I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Toxic Exposures Research Program

Clinical Trial Award

Announcement Type: Initial

Funding Opportunity Number: HT942524TERPCTA

Assistance Listing Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application (Preproposal) Submission Deadline:** 5:00 p.m. Eastern time (ET), August 13, 2024
- **Invitation to Submit an Application:** September 23, 2024
- **Application Submission Deadline:** 11:59 p.m. ET, November 07, 2024
- **End of Application Verification Period:** 5:00 p.m. ET, November 13, 2024
- **Peer Review:** January 2025
- **Programmatic Review:** March 2025

This program announcement must be read in conjunction with the General Application Instructions, version 901. 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

The U.S. Army Medical Research Acquisition Activity (USAMRAA) is soliciting applications to the Fiscal Year 2024 (FY24) Toxic Exposures Research Program (TERP) using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC) is the program management agent for this funding opportunity. The TERP was initiated in FY22 to provide solutions toward the prevention, diagnosis, treatment and mechanistic understanding of the adverse health outcomes associated with a broad range of military-related toxic exposures. Appropriations for the TERP from FY22 through FY23 totaled $60 million (M). The FY24 appropriation is $30M.

The vision of the TERP is to prevent, minimize and mitigate the impact of military-related toxic exposures and improve the health and quality of life of those affected. The mission of the TERP is to support impactful research aimed at identifying the cause and understanding the health outcomes, comorbidities and pathological mechanisms associated with military-related toxic exposures to facilitate the prevention, diagnosis and treatment of the visible and invisible diseases and symptoms impacting Service Members, their Families, Veterans and the American public.

Impactful and highly relevant research will be hypothesis-driven and consider the health care needs of Service Members, their Families, Veterans, and/or the American public with symptoms, diseases, or conditions as a result of military-related toxic exposures and/or the need to minimize toxic exposures for military and civilian populations.

Applicants are strongly encouraged to review Appendix 1, TERP Definitions, before writing and submitting their application.

Collaboration with Department of Defense (DOD) and/or U.S. Department of Veterans Affairs (VA) researchers and clinicians is encouraged.

II.A.1. FY24 TERP Program Goals and Topic Areas

To meet the intent of the award mechanism, applicants to the Clinical Trial Award (CTA) must address at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas. Selection of the Program Goal(s) and Topic Area(s) is the responsibility of the applicant. Selection must be made during the pre-application submission process and addressed in detail in the full application submission.

Program Goals: The FY24 TERP Program Goals are not listed in order of importance. Bulleted items are provided for additional context on current program priorities and, while encouraged, they are not required to be specifically addressed by applications.

1. ***Elucidate mechanisms of how military-related toxic exposures result in adverse effects****, including but not limited to toxicities, malignancies, neurologic and respiratory disorders, cardiac complications, sleep disorders, immune system dysfunction, gastrointestinal issues, etc.*

    - Understand the full range of effects from military-related environmental and toxic exposures, including but not limited to long-term illness such as Gulf War illness (GWI), cancers, cardiopulmonary and airway conditions, Parkinson's disease and other neurologic disorders, etc.

    - Evaluate the effects of epigenetic and genomic mechanisms on potential long-term and/or heritable outcomes.

    - Identify biological and/or psychosocial variables that can impact disease outcomes.

    - Identify risk factors/genetic predictors for various diseases/conditions that may occur as a result of toxic exposure.

    - Understand complex, multi-exposure/physiological or non-chemical stressors (e.g., hormonal, sleep disorders, thermal stress) combinations and how exposure impacts outcome.

    - Address the need for preclinical models that capture the adverse outcomes of human toxic exposures.

2. ***Diagnose the effects of military-related toxic exposures****, understand the phenotypic, pathological and clinical outcomes associated with short-term and long-term exposures, and predict disease progression.*

    - Identify behavioral factors (smoking, substance use, etc.), comorbidities and preexisting medical conditions that may impact exposure outcomes.

    - Identify biomarkers of exposure to individual or multiple toxic substances alone or in combination with physiological/non-chemical stressors.

    - Develop diagnostic screens/assays/devices for toxic exposures.

3. ***Predict and prevent military-related toxic exposures*** *by identifying strategies that can anticipate, identify, monitor and prevent Service Members and the American public from adverse effects of exposures to toxic substances.*

    - Develop assays/devices to identify military-related exposures across environments that lead to adverse health effects.

- Develop personal monitoring devices to detect and characterize toxic exposures.
- Advance exposure assessment methodologies, including but not limited to direct-reading, integrated measurements and machine learning.

4. ***Develop therapeutics, treatments and strategies*** *to minimize symptoms and disease progression associated with military-related toxic exposures.*
   - Evaluate existing therapeutics, treatments and strategies.
   - Advance new therapeutics, treatments and strategies.

Topic Areas: The FY24 TERP Topic Areas are not listed in order of importance.

1. Neurotoxin Exposure
2. Gulf War Illness (GWI) and Its Treatment
3. Airborne Hazards and Burn Pits
4. Other Military Service-Related Toxic Exposures in General, Including Prophylactic Medications, Pesticides, Organophosphates, Toxic Industrial Chemicals, Materials, Metals and Minerals

Requirements for Application Submission	
FY24 TERP Program Goals	Must address at least one.
FY24 TERP Topic Areas	Must address at least one.

II.A.2. FY24 TERP Guidance

Studies focused on the following areas do NOT meet the intent of the FY24 TERP:

- Research data that are classified and/or research in which the anticipated outcomes may be classified or deemed sensitive to national security concerns
- Chemical warfare agents categorized as fourth-generation agents or non-traditional agents
- Biological Select Agents or Toxins (https://www.selectagents.gov/sat/list.htm)
- Anomalous Health Incidents, commonly referred to as Havana Syndrome
- Directed energy weapons
- Development of medical countermeasures intended to diagnose, prevent or treat the immediate (point of injury) health effects of chemical weapons, biological, radiological or nuclear threats

- Treatments or therapeutics for the immediate, adverse health effects of any exposure that would be administered in an acute care setting (i.e., role of care (ROC) 1 or ROC 2)
    - In the military health echelon/ROC, this generally refers to ROC 1 and ROC 2 described below:
        - ROC 1: Unit-level medical care, ranging from point of injury through battalion aid station
        - ROC 2: Advanced trauma management and emergency medical treatment
        - For more information on the military roles of care refer to: Chapter 2, "Roles of Medical Care (United States)," Emergency War Surgery, Fifth United States Revision, 2018, Borden Institute (https://medcoeckapwstorprd01.blob.core.usgovcloudapi.net/pfw-images/dbimages/Ch%202.pdf).

***NOTE* The following examples ARE permitted under the FY24 TERP. These examples are meant to inform prospective applicants in the context of the above exclusions and do not imply that these research areas are prioritized over any others within the scope of the FY24 TERP Program Goals and Topic Areas.**

- Studies focused on the evaluation/treatment of long-term or chronic health impacts of traditional chemical weapons. Examples may include but are not limited to the long-term effects of sarin, soman and sulfur mustard exposures and Gulf War illness.
- Other long-term/chronic effects of military-related exposures that would be diagnosed or treated in a ROC 3 (field hospital) or ROC 4 (definitive care; fixed medical treatment facility) or beyond.

II.A.3. Award History

The TERP CTA mechanism was first offered in FY22. Since then, 15 CTA applications (representing 27 potential awards) have been received, and 2 applications (representing 4 awards) have been recommended for funding.

II.B. Award Information

The FY24 TERP CTA is intended to support the rapid implementation of clinical trials with the potential to have a significant impact on the prevention, treatment or management of symptoms, diseases, or conditions associated with or resulting from military-related toxic exposures. *To meet the intent of the award mechanism,* ***applications must address at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas.***

Proposed projects may range from small proof-of-concept clinical trials (e.g., pilot, first-in-human, phase 0) designed to demonstrate the feasibility or inform the design of more advanced trials through large-scale trials to determine efficacy in relevant patient populations. Clinical

trials may be designed to evaluate promising new products, pharmacologic agents (drugs or biologics), devices, clinical guidance, and/or emerging approaches and technologies. It is anticipated that outcomes from studies funded by this award will follow a clinical development plan that advances the research to U.S. Food and Drug Administration (FDA) device or drug approval and/or establishment of clinical practice guidelines, as applicable.

Applications to the FY24 TERP CTA mechanism must support a clinical trial and may not propose animal or other preclinical research studies. The application will be withdrawn if the proposed research is not a clinical trial.

A clinical trial is defined in the Code of Federal Regulations, Title 45, Part 46.102 (45 CFR 46.102) as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include a placebo or another control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Studies that do not seek to measure safety, effectiveness, and/or efficacy outcome(s) of an intervention are not considered clinical trials.

Applicants seeking funding for research that does not meet this definition should consider one of the other FY24 TERP program announcements being offered. It is the responsibility of the applicant to review the program announcement requirements and select the funding opportunity that aligns with the scope of the proposed research. Applications submitted under a mechanism that is not deemed appropriate for the type and scope of research requested will not be recommended for funding.

For more information, a Human Subjects Resource Document is provided at https://cdmrp.health.mil/pubs/pdf/Human%20Subjects%20Resource%20Document_DEC2022.pdf.

Proposed research may be related to diseases, conditions, or symptoms supported by other CDMRP programs; however, TERP applications must be relevant to military-related toxic exposures and be responsive to the FY24 TERP Program Goals and Topic Areas.

CDMRP encourages research on health areas and conditions that affect women uniquely, disproportionately, or differently from men, including studies analyzing sex as a biological variable. Such research should relate anticipated project findings to improvements in women's health outcomes and/or advancing knowledge for women's health.

