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

Therapeutic/Biomarker Trial Award

Announcement Type: Initial

Funding Opportunity Number: W81XWH-19-GWIRP-TBTA

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), July 12, 2019
- **Invitation to Submit an Application:** August 2019
- **Application Submission Deadline:** 11:59 p.m. ET, October 3, 2019
- **End of Application Verification Period:** 5:00 p.m. ET, October 8, 2019
- **Peer Review:** November 2019
- **Programmatic Review:** January 2020

This Program Announcement must be read in conjunction with the General Application Instructions, version 20190218. 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."

TABLE OF CONTENTS

II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

Applications to the Fiscal Year 2019 (FY19) 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 FY18 totaled $170 million (M). The FY19 appropriation is $22M.

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 pathobiology and symptoms. ***Applicants are strongly encouraged to read and consider The Gulf War Illness Landscape before preparing their applications.*** The Landscape may be found at https://cdmrp.army.mil/gwirp/pdfs/GWIRP_Landscape.pdf.

II.A.2. FY19 GWIRP Overarching Challenges

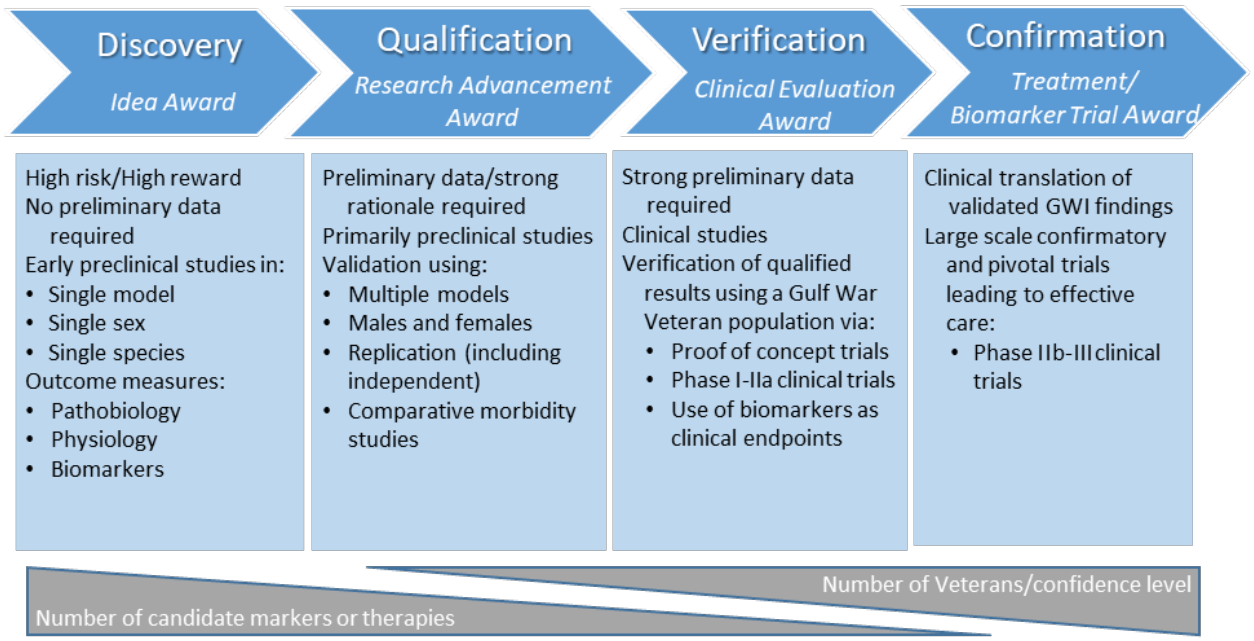
Considering the current Gulf War Illness Landscape and the GWIRP's mission, all FY19 GWIRP applications must address at least one of the following overarching challenges unless adequate justification for exception is provided.*

- Revolutionize treatment and minimize negative side effects
- Eliminate the health consequences associated with Gulf War Illness (GWI)
- Distinguish symptom clusters to better target treatments
- Identify what drives GWI and determine how to intervene
- Identify why GWI is worse for some Veterans than for others
- Validate determinants of GWI susceptibility, latency, and impacts on organs and systems
- Better define and diagnose GWI

- Determine whether GWI puts Veterans at greater risk for developing neurological diseases, cancers, or other serious conditions
- Help Veterans, their caregivers, and clinicians communicate effectively about GWI, its symptoms, and potential treatments
- Primary prevention strategies based on a consistent theory of GWI etiology

*Alternatively, 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 FY19 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 **FY19 GWIRP Idea Award** (Funding Opportunity Number: W81XWH-19-GWIRP-IA).

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 **FY19 GWIRP Research Advancement Award** (Funding Opportunity Number: W81XWH-19-GWIRP-RAA).

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 I through IIa intervention trials. Applicants seeking support for the Verification phase should consider the **FY19 GWIRP Clinical Evaluation Award** (Funding Opportunity Number: W81XWH-19-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 IIb through Phase III 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 **FY19 GWIRP Therapeutic/Biomarker Trial Award** (Funding Opportunity Number: W81XWH-19-GWIRP-TBTA).

The development and maintenance of **strategies to effectively communicate GWI research and clinical recommendations** to diverse audiences, with the goal of informing and raising awareness, shall be considered at each phase of the research pipeline. Applicants seeking support for effective communication strategies should consider the **FY19 GWIRP Patient-Provider and Health Communications Award** (Funding Opportunity Number: W81XWH-19-GWIRP-PPHCA).

NOTE: The scope of research proposed in applications in response to the FY19 GWIRP Program Announcements must align with the research phases outlined above. It is the responsibility of the applicant to select the level 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.B. Award Information

The FY19 GWIRP Therapeutic/Biomarker Trial Award supports large-scale, pivotal (e.g., Phase IIb-III) clinical trials that will revolutionize the clinical management of GWI. **The Therapeutic/Biomarker Trial Award targets the Confirmation phase of the research pipeline as outlined in Section II.A.2.** The proposed research should lead to an approach that is fundamentally better than interventions already approved or in clinical development. Objective biomarkers to measure the biological effect of an investigational therapeutic 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 must be included in the trial design. Development of markers for the purposes of diagnosis, prognosis, or measurement of disease progression without consideration of the therapeutic development process will not be supported.

