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

Investigator-Initiated Research Award

Announcement Type: Initial

Funding Opportunity Number: HT942524TERPIIRA

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."

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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 Investigator-Initiated Research Award (IIRA) 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 IIRA mechanism was first offered in FY22. Since then, 265 IIRA applications have been received, and 27 have been recommended for funding.

II.B. Award Information

The FY24 TERP IIRA is intended to support studies that will make an important contribution toward research and/or patient care for a disease or condition associated with military-related toxic exposures. Research projects may focus on any phase of research from basic laboratory research through translational research, including preclinical studies in animal models and human subjects, as well as correlative studies associated with an existing clinical trial. New Approach Methodologies may also be used.

Impact: Applications should explain how the proposed research will have a significant impact on military-related toxic exposure research and/or patient care with the intent to transition outcome(s)/product(s) (intellectual knowledge and/or tangible materiel) into clinical practice for

Service Members, their Families, Veterans, and/or the American public who have been or could potentially be impacted by toxic exposures. Applications should demonstrate both the short- and long-term impacts and how the successful completion of the proposed research will impact a critical problem or question in the field of research and/or patient care in at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas.

Preliminary data are required. The rationale for a research idea may be derived from laboratory discovery, population-based studies, a clinician's firsthand knowledge of patients, or anecdotal data. Applications must include relevant preliminary data that support the rationale for the proposed study. These data may be unpublished or from published literature.

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.

IIRA applications may include preclinical studies (including research involving animals) and/or research involving human subjects and human anatomical substances; ***however, the FY24 TERP IIRA may not be used to conduct clinical trials***. As stated in Section II.H.2.c, Withdrawal, applications including clinical trials will be withdrawn.

Applications proposing clinical trials may be submitted to the following FY24 TERP funding opportunity:

- Clinical Trial Award (Funding Opportunity Number HT942524TERPCTA)

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.

Studies using human subjects, human anatomical substances, or data sets are strongly encouraged to use relevant military and/or Veteran populations/samples/data sets. Applications not using military or Veteran populations/samples/data sets are strongly encouraged to provide justification for how the chosen populations/samples/data sets are 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/samples/data sets that reflect traditionally underrepresented populations of Service Members, Veterans, and/or their Families.

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 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 (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.

Research Involving Animal Models. If animal models are proposed, consider the following:

- Pairing clinical populations to animal models in order to validate the clinical relevance and development of prevention, assessment, and treatment solutions is encouraged.
- For studies using animal models, the use of an established model is preferred unless there is a compelling scientific justification for the development or use of a new model.
- Proposed animal models should be well-justified, supported within the literature, and clearly align with clinical relevance.
- For studies proposing GWI research with animal models, a list of animal models funded by the former DOD CDMRP Gulf War Illness Research Program (GWIRP) is available at https://cdmrp.health.mil/gwirp/resources/amodels.

Clinical research involving human subjects and human anatomical substances is permitted; *however, the FY24 TERP IIRA may not be used to conduct clinical trials.*

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.

For the purposes of this funding opportunity, research that meets the definition of a clinical trial is distinct from clinical research. Clinical research encompasses research with human data, human specimens, and/or interaction with human subjects. Clinical research is observational in nature and includes:

(1) Research conducted with human subjects and/or material of human origin such as data, specimens, and cognitive phenomena for which an investigator (or co-investigator) does ***not*** seek to assess the safety, effectiveness, and/or efficacy outcomes of an intervention. Research meeting this definition may include but is not limited to: (a) mechanisms of human disease, (b) diagnostic or detection studies (e.g., biomarker or imaging), (c) health disparity studies, and (d) development of new technologies.

(2) Epidemiologic and behavioral studies that do ***not*** seek to assess the safety, effectiveness, and/or efficacy outcomes of an intervention.

(3) Outcomes research and health services research that do not fit under the definition of clinical trial.