Innovative research involving nuclear medicine and related techniques to support early diagnosis, more effective treatment, and improved health outcomes of active-duty Service Members and their Families is encouraged. Such research could improve diagnostic and targeted treatment capabilities through noninvasive techniques and may drive the development of precision imaging and advanced targeted therapies.

Rigorous Study Design. All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of clinical and preclinical research. The standards are described in SC Landis et al., 2012, A call for transparent

reporting to optimize the predictive value of preclinical research, *Nature* 490:187-191 https://www.nature.com/nature/journal/v490/n7419/full/nature11556.html. While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies.

Partnering Principal Investigator (PI) Option: In order to encourage applications that include meaningful and productive collaborations between investigators, the FY24 TERP CTA includes an ***option for up to three PIs to partner*** in one overarching study. Each PI is expected to bring a distinct contribution to the application, and the PIs' unique expertise, when combined as a partnership, should address the research question better than any one investigator could individually. The PIs should have appropriately balanced intellectual input into the design and conduct of the project.

One PI will be identified as the Initiating PI and will be responsible for the majority of the administrative tasks associated with application submission. ***The other PI(s) will be identified as Partnering PI(s).*** All PIs should contribute significantly to the development of the proposed research project, including the Project Narrative, Statement of Work (SOW), and other required components. If recommended for funding, each PI will be named to an individual award within the recipient organization(s). For individual submission requirements for the Initiating PI and Partnering PI(s), refer to Section II.D.2, Content and Form of the Application Submission.

Key aspects of the FY24 TERP CTA:

- **Clinical Trial Start Date:** 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 studies regulated by the Regulatory Agency.

- **Clinical Impact:** Applications should explain how the proposed research will have a significant impact on patient care for Service Members, their Families, Veterans and/or the American public that have been or could potentially be impacted by the effects of military-related toxic exposures. Applications should demonstrate both the short- and long-term impacts and how the successful completion of the proposed research will ultimately lead to new treatments/therapeutics/interventions to improve the quality of life for those that have been impacted by or are likely to encounter toxic substances.

- **Preliminary Data Are Required:** Inclusion of preliminary data relevant to the proposed clinical trial is required. The proposed clinical trial must be based on a sound scientific rationale that is established through logical reasoning and critical review and analysis of the relevant literature.

- **Study Population:** The application should demonstrate the availability of and access to a suitable patient population that will support a meaningful outcome for the study. The application should include a discussion of how accrual goals will be achieved, as well as the strategy for inclusion of women and minorities in the clinical trial appropriate to the objectives of the study. Studies utilizing human biospecimens or data sets that cannot be

linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from Institutional Review Board [IRB] review) are exempt from this requirement.

The recruitment of relevant military and/or Veteran population(s) for the proposed clinical trial(s) is strongly encouraged. Applications not using military or Veteran populations for the proposed studies are strongly encouraged to provide justification for how the chosen population(s) is relevant to military-related toxic exposures and will benefit Service Members, Veterans, and/or their Families. In addition, applicants are also encouraged to consider studying populations that reflect traditionally underrepresented populations of Service Members, Veterans and/or their Families.

- **Intervention Availability:** The application should demonstrate the documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate, for the proposed duration of the study.

- **Personnel and Environment:** The application should demonstrate the study team's expertise and experience in all aspects of conducting clinical trials, including appropriate statistical analysis, knowledge of FDA processes (if applicable), and data management. 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. The application should show 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.

  Participation of at least one military or Veteran consumer as a member of the research team to contribute to the development of the research question, project design, oversight, and evaluation, as well as other significant aspects of the proposed project is strongly encouraged.

  - For the purposes of the FY24 TERP, a consumer is a person living with a disease, injury, or condition or may be a family member or caregiver of a person impacted by a disease/injury/condition associated with military-related toxic exposures. The consumer must be an active participant in an advocacy, outreach, or support organization, or if military personnel on active duty, be approved to participate by their Commanding Officer.

  Inclusion of at least one clinician on the study team is strongly encouraged.

- **Statistical Analysis and Data Management Plans:** The application should include a clearly articulated statistical analysis plan, a power analysis reflecting sample size projections that will answer the objectives of the study, and a data management plan that includes use of an appropriate database to safeguard and maintain the integrity of the data. If required by a Regulatory Agency, the trial must use a 21 CFR 11 compliant database and appropriate data standards.

For the purposes of this funding opportunity, Regulatory Agency refers to the FDA or any relevant international regulatory agency unless otherwise noted.

If the proposed clinical trial involves the use of a drug that has not been approved by the relevant Regulatory Agency for the country where the research will be conducted, then submission of an Investigational New Drug (IND) application, or equivalent, that meets all requirements under 21 CFR 312 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the relevant Regulatory Agency if an IND, or equivalent, is not required. If an IND, or equivalent, is required, the regulatory application ***must be submitted to the relevant Regulatory Agency within 6 months of the award date.*** The IND, or equivalent, should be specific for the product and indication to be tested in the proposed clinical trial. For more information on IND applications specifically, the FDA has provided guidance at https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application.

If the investigational product is a device, then submission of an Investigational Device Exemption (IDE), or equivalent, application that meets all requirements under 21 CFR 812 may be required. It is the responsibility of the applicant to provide evidence if an IDE, or equivalent, is not required. If an IDE, or equivalent, is required, the IDE application, or equivalent, ***must be submitted to the relevant Regulatory Agency within 6 months of the award date.*** The IDE, or equivalent, should be specific for the device and indication to be tested in the proposed clinical trial.

If the clinical trial of an investigational product will be conducted at international sites, evidence that an application to the relevant national regulatory agency of the host country(ies) ***has been submitted within 6 months of the award date*** will be required.

Use of DOD or Department of Veterans Affairs (VA) Resources: Applications from investigators within the military Services and applications involving multidisciplinary collaborations among academia, industry, the military Services, the VA, and other federal government agencies are highly encouraged. These relationships can leverage knowledge, infrastructure, and access to unique clinical populations that the collaborators bring to the research effort, ultimately advancing research that is of significance to Service Members, Veterans, and/or their Families. If the proposed research relies on access to unique populations, resources or databases, the application must describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research.

Resources for Data and/or Previously Collected Biospecimens

The table below is provided as a reference and is not an exhaustive list of all resources that may be applicable to the proposed research. Researchers are not required to use any of the following limited examples or any one particular data set.

The TERP does not provide access to any of the below resources and/or control the information presented on the websites listed below.

Resource	Website
Boston Biorepository, Recruitment and Integrated Network for GWI (BBRAIN)	https://sites.bu.edu/bbrain/

Resource	Website
Defense Health Agency (DHA) Data Sharing Agreement Information	https://www.health.mil/Military-Health-Topics/Privacy-and-Civil-Liberties/Data-Sharing-Agreements
Defense Manpower Data Center (DMDC)	https://dwp.dmdc.osd.mil/dwp/app/main
Defense Medical Surveillance System (DMSS)	https://www.health.mil/Military-Health-Topics/Health-Readiness/AFHSD/Functional-Information-Technology-Support/Defense-Medical-Surveillance-System
Defense Occupational and Environmental Health Readiness System (DOEHRS)	https://phc.amedd.army.mil/topics/envirohealth/hrasm/Pages/DOEHRS_Resources.aspx
DOD Serum Repository (DODSR)	https://www.health.mil/Military-Health-Topics/Health-Readiness/AFHSD/Functional-Information-Technology-Support/Department-of-Defense-Serum-Repository
Gulf War Illness Clinical Trials & Interventions Consortium (GWICTIC)	https://www.nova.edu/nim/GWICTIC/index.html
Individual Longitudinal Exposure Record (ILER)	https://iler.csd.disa.mil/iler/app/hipaa?execution=e2s1
Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC)	https://www.vacsp.research.va.gov/CSP_Centers/Massachusetts_Veterans_Epidemiology_Research_and_Information_Center_MAVERIC_CSP_Coordinating_Cen.asp
Millennium Cohort Study	https://millenniumcohort.org/
The Million Veteran Program (MVP)	https://www.research.va.gov/MVP/default.cfm
VA Environmental Health Registries	https://www.publichealth.va.gov/exposures/benefits/registry-evaluation.asp
VA Gulf War Veterans' Illnesses Biorepository Brain Bank (GWVIB)	https://www.research.va.gov/programs/tissue_banking/gwvib/default.cfm
VA Gulf War Era Cohort and Biorepository (GWECB)	https://www.research.va.gov/programs/csp/585/default.cfm

The funding instrument for awards made under the program announcement will be grants (31 USC 6304).

The anticipated direct costs budgeted for the entire period of performance for an FY24 TERP Clinical Trial Award should not exceed **$1,500,000** for the Single PI Option and **$2,500,000** (combined direct costs) for the Partnering PI Option. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

Awards supported with FY24 funds will be made no later than September 30, 2025.

The CDMRP expects to allot approximately $10.4M to fund approximately three Clinical Trial Award applications. Funding of applications received is contingent upon the availability of federal funds for this program, the number of applications received, the quality and merit of the applications as evaluated by peer 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 FY24 funding opportunity will be funded with FY24 funds, which will expire for use on September 30, 2030.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: Extramural and Intramural organizations are eligible to apply, including foreign or domestic institutions, for-profit and non-profit organizations, and public entities.

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

Intramural DOD Organization: Refers specifically to DOD organizations including DOD laboratories, DOD military treatment facilities, and/or DOD activities embedded within a civilian medical center.

Awards are made to eligible ***organizations***, not to individuals.

Refer to the General Application Instructions, Appendix 1, for additional recipient qualification requirements.

II.C.1.b. Principal Investigator

Extramural and intramural DOD investigators at or above the level of Assistant Professor (or equivalent) may be named by the organization as the Principal Investigator (PI) or Partnering PI(s) on the application.

