

# **I. OVERVIEW OF THE FUNDING OPPORTUNITY**

**Program Announcement for the Department of Defense**

**Defense Health Program**

**Congressionally Directed Medical Research Programs**

**Gulf War Illness Research Program**

**Clinical Evaluation Award**

**Announcement Type: Initial**

**Funding Opportunity Number: W81XWH-21-GWIRP-CEA**

**Catalog of Federal Domestic Assistance Number: 12.420 Military Medical  
Research and Development**

## **SUBMISSION AND REVIEW DATES AND TIMES**

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), May 7, 2021
- **Invitation to Submit an Application:** June 2021
- **Application Submission Deadline:** 11:59 p.m. ET, August 19, 2021
- **End of Application Verification Period:** 5:00 p.m. ET, August 24, 2021
- **Peer Review:** October 2021
- **Programmatic Review:** December 2021

*This program announcement must be read in conjunction with the General Application Instructions, version 601. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the “Package” tab, clicking “Preview,” and then selecting “Download Instructions.”*

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## II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

### II.A. Program Description

Applications to the Fiscal Year 2021 (FY21) Gulf War Illness Research Program (GWIRP) are being solicited for the Defense Health Agency (DHA) J9, Research and Development Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 2358 (10 USC 2358). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The execution management agent for this program announcement is the Congressionally Directed Medical Research Programs (CDMRP). The GWIRP was initiated in 2006 to provide support for research of exceptional scientific merit for studying effects of deployment to the 1990-1991 Persian Gulf War on U.S. Warfighters. Appropriations for the GWIRP from FY06 through FY20 totaled \$214 million (M). The FY21 appropriation is \$22M.

*The proposed research must be relevant to active-duty Service Members, Veterans, military beneficiaries, and/or the American public.*

#### II.A.1. The Gulf War Illness Landscape

The GWIRP has prepared an overview titled, “The Gulf War Illness Landscape,” which describes what is currently known about topics consistent with the mission of identifying treatments, improving definition and diagnosis, and understanding the pathobiology and symptoms of Gulf War Illness (GWI). *Applicants are strongly encouraged to read and consider The Gulf War Illness Landscape before preparing their applications.* The Landscape can be found at [https://cdmrp.army.mil/gwirp/pdfs/GWIRP\\_Landscape\\_2020.pdf](https://cdmrp.army.mil/gwirp/pdfs/GWIRP_Landscape_2020.pdf).

#### II.A.2. FY21 GWIRP Overarching Challenges

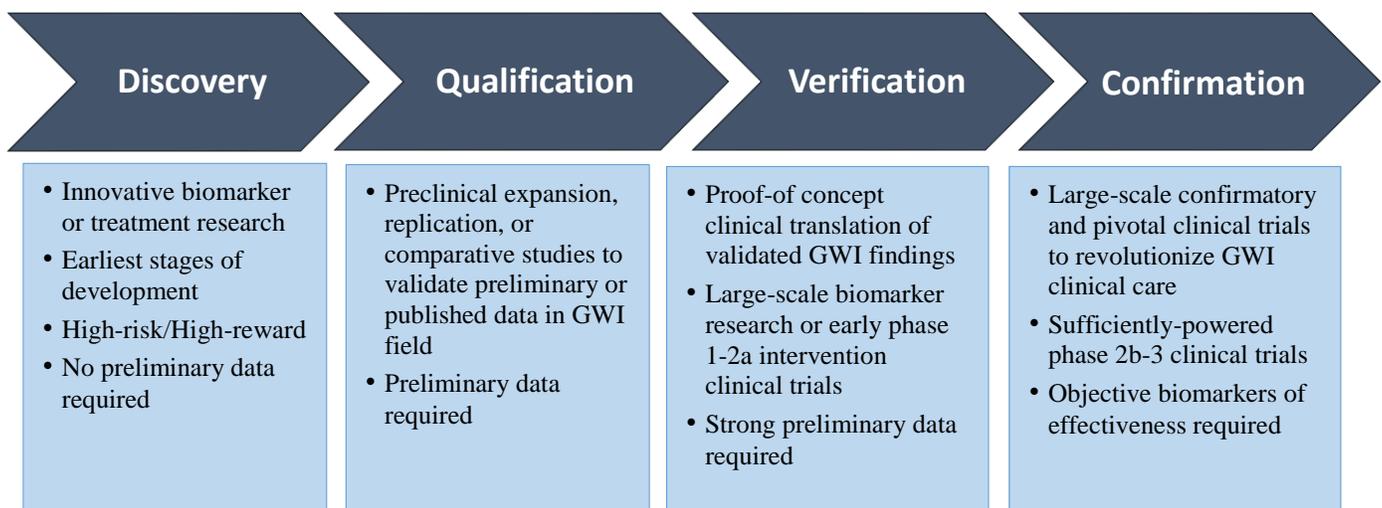
Considering the current Gulf War Illness Landscape and the GWIRP’s mission, all FY21 GWIRP applications must address at least one of the following overarching challenges unless adequate justification for exception is provided.\*

- **Treatments:** Eliminate the health consequences associated with GWI and/or revolutionize treatment
- **Diagnosis:** Better define and diagnose GWI
- **Subtyping:** Distinguish subtypes to better target treatments, monitor therapy, identify severity of GWI, or to identify why GWI is worse for some Veterans than for others
- **Determinants:** Identify and validate determinants of GWI, including latency and impacts on organs and systems

- **Consequences:** Determine whether GWI alters risk for developing neurological conditions, cancers, or other serious conditions; or whether GWI alters outcomes of other infections/diseases
- **Communicate & Educate:** Help Veterans, their caregivers, and clinicians communicate effectively about GWI, its symptoms, and potential treatments

\*With adequate justification, applications may identify and address another overarching challenge related to The Gulf War Illness Landscape. Justification must be provided in the application.

To address the overarching challenges in a step-wise and translational manner, the FY21 GWIRP award mechanisms are aligned to the different phases of the research pipeline illustrated below.



The **Discovery phase** represents innovative biomarker or treatment research that is in the earliest stages of development. Applicants seeking support for research aligning to the Discovery phase should consider the **FY21 GWIRP Idea Award** (funding opportunity number W81XWH-21-GWIRP-IA) or the **FY21 New Investigator Award** (funding opportunity number W81XWH-21-GWIRP-NIA).

The **Qualification phase** represents preclinical research already supported by preliminary or published data in the GWI field that is ready for validation through expansion, replication, or comparative studies. Applicants seeking support for the Qualification phase should consider the **FY21 GWIRP Research Advancement Award** (funding opportunity number W81XWH-21-GWIRP-RAA) or the **FY21 New Investigator Award** (funding opportunity number W81XWH-21-GWIRP-NIA).

The **Verification phase** represents clinical translation of concepts previously validated through expansion, replication, or comparative studies. Examples of projects in the Verification phase include large-scale biomarker trials or phase 1 through 2a intervention trials. Applicants seeking support for the Verification phase should consider the **FY21 GWIRP Clinical Evaluation Award** (funding opportunity number W81XWH-21-GWIRP-CEA).

The **Confirmation** phase represents large-scale confirmatory and pivotal trials that will transform and revolutionize the clinical management of GWI. Sufficiently powered phase 2b through phase 3 clinical trials of previously piloted interventions will be supported. Objective biomarkers to measure the biological effect of an intervention or predictive/cohort-selective biomarkers that indicate whether a specific therapy will be effective in an individual Gulf War Veteran or Gulf War Veteran subgroup are required. Applicants seeking support for the **Confirmation** phase should consider the **FY21 GWIRP Therapeutic/Biomarker Trial Award** (funding opportunity number W81XWH-21-GWIRP-TBTA).

***NOTE: The scope of research proposed in applications in response to the FY21 GWIRP program announcements must align with the research phases outlined above. It is the responsibility of the applicant to select the award mechanism that aligns with the scope of the proposed research. The funding mechanism should be selected based on the research scope defined in the program announcement, and not on the amount of the budget. Applications submitted under a mechanism that is not deemed appropriate for the scope of research proposed will not be funded.***

### **II.A.3. Award History**

The GWIRP Clinical Evaluation Award mechanism was first offered in FY19. Since then, five Clinical Evaluation Award applications have been received, and three have been recommended for funding.

### **II.B. Award Information**

The FY21 GWIRP Clinical Evaluation Award supports translation of validated GWI research, including qualified and replicated preclinical findings, to a Gulf War Veteran population. **The Clinical Evaluation Award targets the Verification phase of the research pipeline as outlined in [Section II.A.2](#).** Statistically powered biomarker trials with the potential to validate use of biomarkers as clinical endpoints or proof-of-concept intervention trials (e.g., pilot, first in human, phase 1-2a) are encouraged under this funding opportunity. Clinical trials may be designed to evaluate pharmacologic agents (drugs or biologics), devices, clinical guidance or other approaches, and technologies supported by strong objective evidence in the GWI field. While studies of treatments repurposed from other disorders sharing GWI symptomatology will be considered (with appropriate rationale), the FY21 GWIRP encourages studies that translate qualified results from the GWI research community. Biomarker investigations must expand preliminary findings in a GWI cohort large enough to produce a statistically meaningful outcome. Biomarker study outcomes shall provide validation of use as clinical endpoints in large-scale (phase 2b-3) clinical trials.