Excluded from the definition of clinical research are in vitro studies that utilize human data or specimens that cannot be linked to a living individual and meet the requirements for exemption under §46.104(d)(4) of the Common Rule.

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/
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

Resource	Website
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 Investigator-Initiated Research Award should not exceed **$500,000**. 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 $3.2M to fund approximately four Investigator-Initiated Research 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 organizations, 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

Independent intramural DOD and extramural investigators at all academic levels (or equivalent) may be named by organizations as the Principal Investigator (PI) on the application.

Postdoctoral fellows are not considered independent investigators.

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

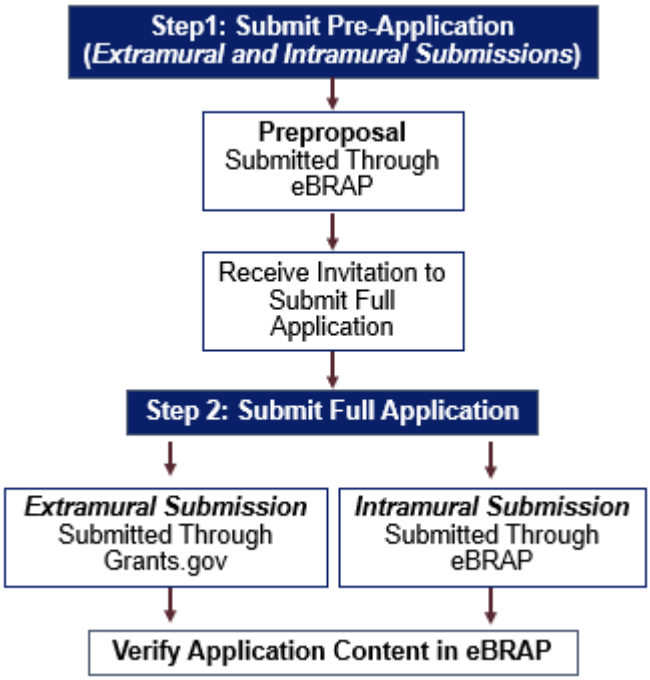
Submission is a two-step process requiring both a ***pre-application*** submitted via the Electronic Biomedical Research Application Portal (eBRAP.org) and a ***full application*** (eBRAP.org or Grants.gov). Depending on the type of submission (i.e., extramural versus intramural), certain aspects of 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 HT942524TERPIIRA 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 HT942524TERPIIRA 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 through eBRAP (https://eBRAP.org/).

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.

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 that ***does not*** involve human subjects, prospective or retrospective human biological samples or human data sets.	**Investigator-Initiated Research Award (IIRA); select "no option"**
Research that ***does*** involve human subjects, prospective or retrospective human biological samples or human data sets but ***does not*** constitute a clinical trial. *Applications that propose only the use of commercially available human primary cells or cell lines do not need to select this option.*	**Investigator-Initiated Research Award – Human Subjects/Samples Option (IIRA-HS)**

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 (two-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.
  - **Specific Aims and Study Design:**
    - Concisely state the specific aims of the proposed study.
    - Briefly describe the experimental methods and approaches.

- As applicable, succinctly describe the proposed model system(s) (cellular, animal, etc.), human samples, human data sets and/or human subjects.
    - If human subjects, samples and/or data sets will be used, indicate whether the proposed project will use military or Veteran populations/samples/data sets OR how the chosen population/samples/data sets are relevant to military-related toxic exposures and will benefit Service Members, Veterans, and/or their Families.

- **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 advance the research field and ultimately lead to new treatments/therapeutics, diagnostic assays, or prevention strategies to improve 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, 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.

- **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 whether the experimental approaches are clearly described.
    - If applicable, to what degree the proposed human populations/samples/data sets include Service Members, Veterans, and/or their Families OR whether the proposed populations/samples/data sets are relevant to military-related toxic exposures and will benefit Service Members, Veterans, and/or their Families.
- **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 advance the research field and ultimately lead to new treatments/therapeutics, diagnostic assays, or prevention strategies to improve 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, 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.