Applicants are discouraged from being named as a Partnering PI on multiple applications unless they are clearly addressing distinct research questions.

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

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 to fulfill the financial and technical deliverable requirements of the award and submit invoices for payment.

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

II.D. Application and Submission Information

II.D.1. Location of Application Package

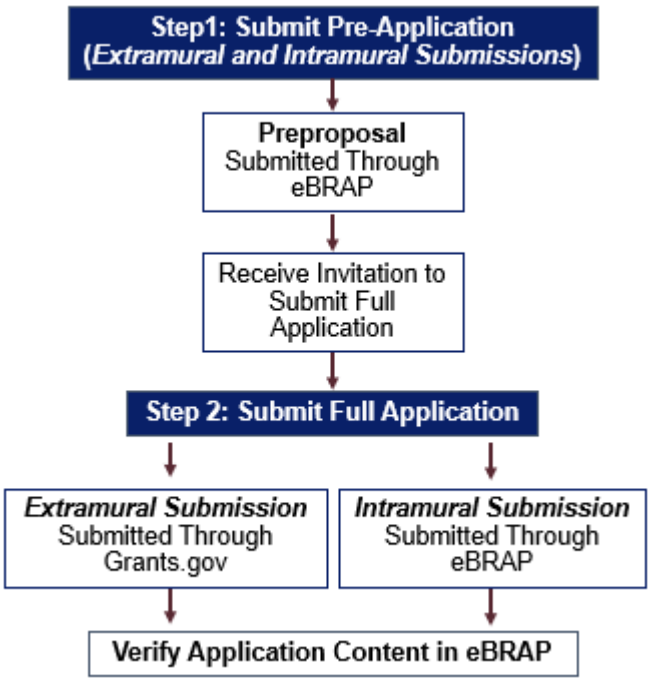
Submission is a two-step process requiring both a ***pre-application*** submitted via the Electronic Biomedical Research Application Portal (eBRAP.org) and a ***full application*** (eBRAP.org or Grants.gov). Depending on the type of submission (i.e., extramural versus intramural), certain aspects of the submission process will differ.

The CDMRP uses two portal systems to accept pre- and full application submissions.

eBRAP (https://ebrap.org) is a secure web-based system that allows PIs and/or organizational representatives from both extra- and intramural organizations to receive communications from the CDMRP and submit their pre-applications. Additionally, eBRAP allows extramural applicants to view and verify full applications submitted to Grants.gov and allows intramural DOD applicants to submit and verify full applications following their pre-application submission.

Grants.gov (https://grants.gov) is a federal system that must be used by funding agencies to announce extramural grant applications. Full applications for CDMRP funding opportunities can only be submitted to Grants.gov after submission of a pre-application through eBRAP.

Application Submission Workflow



Extramural Submission: An application submitted by an extramural organization for an extramural or intramural PI working within an extramural or intramural organization. For example, a research foundation submitting an application for a DOD employee working within a DOD organization would be considered an extramural submission and should follow instructions specific to extramural submissions. Download application package components for HT942524TERPCTA from Grants.gov (https://grants.gov). Full applications from extramural organizations ***must*** be submitted through Grants.gov.

Intramural Submission: An application submitted by an intramural DOD organization for an investigator employed by that organization. Intramural DOD organizations may submit full applications to either eBRAP or Grants.gov. Download application package components for HT942524TERPCTA from the anticipated submission portal eBRAP (https://ebrap.org) or Grants.gov.

The submission process should be started early to avoid missing deadlines. Regardless of submission type or portal used, all pre- and full application components must be submitted by the deadlines stipulated on the first page of this program announcement. There are no grace periods for deadlines; failure to meet submission deadlines will result in application rejection. ***The USAMRAA cannot make allowances/exceptions for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.***

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

Submitting applications that 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).

Unnecessary duplication of funding or accepting funding from more than one source for the same research, is prohibited. See CDMRP's full position on research duplication at https://cdmrp.health.mil/funding/researchDup.

Including classified research data within the application and/or proposing research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns, may result in application withdrawal. Refer to the General Application Instructions Appendix 7, Section B.

FY24 TERP Programmatic Panel members should not be involved in any pre-application or full application. For questions related to panel members and pre-applications or applications, refer to Section II.H.2.c, Withdrawal, or contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

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

All pre-application components must be submitted by the PI or Initiating PI through eBRAP (https://eBRAP.org/), including the submission of contact information for each Partnering PI if exercising the Partnering PI Option.

During the pre-application process, eBRAP assigns each submission a unique log number. This unique log number is required during the full application submission process. The eBRAP log number, application title, 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 eBRAP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application submission deadline.

Partnering PI Option: After the Initiating PI confirms submission of the pre-application, the Partnering PI(s) will be notified of the pre-application submission via an email from eBRAP. ***The Partnering PI(s) must follow the link in the notification email to associate the partnering pre-application with their eBRAP account.*** If not previously registered, the Partnering PI(s) must register in eBRAP.

After associating the pre-application with their eBRAP account, the Partnering PI(s) should email the eBRAP Help Desk (help@ebrap.org) to have the desired contact information associated with their pre-application. The email should include the pre-application log number, the name of the Business Official, the name(s) of the Performing/Contracting Organization(s), and the submission-type for the pre-application (extramural or intramural).

Partnering PI(s) should not initiate a new pre-application based on the same research project submitted by the Initiating PI. Partnering PIs are urged to complete these steps as soon as possible. If they are not completed:

- The Partnering PI(s) will not be able to view and modify their full application during the verification period in eBRAP.
- Any intramural Partnering PI will not be able to submit their full application package components to eBRAP.

When starting the pre-application, applicants will be asked to select a "Mechanism Option". Please be sure to select the correct option appropriate to your pre-application:

Application Includes	Select Option
Research by a **single PI**	**Clinical Trial Award – Single PI Option (CTA); select "no option"**
Research by **multiple PIs** (maximum of three)	**Clinical Trial Award – Partnering PI Option (CTA-PPIO)**

II.D.2.a.i. Pre-Application Components

Pre-application submissions must include the following components (refer to the General Application Instructions, Section III.B, for additional information on pre-application submission).

Note: Upload documents as individual PDF files unless otherwise noted.

- **Preproposal Narrative (three-page limit):** The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs (uniform resource locators) that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

  The Preproposal Narrative should include the following:

  - **Background/Rationale:**
    - State the hypothesis of the proposed study and provide a brief explanation of the study rationale clearly articulating how the hypothesis and rationale are well supported/justified.
    - Specify the intervention to be investigated and indicate the phase of the study and/or class of device, as appropriate.

- **Specific Aims and Study Design:**
  - Concisely state the specific aims of the proposed clinical trial and briefly describe the scientific approach to address them. Include a description of controls, as appropriate.
  - Briefly describe the study population. The recruitment of relevant military and/or Veteran population(s) for the proposed clinical trial(s) is strongly encouraged. Applications not using military or Veteran populations for the proposed studies are strongly encouraged to provide justification for how the chosen population(s) is relevant to military-related toxic exposures and will benefit Service Members, Veterans, and/or their Families.
  - Briefly describe the feasibility of the study including access to patient population(s), plans for recruitment and retention, and how the study will be completed within the proposed period of performance.
- **Alignment:**
  - Describe how the proposed project addresses at least one FY24 TERP Program Goal and at least one FY24 TERP Topic Area.
- **Impact and Relevance to Military Health:**
  - State both the short- and long-term impacts and how the successful completion of the proposed research will ultimately lead to new treatments/therapeutics/interventions to improve patient care and the quality of life for those that have been impacted by, or are likely to encounter, toxic substances.
  - State how the proposed research is responsive to the health care needs of Service Members, Veterans, or their Families that have been or could potentially be exposed to military-related toxic exposures.
  - Describe how research findings could also benefit the general population.

- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application ***must be uploaded as individual files*** and are limited to the following:
  - **References Cited (one-page limit):** List the references cited (including URLs, if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, reference title, and reference source, including volume, chapter, page numbers, and publisher, as appropriate).
  - **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.

- **Key Personnel Biographical Sketches (six-page limit per individual):** ***All biographical sketches should be uploaded as a single combined file.*** Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

II.D.2.a.ii. Pre-Application Screening Criteria

To determine the technical merits of the pre-application and the relevance to the mission of the Defense Health Program (DHP) and the TERP, pre-applications will be screened based on the following criteria:

- **Background/Rationale**:
  - Whether the study rationale and hypothesis are well supported and justified.
- **Specific Aims and Study Design:**
  - How well the specific aims are stated and supported through the scientific rationale.
  - To what degree the proposed study population is appropriate for the proposed clinical trial and whether the study is feasible.
- **Alignment:**
  - How well the proposed project addresses at least one FY24 TERP Program Goal and at least one FY24 TERP Topic Area.
- **Impact and Relevance to Military Health:**
  - To what degree the proposed research project will have both short- and long-term impacts and the successful completion of the project will ultimately lead to new treatments/therapeutics/interventions to improve patient care and the quality of life for those that have been impacted by or are likely to encounter toxic substances.
  - To what degree the proposed research is responsive to the health care needs of Service Members, Veterans, and/or their Families that have been or could potentially be exposed to military-related toxic exposures.
  - To what extent the research findings could benefit the general population.

II.D.2.a.iii. Notification of Pre-Application Screening Results

Following the pre-application screening, Initiating PIs will be notified as to whether they are invited to submit full applications. The estimated date when PIs can expect to receive notification of an invitation to submit a full application is indicated in Section I, Overview of the Funding Opportunity. No feedback (e.g., a critique of the pre-application's strengths and weaknesses) is provided at this stage. Because the invitation to submit a full 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.

II.D.2.b. Step 2: Full Application Submission

Applicants **must** receive an invitation to submit a full application. Uninvited full application submissions will be rejected.