***Funding from this award mechanism must support research in a Gulf War Veteran population.*** Proof of availability and access to necessary cohort(s) and/or critical reagents must be provided. Applications must state a realistic timeline for clinical investigation.

Investigators seeking funding for a preclinical research project should consider one of the other FY21 GWIRP program announcements being offered.

The requested budget must be commensurate with the phase and size of the trial proposed. Refer to [Section II.D.5, Funding Restrictions](#) for detailed funding information.

**Biorepository Contribution Option:** In FY17, the GWIRP awarded infrastructure support for a Gulf War Illness Biorepository. The Boston Biorepository, Recruitment, and Integrative Network (BBRAIN) for GWI has now been established for the retention and distribution of Gulf War Veteran biospecimens and/or data related to GWI research. Applicants to the FY21 GWIRP are encouraged to contribute Gulf War Veteran biospecimens and data to this repository network. The FY21 GWIRP Clinical Evaluation Award offers a Biorepository Contribution Option with higher levels of funding for qualified applications as described in [Section II.D.5, Funding Restrictions](#). For the application to qualify for a higher level of funding, the applicant must submit a Biorepository Contribution Statement (see [Attachment 10](#)) providing a detailed accounting of proposed costs and a commitment to work with protocols and standard operating procedures (SOPs) developed by the BBRAIN for quality assurance purposes. Applicants interested in collaborating with this network should refer to the Research Resources link (<https://cdmrp.army.mil/gwirp/resources/gwirpresources>) on the GWIRP website.

**Clinical Consortium Collaboration Option:** In FY17, the GWIRP awarded a Clinical Consortium Award to create a network of institutions focused on designing and executing phase 1 and 2 clinical trials. The Gulf War Illness Clinical Trials and Interventions Consortium (GWICTIC) has now been established to investigate promising therapeutics for GWI. Applicants to the FY21 GWIRP are encouraged to make use of the established infrastructure of the GWICTIC, such as recruitment networks, existing protocols, Common Data Elements (CDEs), and data management procedures. *Clinical Consortium Collaboration Option applications shall adhere to the GWICTIC policies and procedures with respect to biospecimens and data and therefore are not eligible to also submit under the Biorepository Contribution Option.* A letter of commitment/collaboration from the GWICTIC is required, outlining the services that will be shared to bring value to the government. The FY21 GWIRP Clinical Evaluation Award offers a Clinical Consortium Collaboration Option with higher levels of funding for qualified applications as described in [Section II.D.5, Funding Restrictions](#). For the application to qualify for a higher level of funding, the applicant must submit a Clinical Consortium Collaboration Statement (see [Attachment 10](#)) providing a detailed accounting of proposed costs and a commitment to work with protocols and SOPs developed by the GWICTIC.

**Activities not supported under this Program Announcement include:**

- Studies focusing on psychiatric disease or psychological stress as the primary cause of GWI or implementation of care guidelines placing significant emphasis on psychiatric pathologies or psychiatric remedies.
- Applications focusing on amyotrophic lateral sclerosis (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 CDMRP offers funding opportunities through the ALS Research Program (see <https://cdmrp.army.mil/alsrp>).

The types of awards made under the program announcement will be assistance agreements. An assistance agreement is appropriate when the federal government transfers a “thing of value” to a “state, local government,” or “other recipient” to carry out a public purpose of support or stimulation authorized by a law of the United States instead of acquiring property or service for the direct benefit and use of the U.S. government. An assistance agreement can take the form of a grant or cooperative agreement. The level of involvement on the part of the Department of Defense (DOD) during project performance is the key factor in determining whether to award a grant or cooperative agreement. If “no substantial involvement” on the part of the funding agency is anticipated, a grant award will be made (31 USC 6304). Conversely, if substantial involvement on the part of the funding agency is anticipated, a cooperative agreement will be made (31 USC 6305), and the award will identify the specific substantial involvement. Substantial involvement may include, but is not limited to, collaboration, participation, or intervention in the research to be performed under the award. The award type, along with the start date, will be determined during the negotiation process.

The anticipated direct costs budgeted for the entire period of performance for an FY21 GWIRP Clinical Evaluation award will not exceed **\$1,500,000**. If applying under the Biorepository Contribution Option, direct costs will not exceed **\$1,520,000**. If applying under the Clinical Consortium Collaboration Option, direct costs will not exceed **\$1,700,000**. ***Clinical Consortium Collaboration Option applications shall adhere to the GWICTIC policies and procedures with respect to biospecimens and data and therefore are not eligible to also submit under the Biorepository Contribution Option.*** Refer to [Section II.D.5, Funding Restrictions](#), for detailed funding information.

Awards will be made no later than September 30, 2022. For additional information refer to [Section II.F.1, Federal Award Notices](#).

***The CDMRP expects to allot approximately \$7.2M to fund approximately three Clinical Evaluation Award applications. Funding of applications received is contingent upon the availability of federal funds for this program as well as the number of applications received, the quality and merit of the applications as evaluated by scientific and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY21 funding opportunity will be funded with FY21 funds, which will expire for use on September 30, 2027.***

**Research Involving 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 Development Command (USAMRDC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), prior to research implementation. This administrative review requirement is in addition to the local Institutional Review Board (IRB) or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is *not* required. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes.*** Refer to the General Application Instructions, Appendix 1, and the Human Subject Resource Document available on the electronic Biomedical Research

Application Portal (eBRAP) “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information.

***A clinical trial is defined*** as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. Funded trials are required to post a copy of the IRB-approved informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in the Code of Federal Regulations, Title 32, Part 219 (2 CFR 219).

***Clinical research is defined*** as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies; (2) epidemiologic and behavioral studies; and (3) outcomes research and health services research. Note: Studies that meet the requirements for IRB review Exemption 4 are not considered CDMRP-defined clinical research. IRB Exemption 4 refers to research involving the collection or study of existing de-identified specimens or data, if these sources are publicly available.

If the proposed research is cooperative (i.e., involving more than one institution), a written plan for single IRB review arrangements must be provided at the time of application submission or award negotiation. The lead institution responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements.

**Access to Veterans of the 1990-1991 Gulf War:** Applicants not collaborating with the GWICTIC are encouraged to collaborate with an investigator who has demonstrated access to Gulf War Veterans, particularly investigators within the Department of Veterans Affairs (VA) or other GWIRP-supported investigators, to ensure access to Gulf War Veteran populations as applicable to the proposed project. Applicants interested in leveraging existing cohorts recruited in other GWIRP-supported studies can refer to the Research Resources link (<https://cdmrp.army.mil/gwirp/resources/gwirpresources>) on the GWIRP website. Access to Gulf War patient populations should be confirmed at the time of application submission. A letter of support, signed by the lowest-ranking person with approval authority, should be included for studies involving active-duty military, Veterans, military and/or VA-controlled study materials, and military and/or VA databases.

**Use of DOD or VA Resources:** If the proposed research involves access to active-duty military patient populations and/or DOD or VA resources or databases, the application must describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research. Refer to [Section II.D.2.b.ii, Full Application Submission Components](#), for detailed information. Refer to the General Application Instructions, Appendix 1, for additional information.



- The **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)** statement recommends an evidence-based minimum set of reporting elements for systematic reviews and meta-analyses; was developed by an international group; and was first published in 2009 in multiple journals (*PLOS Medicine*, *Annals of Internal Medicine*, *BMJ*, *Journal of Clinical Epidemiology*, and *Open Medicine*) and was updated in 2015. For more information, see <http://www.prisma-statement.org/>.
- The **Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)** statement, developed by an international collaboration of trialists, methodologists, journal editors, and ethicists, recommends minimum content to include in clinical trial protocols, from study enrollment through closeout, first published in the *Annals of Internal Medicine* and *BMJ* in 2013. For more information, see <https://www.spirit-statement.org>.
- **BEST (Biomarkers, EndpointS, and other Tools) Resource** is an online glossary developed by a Food and Drug Administration and NIH joint committee to clarify terms used in translational science and medical product development, with a focus on study endpoints and biomarkers. For information, see <https://www.ncbi.nlm.nih.gov/books/NBK326791/>.
- **ClinRegs** is a public website developed by NIH's National Institute of Allergy and Infectious Diseases to help researchers navigate country-specific regulatory information as they plan and implement clinical trials. For information, see <https://clinregs.niaid.nih.gov/>.

## II.C. Eligibility Information

### II.C.1. Eligible Applicants

**II.C.1.a. Organization: All organizations, including foreign organizations, foreign public entities, and international organizations, are eligible to apply.**

**Government Agencies Within the United States:** Local, state, and federal government agencies are eligible to the extent that applications do not overlap with their fully funded internal programs. Such agencies are required to explain how their applications do not overlap with their internal programs.

As applications for this program announcement may be submitted by extramural and intramural organizations, these terms are defined below.

**Extramural Organization:** An eligible non-DOD organization. Examples of extramural organizations include academic institutions, biotechnology companies, foundations, federal government organization other than the DOD, and research institutes.

