I. OVERVIEW OF THE FUNDING OPPORTUNITY

United States Army Medical Research and Development Command



DEPARTMENT OF DEFENSE

BROAD AGENCY ANNOUNCEMENT for Extramural Medical Research

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KEY DATES

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This funding opportunity announcement is a broad agency announcement (BAA). It is continuously open for a 5-year period, from October 1, 2022 through September 30, 2027, 11:59 p.m. Eastern Time.

This Broad Agency Announcement must be read in conjunction with the General Submission Instructions, which are available for downloading from Grants.gov. The General Submission Instructions are located under the "package tab" and can be downloaded by selecting the "Download Instructions" icon when previewing the submission package.

Table of Contents

I. OVERVIEW OF THE FUNDING OPPORTUNITY 1

I.A. New for Fiscal Year 2023 – Fiscal Year 2027 4

II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY 5

II.A. Program Descriptions 6

II.A.1. Military Infectious Diseases Research Program 6

II.A.2. Combat Casualty Care Research Program 7

II.A.3. Military Operational Medicine Research Program 9

II.A.4. Medical Biological Defense Research Program 10

II.A.5. Medical Chemical Defense Research Program 11

II.B. Award Information 12

II.B.1. Clinical Trial Support 14

II.B.2. Use of Military and Department of Veterans Affairs Populations or Resources 14

II.B.3. Technology Requirements and Standards 15

II.B.4. Data Sharing 16

II.B.5. Funds Available and Anticipated Number of Awards 17

II.B.6. Award Amounts and Periods of Performance 17

II.B.7. Mechanisms of Support 18

II.C. Eligibility Information 20

II.C.1. Eligible Applicants 20

II.C.2. Cost Sharing 21

II.C.3. Other 21

II.D. Proposal/Application Submission Information 22

II.D.1. Where to Obtain the Proposal/Application Submission Package 22

II.D.2. Content and Form of Proposal/Application Submission 23

II.D.3. Unique Entity Identifier (UEI) and System for Award Management 45

II.D.4. Submission Dates and Times 45

II.D.5. Intergovernmental Review 46

II.D.6. Funding Restrictions 46

II.D.7. Other Submission Requirements 46

II.E. Proposal/Application Review and Selection Information 46

II.E.1. Criteria for Research Proposals/Applications Without a Clinical Trial 46

II.E.2. Proposal/Application Selection Process 50

II.E.3. Integrity and Performance Information 50

II.E.4. Notification of Proposal/Application Review Results 51

II.F. Federal Award Administration Information 51

II.F.1. Federal Award Notices 51

II.F.2. Administrative and National Policy Requirements 52

II.F.3. Reporting Requirements 52

II.G. Federal Awarding Agency Contacts 53
II.G.1. eBRAP Help Desk 53
II.G.2. Grants.gov Contact Center 53
II.H. Other Information....54
II.H.1. Contractor/Recipient Qualification 54
II.H.2. Proprietary Information 54
II.H.3. Administrative Actions....54
II.I. Checklist for Research Proposal/Application Submission Without a Clinical Trial....57
APPENDIX I: RESEARCH AREAS OF INTEREST 59
I. Military Infectious Diseases Research Program 59
II. Combat Casualty Care Research Program 60
III. Military Operational Medicine Research Program....63
IV. Medical Biological Defense Research Program....66
V. Medical Chemical Defense Research Program 68
APPENDIX II: CLINICAL TRIALS 71
I. Important Aspects of Clinical Trials 71
II. Full Proposal/Application Submission Components for Studies With a Clinical Trial....73
III. Review Criteria for Research Proposals/Applications With a Clinical Trial 91
IV. Checklist for Research Proposal/Application Submission With a Clinical Trial....96
APPENDIX III: DOD AND VA WEBSITES....98
APPENDIX IV: PROCEDURES FOR ACQUISITION, PROCESSING, STORAGE, AND SHIPMENT OF BIO-FLUIDS 100
APPENDIX V: NATIONAL INSTITUTE OF MENTAL HEALTH DATA ARCHIVE — INFORMED CONSENT 101
APPENDIX VI: TECHNOLOGY READINESS LEVELS AND KNOWLEDGE READINESS LEVELS....102
APPENDIX VII: ACRONYMS AND ABBREVIATIONS....103