Partnering PI Option: The CDMRP requires separate full application package submissions for the Initiating PI and each Partnering PI, even if the PIs are located within the same organization. Each full application package must be submitted using the unique eBRAP log number received by the Initiating and Partnering PIs during pre-application submission. ***All associated applications (the Initiating PI's and each Partnering PI's) must be submitted by the full application submission deadline.***

II.D.2.b.i. Full Application Submission Type

Extramural Submissions: Full applications from extramural organizations ***must*** be submitted through Grants.gov Workspace. Full applications from extramural organizations, including non-DOD federal organizations, received through eBRAP will be withdrawn. Refer to the General Application Instructions, Section IV, for considerations and detailed instructions regarding extramural full application submission.

Intramural Submissions: Intramural DOD organizations may submit full applications through either eBRAP or Grants.gov. There is no preference from the CDMRP for which submission portal is utilized; submission through one portal or the other does not provide the application any advantage during the review process. Intramural DOD organizations that choose to submit through Grants.gov should follow Extramural Submission instructions. Intramural DOD organizations that are unable to submit through Grants.gov should submit through eBRAP. For the remainder of this program announcement, it will be assumed intramural DOD submissions will proceed through eBRAP. Refer to the General Application Instructions, Section V, for considerations and detailed instructions regarding intramural DOD full application submission.

II.D.2.b.ii. Full Application Submission Components for the PI or Initiating PI

Each application submission must include the completed full application package for this program announcement. See Section II.H.3 of this program announcement for a checklist of the required application components.

(a) SF424 Research & Related Application for Federal Assistance Form *(Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(a), for detailed information.

(b) 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 2.

- **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 that expands the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

  The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-10 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

  Describe the proposed project in detail using the outline below. ***Funding from this award mechanism must support a clinical trial and cannot be used for animal or other preclinical research studies.***

  Background:

  - **Background/Rationale:** Describe in detail the scientific rationale for the study. Applications must include preliminary (published or unpublished clinical or preclinical) data relevant to the proposed clinical trial. The proposed clinical trial must be based on a sound scientific rationale that is established through logical reasoning and critical review and analysis of the relevant literature. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs from other relevant or recently completed research. Describe how the proposed intervention, if applicable, compares/improves on standard of care or other available interventions. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). The background section should clearly support the choice of the study variable and should explain the basis for the study questions and/or hypotheses. State the relevance of the proposed research and the applicability of the anticipated findings to the intent of the mechanism (refer to Section II.B, Award Information) and to ***at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas***.

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

  - **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses. This information should agree with the aims and associated tasks described in Attachment 5, Statement of Work.

- **Study Design:** Describe the type of study to be performed (e.g., treatment, prevention, diagnostic), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to demonstrate a clear course of action. Discuss the feasibility of the proposed project and how it will be completed within the proposed period of performance.

  - Identify the intervention to be tested and describe the projected results.

    Additional details should be provided in Attachment 6, Intervention.

  - Define the primary and any secondary or interim endpoints/outcome measures, outline why they were chosen, and describe how and when they will be measured. Include a description of appropriate controls. Outline the timing and procedures planned during the follow-up period.

  - Describe and justify the study population and the inclusion and exclusion criteria that will be used to meet the needs of the proposed clinical trial.

  - Summarize the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).

    Additional details should be provided in Attachment 7, Human Subject Recruitment and Safety Procedures.

  - 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). 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.

  - If using psychometric measures, describe their reliability and validity.

  - 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 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 and all proposed correlative studies. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be

achieved within the subpopulation study. For phase 3 clinical trials, describe plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity as appropriate for the scientific goals of the study. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations 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. 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.

  - **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 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 and/or organization demonstrating that the PI has the support or resources necessary for the proposed work. If an investigator at an intramural DOD organization is named as a collaborator on a full application submitted through an extramural organization, the application must include a letter from the

collaborator's Commander or Commanding Officer at the intramural DOD organization authorizing the collaborator's involvement.

- **Commercial Entity 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 the availability of the product for the duration of the proposed clinical trial, support for the proposed phase of research, and support for the indication to be tested.

- **Use of DOD Resources *(if applicable)*:** Provide a letter of support signed by the lowest-ranking person with approval authority confirming access to active-duty military populations and/or DOD resources or databases.

- **Use of VA Resources *(if applicable)*:** Provide a letter of support signed by the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the Associate Chief of Staff for Research and Development (ACOS/R&D) or Clinical Service Chief, confirming access to VA patients, resources, and/or VA research space. If the VA-affiliated nonprofit corporation is not identified as the applicant organization 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.

- **Quad Chart:** Provide a Quad Chart for the proposed project. The format for the Quad Chart is available on the eBRAP "Funding Opportunities & Forms" web page at (https://ebrap.org/eBRAP/public/Program.htm).

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf".** The technical abstract is used by all reviewers. ***Abstracts of all funded research projects will be posted publicly.*** 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 abstracts should be written using the outline below. Clarity and completeness within the space limits of the technical abstract are highly important.

  - **Background:** Present the scientific rationale and reasoning 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 research will have a significant impact on patient care for Service Members, their Families, Veterans, and/or the American public that have been or could potentially be impacted by the effects of

military-related toxic exposures. State both the short- and long-term impacts and how the proposed research will ultimately lead to new treatments/therapeutics/interventions to improve patient care and the quality of life for those that have been impacted by, or are likely to encounter, toxic substances.

- **Relevance to the TERP:** Applications should articulate how the proposed research is relevant to at least one of the FY24 TERP Program Goals and addresses at least one of the FY24 TERP Topic Areas.

- **Relevance to Military Health:** State how the proposed research is responsive to the health care needs of Service Members, Veterans, and/or their Families that have been or could potentially be exposed to military-related toxic exposures. Describe how research findings could also benefit the general population.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf".** The lay abstract is used by all reviewers and addresses issues of particular interest to the affected community. ***Abstracts of all funded research projects will be posted publicly.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed. ***Do not duplicate the technical abstract.***

  Lay abstracts should address the points outlined below ***in a manner that will be readily understood by readers without a background in science or medicine***. Avoid overuse of scientific jargon, acronyms, and abbreviations.

  - Clearly describe the objectives and rationale for the proposed study and intervention.

  - If applicable, describe the approach implemented for engagement of military and Veteran consumers in the study.

  - Describe the ultimate applicability of the research and how it addresses at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas.

    - What types of patients will it help and how will it help them?

    - What are the potential clinical applications and short- and long-term benefits?

    - How is the proposed intervention expected to improve patient care and/or quality of life?

  - What is the projected timeline it may take to achieve an impact on the standard of care for adverse health outcomes associated with military-related toxic exposures?

- **Attachment 5: Statement of Work (seven-page limit): Upload as "SOW.pdf".** Refer to the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for the suggested SOW format and recommended strategies for assembling the SOW.

For the FY24 TERP CTA, refer to the "Example: Assembling a Clinical Research and/or Clinical Trial Statement of Work" for guidance on preparing the SOW. Use the "Suggested SOW Format" to develop the SOW for the proposed research. Submit as a PDF.

For the Partnering PI Option: Each PI must submit an identical copy of a jointly created SOW. The specific contributions of the Initiating PI and each Partnering PI should be clearly noted for each task.

The SOW should state the specific aims described in the Project Narrative and include a list of major tasks and subtasks that support the completion of the stated aims, including milestones for completing the aims during the period of performance. The SOW should describe only the work for which funding is being requested by this application and as applicable:

- Include the name(s) of the key personnel for each study site/subaward site.
- Indicate the number (and type, if applicable) of research subjects and/or human anatomical samples projected or required for each task and at each site.
- Indicate timelines required for regulatory approvals relevant to human subjects research (e.g., local IRB and federal USAMRDC Office of Human and Animal Research Oversight [OHARO] approvals, IND and IDE applications, as applicable). Refer to the General Application Instructions, Appendix 6, for additional information regarding regulatory requirements.
- Indicate quarterly enrollment targets.
- If applicable, indicate timelines and approvals required to obtain access to databases, repositories or other resources.

- **Attachment 6: 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 and/or clinical needs as it relates to at least one FY24 TERP Program Goal and at least one FY24 TERP Topic Area. Describe how the intervention addresses current clinical needs and how it compares with currently available interventions and/or standards of care. 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 they 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. Describe measures to ensure consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions). Clearly delineate research procedures from routine clinical procedures. Discuss how compliance with current Good Laboratory Practice (GLP) and Good Manufacturing Practices (GMP) guidelines and other regulatory considerations will be established, monitored, and maintained, as applicable.

- **Laboratory Evaluations:** State the biospecimen that will be collected along with the collection schedule and amount. 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). Describe the specimen storage plan, 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. 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.

- **Questionnaires and Other Research Data Collection Instruments:** If applicable, include a copy of the most recent version of 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.

- **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) Good Clinical Practices (GCP) compliance by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 7: 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 study population (to whom the study findings will be generalized) (i.e., Service Members/Veterans/civilians) and the nature, approximate number, age ranges, sex/gender, race, ethnicity, and other pertinent demographic characteristics, criteria for inclusion/exclusion and methods that will be used for recruitment/accrual/retention of human subjects.

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

  - For studies involving GW Veterans, the use of both the U.S. Centers for Disease Control and Prevention (CDC) and Kansas case definitions are required. Describe and justify any additional case definition of GWI, including any targeted illness subgroups that will be defined for the study.

  - **Enrollment Table:** Provide a table of anticipated enrollment counts at each study site.