**Intramural DOD Organization:** A DOD laboratory, DOD military treatment facility, and/or DOD activity embedded within a civilian medical center. ***Intramural Submission: Application submitted by a DOD organization for an intramural investigator working within a DOD laboratory or military treatment facility or in a DOD activity embedded within a civilian medical center.***

**USAMRAA makes awards to eligible organizations, not to individuals.**

### **II.C.1.b. Principal Investigator**

Independent investigators at any academic level (or equivalent) are eligible to apply.

There are no limitations on the number of applications for which an investigator may be named as a Principal Investigator (PI).

An eligible PI, regardless of ethnicity, nationality, or citizenship status, must be employed by, or affiliated with, an eligible organization.

The CDMRP encourages all PIs to participate in a digital identifier initiative through Open Researcher and Contributor ID, Inc. (ORCID). Registration for a unique ORCID identifier can be done online at <https://orcid.org/>.

### **II.C.2. Cost Sharing**

Cost sharing/matching is not an eligibility requirement.

### **II.C.3. Other**

Organizations must be able to access **.gov** and **.mil** websites in order to fulfill the financial and technical deliverable requirements of the award and submit invoices for payment.

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 3.

Refer to [Section II.H.2, Administrative Actions](#), for a list of administrative actions that may be taken if a pre-application or application does not meet the administrative, eligibility, or ethical requirements defined in this program announcement.

## **II.D. Application and Submission Information**

*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(s).*

### ***Extramural Submission:***

- Pre-application content and forms must be accessed and submitted at [eBRAP.org](http://eBRAP.org).
- Full application packages must be accessed and submitted at Grants.gov.

### ***Intramural DOD Submission:***

- Pre-application content and forms must be accessed and submitted at [eBRAP.org](http://eBRAP.org).

- Full application packages must be accessed and submitted at [eBRAP.org](https://eBRAP.org).

**Note:** *Applications from an intramural DOD organization or from an extramural federal government organization may be submitted to Grants.gov through a research foundation.*

### **II.D.1. Address to Request Application Package**

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance.

Contact information for the CDMRP Help Desk and the Grants.gov Contact Center can be found in [Section II.G, Federal Awarding Agency Contacts](#).

### **II.D.2. Content and Form of the Application Submission**

Submission is a two-step process requiring both *pre-application* (eBRAP.org) and *full application* (eBRAP.org or Grants.gov) as indicated below. The submission process should be started early to avoid missing deadlines. There are no grace periods. Full application submission guidelines differ for extramural (Grants.gov) and intramural (eBRAP.org) organizations (refer to [Table 1, Full Application Guidelines](#)).

***The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent throughout the entire pre-application and full application submission process.*** Inconsistencies may delay application processing and limit or negate the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507 prior to the application submission deadline.

#### **II.D.2.a. Step 1: Pre-Application Submission Content**

***During the pre-application process, eBRAP assigns each submission a unique log number. This unique eBRAP log number is required during the full application submission process.***

To begin the pre-application process, first select whether the submitting organization is extramural or intramural, then confirm your selection or cancel. **Incorrect selection of extramural or intramural submission type will delay processing.**

If an error has been made in the selection of extramural versus intramural and the pre-application submission deadline has passed, the PI or Business Official must contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507 to request a change in designation.

All pre-application components must be submitted by the 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.

The applicant organization and associated PI 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 applicant must contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507.

PIs with an ORCID identifier should enter that information in the appropriate field in the “My Profile” tab in the “Account Information” section of eBRAP.

***When starting the pre-application, PIs should ensure that they have selected the appropriate application category:***

- Clinical Evaluation Award (CEvA)
- Clinical Evaluation Award - Clinical Trial (CEvA-CT)
- Clinical Evaluation Award - Biorepository Contribution Option (CEvA-BCO)
- Clinical Evaluation Award - Clinical Trial - Biorepository Contribution Option (CEvA-CT-BCO)
- Clinical Evaluation Award - Clinical Consortium Collaboration Option (CEvA-CCCO)
- Clinical Evaluation Award - Clinical Trial - Clinical Consortium Collaboration Option (CEvA-CT-CCCO)

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):

- **Tab 1 – Application Information**

Submission of application information includes assignment of primary and secondary research classification codes, which may be found at <https://ebrap.org/eBRAP/public/Program.htm>. Applicants are strongly encouraged to review and confirm the codes prior to making their selection.

- **Tab 2 – Application Contacts**

Enter contact information for the PI. Enter the organization’s Business Official responsible for sponsored program administration (the “person to be contacted on matters involving this application” in Block 5 of the Grants.gov SF424 Research & Related Form). The Business Official must be either selected from the eBRAP list or invited in order for the pre-application to be submitted.

Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 Research & Related Form), and click on “Add

Organizations to this Pre-application.” The organization(s) must be either selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.

It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Tab 3 – Collaborators and Key Personnel**

Enter the name, organization, and role of all collaborators and key personnel associated with the application.

[FY21 GWIRP Programmatic Panel members](#) should not be involved in any pre-application or application. For questions related to panel members and pre-applications or applications, refer to [Section II.H.2.c, Withdrawal](#), or contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507.

- **Tab 4 – Conflicts of Interest**

List all individuals other than collaborators and key personnel who may have a conflict of interest in the review of the application (including those with whom the PI has a personal or professional relationship).

- **Tab 5 – Pre-Application Files**

*Note: Upload documents 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) 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.
  - What [FY21 GWIRP Overarching Challenge\(s\)](#), or other overarching challenge, will the proposed research address? If “other,” state the overarching challenge and provide justification within the context of [The Gulf War Illness Landscape](#).
  - How will the proposed research lead to a solution for the overarching challenge(s)?
  - Briefly describe how the scope of the proposed research is appropriate for the Verification phase of the research pipeline and represents translation of preclinical research already supported by replication and validation studies.
  - If applicable, describe the clinical intervention, subject population(s), and phase of the proposed clinical trial.

- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application *must be uploaded as individual files* and are limited to the following:
  - One page for additional information that the PI can use, at their discretion, to provide supporting data or rationale for the pre-application.

- **Tab 6 – Submit Pre-Application**

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:

- Whether the pre-application addresses at least one of the [FY21 GWIRP Overarching Challenges](#). If a topic outside of the FY21 GWIRP Overarching Challenges is addressed, to what degree the pre-application provides adequate justification within the context of [The Gulf War Illness Landscape](#).
- To what degree the pre-application proposes research that will lead to a solution for the overarching challenge.
- To what degree the pre-application is appropriate for the Verification phase and represents translation of preclinical research already supported by replication and validation studies.
- If the application includes a clinical trial, how well the clinical intervention, subject population(s), and phase of the clinical trial are described.

- **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 in [Section I, Overview of the Funding Opportunity](#). Invitations to submit a full application are based on the Pre-Application Screening Criteria listed above.

### **II.D.2.b. Step 2: Full Application Submission Content**

Applications will not be accepted unless notification of invitation has been received.

*The CDMRP cannot make allowances/exceptions to its policies for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.*

Each application submission must include the completed full application package for this program announcement. The full application package is submitted by the Authorized Organizational Representative through Grants.gov (<https://www.grants.gov/>) for extramural organizations or through eBRAP (<https://ebrap.org/>) for intramural organizations. See Table 1 below for more specific guidelines.

**II.D.2.b.i. Full Application Guidelines**

Extramural organizations must submit full applications through Grants.gov. Applicants must create a Grants.gov Workspace for submission, which allows the application components to be completed online and routed through the applicant organization for review prior to submission. Applicants may choose to download and save individual PDF forms rather than filling out webforms in Workspace. A compatible version of Adobe Reader **must** be used to view, complete, and submit an application package consisting of PDF forms. If more than one person is entering text into an application package, the **same version** of Adobe Reader software should be used by each person. Check the version number of the Adobe software on each user’s computer to make sure the versions match. Using different versions of Adobe Reader may cause submission and/or save errors – even if each version is individually compatible with Grants.gov. Refer to the General Application Instructions, Section III, and the “Apply For Grants” page of Grants.gov (<https://www.grants.gov/web/grants/applicants/apply-for-grants.html>) for further information about the Grants.gov Workspace submission process. Submissions of extramural applications through eBRAP may be withdrawn.

*Do not password protect any files of the application package, including the Project Narrative.*

**Table 1. Full Application Submission Guidelines**

Extramural Submissions	Intramural DOD Submissions
<b>Application Package Location</b>	
Download application package components for W81XWH-21-GWIRP-CEA from Grants.gov ( <a href="https://www.grants.gov/">https://www.grants.gov/</a> ) and create a Grants.gov Workspace. Workspace allows online completion of the application components and routing of the application package through the applicant organization for review prior to submission.	Download application package components for W81XWH-21-GWIRP-CEA from eBRAP ( <a href="https://ebrap.org/">https://ebrap.org/</a> ).
<b>Full Application Package Components</b>	
<b>SF424 Research &amp; Related Application for Federal Assistance Form:</b> Refer to the General Application Instructions, Section III.A.1, for detailed information.	<b>Tab 1 – Summary:</b> Provide a summary of the application information. <b>Tab 2 – Application Contacts:</b> This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.