I.A. New for Fiscal Year 2023 – Fiscal Year 2027

The Fiscal Year 2023 – Fiscal Year 2027 (FY23 – FY27) U.S. Army Medical Research and Development Command's (USAMRDC) Broad Agency Announcement (BAA) for Extramural Medical Research contains several changes from previous USAMRDC BAAs. Read each section carefully. Note the following:

- The open period of the BAA is 5 years and will be amended annually with any updates.
- The "Research Areas of Interest" can be found in Appendix I.
- The type of instrument used to reflect the business relationship between the organization and the government is at the discretion of the government, in accordance with the Federal Grant and Cooperative Agreement Act of 1977, as amended, United States Code, Title 31, Sections 6301-6308 (31 USC 6301-6308), which provides the legal criteria to select a procurement contract or an assistance agreement. The award type, along with the start date, will be determined during the negotiation process.
- For assistance agreements:
    - The total period of performance may be proposed for up to a maximum of 4 years in length; additional periods may be considered.
    - Any assistance agreement (grant or cooperative agreement) awarded under this BAA will be governed by the award terms and conditions that conform to the Department of Defense's (DOD) implementation of Office of Management and Budget guidance in Code of Federal Regulations, Title 2, Part 200 (2 CFR 200), "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards." DOD implementation is located in Chapter XI of 2 CFR.
- For contract awards:
    - The total period of performance may be proposed for up to 5 years in length.
    - Any contract awarded under this BAA will be governed by the various provisions of the Federal Acquisition Regulation (FAR) and the Defense Federal Acquisition Regulation Supplement (DFARS).
- For other transactions:
    - Regarding Other Transaction Agreements (OTAs) that utilize the authority within 10 USC 4021 and 4022, the period of performance will be dependent upon each specific award made.

II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

The USAMRDC's mission is to provide solutions to medical problems of importance to the American Service Member at home and abroad, as well as to the general public at large. The scope of this effort and the priorities attached to specific projects are influenced by changes in military and civilian medical science and technology (S&T), operational requirements, military threat assessments, and national defense strategies. Extramural research and development programs play a vital role in the fulfillment of the objectives established by the USAMRDC. General information on the USAMRDC can be obtained at https://mrdc.health.mil/.

This BAA is intended to solicit extramural research and development ideas using the authority provided by 10 USC 4001. The BAA is issued under the provisions of the Competition in Contracting Act of 1984 (Public Law 98-369), as implemented in FAR 6.102(d)(2) and 35.016 and in Department of Defense Grant and Agreement Regulations (DoDGARs) 22.315. In accordance with FAR 35.016, projects funded under this BAA must be for basic and applied research to support scientific study and experimentation directed toward advancing the state-of-the-art or increasing knowledge or understanding rather than focusing on development of a specific system or hardware solution. Research and development funded through this BAA are intended and expected to benefit and inform both military and civilian medical practice and knowledge. This BAA utilizes competitive procedures in accordance with 10 USC 2302(2)(B) for the selection for award of S&T proposals/applications. For the purposes of this BAA, S&T includes activities involving basic research, applied research, advanced technology development, and, under certain conditions, may include activities involving advanced component development and prototypes.

The selection process is highly competitive, and the quantity of meaningful submissions (both pre-proposals/pre-applications and full proposals/applications) received typically exceeds the number of awards that available funding can support.

This BAA provides a general description of USAMRDC's research and development programs, including Research Areas of Interest, evaluation and selection criteria, pre-proposal/ pre-application and full proposal/application preparation instructions, and general administrative information. Specific submission information and additional administrative requirements can be found in the document titled, "General Submission Instructions," which is available on Grants.gov along with this BAA.

Proposal/application submission by extramural organizations through Grants.gov requires use of the Workspace interface, which separates the proposal/application package into individual forms. Applicants must create a Workspace in Grants.gov, complete the required forms, and submit their proposal/application Workspace package.

The management agent for this BAA is the Congressionally Directed Medical Research Programs (CDMRP). The CDMRP manages the electronic Biomedical Research Application Portal (eBRAP) system, pre-proposal/pre-application and full proposal/application receipt and review, and other key process oversight. Refer to Section II.G, Federal Awarding Agency Contacts, for additional information.