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

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, 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 (13-page limit) *(NEW page limit in FY24)*: 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.

Describe the proposed project in detail using the outline below.

- **Background/Rationale:** Describe in detail the scientific rationale for the study. Applications must include relevant preliminary data that support the rationale for the proposed study; data may be unpublished or from published literature, including preliminary data and/or preclinical data originating from the applicant's laboratory or other external laboratories. The rationale should include a literature review that supports the development of the proposed project. The background section should clearly support the choice of the study variable and should explain the basis for the study questions and/or hypotheses. Provide a summary of relevant prior preclinical and/or clinical work and distinguish how the proposed study differs from other relevant or recently completed research. 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***.

- **Hypothesis or Objective:** Clearly state the hypothesis to be tested or the objective(s) to be reached.

- **Specific Aims:** State and concisely explain the project's specific aims. These aims should agree with the aims and associated tasks described in Attachment 5, Statement of Work (SOW). If the proposed research project is part of a larger study, present only tasks that this TERP award would fund.

- **Research Strategy and Feasibility:**

  - Describe the experimental design, methods, analyses, and models, including appropriate controls, in sufficient detail to allow for their appropriateness and feasibility to be assessed. Identify how the research strategy and approaches will meet the project's goals and milestones.

  - Describe the statistical model and data analysis plan and how the data will be handled and analyzed. If applicable, indicate rules for stopping data collection, primary endpoints and inclusion/exclusion of data.

  - Describe how the proposed project is feasible and will be completed within the proposed performance period.

  - Address potential problem areas and pitfalls, and provide alternative methods and approaches.

  - If cell lines or animals are to be used, justify why the proposed cell line(s) or animal model(s) were chosen and discuss the model's clinical relevance to human biology (including but not limited to routes of human exposures, exposure dose, outcomes [human symptoms, diseases/conditions] associated with exposures and the types of exposures potentially encountered). ***For animal studies, full details will be required in the Animal Research Plan (Attachment 7).***

- If proposing a correlative study, specify how the proposed project complements the existing research efforts and provides additional relevant insight beyond the initial study design.

- If human subjects, human biological samples, or data sets will be used, describe the study population and include an overview of the recruitment of human subjects or the acquisition of samples/data sets. Describe the availability of the proposed study population and past successes in recruiting similar populations. If military, military families, and/or Veteran population(s) or data sets will be used in the proposed research project, describe the feasibility of accessing the population(s)/data set(s). ***For studies proposing recruitment of human subjects, human anatomical substances, or data sets, full details will be required in Human Subjects/Samples Acquisition and Safety Procedures (Attachment 8). Clinical trials are not allowed under the FY24 TERP IIRA.***

- **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 and 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.

- **Intellectual Property:** Information can be found in the 2 CFR 200.315, "Intangible Property."

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

  - Address any impact of intellectual property issues on product development and subsequent government access to products supported by this program announcement.

  - **Commercialization Strategy *(if applicable)*:** Describe the commercialization plan. The plan should include intellectual property, market size, financial analysis, strengths and weaknesses, barriers to the market, competitors, and management team. Discuss the significance of this development effort, when it can be anticipated, and the potential commercial use for the technology being developed.

- **DOD Data Management Plan (two-page limit is recommended):** If a data management plan is included as part of Attachment 8, Human Subjects/Samples Acquisition and Safety Procedures, then submission of the data management plan under Attachment 2 "Supporting Documentation" is not required. Describe the data management plan in accordance with Section 3.c, Enclosure 3, DoD Instructions 3200.12. ***Do not duplicate the Data and Research Resources Sharing Plan.*** Refer to General Application Instructions, Section IV.B, Attachments Form, Attachment: Supporting Documentation, for detailed information regarding Data Management Plan content.