Extramural Submissions	Intramural DOD Submissions
<p>Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> <li>• <a href="#">Attachments</a></li> <li>• <a href="#">Research &amp; Related Personal Data</a></li> <li>• <a href="#">Research &amp; Related Senior/Key Person Profile (Expanded)</a></li> <li>• <a href="#">Research &amp; Related Budget</a></li> <li>• <a href="#">Project/Performance Site Location(s) Form</a></li> <li>• <a href="#">Research &amp; Related Subaward Budget Attachment(s) Form</a></li> </ul>	<p><b>Tab 3 – Full Application Files:</b> Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> <li>• <a href="#">Attachments</a></li> <li>• <a href="#">Key Personnel</a></li> <li>• <a href="#">Budget</a></li> <li>• <a href="#">Performance Sites</a></li> </ul> <p><b>Tab 4 – Application and Budget Data:</b> Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.</p>
<b>Application Package Submission</b>	
<p><b>Create a Grants.gov Workspace.</b> Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission.</p> <p><b>Submit a Grants.gov Workspace Package.</b> An application may be submitted through Workspace by clicking the “Sign and Submit” button on the “Manage Workspace” page, under the “Forms” tab. Grants.gov recommends submission of the application package <b>at least 24-48 hours prior to the close date</b> to allow time to correct any potential technical issues that may disrupt the application submission.</p> <p><b>Note:</b> If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or the budget needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a “Changed/Corrected Application” with the previous Grants.gov Tracking ID <i>prior to</i> the application submission deadline. <b><i>Do not password protect any files of the application package, including the Project Narrative.</i></b></p>	<p><b>Submit package components to eBRAP (<a href="https://ebrap.org">https://ebrap.org</a>).</b></p> <p><b>Tab 5 – Submit/Request Approval Full Application:</b> After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided next to “Enter Your Password Here” and press the “Submit Full Application” button. eBRAP will notify your Resource Manager/ Comptroller/Task Area Manager or equivalent Business Official by email. <b><i>Do not password protect any files of the application package, including the Project Narrative.</i></b></p>

Extramural Submissions	Intramural DOD Submissions
<u><a href="#">Application Verification Period</a></u>	
<p>The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package may be modified <i>with the exception of the Project Narrative and Research &amp; Related Budget Form</i>.</p>	<p>After eBRAP has processed the full application, the organizational Resource Manager/Comptroller/Task Area Manager or equivalent Business Official and PI will receive email notification of this status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package may be modified <i>with the exception of the Project Narrative and Research &amp; Related Budget Form</i>. Your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official should log into eBRAP to review and to approve prior to the application verification deadline.</p>
<b>Further Information</b>	
<p><b>Tracking a Grants.gov Workspace Package.</b> After successfully submitting a Workspace package, a Grants.gov Tracking Number is automatically assigned to the package. The number will be listed on the “Confirmation” page that is generated after submission.</p> <p>Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.</p>	<p>Refer to the General Application Instructions, Section IV, for further information regarding eBRAP requirements.</p>

The full application package must be submitted using the unique eBRAP log number to avoid delays in application processing.

#### II.D.2.b.ii. Full Application Submission Components

- **Extramural Applications Only**

**SF424 Research & Related Application for Federal Assistance Form:** Refer to the General Application Instructions, Section III.A.1, for detailed information.

- **Extramural and Intramural Applications**

**Attachments:**

*Each attachment to the full application components must be uploaded as an individual file in the format specified and in accordance with the formatting guidelines listed in the General Application Instructions, Appendix 4.*

For all attachments, ensure that the file names are consistent with the guidance. Attachments will be rejected if the file names are longer than 50 characters or have incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, there are file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB, and the file size for the entire full application package may not exceed 200 MB.

- **Attachment 1: Project Narrative (15-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) 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 may result in administrative withdrawal of the application.
  - **Outline for Project Narrative: *All applications must describe a large-scale biomarker research study/biomarker trial or a proof-of-concept intervention clinical trial of a drug, device, or other intervention in a Gulf War Veteran population.*** Describe the proposed project in detail using ***one*** of the two outlines below, depending on whether or not a clinical trial is proposed.

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***Outline for applications proposing a large-scale biomarker research study/  
biomarker trial without a clinical trial:***

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- **Background:** Briefly describe the scientific rationale on which the proposed work is based. Provide sufficient preliminary data including but not limited to relevant preclinical validation in GWI models or biological alterations previously identified in Veterans with GWI. Describe the strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the proposed project. Describe plans to address weaknesses in the rigor of the prior research. The application must demonstrate logical reasoning and provide a sound scientific rationale for the proposed project as established through a critical review and analysis of published literature. The PI must clearly demonstrate translatability of research to treatment and/or health care delivery for 1990-1991 Gulf War Veterans with GWI.
- **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 award.
- **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls in sufficient detail for evaluation. Explain how this research strategy will meet the research goals and milestones.
  - ❖ Where relevant, describe the PI’s accessibility to the data, cohort(s), human samples, and/or critical reagents necessary for the project.

- ❖ For studies involving human subjects, both the CDC and Kansas definitions must be used. Describe and justify any additional case definition of GWI, including any targeted illness subgroups that will be defined for the study.
  - ❖ Describe the methods that will be used to recruit Gulf War Veterans, if applicable. Provide information on the availability of and access to the appropriate patient population(s), as well as the ability to accrue sufficient subjects. Applicants are strongly encouraged to consider the outreach and recruitment best practices described online at [https://cdmrp.army.mil/gwirp/pdfs/General%20 Guidance for Gulf War Veteran Outreach and Recruitment.pdf](https://cdmrp.army.mil/gwirp/pdfs/General%20Guidance%20for%20Gulf%20War%20Veteran%20Outreach%20and%20Recruitment.pdf).
  - ❖ Describe the strategy for the inclusion of women and minorities appropriate to the objectives of the study, including a description of the composition of the proposed study population in terms of sex/gender, racial, and ethnic group, and an accompanying rationale for the selection of subjects.
  - ❖ Describe how the use of the newly established GWI CDEs will be incorporated into the collection of clinical data and annotation of clinical samples.
  - ❖ Describe how the research expands preliminary findings and is in a GWI cohort large enough to produce a statistically meaningful outcome.
  - ❖ Explain how biomarker study outcomes could lead to clinical endpoints or subgroup markers useful in large-scale (phase 2b-3) clinical trials.
  - ❖ Address potential pitfalls and problem areas and present alternative methods and approaches.
- **Statistical Model and Data Analysis Plan:** Describe the statistical data analysis plan with respect to the study objectives. Specify, with justification, the rationale for the approximate number of human subjects to be enrolled. *Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study and all proposed correlative studies.* 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. Ensure sufficient information is provided to allow thorough evaluation of all planned statistical procedures during review of the application.
  - **Research Team:** Describe how the combined backgrounds and GWI-related expertise of the research team will enable successful conduct of the project. Describe the PI's record of accomplishments in GWI that demonstrate their ability to perform the proposed work

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***Outline for applications with a clinical trial of a drug, device, or other intervention.***

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**Note:** The Project Narrative is not the formal clinical trial protocol. If recommended for funding, the clinical trial protocol will be requested.

- **Background:** Describe in detail the rationale for the study and how it is supported by previous GWI-relevant investigations, including validated treatments in GWI models, exploitation of qualified biological alterations in Veterans with GWI, or previous pilot trials in Veterans with GWI that are now ready for the Verification phase. Describe the strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the proposed project. Describe plans to address weaknesses in the rigor of the prior research. If the intervention is used for another condition, include a rationale explaining why the proposed intervention would be expected to be effective for GWI. The application must clearly demonstrate translatability of research to treatment and/or healthcare delivery for 1990-1991 Gulf War Veterans with GWI.
- **Hypothesis or Objectives:** State the hypothesis to be tested or the objective to be reached.
- **Specific Aims:** Concisely explain the specific aims of the trial. If the proposed trial is part of a larger study, describe only those aims that will be funded by this award.
- **Research Strategy and Feasibility:** Describe the laboratory research studies that will be performed under this award and how they are *clearly linked* to the clinical trial. Describe the experimental design and methodology, including reagents, assay validation, statistical analysis, potential pitfalls, and alternative approaches.
- **Clinical Trial:** Provide detailed plans for initiating, conducting, and completing the clinical trial during the period of performance. As appropriate, outline a plan for obtaining Investigational New Drug/Investigational Device Exemption (IND/IDE) status (or other FDA approvals). Additional details should be provided in **Attachment 7, Regulatory Strategy**.
  - ❖ Describe the type of clinical trial to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.
  - ❖ Identify the intervention to be tested and describe the projected outcomes.
  - ❖ Describe how subjects and controls will be evaluated using quantitative criteria. Both CDC and Kansas case definitions for GWI must be used for the purpose of comparative analysis. If any additional case definition is to be