The USAMRDC's supporting acquisition office, the U.S. Army Medical Research Acquisition Activity (USAMRAA), will be the awarding and administering office for proposals/applications selected for funding, unless approval is obtained from the USAMRAA Senior Contracting Official to allow another federal acquisition office to execute and administer an award.

II.A. Program Descriptions

II.A.1. Military Infectious Diseases Research Program

Infectious diseases (IDs) pose a significant threat to the operational effectiveness of current and future U.S. Forces. Current and future forces must be prepared to deploy globally and (potentially) on short notice. The U.S. Armed Forces may be called on to operate in areas of the world where infectious diseases present substantial and immediate health risks to DOD personnel. Current national military strategy specifies a worldwide force protection capability that requires surveillance, prevention, diagnosis, and treatment to protect the U.S. Armed Forces against potential infectious disease threats. Future operational scenarios pose increased impact of IDs as natural environmental disease barriers become degraded, enabling rapid spread of diseases across dense urban environments and the population existing within. For example, highly communicable bacterial and viral diseases, multi-drug resistant organisms, and vector-borne diseases will pose significant challenges in dense urban environments during Multi-Domain Operations (MDO).

The mission of the Military Infectious Diseases Research Program (MIDRP) is to plan, coordinate, and oversee the DOD requirements-driven medical solutions that PREVENT, PREDICT, and TREAT infectious diseases threats to the total force maximizing Warfighter readiness and performance.

The vision of the MIDRP is to defeat infection:

- Prevent naturally occurring infectious disease threats to eliminate their impacts on operational readiness of DOD personnel.
    - Prevention is the most desirable infectious disease countermeasure because it prevents disease from occurring (vs. treatment post-infection), is the most cost-effective approach, and reduces unit loss rate.
- Treat naturally occurring infectious disease threats to eliminate their impacts on operational readiness of DOD personnel.
    - Diagnosis centers on prediction of infection to identify the infectious disease BEFORE it is a problem and is integral to appropriate treatment, especially in settings of austere medical capabilities or during near-peer conflict with overwhelming numbers of casualties. Improved diagnosis and treatment of infectious disease casualties is necessary to protect the U.S. Armed Forces. Due to the ever-increasing resistance to presently available treatments, continued countermeasure development needs to be pursued.

Research Areas of Interest to the MIDRP are found in Appendix I.I. ***Applicants are urged to read and consider these before preparing their proposals/applications.***

II.A.2. Combat Casualty Care Research Program

The Combat Casualty Care Research Program (CCCRP) provides integrated capabilities for current and future operations to reduce the mortality and morbidity associated with major combat-related trauma across the spectrum of combat casualty care, including point-of-injury and pre- or out-of-hospital care, the spectrum of en route care, and facilities-based treatment. A primary emphasis of the CCCRP is to identify and develop medical techniques, knowledge products, and materiel[1] (medical devices, drugs, and biologics) for early intervention in life-threatening battle injuries and prolonged care.[2] Because battlefield conditions impose severe constraints on available manpower, equipment, and medical supplies available for casualty care, the CCCRP places an emphasis on medical interventions that can be used within the battle area or as close to it as possible before or during medical evacuation. Preferred medical techniques and materiel that can be used by combat medics must be easily transportable (i.e., small, lightweight, and durable in extreme environments and handling). Devices must be easy to use and require low maintenance, with self-contained power sources as necessary. The CCCRP is interested in existing technologies for which concept and/or patient care efficacy have already been demonstrated, but require improvement to meet military requirements. Development and validation of in vitro and in vivo assessment models that represent military-relevant conditions in wounded Service Members, as well as those that incorporate a systems biology approach, are of interest to the CCCRP when they can be used to identify and describe the safety and efficacy of novel technologies in patients in a predictable manner.

Research efforts are needed in principles, therapies, and technologies to enhance self- and buddy aid, also referred to as tactical care; techniques, methods, or materiel to improve basic and advanced life support for all injured persons; monitoring, sustainment, and management of all injured casualties during episodes of delayed care or prolonged care; and enhanced capability for triage of large numbers of casualties and staged treatment in the field. The principal causes of death among Service Members who die within the first hour of wounding are hemorrhage and traumatic brain injury (TBI). TBI can also occur as a result of blast injuries sustained during training.