Principal Investigators (PIs) are expected to have experience in successfully leading large-scale projects and demonstrated ability (through personal experience or via a commitment from a collaborating clinical investigator) to implement a clinical project successfully.

Funding from this award mechanism must support a clinical trial. Investigators seeking funding for a preclinical research project should consider one of the other FY19 GWIRP Program Announcements being offered.

New FY19 definition: A clinical trial is 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. The term "human subjects" is used in this Program Announcement to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at https://ebrap.org/eBRAP/public/Program.htm.

For proposed research that will require U.S. Food and Drug Administration (FDA) involvement, project readiness requirements at the time of application submission include: proof of availability of and access to clinical reagents (e.g., therapeutics) that meet regulatory compliance guidelines, proof of availability of and access to appropriate subject population(s), validated projections for patient recruitment, and submission of an Investigational New Drug (IND) or Investigational Device Exemption (IDE) application to the FDA that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312). It is the responsibility of the applicant to provide evidence from the Institutional Review Board (IRB) of record or the FDA if an IND or IDE is not required.

If an IND is required, the IND application ***must be submitted to the FDA by the Therapeutic/Biomarker Trial Award application submission deadline.*** The IND should be specific for the product (i.e., the product should not represent a derivative or alternate version of the investigational agent described in the IND application) and indication to be tested in the proposed clinical trial. For more information on IND applications, the FDA has provided guidance at https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm.

If an IDE is required, the IDE application ***must be submitted to the FDA by the Therapeutic/Biomarker Trial Award application submission deadline***. The IDE should be specific for the device (i.e., should not represent a derivative or modified version of the device described in the IDE application) and indication to be tested in the proposed clinical trial.

Refer to Attachment 8, Regulatory Strategy, for additional details on documentation of FDA applications. The Government reserves the right to withdraw funding if an IND or IDE application and/or international regulatory application is necessary but has not been submitted prior to the application submission deadline.

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 FY19 GWIRP are encouraged to contribute Gulf War Veteran biospecimens and data to this repository network. The FY19 GWIRP Therapeutic/Biomarker Trial Award offers a nested 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 13) 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 I and II 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 FY19 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 FY19 GWIRP Therapeutic/Biomarker Trial Award offers a nested 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 13) providing a detailed accounting of proposed costs and a commitment to work with protocols and SOPs developed by the GWICTIC.

The following are important aspects of the GWIRP Therapeutic/Biomarker Trial Award, in addition to the items outlined above:

- **Preliminary Data.** Inclusion of preliminary data from the field of GWI relevant to the proposed clinical trial is required.

- **Start Time.** The proposed clinical trial is expected to begin no later than 12 months after the award date, or 18 months after the award date for FDA-regulated studies.

- **Recruitment Plan and Milestones.** The application must include a sound subject recruitment and retention plan and demonstrate availability of and access to a suitable Gulf War Veteran population that will support a meaningful, statistically significant outcome for the study. Applicants are encouraged to budget sufficient resources to reimburse subjects and their caregivers (as necessary) for travel and lodging expenses and to provide participation incentives. The application must indicate the quarterly enrollment targets across all sites in Attachment 4, Statement of Work. Successful applicants will work with USAMRAA to establish milestones for human subject recruitment. Continued support for the project will be based upon satisfactory progress in meeting the established milestones.

- **Therapeutic Access.** The application should demonstrate availability of and access to the drug/compound, device, and/or other materials needed, as appropriate, for the proposed

duration of the study. The quality and stability of the product should be documented and commensurate with current FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practice [GMP] guidelines).

- **FDA Experience.** If applicable, the application should demonstrate experience on the study team in interacting with the FDA, including previous FDA submissions.

- **Statistical Analysis Plan.** The application should include a clearly articulated statistical analysis plan, demonstrate appropriate statistical expertise on the research team, and include a power analysis reflecting sample size projections that will answer the objectives of the study.

- **Safety Management Plan.** The application should include a clearly articulated safety management plan outlining how safety pharmacovigilance will be conducted, as applicable.

- **Clinical Monitoring Plan.** The application should include a clearly articulated clinical monitoring plan outlining how the study will be monitored for Good Clinical Practice (GCP) compliance.

- **Data Management Plan.** The application should include a clearly articulated data management plan and use of an appropriate database to safeguard and maintain the integrity of the data. If FDA-regulated, the trial must use a 21 CFR 11-compliant database and appropriate data standards. For more on data standards, see https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM511237.pdf.

- **Study Coordinator.** The application should include a study coordinator(s) who will guide the clinical protocol through the local IRB of record and other Federal agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.

- **Transition Plan.** The application should include a Transition Plan (including potential funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to Veterans suffering from GWI after the successful completion of the FY19 GWIRP Therapeutic/Biomarker Trial Award.

- **Institutional Support.** The application should clearly demonstrate strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in 21 CFR 312, Subpart D, are fulfilled.

- **NIH Clinical Trials.gov Registration.** Funded studies are required to register the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 1, Section C, for further details.

- **Costs/Budget.** The requested budget must be commensurate with the phase and size of the trial proposed.

Activities <u>not supported</u> 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 anticipated direct costs budgeted for the entire period of performance for an FY19 GWIRP Therapeutic/Biomarker Trial Award will not exceed **$5,000,000**. If applying under the Biorepository Contribution Option, direct costs will not exceed **$5,020,000.** If applying under the Clinical Consortium Collaboration Option, direct costs will not exceed **$5,500,000.** Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

The CDMRP expects to allot approximately $8.8M to fund approximately one (1) Therapeutic/Biomarker Trial Award application. 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 FY19 funding opportunity will be funded with FY19 funds, which will expire for use on September 30, 2025.

Awards will be made no later than September 30, 2020. For additional information, refer to Section II.F.1, Federal Award Notices.

The type of awards made under the Program Announcement will be assistance agreements (grants or cooperative agreements). 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.

An assistance agreement (grant or cooperative 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. 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 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.