- **Statistical Model and Data Analysis Plan:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the research team member(s) responsible for statistical and data analysis. Specify, with justification, the rationale for the approximate number of human subjects to be enrolled. *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. Ensure sufficient information is provided to allow thorough evaluation of all planned statistical procedures during review of the application.
- **Clinical Team:** Describe the composition of the clinical trial team. Provide details on how the team (including investigator(s), study coordinator, statistician) possesses the appropriate expertise in conducting clinical trials. Describe the PI's record of accomplishments in GWI that demonstrate their ability to perform the proposed work.
- **Attachment 2: Supporting Documentation: Combine and upload as a single file named "Support.pdf".** Start each document on a new page. If documents are scanned to PDF, the lowest resolution (100 to 150 dpi) should be used. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

*There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested or viewed as an extension of the Project Narrative will result in the removal of those items or may result in 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 Patents: Include a list of relevant publication URLs and/or patent abstracts. If articles are not publicly available, then copies of up to five published manuscripts may 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 support not requested in the program announcement, such as those from members of Congress, do not impact application review or funding decisions.
- 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 an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator’s Commander or Commanding Officer at the intramural organization that authorizes the collaborator’s involvement.
- Intellectual Property: Information can be found in Code of Federal Regulations, 2 CFR 200.315, “Intangible Property.”
  - 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 2, Section K, for more information about the CDMRP expectations for making data and research resources publicly available. If applying for the Biorepository Contribution Option, provide details of the commitment to work with protocols and SOPs developed by the BBRAIN in the Biorepository Contribution Statement (see [Attachment 10](#)). If applying for the Clinical Consortium Collaboration Option, provide details in the commitment to work with protocols and SOPs developed by the GWICTIC in the Clinical Consortium Collaboration Option Statement (see [Attachment 10](#)).
- Access to Veterans of the 1990-1991 Gulf War (if applicable): Provide a letter of support from a Department of Veterans Affairs (VA) or GWIRP-supported investigator(s) confirming access to Gulf War Veteran populations. The letter should be signed by the lowest ranking person with approval authority and should be included for studies involving active-duty military, Veterans, military and/or VA-controlled study materials, and military and/or VA databases.
- Use of VA Resources (if applicable): Provide a letter of support from the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the Associate Chief of Staff for Research and Development (ACOS/R&D) or Clinical Service Chief, confirming access to VA patients, resources, and/or VA research

space. For VA PIs, if the VA non-profit corporation is not identified as the applicant institution for administering the funds, include a letter from the VA ACOS/R&D confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.

- Provide an anticipated enrollment table(s) for the inclusion of women and minorities appropriate to the objectives of the study with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The suggested Inclusion Enrollment Report format is a one-page fillable PDF form, which can be downloaded from eBRAP at <https://ebrap.org/eBRAP/public/Program.htm>.”
- **“Attachment 3: Technical Abstract (one-page limit): Upload as “TechAbs.pdf”.** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. *Do not include proprietary or confidential information.* Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

The technical abstract is used by all reviewers. The programmatic reviewers may not have access to the full application and may 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.

- Overarching Challenge(s): State the [FY21 GWIRP Overarching Challenge\(s\)](#) or with adequate justification within the context of [The Gulf War Illness Landscape](#) another overarching challenge that will be addressed.
- Background: Present the ideas and rationale behind the proposed clinical investigation.
- Hypothesis/Objective(s): State the hypothesis to be tested and/or objective(s) to be reached.
- Specific Aims: State the specific aims of the study.
- Study Design: Briefly describe the study design, including appropriate controls.
- Impact: Briefly describe how the proposed project will have an impact on Veterans with GWI.
- **Attachment 4: Lay Abstract (one-page limit): Upload as “LayAbs.pdf”.** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. *Do not include proprietary or confidential information.* Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

Lay abstracts should be written using the outline below. *Do not duplicate the technical abstract.* Minimize use of acronyms and abbreviations. The lay abstract is an important

component of the application review process because it addresses issues of particular interest to the consumer advocate community.

- Overarching Challenge(s): State the [FY21 GWIRP Overarching Challenge\(s\)](#) or other overarching challenge that will be addressed.
- Objective and Rationale: Describe the scientific objective and rationale for the proposed study or intervention in a manner readily understood by readers without scientific or medical backgrounds.
- Applicability: Describe the ultimate applicability and impact of the research.
  - What are the potential clinical applications, benefits, and risks for Veterans with GWI?
  - What is the projected time it may take to achieve a patient-related outcome?
- **Attachment 5: Statement of Work (six-page limit): Upload as “SOW.pdf”.** The suggested Statement of Work (SOW) format and examples specific to different types of research projects are available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>). Recommended strategies for assembling the SOW can be found at <https://ebrap.org/eBRAP/public/Program.htm>.

For the Clinical Evaluation Award mechanism, refer to the “*Suggested SOW Strategy Clinical Research*” document for guidance on preparing the SOW and use the blank SOW format titled “Suggested SOW Format”. The SOW must be in PDF format prior to attaching.

- **Attachment 6: Data Management (no page limit): Upload as “Data\_Manage.pdf”.** Include all components listed below.
  - **Data Management:** Describe all methods used for data collection, including 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 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 the DOD 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. Describe the database lock process. For FDA-regulated studies, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) are 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, including results from any screening or diagnostic tests performed as part of the study.
- **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, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the plan to store specimens for future use, including 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, the applicable quality standard, and 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 7: Regulatory Strategy (no page limit):** *(Attachment 7 is only applicable and required for applications in which a clinical trial is proposed).* **If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “Regulatory.pdf”.**

Describe the regulatory strategy using the following outline and provide supporting documentation as applicable.

- State the product/intervention name.
- State how many months into the award the anticipated clinical trial would be initiated after the award begins, taking into account any required advanced preclinical work (e.g., Good Manufacturing Practice [GMP] production; pharmacokinetics and toxicity testing) and/or clinical trial preparation (IRB and DOD HRPO approval).

***For products/interventions that do not require regulation by the FDA:***

- Provide confirmation that the trial does not require regulation by the FDA in writing from the IRB of record or the FDA. For investigator-sponsored regulatory exemptions (e.g., IND, IDE) provide evidence of institutional support. No further information for this attachment is required.

***For products/interventions that require regulation by the FDA:***

- State whether the product is FDA-approved, -licensed, or -cleared and marketed in the U.S.
- If the product/intervention ***HAS*** already received FDA approval:
  - Provide a copy of the acceptance letter from the FDA.
  - If the product is marketed in the U.S., state the product label indication. State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population. Indicate whether the proposed research involves a change that increases the risks associated with using the product. State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).
- If the product/intervention ***HAS NOT*** already received FDA approval:
  - State the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification.
  - Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.
  - Describe the overall regulatory strategy and product development plan that will support the planned product indication. Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, and the types of FDA meetings that will be held/planned. Include considerations for

compliance with current GMP, Good Laboratory Practice (GLP), and Good Clinical Practice (GCP) guidelines.

- If the clinical trial involves the use of a drug that has not been approved by the FDA for the proposed investigational use, then an IND application to the FDA that meets all requirements under the 21 CFR 312 may be required and must be submitted to the FDA by the application submission deadline. If the investigational product is a device, evidence that an IDE application that meets all requirements under 21 CFR 812 has been submitted to the FDA by the application submission deadline, or that the device is exempt or qualifies for an abbreviated IDE, is required. The government reserves the right to withhold or withdraw funding if an IND or IDE is necessary but has not been submitted to the FDA by the application submission deadline, or if documented status of the IND or IDE has not been obtained within 18 months of the award date.
- If a drug is to be used in the proposed clinical trial, describe the current status for manufacturing development (e.g., manufacturer’s name, GMP-compliant lots available, status of stability testing), non-clinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support phase 1 testing), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).
- If a device is to be used in the proposed clinical trial, indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for the conduct of the clinical trial.
- **Attachment 8: Transition Plan (three-page limit): Upload as “Transition.pdf”.** Describe/discuss the methods and strategies proposed to move the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization’s Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The post-award 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/label. Describe in detail the FDA regulatory strategy, to include considerations for compliance with GMP, GLP, and GCP guidelines (if appropriate).
  - Details of the funding strategy that will be used to bring the outcomes to the next level of development or delivery to Veterans with GWI (e.g., specific potential industry partners, specific funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide feasibility and continuity of development.

- For knowledge products, a description of collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. (A “knowledge product” is a non-materiel product that addresses an identified need, topic area, or capability gap, is based on current evidence and research, aims to transition into medical practice, training, tools, or to support materiel solutions [systems to develop, acquire, provide, and sustain medical solutions and capabilities], and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.)
- A brief schedule and milestones for transitioning the intervention (i.e., next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA).
- Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the government’s ability to access such products or technologies in the future.
- A risk analysis for cost, schedule, manufacturability, and sustainability.
- **Attachment 9: Impact Statement (two-page limit): Upload as “Impact.pdf”.**
  - Summarize how the project addresses one or more of the [FY21 GWIRP Overarching Challenges](#). If the project addresses another overarching challenge, state the overarching challenge and provide justification within the context of [The Gulf War Illness Landscape](#).
  - Identify the Gulf War Veteran population(s) that will participate or be represented in the clinical investigation. Describe how they would benefit from the results obtained from the proposed clinical investigation.
  - ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical investigation and describe anticipated short-term benefits for individuals.
  - ***Describe the long-term impact:*** Explain the long-range vision for implementation of the intervention or biomarker(s) in the clinic. Describe the anticipated long-term benefits for Veterans with GWI. For biomarker investigations, describe how the biomarker(s) will improve therapeutics and interventions for GWI or whether the biomarker(s) will be used as an objective diagnostic or prognostic indicator. For clinical trials, describe how the intervention or therapeutic will improve patient care and/or quality of life of Veterans with GWI.
  - If applicable, identify any issues that could limit the ultimate impact of the research.