The CCCRP supports additional aspects of casualty care. These include drugs, devices, and/or novel surgical techniques to decontaminate, debride, protect, monitor, repair, and/or stabilize complex bone and soft tissue wounds to mitigate secondary tissue damage; improvements to blood products and blood product delivery; novel solutions for non-compressible hemorrhage; treatments for moderate, severe and penetrating TBI; treatments and best practices for management of severe burn injury, to include burn shock and dysregulated metabolism following burn, and care of specialized tissues; acute and chronic pain; regenerative medicine; and, advanced resuscitative care, organ support and critical care solutions. The CCCRP is also interested in the development of sensors; diagnostic and prognostic algorithms; data gathering or capture modalities; processors and autonomous care solutions to improve our capability for

[1] Materiel is defined as equipment and supplies of a military force.

[2] Prolonged care is defined as field medical care, applied beyond "doctrinal planning timelines" by a North Atlantic Treaty Organization (NATO) Special Operations Combat Medic or higher in order to decrease patient mortality and morbidity. It utilizes limited resources and is sustained until the patient arrives at an appropriate level of care. Rasmussen TE, Baer DG, Cap AP, et al. 2015. Ahead of the Curve. *J Trauma Acute Care Surg* 79:S61-64.

remote triage, monitoring, and management of casualties; and products to maintain casualties during prolonged evacuation. Regenerative medicine solutions with potential for early in-theater use will also be considered.

The CCCRP also focuses on the innovations required to reset our wounded Service Members, both in terms of duty performance and quality of life. Innovations developed from CRMRP-supported research efforts are expected to improve restorative treatments and rehabilitative care to maximize function for return to duty (RTD) or civilian life. Medical technologies (drugs, biologics, and devices) and treatment/rehabilitation strategies (methods, guidelines, standards, and information) that will significantly improve the medical care that our wounded Service Members receive within the DOD healthcare system are of particular interest. Implementation of these technologies and strategies should improve the rate of RTD of Service Members, the time to RTD, clinical outcome measures, and quality of life, as well as reduce the hospital stay lengths, clinical workload (patient encounters, treatments, etc.) of caregivers, and initial and long-term costs associated with restorative and rehabilitative or acute care.

The CCCRP supports the conduct of military-relevant clinical research aimed at translating knowledge or materiel from basic and preclinical trauma research into clinical practice. This includes, but is not limited to, single- and multi-center clinical trials performed in the civilian setting to clarify the safety, efficacy, and optimal use of products stemming from the previously mentioned research areas. Comparative effective clinical studies may be encouraged in areas of trauma care where a number of potential known approaches exist and require further investigation to inform selection of the most promising technologies. Novel manufacturing technologies necessary to translate innovative therapies or devices into clinical development are a focus.

The CCCRP supports the conduct of military-relevant, large-data research projects, including the use of large databases of common elements from trauma research projects (preclinical, translational, and clinical). Such studies should directly contribute to or effectively enable the data-driven conduct of combat casualty care. Examples include, but are not limited to, post-hoc analysis of data from completed trauma research projects, meta-analyses of a number of otherwise separate but completed studies, and the ability to harmonize data from planned or ongoing but otherwise separate research studies. All projects should adhere to a core set of reporting standards for rigorous study design.

The CCCRP also supports research related to sustainment of critical expeditionary medical skills. Innovations related to optimized learning, memory permanence, training effectiveness, and sustainment of perishable expeditionary medical skills supplying a comprehensive medical simulation training inventory. Importantly, this program also addresses psychosocial and physiological effects posed by virtual and augmented environments. This ensures the implementation and execution of immersive training events and promotes effective teaching while negotiating scientifically determined safety considerations. Goals include creating standardized training protocols and procedures that promote the effective transfer of knowledge and fosters development of critical medical abilities, while mitigating untoward effects (e.g., cybersickness) produced by modern digital teaching tools, timing, and technologies.

Research related to injuries caused by novel and emerging weapons systems or unique combat environments is also considered. CCCRP supports research in combined injury that focuses on the care of casualties that have sustained both polytrauma and or burn injuries in addition to injuries related to a chemical, biological, radiological, or nuclear scenario. Work is also considered related to medical countermeasures for acute ionizing radiation injury in the areas of post-exposure mitigation and pre-exposure prophylaxis.