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 Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), prior to research implementation. This administrative review requirement is in addition to the local IRB or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB/EC. ***Allow a minimum of 2 to 4 months for HRPO regulatory review and approval processes***. Additional time for regulatory reviews may be needed for clinical studies taking place in international settings. When possible, protocols should be written for research with human subjects and/or human anatomical substances that are specific to the DoD-supported effort outlined in the submitted application as a stand-alone study. Submission to HRPO of protocols involving more than the scope of work in the DoD-funded award will require HRPO review of the entire protocol (DoD and non-DoD funded). DoD human subjects protection requirements may be applied to non-DoD funded work and necessitate extensive revisions to the protocol. Applications that involve recruitment of human subjects must indicate the quarterly enrollment targets across all sites in Attachment 4, Statement of Work. Successful applicants will work with USAMRAA to establish milestones for human subjects recruitment. Continued support for the project will be based upon satisfactory progress in meeting the established milestones. Refer to the General Application Instructions, Appendix 1, Section B, 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.

Multi-Institutional Clinical Trials: If the proposed clinical trial is multi-institutional, plans for the multi-institutional structure governing the research protocol(s) should be outlined in Attachment 9, Study Personnel and Organization. The lead organization 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. A single IRB/EC pathway is strongly recommended whenever possible. The master protocol and consent form must be reviewed by the HRPO prior to distribution to the additional sites for IRB/EC review. Communication and data transfer among the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the application. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials.

If the IRB determines that a trial presents greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consistent with the nature of the risk(s) identified within the research protocol. If applicable, refer to the General Application Instructions, Appendix 1, Section B (Research Monitor Requirement) for more information on study reporting authorities and responsibilities of the research monitor.

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.

Gulf War Veteran Recruitment: Applicants not collaborating with the GWICTIC 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.

GWI Case Definitions for Clinical Research: In 2014 the Institute of Medicine (IOM) (now called National Academy of Medicine) released a report, "Chronic Multisymptom Illness in Gulf War Veterans: Case Definitions Reexamined" (available online at http://www.nationalacademies.org/hmd/Reports/2014/Chronic-Multisymptom-Illness-in-Gulf-War-Veterans-Case-Definitions-Reexamined.aspx). In this report, the IOM recommended the use of both the U.S. Centers for Disease Control and Prevention's (CDC) definition of GWI and the "Kansas" definition of GWI. Applicants proposing clinical research may construct a definition of subgroups or symptom clusters as appropriate to the specific research; however, all cases and controls must additionally be scored and analyzed according to both the CDC and the Kansas definitions of GWI for comparative purposes. Any additional project-specific case definition must recognize the multisymptom nature of GWI. Another resource for clinical investigations includes the 2014 report of the Research Advisory Committee on Gulf War Veterans' Illnesses, "Gulf War Illness and the Health of Gulf War Veterans: Research Update and Recommendations, 2009-2013," which provides information on GWI, including case definitions and research on epidemiology, etiology, pathobiology, and treatment. This report can be found online at https://www.va.gov/RAC-GWVI/RACReport2014Final.pdf.

Common Data Elements for Clinical Research: Through a collaboration between the NIH, CDC, VA, DoD GWIRP, and the GWI community, CDE recommendations are being developed for GWI. The goals of this effort are to increase the efficiency and effectiveness of clinical research studies and treatment, increase data quality, facilitate data sharing and aggregation of information across studies, and help educate new clinical investigators. In early 2018, members from the GWI community participated in a CDE development working group to prepare standard template case report forms and instrument recommendations for clinical research studies. The version 1.0 recommendations were posted on the GWIRP website at https://cdmrp.army.mil/gwirp/default in January 2019. **The GWIRP strongly encourages applicants in the clinical research community, whether or not collaborating with the GWICTIC, to read and consider the CDEs, which are used by GWICTIC, when preparing applications**. Use of CDEs is expected to expedite study start-up, standardize data collection, and allow for future data sharing. CDEs will be required in clinical research going forward and must be considered by investigators submitting samples to the BBRAIN under the Biorepository Contribution

Option. It should be noted that the development of CDEs is an iterative process. Updates will be made to the GWI CDEs as research progresses and feedback is received from the community.

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 2, Section K.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: All organizations, including 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 organizations 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.

Note: Applications from an intramural DoD organization or from an extramural Federal Government organization may be submitted to Grants.gov through a research foundation.

The 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.

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.

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

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: An application submitted by an organization to Grants.gov.

Intramural DoD Submission: An application submitted by a DoD organization to eBRAP.

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.

Extramural Submissions:

- Pre-application content and forms must be accessed and submitted at eBRAP.org.
- Full application packages must be accessed and submitted at Grants.gov.

Intramural DoD Submissions:

- Pre-application content and forms must be accessed and submitted at eBRAP.org.
- Full application packages must be accessed and submitted at eBRAP.org.

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*** and ***full application*** as indicated below. The submission process should be started early to avoid missing deadlines. There are no grace periods.

Pre-Application Submission: All pre-applications for both extramural and intramural organizations must be submitted through eBRAP.org.

Full Application Submission: Full applications must be submitted through the online portals as described below.

Extramural Organization Submissions: Full applications from extramural organizations must be submitted through a Grants.gov Workspace. Applications submitted by extramural organizations (e.g., research foundations) on behalf of intramural DoD or other Federal organizations or investigators will be considered extramural submissions. Applications from extramural organizations, including non-DoD Federal organizations, received through eBRAP will be withdrawn. See definitions in Section II.C.1, Eligible Applicants.

Intramural DoD Organization Submissions: Intramural DoD organizations may submit full applications to either eBRAP or Grants.gov. Intramural DoD organizations that are unable to submit to Grants.gov should submit through eBRAP. Intramural DoD organizations with the capability to submit through Grants.gov may submit following the instructions for extramural submissions through Grants.gov or may submit to 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. 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. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement.

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 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, each submission is assigned a unique log number by. 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 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 PI must contact the CDMRP Help Desk at 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.

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. Note that the codes have recently been revised. 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.

  FY19 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 or 301-682-5507.