- **Data and Research Resources Sharing Plan:** Describe the type of data or research resource 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. Refer to CDMRP's Policy on Data & Resource 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.

- **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 non-profit 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.

- **Inclusion Enrollment Plan *(if applicable)*:** Provide an anticipated enrollment table(s) for the inclusion of women and minorities using the Public Health Service (PHS) Inclusion Enrollment Report, a three-page fillable PDF form, that can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm. The enrollment table(s) should be appropriate to the objectives of the study with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. 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.

- **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 are highly important.

  - **Background/Rationale:** Present the scientific rationale and reasoning behind the proposed research project.

  - **Hypothesis/Objective(s):** State the hypothesis to be tested and/or objective(s) to be reached.

- **Specific Aims:** State the aims of the proposed research project.
- **Study Design:** Briefly describe the experimental design, including model system(s) and appropriate controls.
- **Impact:** Briefly describe how the proposed research will have a significant impact on toxic exposure research and/or patient care with the intent to transition outcomes into clinical practice for Service Members, their Families, Veterans and/or the American public that have been, or could potentially be, impacted by military-related toxic exposures. State both the short- and long-term impacts and how the proposed research will ultimately lead to new treatments/therapeutics, diagnostic assays or prevention strategies to improve 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.

- Summarize the objectives and rationale for the proposed research.
- 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.
- Indicate what population(s) the research will help, and how it will help them.
- Describe potential clinical applications, benefits, and risks.
- If the research is too basic for immediate clinical applicability, then describe the interim outcomes.
- Describe the projected timeline to achieve the expected patient-related outcome.

- Describe the likely contributions of the proposed research project to advance knowledge, lead to new treatments/therapeutics, diagnostic assays or prediction and prevention strategies to improve the quality of life for those that have been impacted by, or are likely to encounter, toxic substances.

- Describe how the proposed project will impact the health and well-being of Service Members, Veterans, and/or their Families.

- **Attachment 5: Statement of Work (five-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 IIRA, refer to either the "Example: Assembling a Clinical Research and/or Clinical Trial Statement of Work" or "Example: Assembling a Generic Statement of Work," whichever example is most appropriate for the proposed effort, for guidance on preparing the SOW. Use the "Suggested SOW Format" to develop the SOW for the proposed research. Submit as a PDF.

  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 (animal or human) and/or human anatomical samples projected or required for each task and at each site.

  - Identify cell line(s) and commercial or organizational source(s) to be used.

  - If applicable, indicate timelines required for regulatory approvals relevant to animal or human subjects research (e.g., local [Institutional Animal Care and Use Committee [IACUC]/IRB] and federal [USAMRDC Office of Human and Animal Research Oversight [OHARO]] approvals). Refer to the General Application Instructions, Appendix 6, for additional information regarding regulatory requirements.

  - For studies with prospective accrual of human subjects, indicate quarterly enrollment targets. If applicable, indicate timelines and approvals required to obtain access to databases, repositories or other resources.

- **Attachment 6: 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 project 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**.**

- **Describe the short-term impact:** Detail the anticipated outcome(s)/product(s) (intellectual knowledge and/or tangible materiel) that will make important scientific advances and improve the understanding, prevention/prediction, diagnosis and/or treatment of military-related toxic exposures.

- **Describe the long-term impact:** Explain the anticipated long-term benefits from this research and how it will impact the field of study and/or the lives of relevant patient or community populations. Explain the anticipated long-term benefits from this research in the clinic or field. Discuss how the proposed materiel or knowledge product represents an improvement to currently available prevention strategies, treatments/interventions, diagnostic approaches, devices, or clinical practice guidelines, if applicable.

- 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 7: Animal Research Plan (five-page limit per animal study): Upload as "AnimalResPlan.pdf".** ***(Attachment 7 is only applicable and required for applications proposing animal studies.)***

  Proposed studies should not rely on samples, reagents, or tools that are contingent upon completion of other ongoing efforts outside the scope of this research project.