The Research Areas of Interest to the CCCRP are found in Appendix I.II. ***Applicants are urged to read and consider these before preparing their proposals/applications.***

II.A.3. Military Operational Medicine Research Program

The mission of the Military Operational Medicine Research Program (MOMRP) is to protect, optimize, sustain, and enhance the readiness and performance of Service Members and their families by developing effective biomedical countermeasures against operational stressors, as well as to prevent and mitigate physical and psychological injuries and threats during training and operations. The MOMRP supports Army Biomedical Performance Enhancement, Human Dimension, MDO, Soldier Lethality, Dense Urban Environment/Subterranean Operations, Army Modernization Priorities, with emphasis on Soldier Lethality and informing Future Vertical Lift Platform Development, Health Services Support, Protection and Survivability, and the DOD Total Force Fitness concepts.

The MOMRP supports research focused on addressing and delivering actionable solutions across the military lifecycle for critical biomedical problems facing the military today and in the future. Service- and platform-specific issues are addressed through close coordination with all Services to prevent unnecessary duplication of effort.

The MOMRP is divided into four Research Areas of Interest (with examples of types of research efforts shown in parentheses): (1) *Environmental Health and Protection* (detecting, monitoring, countermeasure development and performance optimization while operating in extreme environmental [heat/cold/altitude/underwater] and during contaminant/toxicological exposures); (2) *Injury Prevention and Treatment* (validated military performance and readiness assessment tools and metrics, physiological mechanisms, diagnostic capabilities, and optimal treatment of neuromusculoskeletal injury, neuromusculoskeletal injury return-to-duty standards and strategies, neurosensory related injury, and countermeasures against aviation stressors; primary [blast overpressure], secondary [penetrating ballistic fragments or debris], tertiary [accelerative injury], quaternary [burns or exposure to toxic substances], and quinary [illnesses, injuries, or diseases caused by chemical, biological, or radioactive substances] blast injury mechanisms [auditory and non-auditory], blunt trauma, and accelerative injury prevention strategies; and understanding the bioeffects and mitigation of emerging directed energy threats); (3) *Physiological Health and Performance* (biomedical performance enhancement, performance and recovery nutrition, weight balance optimization, cognitive health and performance sustainment in the face of operational challenges, restorative sleep and fatigue management, resilience to operational and environmental stressors, and the medical aspects of manned-unmanned teaming); and (4) *Psychological Health and Resilience* (Post-Traumatic Stress Disorder [PTSD], adjustment disorders and other clinical disorders; combat operational stress

reactions (COSR), suicide prevention and risk reduction, resilience, alcohol and substance misuse prevention, and violence prevention within the military).

More information on these Research Areas of Interest can be found in Appendix I.III. ***Applicants are urged to read and consider these before preparing their proposals/applications.***

The MOMRP is particularly interested in proposals/applications and products that incorporate integrated biomedical approaches (e.g., systems biology). Proposals/applications are encouraged to leverage existing resources and infrastructure to support lifecycle logistics and sustainability as well as consider integrated biomedical approaches (e.g. systems biology).

Guidance for research studies targeting military families and children: (1) In accordance with Department of Defense Instruction (DoDI) 1402.5 and Army Directive 2014-23, Child Care National Agency Check and Inquiries, background investigations are required for all individuals who have regular contact with military dependents under 18 years of age. All individuals who regularly interact with children under 18 years of age in Army-sponsored and -sanctioned programs are required to undergo specific initial background checks and periodic re-verifications. Investigators who propose work involving contact with military dependents under 18 years of age should plan for the additional time and funds required for such investigations. (2) Per Department of Defense Education Activity (DoDEA) Administrative Instruction 2071.3, DoDEA approval is required for research studies involving DoDEA school personnel, school facilities, students, sponsors, and/or data. Investigators proposing to conduct any research activities involving DoDEA schools should plan for the additional time (~3-6 months) and effort required to obtain approval from DoDEA to conduct such activities. Procedures and requirements for the review and approval of a research study request can be found at https://www.dodea.edu/datacenter/research/requests.cfm. (3) Per Army Regulation AR 608-18, "The Family Advocacy Program," the Family Advocacy Research Subcommittee will review, coordinate, and recommend approval and dissemination of all family advocacy research, evaluation projects, and research publications within the Department of the Army.