- **Tab 4 – Conflicts of Interest (COIs)**

  List all individuals other than collaborators and key personnel who may have a COI 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:** Provide responses in the appropriate data fields for the following:

    - What GWIRP overarching challenge(s) will the proposed research address? If "other," state the overarching challenge and provide justification within the context of the Gulf War Illness Landscape. (200-character limit)

    - How will the proposed research lead to a solution for the overarching challenge(s)? (2,000-character limit)

    - State how the scope of the proposed research is appropriate for the **Confirmation phase** of the research pipeline. How will the proposed research lead to a new approach that is fundamentally better than interventions already approved or in clinical development? (2,000-character limit)

    - Project readiness (3,000-character limit): State the clinical intervention and phase of the clinical trial proposed. Describe a plan for project readiness by the application deadline with respect to availability of and access to clinical reagents (e.g., therapeutics) that meet regulatory compliance guidelines, availability of and access to appropriate subject population(s), and submission of an IND or IDE application to the FDA, if applicable.

- **Pre-Application Supporting Documentation:** Supporting documentation for the pre-application ***must be uploaded as an individual file*** limited to the following:

  - One page for additional information that the PI can use, at his/her 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**

  Pre-applications will be reviewed by the GWIRP Programmatic Panel, a group composed of scientists, clinicians, and consumers. Pre-applications that meet the intent of the award mechanism will be invited to submit applications. 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 overarching challenge or other topic that meets the program's goals for which they have provided sufficient justification.

  - To what degree the pre-application proposes research that will lead to a solution for the overarching challenge.

  - To what degree the pre-application moves beyond a minor advancement and has the potential to lead to a new approach that is fundamentally better than interventions already approved or in clinical development.

  - Whether the pre-application describes a feasible plan for project readiness by the application deadline.

- **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.

Table 1. Full Application Submission Guidelines

Extramural Submissions	Intramural DoD Submissions
Application Package Location	
Download application package components for W81XWH-19-GWIRP-TBTA from Grants.gov (https://www.grants.gov) 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-19-GWIRP-TBTA from eBRAP (https://ebrap.org).
Full Application Package Components	
SF424 Research & Related Application for Federal Assistance Form: Refer to the General Application Instructions, Section III.A.1, for detailed information.	**Tab 1 – Summary:** Provide a summary of the application information. **Tab 2 – Application Contacts:** This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.

Extramural Submissions	Intramural DoD Submissions
Descriptions of each required file can be found under Full Application Submission Components: • Attachments • Research & Related Personal Data • Research & Related Senior/Key Person Profile (Expanded) • Research & Related Budget • Project/Performance Site Location(s) Form • Research & Related Subaward Budget Attachment(s) Form (if applicable)	**Tab 3 – Full Application Files:** Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components: • Attachments • Key Personnel • Budget • Performance Sites **Tab 4 – Application and Budget Data:** Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.
Application Package Submission	
Create a Grants.gov Workspace. Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission. **Submit a Grants.gov Workspace Package.** 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 **at least 24-48 hours prior to the close date** to allow time to correct any potential technical issues that may disrupt the application submission. **Note:** 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 ***prior to*** the application submission deadline.	**Submit package components to eBRAP (https://ebrap.org).** **Tab 5 – Submit/Request Approval Full Application:** 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.
Application Verification Period	
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 ***with the exception of the Project Narrative and Research & Related Budget Form***.	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

Extramural Submissions	Intramural DoD Submissions
	application verification period, the full application package may be modified ***with the exception of the Project Narrative and Research & Related Budget Form***. 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.
Further Information	
Tracking a Grants.gov Workspace Package. 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. Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.	Refer to the General Application Instructions, Section IV, for further information regarding eBRAP requirements.

Both Extramural and Intramural organizations: Application viewing, modification, and verification in eBRAP are strongly recommended, but not required. ***The Project Narrative and Research & Related Budget cannot be changed after the application submission deadline.*** Prior to the full application deadline, a corrected or modified full application package may be submitted. 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.

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.

  The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 5-8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

  - **Attachment 1: Project Narrative (20-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: Describe the proposed project in detail using the outline below.

    - **Overarching Challenge(s):** Describe how the proposed research is responsive to one or more of the GWIRP Overarching Challenges.

    - **Background:** Describe in detail the rationale for the study. Include preliminary data collected from relevant previous pilot trials in GWI Veterans, if applicable, and describe how the proposed study validates or confirms findings. If the intervention is used for another condition, include a rationale explaining why the proposed intervention would be expected to be effective for GWI and present preliminary data from the field of GWI that provides a rationale for use of the treatment in a large-scale trial of GWI Veterans. Describe objective biomarkers to be used as clinical endpoints. Biomarkers may originate from the investigators' laboratory or be derived from previously published markers in the context of GWI. Valid biomarker endpoints include a measure of the biological effect of a therapeutic or evidence of a Gulf War Veteran subgroup that will benefit from the proposed intervention.

    - **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses.

This information should agree with the primary aims and associated tasks described in the Statement of Work (Attachment 4).

- **Study Design:** Outline the proposed methodology in sufficient detail to show a clear course of action.

  - Describe the study phase or class and the study model (e.g., single group, parallel, crossover). Define each arm/study group of the proposed trial, if applicable. Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).

  - Outline whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.

  - Describe use of subgroup-selective biomarkers or pharmacodynamics biomarkers to be used as a clinical endpoints. Define other primary, secondary, or interim endpoints/outcome measures, outline why they were chosen, and describe how and when they will be measured. Applicants are encouraged to include multiple endpoints from varied domains as appropriate. Include a description of appropriate controls. Outline the timing and procedures planned during the follow-up period.

  - Briefly describe the inclusion and exclusion criteria that will be used and describe the methods that will be used to recruit Gulf War Veterans. A full description of the recruitment plan should be detailed in Attachment 6, Human Subject Recruitment and Safety Procedures. All subjects and controls must be scored at least according to both CDC and Kansas case definitions for GWI for the purpose of comparative analysis. If an additional case definition other than the CDC or Kansas definition is to be used, describe this definition and how it is quantified, and explain the rationale behind its inception and use.

  - Describe potential problem areas and discuss alternative methods/approaches that may be employed to overcome them. Estimate the potential for subject loss to follow-up and how such loss will be handled/mitigated.

- **Statistical Plan and Data Analysis:** 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 and justify the rationale for the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. ***Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study.*** If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study. Ensure sufficient information is

provided to allow thorough evaluation of all planned statistical procedures during review of the application.