  - **Inclusion of Women and Minorities in the 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 USAMRDC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Describe the strategy for the inclusion of women and minorities in the clinical trial appropriate to the objectives of the study, including a description of the composition of the proposed study population in terms of sex/gender, race, and ethnicity, and an accompanying rationale for the selection of subjects. Studies utilizing human biospecimens or data sets that cannot be linked to a specific individual, sex/gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement. Provide an anticipated enrollment table(s) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The Public Health Service (PHS) Inclusion Enrollment Report is a three-page fillable PDF form, which can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

  - Demonstrate that the research team has access to the proposed study population at each site and describe the efforts of the PI and/or key collaborators that will be made to achieve accrual and retention goals. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials/research, if applicable. Provide a description of the PI and/or key collaborator's experience in recruiting human subjects/acquiring human samples/accessing databases for similar research projects. Identify any potential

barriers to accrual/retention and provide mitigation plans for addressing unanticipated delays (e.g., slow accrual, attrition). Identify ongoing clinical research/trials that may compete for the same patient population and how they may impact enrollment progress.

- If military or Veteran population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of using the population(s). If a non-military population will be used for the proposed research project to simulate a military exposure, explain how the population simulates the targeted population. ***For clinical trials proposing to include DOD or VA patient populations, refer to the General Application Instructions, Appendix 4, for more information.***

- If the proposed research involves access to DOD and/or VA patient populations and/or DOD or VA resources or databases, describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research. ***Refer to the General Application Instructions, Appendix 4, for additional considerations***.

– **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, healthcare provider identification).

- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.

- If human subjects will be compensated for participation in the study, include a detailed description of and justification for the compensation plan.

- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.

– **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.*** It is recommended that informed consent allows for the use of samples for future studies.

- 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 the potential human subject will be allowed to discuss the study with anyone before making a decision.

- Address the need (if applicable) for obtaining ongoing consent or for reassessing 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.govinfo.gov/content/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.

– **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.

– **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 how the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study. 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:**

  - Appropriate to the study's level of risk, describe how safety monitoring and reporting to the IRB and Regulatory Agency (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.

- **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. ***Payment and/or other compensation for participation are not considered benefits and must be addressed in Recruitment Process.***

- **Attachment 8: Data Management and Sharing (no page limit): Upload as "Data_Manage.pdf".** The Data Management attachment should include the components listed below.

  - **Data Management:** Describe the data to be gathered and all methods used for collection, including the following:

    - **Data:** The types of data, software, or other materials to be produced.

    - **Acquisition and Processing:** How the data will be acquired, including the time and location of data acquisition, if scientifically pertinent. If use of existing data resources is proposed, describe the origin of the data set. Provide an account of the standards to be used for data and metadata format and content. Explain how the data will be processed.

    - **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, including the quality assurance and quality control measures taken during collection, analysis, and processing. Describe where data (both electronic and hard copy) will be stored; who will keep the data; how the data will be stored, if applicable; the file formats and the naming conventions that will be used; the process for locking the database at study completion; and the length of time that data will be stored, along with a justification for the time frame of preservation, which may include considerations related to the balance between the relative value of data preservation and other factors such as the associated cost and administrative burden of data storage. 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 studies requiring Regulatory Agency oversight, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.

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

- **Common Data Elements (CDEs) for GWI Clinical Trials:** If proposing clinical trials with GW Veterans, the use of CDEs is strongly encouraged. If applicable, describe how the use of GWI CDEs was considered when developing the plans for the collection of clinical data and annotation of clinical samples.

– **Data and Research Resources Sharing Plan:** Describe the type of data or research resources to be made publicly available as a result of the proposed work. Describe how data and resources generated during the performance of the project will be shared with the research community. Include the name of the repository(ies) where scientific data and resources arising from the project will be archived, if applicable. If a public repository will not be used for data or resource sharing, provide justification. Provide a milestone plan for data/results dissemination that includes when data and resources will be made available to other users, including

dissemination activities with a particular focus on feeding back the data to affected communities and/or research participants. In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether 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. In cases of national security or controlled unclassified information concerns, include a statement that the data cannot be made available to the public (e.g., "This data cannot be cleared for public release in accordance with the requirements in DoD Directive 5230.09."). Refer to CDMRP's Policy on Data & Resources Sharing located on the eBRAP "Funding Opportunities & Forms" web page https://ebrap.org/eBRAP/public/Program.htm for more information about CDMRP's expectations for making data and research resources publicly available.

- **Attachment 9: 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 a Regulatory Agency:

  - For investigator-sponsored regulatory exemptions (e.g., IND, IDE) provide evidence of institutional support. Provide evidence that the clinical trial does not require regulation by a Regulatory Agency. No further information for this attachment is required.

  For products that require regulation by a Regulatory Agency:

  - State whether the product is FDA-approved, -licensed, or -cleared, and marketed in the United States.

  - If the product is marketed in the United States, 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 FY24 TERP CTA, ***if an IND or IDE is required, the application must be submitted to the FDA within 6 months of award.*** 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). 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 Regulatory 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.

- If the clinical trial will be conducted at international sites, provide equivalent information and supporting documentation relevant to the product indication/label and regulatory approval and/or filings in the host country(ies).

- Provide the current status for manufacturing development (e.g., manufacturer's name, GMP-compliant lots available, status of stability testing), nonclinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support phase 1 testing), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).

- Describe the overall regulatory strategy and product development plan that will be performed during the project's period of performance to support the planned product indication/label. Include, as appropriate, a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of Regulatory Agency meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.

- **Attachment 10: 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 Regulatory Agency sponsor and any external consultants or other experts who will assist with Regulatory Agency sponsor 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 composition of the study team, including roles of the individuals listed in the organizational chart on the project along with any external consultants or advisors who will provide critical guidance and input to the study team (e.g., statistician, regulatory expert, commercialization consultant, clinical ethicist, patient advocate). Study coordinator(s) and statisticians should be included. Describe how the levels of effort for each individual are appropriate to successfully support the proposed research. Describe relevant background and qualifications that demonstrate appropriate expertise to accomplish the proposed work (e.g., statistical expertise, expertise in the disease and in conducting clinical studies), including previous interactions with the relevant Regulatory Agency, if applicable.

- **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial involves more than one institution, 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 institution. If the research involves more than one institution, a single IRB is required for all institutions located in the United States. If applicable, describe how communication and data transfer between/among the collaborating institutions will occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.

  The inclusion of at least one clinician on the study team is strongly encouraged.

  Participation of at least one military or Veteran consumer as a member of the research team to contribute to the development of the research question, project design, oversight, and evaluation, as well as other significant aspects of the proposed project is strongly encouraged.

  - For the purposes of the FY24 TERP, a consumer is a person living with a disease, injury, or condition or may be a family member or caregiver of a person impacted by a disease/injury/condition associated with military-related toxic exposures. The consumer must be an active participant in an advocacy, outreach, or support organization, or if military personnel on active duty, be approved to participate by their Commanding Officer.

- **Attachment 11: Partnership Statement (one-page limit): Upload as "Partnership.pdf".** ***(Attachment 11 is only applicable and required for applications submitted under the Partnering PI Option (CTA-PPIO)).***

  Describe the partnership including how the combined unique expertise of the Initiating and Partnering PI(s) will better address the research question and why the work should be done together rather than through separate individual efforts. Explain how the partnership and combined expertise of the PIs are critical for the research strategy and completion of the SOW. Explain how all PIs have appropriately balanced intellectual input into the design of the project and will devote appropriate levels of effort to conduct the project.

- **Attachment 12: 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 proposed effort. 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 transition plan should include the components list below, as appropriate and applicable to the research proposed.

  - A description of the anticipated outcomes/products expected upon completion of the proposed research efforts. Outcomes should be relevant, measurable, and include the intended end-user.

  - Provide a description of how the anticipated outcomes/products of the proposed research will be disseminated to both the scientific and consumer/stakeholder communities.

  - Details of the funding strategy that will be used to advance the outcome(s) to the next phase of development and/or commercialization (e.g., specific industry partners, specific funding opportunities to be applied for).

  - A description of collaborations and other resources that will be used to provide continuity of development.

  - Provide a brief schedule and milestones for transitioning the intervention to the next phase of development (e.g., further research, next-phase clinical trials, commercialization/transition to industry, delivery to the military or civilian market, incorporation into clinical practice, and/or clearance/approval by a Regulatory Agency).

  - For knowledge products, include a description of collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of clinical practice guidelines and recommendations,

provider training materials, patient brochures, clinical support tools, scientific journal publications, models, simulations, and applications. (A "knowledge product" is a non-materiel product that addresses an identified need, topic area, or capability gap; is based on current evidence and research; aims to transition into medical practice, training, or tools or to support materiel solutions [systems to develop, acquire, provide, and sustain medical solutions and capabilities]; and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.)

- Provide a plan for resolving intellectual and material property issues among participating organizations.

- Clearly articulate ownership rights and/or access to the appropriate 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.

- If applicable, provide a risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 13: Impact and Relevance to Military Health Statement (three-page limit): Upload as "Impact.pdf".** The Impact and Relevance to Military Health Statement must demonstrate how a successful outcome of the proposed research project will advance at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas. ***The Impact and Relevance to Military Health Statement should be written in a manner that will be readily understood by readers without a background in science or medicine.***

  - Describe how a successful outcome of the proposed research will reduce the burden (effects/outcomes, new exposures, etc.) of military-related toxic exposures for Service Members, their Families, Veterans, and/or the American public.

  - Identify the sample population(s) that will participate in the proposed intervention, inclusive of sex, gender, and/or minorities, if applicable; describe how they represent the target population that would benefit from the intervention and describe the potential impact a successful outcome of the proposed clinical trial would have on the lives and health of the target population.

  - **Describe the short-term impact:** Detail the anticipated outcomes/products (intellectual knowledge and/or tangible materiel) that will be directly attributed to the results of the proposed clinical trial and describe anticipated short-term benefits for individuals impacted by military-related toxic exposures.