- **Attachment 10: Option Statements (three-page limit): Upload as “Options.pdf”.** *(Required for applications submitted under the Biorepository Contribution Option OR the Clinical Consortium Collaboration Option. Clinical Consortium Collaboration Option applications will adhere to the GWICTIC policies and procedures with respect to biospecimens and data and may not submit a separate Biorepository Contribution Statement.)* If the applicant is not applying to the Biorepository Contribution Option or the Clinical Consortium Collaboration Option, leave Attachment 10 blank.
  - **Biorepository Contribution Statement:** Describe the types of datasets and/or Gulf War Veteran biospecimens to be contributed to the BBRAIN, giving the approximate number of each. Provide a detailed accounting of proposed costs (per-sample basis as well as in aggregate). Describe any special preparation required and the facilities and technical capabilities necessary for collection, storage, and transfer of data and/or specimens. Contributing sites must adhere to the SOPs, quality assurance measures, and annotation standards for clinical and pathological specimens and data established by the BBRAIN members. Clearly explain how the applicant plans to coordinate with the BBRAIN and provide a plan for resolving any intellectual and material property issues related to contribution of samples and/or data. State whether clinical data will be associated with samples or research datasets and, if applicable, describe how patient data confidentiality will be maintained in compliance with federal and state regulations. Contributing sites must ensure IRB approval and informed consent to share samples and data.
  - **Clinical Consortium Collaboration Statement:** The GWICTIC currently consists of five Clinical Research Sites and one Coordinating Center. The Coordinating Center, in addition to functioning as a Clinical Research Site, serves as the Consortium information and planning nexus, providing administrative, operational, and data management support services to participating Clinical Research Sites to implement clinical trials in a timely manner. Institutions collaborating with the GWICTIC will leverage capabilities and integrate SOPs, quality assurance measures, CDEs, and data management procedures into the project. It is the responsibility of the applicant to clearly articulate the qualifications of the research team and institution to participate as a new Clinical Research Site in the Consortium. A Letter of Collaboration is required for applications submitted under the Clinical Consortium Collaboration Option to demonstrate engagement of the GWICTIC. Provide this letter as part of the Clinical Consortium Collaboration Statement.

Provide evidence that the research team and institution fulfill each of the following criteria for participation in the Consortium:

- Describe the PI’s experience in conducting multi-institutional clinical trials that demonstrate willingness and ability to participate in collaborative clinical trials and function in the Consortium.
- Include a named institutional Clinical Research Coordinator who will interact with the Supervising Clinical Research Coordinator at the Coordinating Center to

guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.

- Clearly explain how intellectual and material property issues related to contribution of samples and/or data will be resolved.

Provide an accounting of proposed costs, including but not limited to costs for personnel integral to collaboration, data and sample sharing and storage

- **Attachment 11: Outcomes Statement (if applicable; one-page limit): Upload as “Outcomes.pdf”.** If applicable, list all of the PI’s 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. Attachment 11 will be available for programmatic review only.
  - **Attachment 12: Representations, if applicable (extramural submissions only): Upload as “RequiredReps.pdf”.** All extramural applicants must complete and submit the Required Representations template available on eBRAP (<https://ebrap.org/eBRAP/public/Program.htm>). For more information, see the General Application Instructions, Appendix 5, Section B, Representations.
  - **Attachment 13: Suggested Collaborating DOD Military Facility Budget Format, if applicable: Upload as “MFBudget.pdf”.** If a military facility (Military Health System facility, research laboratory, medical treatment facility, dental treatment facility, or a DOD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete a separate budget, using “Suggested Collaborating DOD Military Facility Budget Format”, available for download on the eBRAP “Funding Opportunities & Forms” web page <https://ebrap.org/eBRAP/public/Program.htm>), including a budget justification, for each military facility as instructed. The costs per year should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section III.A.8, for detailed information.
- **Extramural and Intramural Applications**

To evaluate compliance with Title IX of the Education Amendments of 1972 (20 USC 1681(a) et seq.), the DOD is collecting certain demographic and career information to be able to assess the success rates of women who are proposed for key roles in applications in science, technology, engineering, and/or mathematics (STEM) disciplines. To enable this assessment, each application must include the following forms completed as indicated.

**Research & Related Personal Data:** For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.3, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.2, for detailed information.

**Research & Related Senior/Key Person Profile (Expanded):** For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.4, and for

intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.3, for detailed information.

- PI Biographical Sketch (five-page limit): Upload as “Biosketch\_LastName.pdf”. The suggested biographical sketch format is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP. The National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in uneditable PDF format.
- PI Previous/Current/Pending Support (no page limit): Upload as “Support\_LastName.pdf”.

For extramural submissions, refer to the General Application Instructions, Section III.A.4 for detailed information.

For intramural submissions, refer to the General Application Instructions, Section IV.A.3, for detailed information.

- Key Personnel Biographical Sketches (five-page limit each): Upload as “Biosketch\_LastName.pdf”.
- Key Personnel Previous/Current/Pending Support (no page limit): Upload as “Support\_LastName.pdf”.

**Research & Related Budget:** For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.5, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.4, for detailed information.

**Budget Justification (no page limit): Upload as “BudgetJustification.pdf”.** The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.

**Project/Performance Site Location(s) Form:** For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.6, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.5, for detailed information.

- **Extramural Applications Only**

**Research & Related Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section III.A.7, for detailed information.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov. (Refer to the General Application Instructions, Section III.A.7, for detailed information.) Verify subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period.

- **Intramural DOD Collaborator(s):** Complete the “Suggested Collaborating DOD Military Facility Budget Format” and upload to Grants.gov attachment form as [Attachment 13](#). (Refer to the General Application Instructions, Section IV.A.4, for detailed information.) Each Intramural DOD Collaborator should include costs per year on the Grants.gov Research & Related Budget Form under subaward costs.
  - **Research & Related Budget:** For extramural submissions, refer to the General Application Instructions, Section III.A.5, and for intramural submissions, refer to the General Application Instructions, Section IV.A.4, for detailed information.

### **II.D.3. Dun and Bradstreet Data Universal Numbering System (DUNS) Number and System for Award Management (SAM)**

Applicant organizations and all sub-recipient 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. Verify the status of the applicant organization’s Entity registration in SAM well in advance of the application submission deadline. Allow several weeks to complete the entire SAM registration process. If an applicant has not fully complied with the requirements at the time the federal awarding agency is ready to make a federal award, the federal awarding agency may determine that the applicant is not qualified to receive a federal award and use that determination as a basis for making a federal award to another applicant. Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.

***Announcement of Transition to SAM-Generated Unique Entity Identifier (UEI):*** Through April 2022, a transition from DUNS to the SAM-generated UEI will occur. Refer to the General Application Instructions, Section III.1, DUNS Number, for more information on the transition and timing.

### **II.D.4. Submission Dates and Times**

All submission dates and times are indicated in [Section I, Overview of the Funding Opportunity](#). Pre-application and application submissions are required. The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Failure to meet either of these deadlines will result in submission rejection.

### **Applicant Verification of Full Application Submission in eBRAP**

***For Both Extramural and Intramural Applicants:*** eBRAP allows an organization’s representatives and PIs to view and modify the full application submissions associated with them. Following retrieval and processing of the full application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the full application submission. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in an email to the PI and in the “Full Application Files” tab in eBRAP. eBRAP does not confirm the accuracy of file content. Application viewing, modification, and verification in eBRAP are strongly recommended, but not required. It is the applicant’s responsibility to review all application components and ensure proper ordering as specified in the program announcement. ***If either the***

***Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the application submission deadline. The Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline.*** Other application components may be changed until the end of the application verification period. Verify that subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

***Extramural Submission:*** The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package, ***with the exception of the Project Narrative and Budget Form***, may be modified.

***Intramural DOD Submission:*** After eBRAP has processed the full application, the organizational Resource Manager/Comptroller/Task Area Manager or equivalent Business Official and PI will receive email notification of the status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package, ***with the exception of the Project Narrative and Budget Form***, may be modified. The Resource Manager/Comptroller/Task Area Manager or equivalent Business Official should log into eBRAP to review and to approve the application package prior to the application verification deadline.

***For All Submissions:*** Verify that subaward budget(s) with budget justification are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period.

#### **II.D.5. Funding Restrictions**

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

The anticipated direct costs budgeted for the entire period of performance will not exceed **\$1,500,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **\$1,500,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

**Application to the Clinical Evaluation Award with the Biorepository Contribution Option:** If applying for the **Biorepository Contribution Option**, PIs may include additional direct costs up to **\$20,000** associated with the contribution of samples and data to the BBRAIN.