- **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.

- Letters of Commitment (if applicable): If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.

- Intellectual Property: Information can be found in 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 13). 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 (see Attachment 13).

- Access to Veterans of the 1990-1991 Gulf War (if applicable): Provide a letter of support from a 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 ACOS/R&D or Clinical Service Chief confirming access to VA patients, resources, and/or VA research space. For VA PIs, if the VA NPC 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.

- **Attachment 3: Technical and Lay Abstracts (two-page limit): Upload as Abstracts.pdf.** Use one page for technical abstract (page should be titled "Technical Abstract"). Begin lay abstract on a separate page (page should be titled "Lay Abstract").

  The technical and lay abstracts are 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.

Technical abstract. 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 overarching challenge(s) that will be addressed.
- Background: Present the ideas and rationale behind the proposed clinical trial.
- 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.
- Clinical Impact: Briefly describe how the proposed project will transform and revolutionize the clinical management of GWI.

Lay abstract. 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.

- State the overarching challenge(s) that will be addressed.
- Describe the scientific objective and rationale for the proposed study and intervention in a manner readily understood by readers without scientific or medical backgrounds.
- Describe the ultimate applicability and impact of the research.
  - What are the clinical applications, benefits, and risks for Veterans with GWI?
  - What is the projected time it may take to achieve a patient-related outcome?

- **Attachment 4: Statement of Work (six-page limit): Upload as "SOW.pdf".** The suggested 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). For the Therapeutic/Biomarker Trial Award mechanism, use the SOW format example titled "SOW for Clinical Research (Including Trials, Special Populations)." The SOW must be in PDF format prior to attaching.

  The SOW should include a list of major tasks that support the proposed specific aims, followed by a series of subtasks outlined related to the major tasks and milestones within the period of performance. The SOW should describe only the work for which funding is being requested by this application and, as applicable, should also:

- Include the name(s) of the key personnel and contact information for each study site/ subaward site.

- Indicate the number (and type, if applicable) of research subjects projected or required for each task and at each site. Indicate quarterly enrollment targets. Refer to the General Application Instructions, Appendix 1, for additional information regarding regulatory requirements.

- If applicable, indicate timelines required for regulatory approvals relevant to human subjects research (e.g., IND or IDE applications) by the FDA or other Government agency.

- The SOW should include a feasible timeline to conduct the clinical trial.

- The GWIRP strongly encourages timely dissemination of the results of GWIRP-sponsored research. The SOW should include at least one task or aim focused on preparation of final study results including lay-oriented materials for study participants as well as submission of scientific publications.

- **Attachment 5: Intervention (no page limit): Upload as "Intervention.pdf".** The Intervention attachment should include the components listed below.

  - Description of the Intervention: Identify the intervention to be tested and describe the particular outcomes. As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for conduct of the clinical trial.

  - Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety and stability (as appropriate) of the intervention.

  - Study Procedures: Describe the interaction with the human subject, including the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Clearly delineate research procedures from routine clinical procedures. Discuss how compliance with current Good Laboratory Practice (GLP) guidelines, GMP, and other regulatory considerations will be established, monitored, and maintained, as applicable.

  - Clinical Monitoring Plan: Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of

Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 6: Human Subject Recruitment and Safety Procedures (no page limit): Upload as "HumSubProc.pdf".** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  - Study Population: Describe the nature, approximate number, and pertinent demographic characteristics of the target 1990-1991 Gulf War Veteran population. Include information about specific symptom profiles relevant to GWI and the proposed clinical trial.

  - Inclusion/Exclusion Criteria: List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender.

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

  - Gulf War Veteran Outreach and Recruitment Plan: Outreach and positive recruitment and retention have historically been an issue in the study of Gulf War Veterans. Recruiting and retaining participants requires careful consideration. Outreach and recruitment activities need to be identified early in the planning process and should include the involvement of appropriate sources within the community and considerations for Veteran subject compensation. The Gulf War Veteran Outreach and Recruitment Plan must include the components listed below. A resource containing additional guidance for successful access to Gulf War Veterans titled, "General Guidance for Gulf War Veteran Subject Outreach and Recruitment" can be found on the GWIRP webpage at https://cdmrp.army.mil/gwirp/pdfs/General%20_Guidance_for_Gulf_War_Veteran_Outreach_and_Recruitment.pdf.

    - Describe the activities that will be used to identify and recruit potential subjects using the outline below. All advertisements and recruitment materials must be

approved by the respective IRB/EC prior to use. Local IRB/EC approval at the time of application submission is not required.

- Specific Approaches: Summarize the outreach and recruitment plan in detail including drawing on an existing cohort, partnering with an established GWI researcher, advertising, appearances at events, direct mail, and other approaches. Provide a table of anticipated enrollment counts at each study site.

- Organizations: Name the specific organizations that will participate in recruitment efforts

  - When collaborating with VA researchers, a letter of support confirming access to VA patients and signed by the lowest-ranking person with approval authority, is required. Include this letter in Attachment 2, Supporting Documentation.

  - Media Outlets: Name specific broadcast or social media outlets that will be used to advertise the study.

- Staff: Describe the composition and duties of the outreach/recruiting staff. Demonstrate that the research team has access to the proposed study population at each site, and describe the efforts that will be made to achieve accrual goals. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Describe training they will receive for interacting with and recruiting Veterans.

- Recruitment Materials: The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study. Encouraging themes describing how the research might benefit fellow Gulf War Veterans or Veterans of later deployments suffering from similar exposures are acceptable. Describe electronic, paper, or other recruitment materials to be employed.

  - If advertising materials are to be posted at VA or civilian facilities, a signed statement indicating permission must be included. Include this letter in Attachment 2.

  - Compensation and incentives: Include a description of the compensation plan for travel, meals, lodging, participation incentives, and any other compensation or incentives.

- Physical and Logistical Accommodation of Subjects: Describe measures that will be taken at the trial facility to accommodate subjects including aid in

reaching the facility, moving or navigation within the facility, and assignment of and access to staff points of contact for inquiries or requests for assistance.