  - **Describe the long-term impact:** Explain the anticipated long-term impact of implementing the intervention in the clinic and describe the anticipated long-term benefits on patient care and/or quality of life for the targeted population(s).

- Describe any relevant controversies or treatment issues that will be addressed by the proposed clinical trial.
- Describe how the intervention represents an improvement over currently available interventions and/or standards of care.
- Describe how the proposed effort is responsive to the health care needs and quality of life of Service Members, Veterans, and/or their Families.
  - Provide a description of how the knowledge, information, products, or technologies gained from the research could be implemented in a dual-use capacity to benefit the civilian population and address a military need, as appropriate.
  - Describe potential issues that might limit the impact of the proposed research even if the study is successful.

- **Attachment 14: Representations *(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 8, Section B.
- **Attachment 15: Suggested Intragovernmental/Intramural Budget Form *(if applicable)*: Upload as "IGBudget.pdf".** If an intramural DOD organization will be a collaborator in performance of the project, complete a separate budget using the "Suggested Intragovernmental/Intramural Budget Form" available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). The budget should cover the entire period of performance for each intramural DOD site and include a budget justification as instructed. The ***total*** costs per year for each subaward (direct and indirect costs) should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section V.A.(e), for additional information and considerations.

(c) Research & Related Personal Data: For extramural submissions, refer to the General Application Instructions, Section IV.B.(c), and for intramural submissions, refer to the General Application Instructions, Section V.A.(c), for detailed instructions.

(d) Research & Related Senior/Key Person Profile (Expanded): For extramural submissions, refer to the General Application Instructions, Section IV.B.(d), and for intramural submissions, refer to the General Application Instructions, Section V.A.(d), for detailed instructions.

- **PI Biographical Sketch (six-page limit):** Upload as "Biosketch_LastName.pdf".
- **PI Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".

- **Key Personnel Biographical Sketches (six-page limit each):** Upload as "Biosketch_LastName.pdf".

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

(e) Research & Related Budget: For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), for detailed instructions.

- **Budget Justification (no page limit):** For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Section L. For intramural submissions, refer to General Applications Instructions, Section V.A.(e), Budget Justification Instructions.

- ***Partnering PI Option:*** Initiating and Partnering PIs must have a separate budget and justification specific to their distinct portions of the effort that the applicant organization will submit as separate Grants.gov or eBRAP application packages. The Initiating PI should not include budget information for Partnering PI(s) even if they are located within the same organization. Refer to Section II.D.5, Funding Restrictions, for detailed information.

(f) Project/Performance Site Location(s) Form: For extramural submissions, refer to the General Application Instructions, Section IV.B.(f), and for intramural submissions, refer to the General Application Instructions, Section V.A.(f), for detailed instructions.

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(g), for detailed information.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov.

- **Intramural DOD Subaward:** Complete a separate "Suggested Intragovernmental/Intramural Budget Form" for each intramural DOD subaward and upload as a single document titled **IGBudget.pdf** to Grants.gov as Attachment 15.

II.D.2.b.iii. Full Application Submission Components for Each Partnering PI if Applying Under the Partnering Principal Investigator Option

The application submission process for each Partnering PI uses an abbreviated full application package. Refer to the equivalent attachment above for details specific to each of the following application components.

(a) SF424 Research & Related Application for Federal Assistance Form *(Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(a), for detailed information.

(b) Attachments:

- **Attachment 5: Statement of Work (seven-page limit): Upload as "SOW.pdf".** Each PI must submit an identical copy of a jointly created SOW.

- **Attachment 14: Representations *(Extramural Submissions Only)*: Upload as "RequiredReps.pdf".**

- **Attachment 15: Suggested Intragovernmental/Intramural Budget Form *(if applicable)*: Upload as "IGBudget.pdf".**

(c) Research & Related Personal Data: For extramural submissions, refer to the General Application Instructions, Section IV.B.(c), and for intramural submissions, refer to the General Application Instructions, Section V.A.(c), for detailed information.

(d) Research & Related Senior/Key Person Profile (Expanded): For extramural submissions, refer to the General Application Instructions, Section IV.B.(d), and for intramural submissions, refer to the General Application Instructions, Section V.A.(d), for detailed information.

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

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

- **Key Personnel Biographical Sketches (six-page limit each):** Upload as "Biosketch_LastName.pdf".

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

(e) Research & Related Budget: For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), for detailed information.

- **Budget Justification (no page limit):** Upload as "BudgetJustification.pdf".

The Initiating and Partnering PI(s) must each submit a budget and justification specific to their own portion of the efforts as part of their separate Grants.gov or eBRAP application packages. The Research & Related Budget for each Partnering PI should not include budget information for the Initiating PI, even if they are located within the same organization. Refer to Section II.D.5, Funding Restrictions, for detailed information.

(f) Project/Performance Site Location(s) Form: For extramural submissions, refer to the General Application Instructions, Section IV.B.(f), and for intramural submissions, refer to General Application Instructions, Section V.A.(f), for detailed information.

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(g), for detailed information.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov.

- **Intramural DOD Subaward:** Complete the Suggested Intragovernmental/Intramural Budget Form for each intramural DOD subaward and upload as a single document titled **IGBudget.pdf** to Grants.gov as Attachment 15.

II.D.2.c. Applicant Verification of Full Application Submission in eBRAP

Independent of submission type, once the full application is submitted it is transmitted to and processed in eBRAP. At this stage, the PI and organizational representatives will receive an email from eBRAP instructing them to log into eBRAP to review, modify, and verify the full application submission. Verification is strongly recommended but not required. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in the "Full Application Files" tab in eBRAP. However, 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. ***The Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline. 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 full application submission deadline.*** Other application components, including subaward budget(s) and subaward budget justification(s), may be changed until the end of the application verification period. The full application cannot be modified once the application verification period ends.

II.D.3. Unique Entity Identifier (UEI) and System for Award Management (SAM)

The applicant organization must be registered as an entity in SAM (https://www.sam.gov/content/home) and receive confirmation of an "Active" status before submitting an application through Grants.gov. Organizations must include the UEI generated by SAM in applications to this funding opportunity.

II.D.4. Submission Dates and Times

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.

All submission dates and times are indicated in Section I, Overview of the Funding Opportunity.

II.D.5. Funding Restrictions

Single PI Option:

The maximum period of performance is **4** years.

The application's direct costs budgeted for the entire period of performance should not exceed **$1,500,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

All direct and indirect costs of any subaward or contract must be included in the 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.

Partnering PI Option:

The maximum period of performance is **4** years.

The applications' combined direct costs budgeted for the entire period of performance in the applications of the Initiating PI and each Partnering PI should not exceed **$2,500,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

A separate award will be made to each PI's organization.

The PIs are expected to be partners in the research, and direct cost funding should be divided accordingly unless otherwise warranted and clearly justified.

All direct and indirect costs of any subaward or contract must be included in the 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 may be requested for (not all-inclusive):

Single PI Option:

- Travel in support of multi-institutional collaborations.
- Costs for one investigator to travel to one scientific/technical meeting per year. The intent of travel to scientific/technical meetings should be to present project information and/or disseminate project results from the FY24 TERP CTA.

- Costs for the PI to present project information or disseminate project results at one DOD-sponsored meeting (e.g., Military Health System Research Symposium) during the lifetime of the award. For budget purposes, it is suggested that these costs be included in year 2 of the award. These travel costs are in addition to those allowed for annual scientific/technical meetings.

- Research subject compensation and reimbursement for trial-related out-of-pocket costs (e.g., travel, lodging, parking, costs associated with caregiving, and resources/equipment to enable participation).

Partnering PI Option:

- Travel in support of multi-institutional collaborations.

- Costs for one investigator from each partnering application to travel to one scientific/technical meeting per year. The intent of travel to scientific/technical meetings should be to present project information and/or disseminate project results from the FY24 TERP CTA.

- Costs for the Initiating and Partnering PI(s) to present project information or disseminate project results at one DOD-sponsored meeting (e.g., a Military Health System Research Symposium) during the lifetime of the award. For budget purposes, it is suggested that these costs be included in year 2 of the award. These travel costs are in addition to those allowed for annual scientific/technical meetings.

- Research subject compensation and reimbursement for trial-related out-of-pocket costs (e.g., travel, lodging, parking, costs associated with caregiving, and resources/equipment to enable participation).

For all options within this award mechanism, direct costs must not be requested for:

- Travel to scientific/technical meeting(s) beyond the limits stated above.

- Preclinical or animal research.

II.D.6. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, 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 individually evaluated according to the following **scored criteria**, which are of equal importance:

- **Clinical Impact and Relevance to Military Health**
    - To what extent a successful outcome of the proposed research project will advance at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas.
    - How well the sample population represents the target population that would benefit from the intervention and how impactful a successful outcome of the proposed clinical trial would be on the lives and health of the target population.
    - How impactful a successful outcome of the proposed clinical trial would be on patient care for Service Members, Veterans, and/or the American public that have been or could potentially be impacted by the effects of military-related toxic exposures.
    - How the anticipated short- and long-term impacts of the proposed clinical trial will ultimately lead to new treatments/therapeutics/interventions to improve the quality of life for those that have been impacted by or are likely to encounter toxic substances.
    - How well the short-term impact including the anticipated outcomes/products (intellectual and/or tangible materiel) that will be directly attributed to the results of the proposed clinical trial and the short-term benefits for individuals are described.
    - How well the anticipated long-term impact of implementing the intervention in the clinic and long-term benefits on patient care and/or quality of life for the targeted populations are described.
    - Whether the application provides a description of how the knowledge, information, products, or technologies gained from the research could be implemented in a dual-use capacity to benefit civilian population and address military need (as appropriate).
    - Whether the application describes potential issues that might limit the impact of the proposed research even if the study is successful.
- **Research Strategy and Feasibility**
    - How well the application describes the scientific rationale for the clinical trial including preliminary (published or unpublished clinical or preclinical) data relevant to the proposed clinical trial and whether the clinical trial is based on a sound scientific rationale.
    - Whether the hypothesis or objectives of the study are clearly stated and how well the detailed specific aims, are described and aligned with the tasks in the SOW.
    - Whether the proposed project is feasible and will be completed within the proposed period of performance.
    - How well the application addresses measures to reduce bias.

