coordinator(s) who will guide the clinical protocol through the local Institutional Review Board (IRB) of record and other

regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.

- The application should include a Transition Plan (including potential funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the GWIRP Clinical Trial Award.
- The application should clearly demonstrate strong institutional support.
- The application should acknowledge the commitment to filing the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov.

Use of Human Subjects and Human Anatomical Substances: All DoD-funded research involving new and ongoing research with human subjects and human anatomical substances 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 IRB of record. Local IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DoD. These laws and directives will require information in addition to that supplied to the IRB. Allow a minimum of 2-3 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for more information.

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

- Independent investigators at any academic level (or equivalent) are eligible to apply as a single PI, Initiating PI, or Partnering PI.
- 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 **4** years.
- The maximum allowable direct costs for the entire period of performance are **\$1,500,000** plus indirect costs for applications submitted by a single PI or for the Initiating PI under the Multiple PI Option.

- **Multiple PI Option:** Up to 3 Partnering PIs may be included in the application. The maximum allowable direct costs for each Partnering PI's application are **\$1,000,000** plus indirect cost. A separate award will be made to each PI's organization.
- 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 **4** 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-related research 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. ***For applications submitted under the Multiple PI Option, travel costs should be requested separately for each of the PIs in their separate budget.***

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 \$5.25M of the \$20M FY14 GWIRP appropriation to fund approximately one Clinical Trial Award application, 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 or may be subject to administrative rejection (see [Section IV.A., Rejection](#)).

Multiple PI Option: This option is structured to accommodate up to four PIs in total. One PI will be identified as the Initiating PI and will be responsible for the majority of the administrative tasks associated with application submission. The other PI(s) will be identified as Partnering PI(s). Initiating and Partnering PIs each have different submission requirements; however, all PIs should contribute significantly to the development of the proposed research project including the Project Narrative, Statement of Work, and other required components. ***The Initiating PI must complete the pre-application submission process and submit the contact information for each Partnering PI.*** Each Partnering PI will then be notified of the pre-application submission separately by email. Each Partnering PI must follow the link in this email and register with eBRAP in order to associate his/her grant application package with that of the Initiating PI. If an application is invited, only the Initiating PI will receive notification of invitation via email from CDMRP. The letter will provide the information necessary to begin application submission through Grants.gov.

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-CTA.

B. Pre-Application Submission and Content Form

All pre-application components must be submitted by the Initiating PI through eBRAP (<https://eBRAP.org/>). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

All 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.

A change in PI or organization after submission of the pre-application will be allowed only at the discretion of the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/ Grants Officer.

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 (COI) – 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 Help Desk at help@eBRAP.org or 301-682-5507.

Multiple PI Option: The Initiating PI must enter the contact information for each Partnering PI in the Partnering PI section. This Program Announcement/Funding Opportunity allows a maximum of three Partnering PIs.

- **Required Files – Tab 4**

Notes: Upload document(s) as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

Preproposal Narrative (three-page limit): The Preproposal Narrative page limit 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 Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

The Preproposal Narrative should include the following:

- **Research Idea:** State the ideas and reasoning on which the proposed intervention is based. Explain the mechanistic rationale of the treatment. Describe how the rationale and preliminary data support the research.
- **Research Strategy:** Concisely state the project's objectives and specific aims. Describe the published case definition of GWI to be used in the proposed project. Clearly specify the intervention to be tested, and indicate the phase of the trial and/or class of device, as appropriate.
- **Impact:** State how the proposed intervention will accelerate the movement of a promising treatment for GWI into clinical application. Describe how the results of the proposed clinical trial will, if successful, positively impact the health and lives of veterans with GWI.
- **Personnel:** Briefly state the qualifications of the PI(s) to perform the described research.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application *must be uploaded as individual documents* and are limited to:

- References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal 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 used in the Preproposal Narrative.
- Key Personnel Biographical Sketches (four-page limit per individual).
 - For applications submitted under the Multiple PI Option, include biographical sketches for the Initiating and Partnering PIs.
- **Submit Pre-Application – Tab 5**