- ❖ Alternate Approaches: Address any potential barriers to accrual or other potential unanticipated delays. Include detailed plans for alternate approaches to be employed if recruitment lags behind schedule. Include a mitigation plan for slow or low enrollment. Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress.

- Sharing of Study Results: Describe plans for dissemination of study results to participants including:

  - Aggregate, final study results including any lay-oriented materials other than scientific publications.

  - Individual study test results for individual subjects.

- Description of the Informed Consent Process: Specifically describe the plan for obtaining informed consent from human subjects.

  - ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***

  - Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial.

  - Include information regarding the timing and location of the consent process.

  - Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.

  - Address how privacy and time for decision-making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.

  - Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.

  - Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. ***Note:*** In compliance with 10 USC 980 (https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-

chap49-sec980.pdf), the application must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial. If applicable, refer to the General Application Instructions, Appendix 1, for more information.

- ***Assent.*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

- Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. ***Note:*** Some screening procedures may require a separate consent or a two-stage consent process.

- Risks/Benefits Assessment:

  - **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is exposed to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

  - **Risk management and emergency response:**

    - Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.

    - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.

    - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, including who will be responsible for the cost of such care.

    - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).

    - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.

- ❖ If the IRB determines that a trial presents greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research protocol. If applicable, refer to the General Application Instructions, Appendix 1, Section B (Research Monitor Requirement), for more information on study reporting authorities and responsibilities of the research monitor.

– Potential benefits: Describe known and potential benefits of the study to the human subjects who will participate in the study. Articulate the importance of the knowledge to be gained as a result of the proposed research. Discuss why the potential risks to human subjects are reasonable in relation to the anticipated benefits to the human subjects and others that may be expected to result.

○ **Attachment 7: Data Management (no page limit): Upload as "Data_Manage.pdf".** The Data Management attachment should include the 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.

- **GWI CDEs:** Describe how the newly established GWI CDEs are being considered and implemented into the clinical trial design.

- **Data reporting:** Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA, if applicable.

- **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 8: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** Answer the following questions and provide supporting documentation as applicable.

– State the product/intervention name.

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

– Explain why the product/intervention is exempt from FDA oversight. Provide confirmation that the trial does not require regulation by the FDA in writing from the IRB of record or the FDA. 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 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 is not currently FDA-approved, -licensed, or -cleared, 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.

- For the FY19 GWIRP Therapeutic/Biomarker Trial Award, ***if an IND or IDE is required, the application must be submitted to the FDA prior to the FY19 GWIRP Therapeutic/Biomarker Trial Award application submission deadline.*** The IND or IDE should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical trial. Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold, etc.). If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of this product. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.

- If available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed.

- If an active IND or IDE for the investigational product is in effect, but an amendment is needed to include the proposed trial, describe the type and nature of the amendment(s) and the timeline for submission. Indicate whether the amendment increases the risk of the intervention.

- Provide the current status for manufacturing development (e.g., manufacturer's name, GMP-compliant lots available, status of stability testing, etc.), non-clinical development (e.g., test facility name, status of pivotal GLP toxicology studies to

support Phase I testing, etc.), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).

- 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, the types of FDA meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.

- **Attachment 9: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as "Personnel.pdf".** The Study Personnel and Organization attachment should include the components listed below.

  - Organizational Chart: Provide an organizational chart that identifies key members of the study team and provides an outline of the governing structure for multi-institutional studies. Identify collaborating organizations, centers, and/or departments and name each person's position on the project. Include any separate laboratory or testing centers. Identify the data and clinical coordinating center(s) and note any involvement from Contract Research Organizations, as appropriate. Identify and provide justification for the inclusion of international sites, as appropriate. If applicable, identify the FDA regulatory sponsor and any external consultants or other experts who will assist with FDA applications. While there is no specified format for this information, a table(s) or diagram is recommended. ***Note:*** This item may be made available for programmatic review.

  - Study Personnel Description: Briefly describe the roles of the individuals listed in the organizational chart on the project. Describe relevant experience and qualifications that demonstrate appropriate expertise for the given role, including previous interactions with the FDA, if applicable. An external research monitor (if applicable) and study coordinator(s) should be included.

  - Study Management Plan: Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions. Provide a regulatory submission plan for the master protocol and master consent form by the lead organization; include a single IRB/EC pathway whenever possible. If applicable, describe how communication and data transfer between the collaborating institutions will occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.

- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit): Upload as "Surveys.pdf".** The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information

collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.

- **Attachment 11: 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.

  - 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 continuity of development.

  - A brief schedule and milestones for transitioning the intervention to the next phase of development (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 12: Impact Statement (two-page limit): Upload as "Impact.pdf".**

  - Identify the Gulf War Veteran population(s) that will participate in the proposed clinical trial, describe how they represent the target population that would benefit from the proposed intervention, and describe the potential impact of the proposed clinical trial on the outcomes of Veterans with GWI.

  - ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial.

  - ***Describe the long-term impact:*** Explain the long-range vision for implementation of the intervention in the clinic, field, or quality of life for the Veteran with GWI and describe the anticipated long-term benefits for the targeted population.

  - Describe any relevant controversies or treatment issues that will be addressed by the proposed clinical trial.

- Describe any potential issues that might limit the impact of the proposed clinical trial.

- Describe how the intervention represents an approach that is fundamentally better than interventions already approved or in clinical development.

- **Attachment 13: Option Statements (three-page limit): Upload as "Options.pdf". (*Required for applications submitted under the Biorepository Contribution Option <u>OR</u> 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 13 blank.

  - Biorepository Contribution Statement: Describe the types of datasets and/or 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 PI 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 if the PI is requesting the Clinical Consortium Collaboration Option to demonstrate commitment and collaboration of the PI to the GWICTIC.***

    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 expenses, quality assurance considerations, and data management considerations.

- **Attachment 14: 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 15: DoD Military Budget Form(s), 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 the DoD Military Budget Form, 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 and 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 A§1681 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".

- 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 DoD Military Budget Form and upload to Grants.gov attachment form as Attachment 15. (Refer to the General Application Instructions, Section IV.A.4, for detailed information.) Intramural DoD Collaborator(s) costs per year should be included on the Grants.gov Research and Related Budget Form under subaward costs.

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's 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.