- How well the application discusses potential problem areas, alternative methods/ approaches and mitigation strategies to address the potential for subject loss to follow-up.
- To what degree the data collection instruments, if applicable, are appropriate to the proposed study.

- **Intervention**
  - Whether there is evidence of who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for the proposed clinical trial.
  - To what degree the intervention addresses the clinical need(s) described.
  - How the intervention compares with currently available interventions and/or standards of care.
  - To what degree the application includes preclinical and/or clinical evidence to support the safety and stability (as appropriate) of the intervention.
  - How well research procedures are clearly delineated from routine clinical procedures.
  - How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
  - Whether measures are described to ensure the consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions).
  - How well the application describes interactions with human subjects including the study intervention that they will experience.
  - Whether the monitoring plan describes 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.

- **Regulatory Strategy and Transition Plan**
  - How the regulatory strategy and product 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 the FDA or other international regulatory agency, or that the IND or IDE application (and/or international equivalent) can feasibly be submitted within 6 months of award, as appropriate.
  - How well the documentation provided supports the feasibility of acquiring an active IND or IDE (and/or international equivalent) covering the proposed trial, if applicable.

- For investigator-sponsored regulatory exemptions (e.g., IND/IDE or other international equivalent), whether there is evidence of appropriate institutional support.

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

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

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

- For knowledge products, whether the proposed collaborations and other resources are achievable to provide continuity of development.

- Whether the schedule and milestones for bringing the intervention to the next phase of development (e.g., further research, next-phase clinical trials, commercialization/transition to industry, delivery to the market, incorporation into clinical practice, and/or clearance/approval by a Regulatory Agency) are achievable.

- If applicable, whether the potential 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/or commercialization, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this program announcement.

- How well the application describes the manner by which outcomes/products of the proposed research will be disseminated to both the scientific and consumer/stakeholder communities.

- **Recruitment, Accrual, and Access to Appropriate Subject Populations**

  - How well the application addresses the availability of human subjects for the clinical trial and the prospect of their participation.

  - Whether there is sufficient evidence provided to support availability of and access to human samples/study populations required for the study and documentation of experience of the PI and/or key collaborators in recruiting human subjects/acquiring human samples/accessing databases for similar projects.

  - How well the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random) are described.

- The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
- How well the inclusion/exclusion criteria and group assignment process meet the needs of the proposed clinical trial.
- How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate mitigation 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.
- Whether the strategy for the inclusion of women and minorities is appropriate to the objectives of the study.
- Whether the distribution of the proposed enrollment on the basis of sex/gender, race, and/or ethnicity is appropriate for the proposed research.
- If applicable, whether studies including GW Veterans use both the CDC and Kansas case definitions and whether any additional case definitions of GWI are justified and well-defined for the study.

- **Statistical Plan and Data Analysis**
  - To what degree the statistical model and data analysis plan are suitable for the study objectives.
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - 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.
  - Whether the plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity for phase 3 clinical trials are appropriate for the proposed research.
  - If applicable, to what extent the use of GWI CDEs was considered when developing the plans for the collection of clinical data and annotation of clinical samples.
- **Ethical Considerations**
  - Whether the population selected to participate in the trial stands to benefit from the knowledge gained.
  - If applicable, how well the inclusion of international sites is justified.
  - How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.

- To what degree privacy and confidentiality issues are appropriately considered.
- To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Personnel and Communication**
  - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
  - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
  - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
  - If applicable, 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.
  - For clinical trials that involve more than one institution, to what degree the multi-institutional structure governing the research protocol(s) across all participating institutions and regulatory submission plan are described and appropriate.
- **Partnership (Only Applicable to Partnering PI Option Applications)**
  - Whether the partnership and combined unique expertise of the Initiating and Partnering PIs will better address the research question together rather than through separate individual efforts.
  - To what degree the partnership and combined expertise of the PIs are critical to the research strategy and completion of the SOW.
  - How well the application reflects that all PIs contributed an appropriately balanced intellectual input into the design of the project and will devote appropriate levels of effort to conduct the project.

In addition, the following criteria will also contribute to the overall evaluation of the application, but will not be individually scored and are therefore termed **unscored criteria**:

- **Data and Research Resources Sharing Plan**
  - Whether the data and research resources will be shared with the research community.
  - To what extent the plan for sharing data and resources is appropriate and reasonable. If applicable, whether the name of the repository(ies) where scientific data and resources arising from the project will be archived is provided.

- Whether data and outcome dissemination activities, with particular focus on feeding back the data to affected communities and/or research participants, are described and appropriate.

- **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.

- **Budget**
  - Whether the **direct** costs exceed the allowable direct costs as published in the program announcement.
  - Whether the budget is appropriate for the proposed research.

- **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 priorities of the DHP and FY24 TERP, as evidenced by the following:
  - Adherence to the intent of the award mechanism
  - Program portfolio composition and balance
  - Relative clinical impact and relevance to military health

II.E.2. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding

General, USAMRDC. ***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.health.mil/about/2tierRevProcess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement declaring that application and evaluation information will not be disclosed outside the review panel. Violations of confidentiality can result in the dissolution 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 a 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 200.1, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in SAM.

An applicant organization may review SAM and submit comments on any information currently available about the organization that a federal awarding agency previously entered. 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.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Each applicant organization and PI will receive email notification when the funding recommendations are posted to eBRAP. At this time, each PI will receive a peer review summary statement on the strengths and weaknesses of the application and an information paper describing the funding recommendation and review process for the FY24 TERP award mechanisms. The information papers and a list of organizations and PIs recommended for funding are also posted on the program's page within the CDMRP website.

If an application is recommended for funding, after the email notification is posted to eBRAP, a government representative will contact the person authorized to negotiate on behalf of the recipient organization.

Only an appointed USAMRAA Grants Officer may obligate the government to the expenditure of funds to an extramural organization. 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 (i.e., assistance agreement).***

Intra-DOD obligations of funding will be made according to the terms of a negotiated Inter-Agency Agreement and managed by a CDMRP Science Officer.

Funding obligated to ***intragovernmental and intramural DOD organizations*** will be sent through the Military Interdepartmental Purchase Request (MIPR), Funding Authorization Document (FAD), or Direct Charge Work Breakdown Structure processes. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intragovernmental and intramural DOD investigators and collaborators must coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

An organization may, at its own risk and without the government's prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new award. For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Pre-Award Costs section, and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), Pre-Award Costs section, for additional information about pre-award costs.

If there are technical reporting requirement delinquencies for any existing CDMRP awards at the applicant organization, no new awards will be issued to the applicant organization until all delinquent reports have been submitted.

II.F.2. PI Changes and Award Transfers

Unless otherwise restricted, changes in PI (Initiating or Partnering) will be allowed on a case-by-case basis, provided the intent of the award mechanism is met.

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.

Refer to the General Application Instructions, Appendix 7, Section F, for general information on organization or PI changes.

II.F.3. Administrative and National Policy Requirements

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

Refer to the General Application Instructions, Appendix 7, for general information regarding administrative requirements.

Refer to the General Application Instructions, Appendix 8, for general information regarding national policy requirements.

Refer to full text of the latest DoD R&D General Terms and Conditions and the USAMRAA General Research Terms and Conditions: Addendum to the DoD R&D General Terms and Conditions for further information.

Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to register the study in the NIH clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 6, Section F, for further details.

Applications recommended for funding that involve animals, human data, human specimens, human subjects, or human cadavers must be reviewed for compliance with federal and DOD animal and/or human subjects protection requirements and approved by the USAMRDC OHARO, prior to implementation. This administrative review requirement is in addition to the local Institutional Animal Care and Use Committee, IRB, or Ethics Committee review. Refer to the General Application Instructions, Appendix 6, for additional information.

II.F.4. Reporting

Quarterly technical progress reports and quad charts, annual technical progress reports and quad charts, as well as a final technical progress report and a final quad chart will be required. Annual and final technical reports must be prepared in accordance with the Research Performance Progress Report (RPPR).

The Award Terms and Conditions will specify whether additional and/or more frequent reporting is required.

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

PHS Inclusion Enrollment Reporting Requirement: Enrollment reporting on the basis of sex/gender, race, and ethnicity will be required with each annual and final progress report. The

PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP.

Awards resulting from this program announcement may entail 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 $10M are required to provide information to SAM 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. These recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 8, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

Questions regarding program announcement content or submission requirements as well as technical assistance related to pre-application or intramural application submission:

Phone: 301-682-5507

Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

Questions regarding Grants.gov registration and Workspace:

Phone: 800-518-4726; International 1-606-545-5035

Email: support@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 901Ta. The program announcement numeric version code will match the General Application Instructions version code 901.

II.H.2. Administrative Actions

After receipt of pre-applications or full 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 exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the full application:

- Submission of an application for which a letter of invitation was not issued.
- Project Narrative is missing.
- Project Narrative exceeds page limit.
- Budget is missing.
- Intervention (Attachment 6) is missing.
- Human Subject Recruitment and Safety Procedures (Attachment 7) is missing.
- Data Management and Sharing (Attachment 8) is missing.
- Regulatory Strategy (Attachment 9) is missing.
- Study Personnel and Organization (Attachment 10) is missing.
- For applications including the Partnering PI Option, the Partnership Statement (Attachment 11) is missing.
- Transition Plan (Attachment 12) is missing.