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

Pre-Application Screening

- **Pre-Application Screening Criteria**

To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the GWIRP, pre-applications will be screened based on the following criteria:

- **Research Idea:** How the proposed intervention is based on ideas and reasoning that appropriately support the study. How well the preliminary data and rationale support the research idea.
- **Research Strategy:** How well the specific aims support the research idea. Whether the pre-application described a published case definition of GWI to be used in conducting the trial. Whether the phase of the proposed clinical trial is appropriate for the Clinical Trial Award mechanism.
- **Impact:** How the research describes a potentially effective treatment or intervention for GWI. How the proposed clinical trial, if successful, will positively impact the health and lives of veterans with GWI.
- **Personnel:** How the qualifications of the PI(s) are appropriate to perform the proposed research project.
- **Notification of Pre-Application Screening Results**

Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the [title page](#) of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Forms

Applications will not be accepted unless the (Initiating) PI has received notification of invitation.

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).*

Multiple PI Option: *The CDMRP requires separate Grants.gov application package submissions for the Initiating PI and each Partnering PI, even if the PIs are located within the same organization. Initiating and Partnering PIs will each be assigned unique log numbers by eBRAP. Each Grants.gov application package must be submitted using the unique log number. Note: All associated applications (Initiating and each Partnering PI) must be submitted by the Grants.gov deadline.*

Application Components for Single PIs or for Initiating PIs under the Multiple PI Option

Grants.gov application package components: For the Clinical Trial 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**

The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

- **Attachment 1: Project Narrative (12-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.

- **Background:** Describe in detail the rationale for the study including a description of the pathobiological mechanism being targeted by the proposed intervention. Include a literature review, preliminary studies, and/or preclinical data that led to the development of the proposed clinical trial. The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study for veterans with GWI and explain the applicability of the proposed findings.

If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses.
- **Study Design:** Describe the type of study to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action.
 - Describe the case definition of GWI to be used in the study. Use of a published case definition is required. Any case definition must recognize the multi-symptom nature of GWI.
 - Identify the intervention to be tested and describe the projected outcomes.
 - Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
 - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
 - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
 - If using psychometric measures, describe their reliability and validity.

- Describe potential challenges and alternative strategies where appropriate.
- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study.
- **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. If the PI is a clinician, the organization must clearly demonstrate a commitment to the clinician’s research.
 - Letters of Collaboration (if applicable): 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. If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating

availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.

- 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.
- 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.

- **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.

Technical abstracts should be written using the outline below:

- Background: Present the ideas and reasoning behind the proposed work. Identify the specific pathobiological mechanism being targeted.
- 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.
- Clinical Impact: Briefly describe how the proposed project will have an impact on veterans with GWI including the intervention to be tested, the study population, outcome measures, and appropriate controls.

- **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.

- Clearly 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. Indicate the *pathobiological* mechanism being targeted.
 - Do not duplicate the technical abstract.
- Describe the ultimate applicability and impact 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 GWI?
- **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 CTA mechanism, use the SOW format example titled “SOW for Clinical 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.

If proposing the Multiple PI Option, each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and each Partnering PI should be noted for each task.

- **Attachment 6: Human Subject Recruitment and Safety Procedures (no page limit):** Upload as “HumSubProc.pdf.” The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.
 - a. **Study Population:** Describe the target Gulf War veteran population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site (population from whom the sample will be recruited/drawn). Demonstrate that the research team has access to the proposed study population in numbers that will support a meaningful outcome. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials

(if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided.

- b. Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, “Ethical Principles and Guidelines for the Protection of Human Subjects,” and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical trial.