II.A.4. Medical Biological Defense Research Program

The Defense Threat Reduction Agency (DTRA) Joint Science and Technology Office for Chemical and Biological Defense (JSTO-CBD) manages research directed toward medical biological defense. The DTRA JSTO-CBD has limited funding for proposals/applications submitted through the USAMRDC BAA. DTRA also seeks proposals/applications for its requirements through SAM.gov Contract Opportunities and the DOD Small Business Innovation Research (SBIR) Program solicitations. For information regarding DTRA business opportunities, visit the website at https://www.dtra.mil/Work-With-Us/Contracts/DTRA-Business-Opportunities/.

The Medical Biological Defense Research Program (MBDRP) provides medical countermeasures for biological warfare agents. These countermeasures include specialized medical materiel or procedures designed to enhance protection. The priorities of the program are (1) prophylaxis or pretreatment to prevent any casualty; (2) identification and diagnosis of biological agents; and (3) treatment or supportive care regimens. The MBDRP is interested in applications and products incorporating a systems biology approach.

Examples of some of the infectious agents of interest are those causing anthrax, plague, and glanders; the Ebola, Marburg, Venezuelan, Western and Eastern equine encephalitis viruses; and poxvirus models of variola virus. Examples of toxins of interest include those from plants (Ricin) and bacteria (Staphylococcal enterotoxins, botulinum).

The Research Areas of Interest to the MBDRP are found in Appendix I.IV. ***Applicants are urged to read and consider these before preparing their proposals/applications.***

II.A.5. Medical Chemical Defense Research Program

The DTRA JSTO-CBD manages research directed toward medical chemical defense. The DTRA JSTO-CBD has limited funding for proposals/applications submitted through the USAMRDC BAA. DTRA also seeks proposals/applications for its requirements through SAM.gov Contract Opportunities and DOD SBIR program solicitations. For information on DTRA business opportunities, visit its website at https://www.dtra.mil/Work-With-Us/Contracts/DTRA-Business-Opportunities.

The Medical Chemical Defense Research Program (MCDRP) seeks to preserve combat effectiveness through timely provision of medical countermeasures in response to Joint Service Chemical Warfare Defense Requirements. The fundamental orientation of the program is to protect U.S. Armed Forces from the effects of chemical warfare agents by developing protective, pretreatment, and prophylactic products, providing products usable by the individual Service Member for immediate treatment of chemical warfare agent exposures, developing antidotes/ therapeutics to chemical warfare agents, defining care procedures for chemical warfare agent casualties, and advancing management of these casualties. The medical countermeasures are intended to preserve and sustain the Service Members' combat effectiveness in the face of combined threats from chemical and conventional munitions on the integrated battlefield. For combined chemical and conventional injuries that focus on the care of the casualties' conventional injuries in a chemical or biological environment, please refer to CCCRP (Section II.A.2 and Appendix I.II). The MCDRP is interested in applications and products incorporating a systems biology approach.

The broad goals of this program are described below.

- ***Maintain the technological capability to meet present requirements and counter future chemical warfare agent threats:*** The program will maintain the scientific base and technological capability to develop timely medical countermeasures for both current and future chemical warfare agent threats. Research funded by this program will be used to identify concepts and candidate medical countermeasures for use by the individual Service Member or by medical personnel. Basic and applied research are both supported and may address topics as diverse as determining sites/mechanisms of action and effects of exposure to chemical warfare agents with emphasis on exploitation of neuroscience technology and respiratory, ocular, and dermal pathophysiology; identifying sites and biochemical mechanisms of action of medical countermeasures; exploiting molecular biological and biotechnological approaches for development of new approaches for medical countermeasures to chemical warfare agents; and exploiting molecular modeling and quantitative structure-activity relationships in support of drug discovery and design.

- ***Provide medical countermeasures for the individual Service Member to maintain combat effectiveness and prevent or reduce injury from chemical warfare agents:*** This goal encompasses research supporting development of new concepts for prophylaxes, pretreatments, antidotes, and therapeutic countermeasures; development of skin protectants and decontaminants; identification of factors that influence safety and efficacy of candidate medical countermeasures; and development and maintenance of preformulation, formulation, and radiolabeling capabilities.

- ***Provide medical management of chemical casualties to enhance survival and expedite the RTD of chemical warfare agent casualties through definitive therapies and life support technologies:*** This goal includes developing concepts and therapeutic regimens and procedures for the management of chemical warfare agent casualties; developing diagnostic and prognostic indicators for chemical warfare agent casualties; developing life-support equipment for definitive care of chemical warfare agent casualties; and addressing the unique challenges of combined injuries due to both physical trauma from kinetic weapons and exposure to chemical agents. When the focus of the research is on the care of the casualties' conventional injuries in a chemical or biological environment, please see the CCCRP (Section II.A.2 and Appendix I.II).