- The anticipated direct costs budgeted for the entire period of performance will not exceed **\$1,520,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **\$1,520,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

- A Clinical Evaluation Award application including the Biorepository Contribution Option that does not meet the criteria specified may be funded at the lower maximum direct costs of **\$1,500,000** (i.e., at the level of the standard Clinical Evaluation Award) as described above.

**Application to the Clinical Evaluation Award with the Clinical Consortium Collaboration**

**Option:** If applying for the **Clinical Consortium Collaboration Option**, PIs may include additional direct costs up to **\$200,000** associated with collaborative activities involving participation of the GWICTIC.

- The anticipated direct costs budgeted for the entire period of performance will not exceed **\$1,700,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **\$1,700,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.
- A Clinical Evaluation Award application including the Clinical Consortium Collaboration Option that does not meet the criteria specified may be funded at the lower maximum direct costs of **\$1,500,000** (i.e., at the level of the standard Clinical Evaluation Award) as described above.

All direct and indirect costs of any subaward or contract 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.

For this award mechanism, direct costs may be requested for (not all-inclusive):

- Veteran subject reimbursement and compensation including:
  - Transportation
  - Lodging
  - Participation incentives
- Travel in support of multidisciplinary collaborations.
- Travel costs for one investigator to travel to one scientific/technical meeting per year to present project information or disseminate project results from the FY21 GWIRP Clinical Evaluation Award

For extramural awards with an intragovernmental component, direct transfer of funds from an extramural award recipient to a DOD or other federal agency is not allowed except under very limited circumstances. Funding to intramural DOD and other federal agencies will be managed through a direct funds transfer. Intramural applicants are responsible for coordinating through their agency's procedures the use of contractual or assistance funding awards or other appropriate agreements to support extramural collaborators.

Refer to the General Application Instructions, Section III.A.5, for budget regulations and instructions for the Research & Related Budget. *For federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in the General Application Instructions, Section III.A.5.*

## **II.D.6. Other Submission Requirements**

Refer to the General Application Instructions, Appendix 4, for detailed formatting guidelines.

## **II.E. Application Review Information**

### **II.E.1. Criteria**

#### **II.E.1.a. Peer Review**

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

- **Impact**
  - To what degree the proposed research is responsive to one or more of the [FY21 GWIRP Overarching Challenges](#) or, with adequate justification, another identified overarching challenge related to [The Gulf War Illness Landscape](#).
  - To what degree the anticipated short-term outcomes will benefit Veterans with GWI.
  - Considering either an intervention or marker, to what degree could the project, if successful, lead to long-term improvements in diagnostics, prognostics, or therapeutic interventions and quality of life for Veterans with GWI.
  - How well potential issues that may limit impact of the proposed research are addressed.
- **Research Strategy and Feasibility**
  - How well the scientific rationale is supported by prior evidence collected from GWI-relevant investigations.
  - How well the application addresses weaknesses in the rigor of prior research that serves as the key support for the proposed project.
  - How well the application demonstrates translatability of research to treatment and/or healthcare delivery for 1990-1991 Gulf War Veterans with GWI.
  - How well hypotheses and/or objective(s), experimental design, methods, data collection and management procedures, and analyses are developed.
  - Whether there is documented availability of and access to all data, cohort(s), and/or critical reagents.

- If applicable, to what degree the process for recruitment is appropriate. Whether the application describes use of the CDC and Kansas case definitions. If the application proposes use of a case definition in addition to CDC and Kansas case definitions, how well that case definition is described and its use justified including any targeted illness subgroups that will be defined for the study.
- To what extent the strategies for the inclusion of women and minorities and distribution of proposed enrollment, if applicable, are appropriate for the proposed research.
- How well the newly established GWI CDEs are incorporated for the collection of clinical data and annotation of clinical samples.
- How well the research expands preliminary findings in a GWI cohort large enough to produce a statistically meaningful outcome.
- The potential utility of the biomarker study outcomes as clinical endpoints or subgroup markers in large-scale (phase 2b-3) clinical trials.
- How well plans to collect specimens and conduct laboratory evaluations are addressed.
- Whether potential challenges and alternative strategies are appropriately identified.
- **Clinical Trial (*for applications submitted to the Clinical Trial Option*)**
  - Whether proposed laboratory research studies are clearly linked to the clinical trial.
  - How well the rationale for clinically testing the intervention is supported by the preliminary data collected from GWI-relevant preclinical studies
  - Whether the type of clinical trial (e.g., prospective, randomized, controlled) proposed is appropriate and the methodology demonstrates a clear course of action.
  - How well the intervention to be tested and projected outcomes are described.
  - How well the plans for initiating, conducting, and completing the clinical trial demonstrate feasibility over the period of performance.
  - How well the clinical trial is designed with appropriate study variables, controls, and endpoints and whether subjects and controls will be evaluated using quantitative criteria.
  - How well the application describes the availability of and accessibility to critical reagents (e.g., therapeutic molecules) necessary for the clinical trial.
  - How well the application demonstrates the availability of and access to a GWI Veteran population, as well as the ability to accrue a sufficient number of subjects.
  - How well the human subject-to-group assignment process is described as well as the specific actions to accomplish the group assignment. Whether subjects, clinicians, data

analysts, and/or others will be blinded during the study and/or other measures to be taken to reduce bias are described.

- **Regulatory Strategy (*for applications submitted to the Clinical Trial Option*)**
  - Whether the clinical trial design, methods, and analysis plan meet the requirements for applying for and obtaining IND/IDE status (or other FDA approval), if appropriate.
  - How well the regulatory strategy and development plan to support the product indication or product label change, if applicable, are appropriate and well-described.
  - Whether the application includes documentation that the study is exempt from FDA regulations, or that the IND or IDE application has been submitted to the FDA, as appropriate.
  - For investigator-sponsored regulatory exemptions (e.g., IND, IDE), whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
  - Whether the plans to comply with current GMP, GLP, and GCP guidelines are appropriate.
- **Statistical Model and Data Analysis Plan**
  - To what degree the statistical data analysis plan is suitable for the planned study.
  - Whether a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study is provided.
  - The extent to which methods used for data collection (data capture, verification, disposition, and data reporting) are feasible.
- **Transition Plan**
  - To what degree the application demonstrates feasible methods and strategies to move the research findings to the next phase of development, clinical trials, and/or delivery to the commercial market after successful completion of the award.
  - Whether the application has a risk analysis for cost, schedule, and sustainability.
- **Personnel**
  - Whether the levels of effort by the PI and other key personnel are appropriate to ensure success of the project.
  - How appropriate the PI and research team's background and expertise are with regard to the ability to accomplish the proposed work.

- How well the PI's record of accomplishments in GWI demonstrate their ability to perform the proposed work.
- Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
- How well the logistical aspects (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed study.
- Whether a written plan for single IRB review arrangements is provided if multi-site clinical trials are proposed.
- **Ethical Considerations**
  - Whether the population selected to participate in the trial stands to benefit from the knowledge gained.
  - Whether the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
  - To what degree privacy and confidentiality issues are appropriately considered.
  - To what degree the process seeking informed consent are appropriate.
- **Biorepository Contribution Statement (*Biorepository Contribution Option only*)**
  - How well the types of datasets and/or biospecimens to be contributed to the BBRAIN are described.
  - To what extent the application describes any special preparation, facilities and/or technical capabilities necessary for collection, storage, and transfer of data and specimens to BBRAIN.
  - How well technical capabilities necessary for collection, storage, and transfer of data and/or Gulf War Veteran specimens to BBRAIN are described.
  - Whether plans for adherence to the SOPs, quality assurance measures, and annotation standards for clinical and pathological specimens and data established by the BBRAIN members are adequately detailed.
  - How well the application describes plans to coordinate with the BBRAIN for the resolution of any intellectual and material property issues related to contribution of samples and/or data.
  - How well the application addresses the informed consent processes and how patient data confidentiality will be maintained in compliance with federal and state regulations, if applicable.

- **Clinical Consortium Collaboration Statement** (*Clinical Consortium Collaboration Option only*)
  - How well the PI's experience in conducting multi-institutional clinical trials demonstrates willingness and ability to participate in collaborative clinical trials and function in the Consortium.
  - How well the application describes the extent to which the existing GWICTIC infrastructure will be leveraged and integrated into the clinical trial, including interaction of a named Clinical Research Coordinator.
  - How well the application describes commitment to adhere to the SOPs, quality assurance measures, clinical protocols, CDEs, and data management procedures of the GWICTIC.
  - How well a letter of collaboration from the GWICTIC demonstrates endorsement of the clinical trial.