- c. Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification).
- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
 - Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study. Note: PIs are urged to consider including reimbursement for travel and accommodations and/or other appropriate expenses for Gulf War veterans participating in clinical trials.
 - Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.
 - Provide a letter(s) from an appropriate authority showing approved access to Gulf War veterans or use of data from veterans (e.g., Defense Manpower Data Center Data Request System, collaborating investigator(s) from the Department of Veterans Affairs, etc.), if applicable. 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.
 - Description of the Informed Consent Process: Specifically describe the plan for obtaining informed consent from human subjects.
 - ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial.
 - Include information regarding the timing and location of the consent process.
 - Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
 - Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
 - Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
 - Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (<http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf>). If applicable, please refer to the General Application Instructions, Appendix 5, for more information.
 - **Assent.** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.
- d. Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. Please note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.
- e. Risks/Benefits Assessment:**
- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is subjected to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical

risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:**
 - Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.
 - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
 - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
 - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
 - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.
- **Attachment 7: Intervention (no page limit):** Upload as “Intervention.pdf.” The Intervention attachment should include the components listed below.
 - a. **Description of the Intervention:** As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described.

Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety of the intervention.
 - b. **Study Procedures:** Describe the interaction with the human subject to include the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Discuss how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.

- c. **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Good Clinical Practices (GCP) compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.
- **Attachment 8: Data Management (no page limit):** Upload as “Data_Manage.pdf.” The Data Management attachment should include the components listed below.
 - a. **Data Management:** Describe all methods used for data collection to include the following:
 - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
 - **Confidentiality:**
 - Explain measures taken to protect the privacy of study human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
 - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of USAMRMC are eligible to review study records.
 - Address requirements for reporting sensitive information to state or local authorities.
 - **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time data will be stored. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. For FDA-regulated studies, compliance with 21 CFR 11 is required.
 - **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.
 - b. **Laboratory Evaluations:**
 - **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.

- **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).
- **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
- **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.
- **Attachment 9: Study Personnel and Organization (no page limit):** Start each document on a new page. Combine into one document and upload as “Personnel.pdf.” The Study Personnel and Organization attachment should include the components listed below.
 - a. **Organizational Chart:** Provide an organizational chart identifying key members of the study team including institution/center/department and name each person’s position on the project. A medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included. If applicable, include any external consultants or other experts who will assist with FDA applications. While there is no specified format for this information, a table(s) or diagram is recommended.
 - b. **Study Personnel Description:** Briefly describe the roles of the individuals listed in the organizational chart on the project. Describe relevant experience and qualifications that demonstrate appropriate expertise for the given role.
 - c. **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included. Provide a plan for real-time communication among collaborating institutions (if applicable).
- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit):** Upload as “Surveys.pdf.” The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study.

- **Attachment 11: Impact Statement (one-page limit).** Upload as “Impact.pdf.”
 - Identify the Gulf War veteran population that will participate in the proposed intervention, and describe the potential impact of the proposed clinical trial on veterans with GWI.
 - Describe the short-term impact: Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial.
 - Describe the long-term impact: Explain the long-range vision for implementation of the intervention in the clinic or field, and describe the anticipated long-term benefits for veterans with GWI.
- **Attachment 12: Transition Plan (one-page limit).** Upload as “Transition.pdf.” Provide information on the methods and strategies proposed to move the product or knowledge outcomes to the next phase of clinical trials, commercialization, and/or delivery to the civilian or military market after successful completion of the award. The transition plan should include the components listed below.
 - The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication.
 - Details of the funding strategy that will be used to bring the outcomes to the next level of development and/or commercialization (e.g., specific potential industry partners, specific funding opportunities to be applied for).
 - For knowledge products, a description of how the knowledge will be further developed, disseminated, and incorporated into clinical care.
 - A description of collaborations and other resources that will be used to provide continuity of development.
 - A brief schedule and milestones for bringing the intervention to the next phase of clinical trials and/or delivery to veterans with GWI.
 - A risk analysis for cost, schedule, manufacturability, and sustainability.
- **Attachment 13: IND/IDE Documentation:** If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “IND-IDE.pdf.”
 - Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov.
 - If an IND or IDE application has been submitted, provide an explanation of the status of the IND or IDE application (e.g., past the critical 30-day period, pending response to questions raised by the Agency, on clinical hold). Provide a summary of previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.