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

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 retrieved files against the specific Program Announcement requirements, and discrepancies will be noted in both the email and in the "Full Application Files" tab in eBRAP. eBRAP does not confirm the accuracy of file content. 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 Budget Form cannot be changed after the application submission deadline.

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(s) 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 **4** years.

Application to the standard Therapeutic/Biomarker Trial Award:

- The anticipated direct costs budgeted for the entire period of performance will not exceed **$5,000,000**. 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 **$5,000,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

Application to the Therapeutic/Biomarker Trial 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 **$5,020,000**. 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 **$5,020,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

- A Therapeutic/Biomarker Trial Award application including the Biorepository Contribution Option that does not meet the criteria specified may be funded at the lower maximum direct costs of **$5,000,000** (i.e., at the level of the standard Therapeutic/Biomarker Treatment Award) as described above.

Application to the Therapeutic/Biomarker Trial Award with the Clinical Consortium Collaboration Option: If applying for the **Clinical Consortium Collaboration Option**, PIs may include additional direct costs up to **$500,000** associated with collaborative activities involving participation of the GWICTIC. ***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.***

- The anticipated direct costs budgeted for the entire period of performance will not exceed **$5,500,000**. 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 **$5,500,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

- A Therapeutic/Biomarker Trial 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 **$5,000,000** (i.e., at the level of the standard Therapeutic/Biomarker Trial Award) as described above.

Milestone Meetings: Research milestones to be accomplished by the end of each year in the period of performance must be clearly defined in the project SOW and will be finalized during award negotiations. The PI will be required to present an update on progress toward accomplishing research milestones and goals of the project at an annual Milestone Meeting to be held in the National Capital Region. Annual Milestone Meetings will be held at the conclusion of Year 1 and every subsequent year in the period of performance and will be attended by members of the GWIRP Programmatic Panel, CDMRP staff, and the USAMRAA Grants Officer.

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 **4** years.

- For this award mechanism, direct costs must be requested for:
    - Travel costs for the PI to attend annual Milestone Meetings in the National Capital Region. Costs associated with travel to these meetings should be included in Years 1, 2, 3, and 4 of the budget. These travel costs are in addition to those allowed for annual scientific/technical meetings.

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

- Salary
- Research-related subject costs
- Veteran subject reimbursement and compensation including:
    - Transportation
    - Lodging
    - Participation incentives
- Clinical trial costs
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs for up to three investigators to travel to one scientific/technical meeting per year to present project information or disseminate project results, in addition to the required Milestone Meetings described above

Awards made to extramural organizations will consist solely of assistance agreements (grants and cooperative agreements). 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 fund 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***.

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. The time is considered when establishing the award's period of performance. It is anticipated that awards made from this FY19 funding opportunity will be funded with FY19 funds, which will expire for use on September 30, 2025.

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:

- **Clinical Impact**
    - To what degree the proposed research could lead to a solution for an overarching challenge in GWI.
    - To what degree the anticipated outcomes of the proposed clinical trial are relevant to Veterans with GWI.
    - To what degree the anticipated short-term outcomes of the proposed clinical trial will benefit Veterans with GWI.
    - To what degree the anticipated long-term outcomes of the proposed clinical trial may impact treatment of GWI and quality of life for Veterans with GWI.
    - To what degree the proposed intervention represents an approach that is fundamentally better than interventions already approved or in clinical development.

- **Research Strategy**

  - How well the scientific rationale for clinically testing the intervention is supported by previous pilot trials in GWI Veterans or by outcomes from other conditions related to GWI. For interventions repurposed from other conditions, the extent to which the intervention is expected to be effective in GWI based on pathobiological data from the field of GWI.

  - To what degree the application provides preliminary data and evidence to support the applicability of the biomarker(s) as a diagnostic or prognostic clinical endpoint and whether the proposed clinical trial will lead to broad acceptance of its use.

  - How well the evidence presented supports moving this research into the clinical trial phase proposed by the application. To what degree the application provides clinical evidence to support the safety of the intervention.

  - Whether the type of clinical trial (e.g., prospective, randomized, controlled) proposed is appropriate to meet the project's objectives.

  - How well the study aims, hypotheses and/or objective(s), experimental design, methods, data collection and management procedures, and analyses are designed to clearly answer the clinical objective.

  - How well the newly established GWI CDEs are incorporated into the clinical trial plan.

  - 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.

  - If applicable, how well plans to collect specimens and conduct laboratory evaluations are addressed in terms of technical/methodological, operational, and logistical considerations.

  - To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.

  - How well potential challenges and alternative strategies are discussed.

  For applications submitted to the Biorepository Contribution Option:

  - How well any special preparation required and the facilities and technical capabilities necessary for collection, storage, and transfer of data and/or specimens to BBRAIN are described.

  - How well the application describes commitment to adhere to the SOPs, quality assurance measures, and annotation standards for clinical and pathological specimens and data established by the BBRAIN members.

- To what extent the proposed costs are appropriate for the collection, processing, and contribution of samples and/or data to BBRAIN.

- To what extent the application describes an appropriate plan for resolving any intellectual and material property issues.

For applications submitted to the Clinical Consortium Collaboration Option:

- 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.

- To what extent the proposed costs are appropriate, including but not limited to costs for personnel integral to collaboration, data and sample sharing and storage expenses, quality assurance considerations, and data management considerations.

- To what extent the application describes an appropriate plan for resolving any intellectual and material property issues.

- **Intervention**

  - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable) and for future translation to clinical care.

  - To what degree the intervention addresses the clinical need(s) described.

  - To what degree the application has provided clinical evidence to support the safety of the intervention.

  - How well research procedures are clearly delineated from routine clinical procedures.

  - If using nutritional supplements and/or over-the-counter drugs, whether measures are described to guarantee the consistency of dosing of active ingredients (if applicable).

- **Regulatory Strategy and Transition Plan**

  - How 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 regulation, or that the IND or IDE application has been submitted to the FDA, as appropriate.

- How well the documentation provided supports the feasibility of acquiring an active IND or IDE covering the proposed trial, if applicable.

- 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 plans to comply with GMP, GLP, and GCP guidelines are appropriate.

- Whether the identified next level of development and/or commercialization is realistic.