  If the proposed study involves animals, a summary describing the animal research that will be conducted must be included in the application. Consult the ARRIVE guidelines 2.0 (Animal Research: Reporting *In Vivo* Experiments) to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines 2.0 can be found at https://arriveguidelines.org/arrive-guidelines. The Animal Research Plan may not be an exact replica of the protocol(s) submitted to the IACUC. The Animal Research Plan should address the following points to achieve reproducible and rigorous results for each proposed animal study:

- Briefly describe the research objective(s) of the animal study. If using an existing animal model, provide evidence that the chosen animal model(s) is validated and well-justified in the literature. If developing a novel animal model, explain how the animal model is expected to be superior to other existing models (if others exist) and indicate how this model will be suitable to address the study aims.

- Explain how and why the animal species, strain, and model(s) being used/developed can address the scientific objectives and the relevance to human biology.

- If applicable, describe approaches that will be undertaken to validate or corroborate findings from animal studies to relevant human data sources/populations. Describe how the proposed validation approaches or corroborative studies "de-risk" the possibility that the findings from the animal study cannot be translated into human populations.

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

- Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during the review of the application.

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

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

- Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with a Regulatory Agency or next stage of development, if applicable.

- **Attachment 8: Human Subjects/Samples Acquisition and Safety Procedures *(if required; no page limit)*: Upload as "HumSubProc.pdf".**

  Attachment 8 is required for all applications submitted under the Human Subjects/Samples Option (IIRA-HS) where the proposed research involves human subjects, prospective or retrospective human biological samples, or human data sets.

  Attachment 8 is NOT required if applications propose only the use of commercially available human cell lines or commercially available primary human cells as those applications are not required to submit under the Human Subjects/Samples Option (IIRA-HS).

Proposed studies should not rely on samples, reagents, or tools that are contingent upon completion of other ongoing efforts outside the scope of this proposed project.

Include the components listed below as applicable.

- **Human Samples and/or Data Sets:** Describe the types and source(s) of specimens, records, or data to be collected and evaluated.
  - All specimens that will be collected for study purposes must be clearly stated and relevance to the study objectives described. The collection schedule and amount of material collected must also be clearly described.
  - Include information about specimen storage (i.e., location, duration, special handling conditions). Describe the identifiers that will be associated with the human specimens and data and provide a list of who has access to subjects' identities. Describe how individually identifiable private information will be protected.
  - If retrospectively collected human biological samples or correlated data from biorepositories or databases will be used, describe how those curated samples or data are representative of well-pedigreed cohorts of uniformly documented patients by providing their defining inclusion/exclusion criteria.
  - For studies involving the use of banked human specimens, include a detailed plan for the acquisition of samples and/or data. Describe procedures to be used to assess the quality of the materials and identify and correct for effects and/or artifacts of sample processing and storage.
- **Human Subjects Study Population:** Describe the study population (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 the methods that will be used for recruitment/accrual/retention of human subjects.
  - Describe the rationale for the selection of 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.
  - 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:** Describe the strategy for the inclusion of women and minorities appropriate to the objectives of the study,

including a description of the composition of the proposed study population in terms of sex/gender, race, and ethnicity, and an accompanying rationale for the selection of 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. 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. Anticipated enrollment table(s) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity should be provided as part of the application's Supporting Documentation, Attachment 2.

- Demonstrate that the research team has access to the proposed study population at each site and describe the efforts that will be made to achieve accrual and retention goals. If applicable, discuss past efforts of the PI and/or key collaborators in recruiting human subjects from the target population for previous clinical research. 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-related toxic exposure, explain how the population simulates the targeted population. ***For clinical research 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.***

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

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

- 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.

– **Informed Consent Process:** Specifically describe the plan for obtaining informed consent from human subjects and 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 study.