- If the IND or IDE application is not yet submitted, provide evidence that an IND or IDE will be submitted within 60 days of award. Examples include results and minutes of a pre-IND or pre-IDE meeting with the FDA, a pre-IND/pre-IDE meeting request to the FDA, or other communication with the FDA. Provide the anticipated date of IND/IDE submission.
 - If an IND or IDE is not required for the proposed study, provide evidence in the form of communication from the FDA or the IRB of record to that effect.
 - **Attachment 14: Outcomes Statement (one-page limit):** Upload as “Outcomes.pdf.” If applicable, list all prior research projects/awards relating to GWI, including resulting publications, abstracts, patents or other tangible outcomes. Only research and outcomes directly relevant to GWI should be listed. Note: This item will be made available for programmatic review.
- 3. Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information.
- 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.”
 - *If proposing the Multiple PI Option, include biographical sketches for the Partnering PI(s).*
 - Key Personnel Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”
 - *If proposing the Multiple PI Option, include previous/current/pending support for Partnering PI(s).*
- 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.”
- If proposing the Multiple PI Option, Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the effort as part of their separate Grants.gov application packages. The Research & Related Budget for the Initiating PI should not include budget information for the Partnering PI(s), even if they are located within the same organization. The total direct costs in each Partnering PI’s budget cannot exceed \$1,000,000.*
- 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.

Application Components for the Partnering PI(s)
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Each Partnering PI MUST follow the link in the email from eBRAP and complete the registration process prior to the application submission deadline in order to associate his/her grant application package with that of the Initiating PI.

The application submission process for Partnering PI(s) uses an abbreviated application package of forms and attachments from Grants.gov that includes:

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

2. **Attachments Form**

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as “SOW.pdf.” Refer to the General Application Instructions, Section II.C., for detailed information on completing the SOW. *Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI(s) should be noted for each task.*
- **Attachment 14: Outcomes Statement (one-page limit):** Upload as “Outcomes.pdf.” List all prior research projects/awards relating to GWI, including resulting publications, abstracts, patents or other tangible outcomes. Only research and outcomes directly relevant to GWI should be listed. Note: This item will be made available for programmatic review. Note: This item will be made available for programmatic review.”

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

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

Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the effort as part of their separate Grants.gov application packages. The Research & Related Budget for the Partnering PI(s) should not include budget information for the Initiating PI, even if they are at the same organization. The total direct costs in each Partnering PI’s budget cannot exceed \$1,000,000.

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

5. **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 DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the 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.shtml>.

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 18 USC 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:

- **Clinical Impact**
 - How relevant the anticipated outcomes of the proposed clinical trial are to veterans with Gulf War Illness. If a multi-armed trial comparing different interventions is proposed, how relevant each proposed arm is to GWI.
 - How well the sample population represents the targeted patient population of veterans with GWI that might benefit from the proposed intervention.
 - How the potential outcomes of the proposed clinical trial will provide/improve short-term benefits for ill Gulf War veterans.
 - How significantly the long-term benefits of the intervention may impact treatment of GWI and quality of life for veterans with GWI.
- **Research Strategy**
 - How well the scientific rationale for testing the intervention, including the description of the pathobiological mechanism being targeted, is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.
 - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective(s).
 - How well the application describes the published case definition of GWI to be used in the proposed clinical trial.
 - How well the inclusion and randomization criteria meet the needs of the proposed clinical trial, if applicable.