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 the intellectual and material property plan is appropriate for the proposed clinical trial.
- **Budget**
  - Whether the direct costs exceed the allowable direct costs as published in the program announcement.
  - Whether the budget is appropriate for the proposed research.
  - If applicable, the extent the proposed costs for contribution of samples and/or data to BBRAIN are appropriate.
  - If applicable, the extent the accounting of proposed costs for collaboration with the GWICTIC are appropriate.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

### **II.E.1.b. Programmatic Review**

To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following criteria are used by programmatic reviewers:

- Ratings and evaluations of the peer reviewers
- Relevance to the mission of the DHP and FY21 GWIRP, as evidenced by the following:
  - Adherence to the intent of the award mechanism
  - Program portfolio composition
  - Relative impact
  - Relative outcomes from the PI's previous GWI-related (if applicable)

### **II.E.2. Application Review and Selection Process**

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding General, USAMRDC, on behalf of the DHA and the OASD(HA). ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in [Section II.E.1.b, Programmatic Review](#).*** Additional information about the two-tier process used by the CDMRP can be found at <https://cdmrp.army.mil/about/2tierRevProcess>. An information paper describing the funding recommendations and review process for the award mechanisms for the GWIRP will be provided to the PI and posted on the CDMRP website.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement declaring 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 and approval 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 and approval 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.

### **II.E.3. Integrity and Performance Information**

Prior to making an assistance agreement award where the federal share is expected to exceed the simplified acquisition threshold, as defined in 2 CFR 200.88, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in the Federal Awardee Performance and Integrity Information System (FAPIIS).

An applicant organization may review FAPIIS, accessible through SAM, and submit comments to FAPIIS on any information about the organization that a federal awarding agency previously entered and is currently available in FAPIIS.

The federal awarding agency will consider any comments by the applicant, in addition to other information in the designated integrity and performance system, in making a judgment about the applicant's integrity, business ethics, and record of performance under federal awards when determining a recipient's qualification prior to award, according to the qualification standards of the Department of Defense Grant and Agreement Regulations (DODGARs), Section 22.415.

### **II.E.4. Anticipated Announcement and Federal Award Dates**

All application review dates and times are indicated in [Section I, Overview of the Funding Opportunity](#).

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.

## **II.F. Federal Award Administration Information**

### **II.F.1. Federal Award Notices**

Awards supported with FY21 funds are anticipated to be made no later than September 30, 2022. Refer to the General Application Instructions, Appendix 2, for additional award administration information.

After email notification of application review results through eBRAP, and if selected for funding, a representative from USAMRAA will contact the Business Official authorized to negotiate on behalf of the PI's organization.

**Pre-Award Costs:** An institution of higher education, hospital, or other non-profit organization may, at its own risk and without the government's prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new award. Refer to the General Application Instructions, Section III.A.5.

***Only an appointed USAMRAA Grants Officer may obligate the government to the expenditure of funds.*** No commitment on the part of the government should be inferred from discussions

with any other individual. **The award document signed by the Grants Officer is the official authorizing document.**

**Federal Government Organizations:** Funding made to federal government organizations (to include intramural DOD organizations) will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

### **II.F.1.a. PI Changes and Award Transfers**

The organizational 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. An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

Unless otherwise restricted, changes in PI will be allowed at the discretion of the Grants Officer, provided the intent of the award mechanism is met.

An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

Refer to the General Application Instructions, Appendix 2, Section B, for general information on organization or PI changes.

### **II.F.2. Administrative and National Policy Requirements**

Applicable requirements in the DODGARs found in 32 CFR, Chapter I, Subchapter C, and 2 CFR, Chapter XI, apply to grants and cooperative agreements resulting from this program announcement.

Refer to the General Application Instructions, Appendix 2, for general information regarding administrative requirements.

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

Refer to full text of the latest [DoD R&D General Terms and Conditions](#); the [USAMRAA General Research Terms and Conditions with Institutions of Higher Education, Hospitals, and Non-Profit Organizations: Addendum to the DoD R&D General Terms and Conditions](#); and the [USAMRAA General Research Terms and Conditions with For-Profit Organizations](#) for further information.

### **II.F.3. Reporting**

Refer to the General Application Instructions, Appendix 2, Section A, for general information on reporting requirements. ***If there are technical reporting requirement delinquencies for any***

*existing USAMRAA-sponsored awards at the applicant organization, no new awards will be issued to the applicant organization until all delinquent reports have been submitted.*

Annual progress reports as well as a final progress report will be required.

The Award Terms and Conditions will specify if more frequent reporting is required.

**Award Expiration Transition Plan:** An Award Expiration Transition Plan must be submitted with the final progress report. Use the one-page template “Award Expiration Transition Plan,” available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) under the “Progress Report Formats” section. The Award Expiration Transition Plan must outline if and how the research supported by this award will progress and must include source(s) of funding, either known or pending.

**Inclusion Enrollment Reporting Requirement:** Enrollment on the basis of sex/gender, race, and/or ethnicity will be required with each annual and final technical report. The suggested Inclusion Enrollment Report format is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP.

Awards resulting from this program announcement will incorporate additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have federal contract, grant, and cooperative agreement awards with a cumulative total value greater than \$10,000,000 are required to provide information to FAPIIS about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a federal award. Recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 5, Section B).

## **II.G. Federal Awarding Agency Contacts**

### **II.G.1. CDMRP Help Desk**

Questions related to program announcement content or submission requirements as well as questions related to the pre-application or intramural application submission 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](mailto:help@eBRAP.org)

### **II.G.2. Grants.gov Contact Center**

Questions related to extramural 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; International 1-606-545-5035

Email: [support@grants.gov](mailto: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 or by responding to the prompt provided by Grants.gov when first downloading the Grants.gov application package. If the Grants.gov application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

## **II.H. Other Information**

### **II.H.1. Program Announcement and General Application Instructions Versions**

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 601a. The program announcement numeric version code will match the General Application Instructions version code 601.

### **II.H.2. Administrative Actions**

After receipt of pre-applications or applications, the following administrative actions may occur:

#### **II.H.2.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:

- 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.

#### **II.H.2.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.

### II.H.2.c. Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- An FY21 GWIRP Programmatic Panel 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 FY21 GWIRP Programmatic Panel members can be found at <https://cdmrp.army.mil/gwirp/panels/panels21>.*
- The application fails to conform to this program announcement description.
- 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).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY21, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<https://cdmrp.army.mil/about/2tierRevProcess>). Applications that include names of personnel from either of these companies may be administratively withdrawn.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP may be withdrawn.
- Applications submitted by an intramural DOD organization may be withdrawn if the intramural organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to extramural collaborators.
- The proposed research is not a large-scale biomarker research study/biomarker trial or a clinical trial.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The invited application proposes a different research project than that described in the pre-application.
- The application describes research focusing on ALS.
- 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.

#### **II.H.2.d. Withhold**

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization 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.

### II.H.3. Application Submission Checklist

Application Components	Action	Completed
SF424 Research & Related Application for Federal Assistance ( <b>extramural submissions only</b> )	Complete form as instructed	
Summary (Tab 1) and Application Contacts (Tab 2) ( <b>intramural submissions only</b> )	Complete tabs as instructed	
Attachments	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"	
	Data Management: Upload as Attachment 6 with file name "Data_Manage.pdf"	
	Regulatory Strategy: Upload as Attachment 7 with the file name "Regulatory.pdf" if applicable	
	Transition Plan: Upload as Attachment 8 with file name "Transition.pdf"	
	Impact Statement: Upload as Attachment 9 with file name "Impact.pdf"	
	Option Statements: Upload as Attachment 10 with file name "Options.pdf" if applicable	
	Outcomes Statement: Upload as Attachment 11 with file name "Outcomes.pdf" if applicable	
	Representations (extramural submissions only): Upload as Attachment 12 with file name "RequiredReps.pdf" if applicable	
	Suggested Collaborating DOD Military Facility Budget Format: Upload as Attachment 13 with file name "MFBudget.pdf" if applicable	

<b>Application Components</b>	<b>Action</b>	<b>Completed</b>
Research & Related Personal Data	Complete form as instructed	
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 ( <b>extramural submissions only</b> )	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field	
Budget ( <b>intramural submissions only</b> )	Suggested DOD Military Budget Format, including justification	
Project/Performance Site Location(s) Form	Complete form as instructed	
Research & Related Subaward Budget Attachment(s) Form, if applicable	Complete form as instructed	

## APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
ALS	Amyotrophic Lateral Sclerosis
BBRAIN	Boston Biorepository, Recruitment, and Integrative Network
CDC	Centers for Disease Control and Prevention
CDE	Common Data Element
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
DHA	Defense Health Agency
DHP	Defense Health Program
DOD	Department of Defense
DODGARs	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Numbering System
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FAPIIS	Federal Awardee Performance and Integrity Information System
FDA	U.S. Food and Drug Administration
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GWI	Gulf War Illness
GWICTIC	Gulf War Illness Clinical Trials and Interventions Consortium
GWIRP	Gulf War Illness Research Program
HRPO	Human Research Protection Office
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use)
IDE	Investigational Device Exemption
IND	Investigational New Drug
IOM	Institute of Medicine (now, National Academy of Medicine)
IRB	Institutional Review Board
LAR	Legally Authorized Representative
M	Million
MIPR	Military Interdepartmental Purchase Request
OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
ORCID	Open Researcher and Contributor ID, Inc.
ORP	Office of Research Protections
PI	Principal Investigator
RDT&E	Research, Development, Test, and Evaluation
SAM	System for Award Management

SOPs	Standard Operating Procedures
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
UEI	Unique Entity Identifier
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	Department of Veterans Affairs