Recent changes in the security situation facing the United States have not materially reduced the threat that chemical weapons present to the U.S. Armed Forces in the field. Many countries and terrorist groups have the capability of producing and delivering chemical warfare agents, thus posing a substantial and serious threat to the U.S. Armed Forces.

Classical chemical agent threat categories include vesicant or blister agents (e.g., sulfur mustard), blood agents (e.g., cyanide), respiratory agents (e.g., phosgene), and nerve agents (e.g., GA, or Tabun; GB, or Sarin; GD, or Soman; and VX).

The Research Areas of Interest to the MCDRP are found in Appendix I.V. ***Applicants are urged to read and consider these before preparing their proposals/applications.***

II.B. Award Information

This BAA may be used to support applied research, preclinical research, clinical research, and clinical trials/testing (or equivalent). BAA proposals/applications that include a clinical trial have additional proposal/application and review requirements (see Appendix II). ***The proposed research must be relevant to active-duty Service Members, Veterans, military beneficiaries, and/or the American public.***

Clinical research is defined as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research. ***Note:*** Studies that meet the requirements for Institutional Review Board (IRB) Exemption 4 are not considered

clinical research. IRB Exemption 4 refers to research involving the collection or study of existing de-identified specimens or data, if these sources are publicly available.

A clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. Funded trials are required to post a copy of the IRB-approved informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. ***Note:*** Food and Drug Administration (FDA)-regulated clinical investigation is always a clinical trial, but not all clinical trials are FDA clinical investigations.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DOD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRDC Office of Human and Animal Research Oversight (OHARO), Office of Human Research Oversight (OHRO), prior to research implementation. This administrative review requirement is in addition to the local IRB or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is ***not*** required. Allow up to 3 months to complete the OHRO regulatory review and approval processes following submission of ***all required and complete*** documents to the OHRO. Refer to the General Submission Instructions, Appendix 1, and the Human Research Protections Office Resources and Overview document available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

If the proposed research involves more than one institution, plans for the multi-institutional structure governing the research protocol(s) should be outlined. In addition, a written plan for single IRB review arrangements must be provided for research conducted in the United States involving more than one institution. The lead institution responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements. Communication and data transfer between or among the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the application. A separate intellectual and material property plan agreed on by all participating institutions is also required for multi-institutional clinical research/trials.

Research Involving Animals: All research funded by the BAA involving new and ongoing research with animals must be reviewed and approved by the USAMRDC OHARO Animal Care and Use Review Office (ACURO), in addition to the local Institutional Animal Care and Use Committee (IACUC) of record. IACUC approval at the time of submission is ***not*** required. ***Allow at least 3 to 4 months for ACURO regulatory review and approval processes for animal studies.*** Refer to the General Application Instructions, Appendix 1, for additional information.

Rigor of Experimental Design: All projects should adhere to accepted standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. Core standards are described in S.C. Landis et al., "A call for transparent reporting to optimize the predictive value of preclinical research," *Nature* 2012, 490:187-191

(https://www.nature.com/articles/nature11556). 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. Applicants should consult the Animal Research: Reporting *In Vivo* Experiments (ARRIVE) guidelines 2.0 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.

II.B.1. Clinical Trial Support

Investigator(s) proposing a clinical trial should refer to Appendix II for a detailed description of the requirements for such a proposal/application. The pre-proposal/pre-application submission process should be performed as described in Section II.D.2.a. Full proposal/application submission is described in Appendix II. Refer to Appendix II, Section IV, Checklist for Research Proposal/Application Submission With a Clinical Trial, in preparing the full proposal/application.

For projects proposing a clinical trial:

- ***If an Investigational New Drug (IND) or Investigational Device Exemption (IDE) is required for the study, the IND/IDE application must be submitted to the FDA by the proposal/application submission. It is the responsibility of the applicant to provide evidence from the IRB of record or the FDA if an IND/IDE is not required.*** Refer to Attachment 12, Regulatory Strategy (Appendix II), for further details.