- How well the exclusion criteria are justified.
- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
- **Statistical Plan**
 - To what degree the statistical model and data analysis plan are suitable for the planned study.
 - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
- **Intervention**
 - To what degree the intervention addresses the needs of veterans with GWI. For a clinical trial with multiple arms, the applicability of each intervention for Gulf War Illness.
 - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
 - To what degree the application has provided preclinical and/or clinical evidence to support the safety of the intervention.
 - To what extent the intervention has the potential to provide an improvement over currently available interventions and/or standards of care.
 - To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.
 - Whether a member of the study team holds the IND/IDE for the indication proposed, or whether the timeline proposed for obtaining the IND/IDE is appropriate (if applicable).
 - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
 - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate, as applicable.
 - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **Recruitment, Accrual, and Feasibility**
 - How well the PI addresses the availability of and access to Gulf War veterans for the clinical trial and the prospect of their participation.
 - Whether the PI has demonstrated access to the proposed Gulf War veteran population in numbers that will support a meaningful outcome. Whether the PI has provided a letter from an appropriate authority showing approved access to Gulf War veterans or use of data from veterans.
 - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.

- How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
- To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital? Will there be reimbursement for expenses e.g. travel and accommodations?).
- **Ethical Considerations**
 - How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
 - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
 - To what degree privacy issues are appropriately considered.
 - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
- **Personnel and Communication**
 - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
 - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
 - For Multiple PI Option: How the team is poised to accomplish work synergistically to a greater extent than would be possible than by each one working independently.
 - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
 - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.
- **Transition Plan**
 - Whether the funding strategy described to bring the outcome(s) to the next level of clinical trials or to veterans with GWI is appropriate is appropriate.
 - How the development plan to support a product label change, if applicable, is appropriate and well described.
 - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
 - How the schedule and milestones for bringing the outcome(s) to the next level clinical trials or to veterans with GWI is appropriate.

- How well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.

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

- **Environment**

- To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
- Whether there is evidence for appropriate institutional commitment from each participating institution.
- If applicable, to what degree intellectual and material property plan that is agreed upon by each participating institution is appropriate for the proposed clinical trial.

- **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 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
- Relative outcomes from the PI's previous GWI-related research, if applicable

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 pre-applications from eBRAP 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 is missing.

The following will result in administrative rejection of the application:

- All associated (Initiating and Partnering PI) applications are not submitted by the deadline.
- Submission of an application for which a letter of invitation was not received.
- 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.
- Human Subject Recruitment and Safety Procedures (Attachment 6) is missing.
- Intervention (Attachment 7) is missing.
- Data Management (Attachment 8) is missing.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and 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 pre-application or 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 GWIP IP members can be found at <http://cdmrp.army.mil/gwirp/panels/panels14.shtml>.
- 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 PI does not meet the eligibility criteria.
- The proposed research is not a clinical trial.
- The proposed study is primarily focused on ALS or the psychological basis for GWI.

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.

Quarterly technical progress reports will be required.

In addition to written progress reports, oral presentations may be requested.

For the Multiple PI Option: Each PI, whether Initiating or Partnering, must submit individual progress reports as required by his or her individual assistance agreement; however, PIs are expected to work together in preparing the reports.

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.

The institution transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

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

F. Pre-Award Meeting

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

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	Initiating PI Completed	Partnering PI 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."		
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 6 with file name "HumSubProc.pdf."		
	Intervention: Upload as Attachment 7 with file name "Intervention.pdf."		
	Data Management: Upload as Attachment 8 with file name "Data_Manage.pdf."		
	Study Personnel and Organization: Upload as Attachment 9 with file name "Personnel.pdf."		
	Surveys, Questionnaires, and Other Data Collection Instructions: Upload as Attachment 10 with file name "Surveys.pdf" if applicable.		
	Impact Statement: Upload as Attachment 11 with file name "Impact.pdf."		
	Transition Plan: Upload as Attachment 12 with file name "Transition.pdf."		
	IND/IDE Documentation: Upload as Attachment 13 with file name "IND-IDE.pdf."		
	Outcomes Statement: Upload as Attachment 14 with file name "Outcomes.pdf" if applicable.		
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.		

Grants.gov Application Components	Action	Initiating PI Completed	Partnering PI Completed
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.		