  - 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 research, 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 research. Consider how the proposed clinical research 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 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 or stopping criteria.

    - 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 or 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 the Recruitment Process.***

- **Statistical Plan:** Clearly describe the statistical plan and sample size estimate for each study arm, including power analysis calculations to demonstrate that the sample size is appropriate to meet the objectives of the study given the constraints of the award mechanism. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during the review of the application. As applicable, describe how the randomization and blinding procedures for the study are appropriate, and specify any other measures to be taken to minimize the effects of subjective bias.

- **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.

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

- **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 Research:** If proposing clinical research 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.

- **Sharing Study Results:** 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.").

– **Laboratory Evaluations:**

  - **Specimens to be Collected, Schedule, and Amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.

  - **Evaluations to Be Made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study.

  - **Storage:** Describe specimen storage, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the plan to store specimens for future use, including considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.

  - **Labs Performing Evaluations and Special Precautions:** Identify the laboratory performing each evaluation, the applicable quality standard, and any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Attachment 9: Use of Hazardous Chemical or Biological Agents *(if applicable; no page limit)*: Upload as "Hazardous.pdf".** The applicant must submit a plan for acquiring, using, and maintaining hazardous agents if such agents are to be used in the study. The plan must contain all applicable information such as CDC registration, an approved organizational safety plan to use the agent(s), and letters of collaboration, agreement, or approval from government sites issuing any agent(s). Indicate whether agents used are purchased commercially, and, if so, confirm that the

amount is under regulated limits. Include a statement addressing this requirement along with accompanying letters of collaboration, approvals, and certifications.

- **Attachment 10: Study Personnel and Organization (one-page limit): Upload as "Personnel.pdf".**
  - Discuss the qualifications and experience/expertise of the research team and each individual's specific contributions to the project, including how the appropriate experience is incorporated to address the research question and enable the success of the proposed project.
  - Clearly state whether key personnel are not receiving salary from the award. If applicable, provide assurances/letters of commitment that the unpaid personnel will contribute the required level of effort to complete the project.
  - Describe the PI's record of accomplishment and their ability to lead the research team to accomplish the proposed research project. Describe previous experience most pertinent to this project.
- **Attachment 11: 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, Representations.
- **Attachment 12: 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 instructions. For intramural submissions, refer to General Application Instructions, Section V.A.(e), Budget Justification Instructions.

(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 instructions.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form and upload 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 12.

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

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

The application's direct costs budgeted for the entire period of performance should not exceed **$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 **3** years.

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

- 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 IIRA.
- Costs for the PI 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 study-related out-of-pocket costs (e.g., travel, lodging, parking, costs associated with caregiving, and resources/equipment to enable participation).

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

- Costs for travel to scientific/technical meeting(s) beyond the limits stated above.
- Clinical trial costs.

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.

- **Research Strategy and Feasibility**
    - How well the application describes the scientific rationale for the study including relevant preliminary data that support the rationale for the proposed study and a literature review that supports the development of the proposed project and provides the basis for the study questions and/or hypotheses.
    - 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.
    - How well the experimental design, methods, analyses, and models, including the appropriate controls, are described; how well the approaches will meet the project's goals and milestones; and whether the project is feasible and can be completed within the proposed period of performance.
    - If applicable, how well the proposed correlative study complements the existing research efforts and provides additional relevant insight beyond the initial study design.
    - How thoroughly the application acknowledges potential problem areas and pitfalls and provides alternative methods and approaches.
    - For studies involving hazardous agents, whether the application includes an appropriate plan for acquiring, using, and maintaining the hazardous agents.
    - If applicable, to what degree the intellectual and material property plan is appropriate.