- Whether the funding strategy described to bring the intervention to the next level of development (e.g., specific industry partners, specific funding opportunities to be applied for) is reasonable and achievable.

- Whether the schedule and milestones for bringing the intervention to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into standard practice, and/or approval by the FDA) are achievable.

- If applicable, whether the risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.

- How well the application identifies intellectual property ownership, demonstrates the appropriate access to all intellectual property rights necessary for development and commercialization, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product or technology development and subsequent Government access to products or technologies supported by this Program Announcement.

- **Recruitment, Accrual, and Feasibility**

  - How well the application addresses the availability of 1990-1991 Gulf War Veterans for the clinical trial and the prospect of their participation.

  - Whether the application has demonstrated access to the proposed 1990-1991 Gulf War Veteran population and whether the application includes a letter from an appropriate authority showing approved access to 1990-1991 Gulf War Veterans or use of data from 1990-1991 Gulf War Veterans with GWI.

  - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.

- To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital? Is the excess fatigue and post-exertional malaise common in GWI adequately considered?).

- **Statistical Plan**

  - To what degree the statistical model and data analysis plan are suitable for the planned study.

  - Whether the statistical plan, including randomization methods, sample size projections, power analysis, and the inclusion and exclusion criteria, is adequate for the study and all proposed correlative studies.

  - To what extent will the statistical power of the study support future trials or other translational goals.

  - How well the sample population represents the targeted patient population in a statistical sense taking into account the stated inclusion and exclusion criteria.

  - Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.

- **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.

  - Whether a research monitor with expertise consistent with the nature of the potential risk(s) is identified.

  - To what degree privacy and confidentiality issues are appropriately considered.

  - To what degree the processes for recruitment and seeking informed consent are appropriate.

  - To what extent are sample collection and laboratory evaluations planned to coincide with standard clinical care and to otherwise minimize risk, invasiveness, pain, side-effects, discomfort, and inconvenience to study subjects.

- **Personnel and Communication**

    - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.

    - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., expertise in GWI, statistical expertise, expertise in conducting clinical trials, and FDA experience, if applicable).

    - How appropriate the study team members' levels of effort are to ensuring successful completion of the proposed trial.

    - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial. ***The Clinical Consortium Collaboration Statement will be considered for applications submitted under the Clinical Consortium Collaboration Option.***

    - For multi-site clinical trials, how well-defined and well-planned the lead site responsibilities and human research protections regulatory coordination are. ***The Clinical Consortium Collaboration Statement will be considered for applications submitted under the Clinical Consortium Collaboration Option.***

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** maximum costs are equal to or less than the allowable direct maximum costs as published in the Program Announcement.

    - Whether the budget is both adequately justified and appropriate for the proposed research.

    - If applicable, whether the optional collaboration proposed brings value to the study.

- **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 FY19 GWIRP, as evidenced by the following:
    - Adherence to the intent of the award mechanism
    - Program portfolio composition
    - Relative clinical impact

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, USAMRMC, 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. A PI 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 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 FY19 funds are anticipated to be made no later than September 30, 2020. 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 the USAMRAA will contact the Business Official authorized to negotiate on behalf of the PI's organization.

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.

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

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.

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 1, 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 the 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.

Report out at annual Milestone Meetings is required for this award mechanism.

Quarterly technical progress reports and quad charts will be required. For format examples, refer to the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm).

Award Chart: An Award Chart will be required within 20 business days after award. For the Therapeutic/Biomarker Trial Award mechanism, use the generic format example titled "Award Charts," available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm).

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the final progress report. Use the one-page template titled "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.

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

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

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 20190218e. The Program Announcement numeric version code will match the General Applications Instructions version code 20190218.

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.
- Intervention (Attachment 5) is missing.
- Human Subject Recruitment and Safety Procedures (Attachment 6) is missing.
- Data Management (Attachment 7) is missing.

- Regulatory Strategy (Attachment 8) 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 FY19 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 FY19 GWIRP Programmatic Panel members can be found at https://cdmrp.army.mil/gwirp/panels/panels19***.

- 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 FY19, 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 clinical trial.

- Submission of the same research project to different funding opportunities within the same program and fiscal year.

- The invited application does not propose the same research project described in the pre-application.
- For studies requiring an IND or IDE, documentation of IND/IDE submission and/or active status is not provided.
- The proposed project includes preclinical research.
- The applicant fails to demonstrate access to the relevant study population or resources.
- 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.

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 **(Extramural submissions only)**	Complete form as instructed.	
Summary (Tab 1) and Application Contacts (Tab 2) **(Intramural submissions only)**	Complete these 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 and Lay Abstracts: Upload as Attachment 3 with file name "Abstracts.pdf"	
	Statement of Work: Upload as Attachment 4 with file name "SOW.pdf"	
	Intervention: Upload as Attachment 5 with file name "Intervention.pdf"	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 6 with file name "HumSubProc.pdf"	
	Data Management: Upload as Attachment 7 with file name "Data_Manage.pdf"	
	Regulatory Strategy: Upload as Attachment 8 with the file name "Regulatory.pdf"	
	Study Personnel and Organization: Upload as Attachment 9 with file name "Personnel.pdf"	
	Surveys, Questionnaires, and Other Data Collection Instruments: Upload as Attachment 10 with file name "Surveys.pdf"	
	Transition Plan: Upload as Attachment 11 with file name "Transition.pdf"	
	Impact Statement: Upload as Attachment 12 with file name "Impact.pdf"	
	Option Statements: Upload as Attachment 13 with file name "Options.pdf"	
	Representations (extramural submissions only): Upload as Attachment 14 with file name "RequiredReps.pdf" if applicable	
	DoD Military Budget Form(s): Upload as Attachment 15 with file name "MFBudget.pdf" if applicable	

Application Components	Action	Completed
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 **(Extramural submissions only)**	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field	
Budget **(Intramural submissions only)**	Complete the DoD Military Budget Form and 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

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
COI	Conflict of Interest
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
NIH	National Institutes of Health
NPC	Non-Profit Corporation

OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
OMB	Office of Management and Budget
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
SOP	Standard Operating Procedure
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRMC	U.S. Army Medical Research and Materiel Command
USC	United States Code
VA	Department of Veterans Affairs