II.H.2.b. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.

II.H.2.c. Withdrawal

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

- An FY24 TERP 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, including letters of support/recommendation.

A list of the FY24 TERP Programmatic Panel members can be found at https://cdmrp.health.mil/terp/panels/panels24.

- 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.
- Applications that include names of personnel from either of the CDMRP peer or programmatic review companies. For FY24, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.health.mil/about/2tierRevProcess).
- 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.
- Applications submitted by a federal government organization (including an intramural DOD organization) may be withdrawn if (a) the organization cannot accept and execute the entirety of the requested budget in current fiscal year (FY24) funds and/or (b) the federal government organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to collaborators.
- Application includes research data that are classified and/or proposes research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The proposed research is not a clinical trial.
- The proposed project includes animal or other preclinical research.
- The application fails to address at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas.
- The PI, Initiating PI, or Partnering PI does not meet the eligibility criteria.
- The invited application proposes a different research project than that described in the pre-application.
- Failure to submit all associated (Initiating and Partnering PI[s]) applications by the deadline.

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. Full Application Submission Checklist

Full Application Components	Uploaded	
	Single or Initiating PI	Partnering PI
SF424 Research & Related Application for Federal Assistance *(Extramural submissions only)*	☐	☐
Summary (Tab 1) and Application Contacts (Tab 2) *(Intramural submissions only)*	☐	☐
Attachments		
Project Narrative – Attachment 1, upload as "ProjectNarrative.pdf"	☐	
Supporting Documentation – Attachment 2, upload as "Support.pdf"	☐	
Technical Abstract – Attachment 3, upload as "TechAbs.pdf"	☐	
Lay Abstract – Attachment 4, upload as "LayAbs.pdf"	☐	
Statement of Work – Attachment 5, upload as "SOW.pdf"	☐	☐
Intervention – Attachment 6, upload as "Intervention.pdf"	☐	
Human Subject Recruitment and Safety Procedures – Attachment 7, upload as "HumSubProc.pdf"	☐	
Data Management and Sharing – Attachment 8, upload as "Data_Manage.pdf"	☐	
Regulatory Strategy – Attachment 9, upload as "Regulatory.pdf"	☐	
Study Personnel and Organization – Attachment 10, upload as "Personnel.pdf"	☐	
Partnership Statement – Attachment 11, upload as "Partnership.pdf"	☐	
Transition Plan – Attachment 12, upload as "Transition.pdf"	☐	
Impact and Relevance to Military Health Statement – Attachment 13, upload as "Impact.pdf"	☐	
Representations *(Extramural submissions only)* – Attachment 14, upload as "RequiredReps.pdf"	☐	☐
Suggested Intragovernmental/Intramural Budget Form *(if applicable)* – Attachment 15, upload as "IGBudget.pdf"	☐	☐
Research & Related Personal Data	☐	☐
Research & Related Senior/Key Person Profile (Expanded)	☐	☐
Attach PI Biographical Sketch (Biosketch_LastName.pdf)	☐	☐

Full Application Components	Uploaded	
	Single or Initiating PI	Partnering PI
Attach PI Previous/Current/Pending Support (Support_LastName.pdf)	☐	☐
Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person	☐	☐
Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person	☐	☐
Research & Related Budget *(Extramural submissions only)* Include budget justification	☐	☐
Budget *(Intramural submissions only)* Include budget justification	☐	☐
Project/Performance Site Location(s) Form	☐	☐
Research & Related Subaward Budget Attachment(s) Form *(if applicable)*	☐	☐

APPENDIX 1: TERP DEFINITIONS

The TERP uses the following definitions:

- **Fourth Generation Agents (FGA):** "Fourth generation agents, also known as Novichoks or A-series nerve agents, belong to a category of chemical warfare agents that are unique organophosphorus compounds. They are more persistent than other nerve agents and are at least as toxic as VX." (https://chemm.hhs.gov/nerveagents/FGA.htm.)

- **Gulf War (GW):** The 1990-1991 Persian Gulf War

- **Gulf War Illness (GWI):**

    - **Case Definitions:** 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 https://www.ncbi.nlm.nih.gov/books/NBK268875/pdf/Bookshelf_NBK268875.pdf). In this report, the IOM recommended the use of both the CDC definition of GWI and the "Kansas" definition of GWI. Applicants are encouraged to review this report, as the use of these case definitions is required when proposing clinical research/clinical trials with GW Veterans. Additional information on GWI can also be found in 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." This report can be found online at https://www.va.gov/RAC-GWVI/RACReport2014Final.pdf.

    - The former DOD CDMRP Gulf War Illness Research Program (GWIRP) assembled multiple resources that applicants may find helpful if proposing studies on GWI. These resources can be found at https://cdmrp.health.mil/gwirp/.

    - **Common Data Elements (CDEs) for GWI Clinical Research:** Through a collaboration among the National Institutes of Health (NIH), CDC, VA, former DOD CDMRP GWIRP, and the GWI community, CDE recommendations were developed for GWI. Applicants proposing clinical research under the Topic Area of "Gulf War Illness and Its Treatment" are strongly encouraged to review and consider the CDEs when preparing applications. Information on the GWI CDEs can be found at https://cdmrp.health.mil/gwirp/ and in: Cohen DE, Sullivan KA, McNeil RB, et al. 2022. A common language for Gulf War Illness (GWI) research studies: GWI common data elements. *Life Sciences Journal* 290:119818. doi:10.1016/j.lfs.2021.119818.

- **Medical Countermeasures (MCMs):** Medicines and medical products that can be used to diagnose, prevent, or treat diseases/conditions/symptoms related to chemical, biological, radiological, or nuclear (CBRN) threats.

- **Military-Related Toxic Exposures:** Exposures to known or unknown, naturally occurring or manmade substances associated with deployed, garrison, or other military-linked environments that result in adverse health effects. For the purposes of this TERP program announcement, exposures solely focused on environmental extremes are not considered military-related toxic exposures.

- **New Approach Methodologies (NAMs):** "Technologies and approaches that can potentially provide the same hazard and risk assessment information without the use of animal testing" (https://www.nationalacademies.org/event/12-09-2021/new-approach-methods-nams-for-human-health-risk-assessment-workshop-1).

- **Neurotoxin:** "Synthetic or naturally occurring substances that damage, destroy, or impair the functioning of the central and/or peripheral nervous system" (https://emedicine.medscape.com/article/1743954-overview).

- **Non-Traditional Agents (NTAs):** "Novel chemical threat agents or toxicants requiring adapted countermeasures" (https://www.govinfo.gov/content/pkg/PPP-2007-book1/pdf/PPP-2007-book1-doc-pg109.pdf).

- **Roles of Medical Care:** "The characterization of health support for the distribution of medical resources and capabilities" (https://www.health.mil/Reference-Center/Glossary-Terms/2018/06/22/Roles-of-Medical-Care#:~:text=Definition%3A,resuscitation%2C%20not%20including%20surgical%20care). For more information on the military roles of care refer to: Chapter 2, "Roles of Medical Care (United States)," Emergency War Surgery, Fifth United States Edition, 2018, Borden Institute (https://medcoeckapwstorprd01.blob.core.usgovcloudapi.net/pfw-images/dbimages/Ch%202.pdf).

- **Toxicant:** "A poison that is made by humans or that is put into the environment by human activities" (https://www.cancer.gov/publications/dictionaries/cancer-terms/def/toxicant).

- **Toxic Exposures:** Exposures to known and unknown naturally occurring or manmade, harmful substances that result in adverse health effects.

APPENDIX 2: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
BBRAIN	Boston Biorepository, Recruitment and Integrated Network for GWI
CDC	U.S. Centers for Disease Control and Prevention
CDE	Common Data Elements
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
CTA	Clinical Trial Award; when selecting a "Mechanism Option" in eBRAP, CTA also refers to the Clinical Trial Award – Single PI Option
CTA-PPIO	Clinical Trial Award – Partnering PI Option
DHA	Defense Health Agency
DHP	Defense Health Program
DMDC	Defense Manpower Data Center
DMSS	Defense Medical Surveillance System
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
DODSR	Department of Defense Serum Repository
DOEHRS	Defense Occupational and Environmental Health Readiness System
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FDA	U.S. Food and Drug Administration
FGA	Fourth Generation Agent
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GW	Gulf War
GWECB	Gulf War Era Cohort and Biorepository
GWI	Gulf War Illness
GWICTIC	Gulf War Illness Clinical Trials and Interventions Consortium
GWIRP	Gulf War Illness Research Program
GWVIB	Gulf War Veterans' Illness Biorepository Brain Bank
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

IDE	Investigational Device Exemption
IIRA	Investigator-Initiated Research Award
ILER	Individual Longitudinal Exposure Record
IND	Investigational New Drug
IOM	Institute of Medicine
IRB	Institutional Review Board
LAR	Legally Authorized Representative
M	Million
MAVERIC	Massachusetts Veterans Epidemiology Research and Information Center
MCM	Medical Countermeasure
MIPR	Military Interdepartmental Purchase Request
MVP	The Million Veteran Program
NAMs	New Approach Methodologies
NIH	National Institutes of Health
NTA	Non-Traditional Agent
OHARO	Office of Human and Animal Research Oversight (previously Office of Research Protections)
PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
ROC	Roles of Care, Role of Care
RPPR	Research Performance Progress Report
SAM	System for Award Management
SOW	Statement of Work
TERP	Toxic Exposures Research Program
TRA	Translational Research Award
UEI	Unique Entity Identifier
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	U.S. Department of Veterans Affairs