For research involving cell line(s) and/or animals:

- How well the choice of proposed cell line(s) and/or animal model is justified and relevant to human biology (including but not limited to routes of human exposures, exposure dose, outcomes [human symptoms, diseases/conditions] associated with exposures, and types of exposures potentially encountered).
- How well and why the animal species, strain, and model(s) being used can address the scientific objectives.
- If applicable, whether the Animal Research Plan (Attachment 7) includes and describes the appropriate control groups to meet the objectives of the study.
- If applicable, whether appropriate approaches are being undertaken to validate or corroborate findings from animal studies to human data sources/populations.
- If applicable, to what extent the proposed validation approaches or corroborative studies "de-risk" the possibility that the findings from the animal study cannot be translated into human populations.
- To what extent the data and documentation support a regulatory filing with a Regulatory Agency or next stage of development, if applicable.
- To what extent the primary endpoint(s) identified in the Animal Research Plan (Attachment 7) are appropriate, as applicable.

For applications submitted under the Human Subjects/Samples Option (IIRA-HS):

- Whether the study population, methods for sample acquisition or proposed data/samples are appropriate to accomplish the proposed work.
- Whether there is sufficient evidence provided to support availability of and access to samples/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 inclusion/exclusion criteria meet the needs of the proposed clinical research.
- If recruiting human subjects:
  - To what degree the recruitment, screening, and retention processes for human subjects will meet the needs of the proposed clinical research.
  - Whether the strategy for the inclusion of women and minorities and distribution of proposed enrollment are appropriate for the proposed 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 IRB review) are exempt from this requirement.

- To what degree the distribution of the proposed enrollment or data set on the basis of sex/gender, race, and/or ethnicity is appropriate and is related to the scientific goals of the proposed research.
- How well the application identifies any potential barriers to accrual/retention and provides mitigation plans for addressing unanticipated delays (e.g., slow accrual, attrition).
- To what degree the process for seeking informed consent is appropriate.

- If applicable, to what degree the plans to collect specimens and conduct laboratory evaluations are relevant to the study objectives.
- 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.
- 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.
- How well the types of specimens or data to be collected and evaluated and specimen storage and maintenance are described.
- If applicable, to what extent retrospectively collected human biological samples or correlated data from biorepositories or databases are from well-pedigreed cohorts that include patient inclusion/exclusion criteria.
- To what extent the methods for data collection including confidentiality, methods for data capture, verification, and disposition are described.
- If applicable, whether the measures of risk management and plans for emergency response are well described.
- Whether there is sufficient information provided regarding data reporting and how it will be assured that data will support a regulatory filing with a Regulatory Agency, if applicable.
- How well the application describes whether the results of any screening and/or study participation will be shared with the human subject or their primary care provider, if applicable.

- **Impact and Relevance to Military Health**
    - To what extent a successful outcome of the proposed research project will have an impact on military-related toxic exposure research and/or patient care and will advance at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas.
    - To what extent a successful outcome of the proposed research project will reduce the burden (effects/outcomes, new exposures, etc.) of military-related toxic exposures for Service Members, Veterans, their Families, and/or the American public.
    - Whether the anticipated short-term outcome(s)/products (intellectual knowledge and/or tangible materiel) will make an important scientific advancement and improve the understanding, prevention/prediction, diagnosis, and/or treatment of military-related toxic exposures.
    - Whether the anticipated long-term benefits will impact the field of study and/or the lives of relevant patient or community populations and whether the anticipated outcomes will benefit the clinic or the field.
    - To what extent the proposed materiel or knowledge product represents an improvement to currently available prevention or treatments/interventions, diagnostic approaches, devices or clinical practice guidelines (if applicable).
    - How well the proposed effort is responsive to the health care needs and quality of life of Service Members, Veterans, and/or their Families.
    - 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.
- **Statistical Plan and Data Analysis**
    - Whether the application provides a description of how the data will be handled and statistically analyzed.
    - How well the statistical model and data analysis plan are explained and, whether they are appropriate for the proposed study objectives.
    - Whether the application identifies rules for stopping data collection, primary endpoints, and inclusion/exclusion of data.
    - If applicable, to what extent the statistical plan and sample size, including power analysis, are appropriate for the study objectives.

- If applicable, whether the randomization and blinding procedures for the study are appropriate and discuss other measures taken to minimize the effects of subjective bias during animal treatment and assessment of results.

- **Personnel**

  - To what degree the research team's qualifications and experience/expertise and each individual's specific contributions, including how their appropriate experience is incorporated, address the research question and enable the success of the proposed project.

  - Whether the PI's record of accomplishment and their ability to lead the research team to accomplish the proposed research project is clearly stated and whether their previous experience most pertinent to this project is sufficient to achieve the project's goals.

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

- **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.

- **Environment**

  - To what extent the scientific environment is appropriate for the proposed research project.

  - How well the research requirements are supported by the availability of and accessibility to facilities and resources.

- To what extent the quality and level of institutional support are appropriate for the proposed research project.

- **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 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 or organization will be allowed on a case-by-case basis, provided the intent of the award mechanism is met.

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

Refer to the General Application Instructions, Appendix 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 Terms and Conditions and the USAMRAA Research Terms and Conditions: Addendum to the DoD R&D Terms and Conditions for further information.

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 IACUC, IRB, or Ethics Committee review. Refer to the General Application Instructions, Appendix 6, for additional information.

II.F.4. Reporting

Annual technical progress reports and quad charts as well as a final technical progress report and quad chart will be required. Annual and final technical reports must be prepared in accordance with the Research and 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 *(only required for clinical research studies)*: Enrollment reporting on the basis of sex/gender, race, and/or 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 901a. 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.
- For applications involving animal research, the Animal Research Plan (Attachment 7) is missing.
- For applications involving human subjects, human samples, or human data sets, the Human Subjects/Samples Acquisition and Safety Procedures (Attachment 8) is missing.

II.H.2.b. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the 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.
- The application fails to address at least one of the FY24 TERP Program Goals and at least one of the FY24 TERP Topic Areas.

- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The PI does not meet the eligibility criteria.
- A clinical trial is proposed.
- The invited application proposes a different research project than that described in the pre-application.

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
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"	☐
Impact and Relevance to Military Health Statement – Attachment 6, upload as "Impact.pdf"	☐
Animal Research Plan *(if applicable)* – Attachment 7, upload as "AnimResPlan.pdf"	☐
Human Subjects/Samples Acquisition and Safety Procedures *(if applicable)* – Attachment 8, upload as "HumSubProc.pdf"	☐
Use of Hazardous Chemical or Biological Agents *(if applicable)* – Attachment 9, upload as "Hazardous.pdf"	☐
Study Personnel and Organization – Attachment 10, upload as "Personnel.pdf"	☐
Representations *(Extramural submissions only)* – Attachment 11, upload as "RequiredReps.pdf"	☐
Suggested Intragovernmental/Intramural Budget Form *(if applicable)* – Attachment 12, upload as "IGBudget.pdf"	☐
Research & Related Personal Data	☐
Research & Related Senior/Key Person Profile (Expanded)	☐
Attach PI Biographical Sketch (Biosketch_LastName.pdf)	☐
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
ARRIVE	Animal Research: Reporting *In Vivo* Experiments
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
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
ET	Eastern Time
FAD	Funding Authorization Document
FGA	Fourth Generation Agent
FY	Fiscal Year
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' Illnesses Biorepository Brain Bank
IACUC	Institutional Animal Care and Use Committee
IIRA	Investigator-Initiated Research Award; when selecting a "Mechanism Option" in eBRAP, IIRA also refers to the Investigator-Initiated Research Award for applications that do not involve human subjects, prospective or retrospective human biological samples or human data sets.
IIRA-HS	Investigator-Initiated Research Award – Human Subjects/Samples Option
ILER	Individual Longitudinal Exposure Record
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