- If the clinical trial of an investigational product will be conducted at international sites, evidence that an application has been submitted to the relevant national regulatory agency of the host country(ies) is required by the above deadlines.

- Clinical trials must be initiated no later than 12 months after the award date.
  Note: The government reserves the right to withhold or withdraw funding if an IND or IDE is necessary to conduct the study but has not been obtained within 6 months of the award date.

II.B.2. Use of Military and Department of Veterans Affairs Populations or Resources

Principal Investigators (PIs) are encouraged to integrate and/or align their research projects with DOD and/or Department of Veterans Affairs (VA) research laboratories and programs and existing clinical trial networks. Collaboration with the DOD or VA is also encouraged. A list of websites that may be useful in identifying additional information about ongoing DOD and VA areas of research interest or potential opportunities for collaboration can be found in Appendix III.

Use of DOD or VA Resources: If the proposed research involves access to active-duty military or Veteran patient populations and/or DOD or VA resources or databases, the proposal/application must describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research. Use Attachment 2: Supporting Documentation, to provide relevant documentation to demonstrate access to DOD or VA

populations or resources. Refer to the General Submission Instructions, Appendix 1, for additional information.

45 CFR Section 46.114 (Cooperative Research) of the Common Rule requires any institution located in the United States that is engaged in cooperative research to rely upon approval by a single IRB for that portion of the research that is conducted in the United States. For multi-site studies with collaborating VA institutions engaged in non-exempt human subjects research, and for which the use of a single IRB is determined to be not appropriate for the particular research context, a memorandum from the VA Office of Research and Development approving exception of the single IRB requirement must be sought and provided to the OHARO OHRO during the human research protection official review of the project.

Access to certain DOD or VA patient populations, resources, or databases may only be obtained by collaboration with a DOD or VA investigator who has a substantial role in the research and may not be available to a non-DOD or non-VA investigator if the resource is restricted to DOD or VA personnel. Investigators should be aware of which resources are available to them if the proposed research involves a non-DOD or non-VA investigator collaborating with the DOD and/or VA. ***If the proposal/application is recommended for funding, the government reserves the right to withdraw or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resource(s).***

Conducting DOD-Funded Human Research with Military Populations: There are unique requirements and prohibitions for compensating DOD-affiliated personnel for study participation and for conducting research with military families/children and U.S. Army Special Operations Command populations. Additional information regarding conducting DOD-funded human research with military populations can be found at https://mrdc.health.mil/assets/docs/orp/conducting_research_military_Pop_dod_may_2021.pdf.

Guidance for Research Studies Involving U.S. Army Special Operations Command (USASOC): Per USASOC policy 24-18, studies involving USASOC Soldiers as human subjects require additional review by the USASOC Research Advisory Committee (RAC) and Human Subjects Research Board (HSRB).

II.B.3. Technology Requirements and Standards

Any technology-based research products/prototypes (such as devices, mobile apps, software, information technology (IT) infrastructure, etc.) that expect to interact with military health IT systems should conform with accepted industry and DOD Information Management/IT standards for interoperability, cybersecurity, as well as the DOD Architecture Framework (DoDAF) and viewpoints, as follows:

a. DoDAF and viewpoints

b. DoDI 8500.01 March, 14, 2014, “Cybersecurity”

c. DoDI 8510.01 March 12, 2015, “Risk Management Framework (RMF)”

d. Any products expected to provide data to Military Health System (MHS) Genesis, the new DOD Military Electronic Health Record system (which is the military version of Cerner Millennium commercial-off-the-shelf electronic health record), should be aimed toward meeting the Health Level 7 and Fast Healthcare Interoperability Resources standards in order to ultimately provide integration with MHS Genesis.

e. All software-based research products including computer code, software code, data, and metadata should be provided as deliverables, and electronic versions need to be able to be uploaded to standards-based electronic repositories. Metadata (i.e., the data dictionary and data model) as well as data (i.e., cases) generated in the research should be provided in an industry standard format for access by the government in an open source data repository of electronic deliverables.

f. Any information systems that are owned or operated by the contractor that processes, stores, or transmits Federal contraction information, not intended for public release, is subject to the basic safeguarding requirements detailed under FAR 52.204-21, Basic Safeguarding of Covered information Systems

g. OTAs may establish non-standard requirements.

II.B.4. Data Sharing

The USAMRDC intends that information, data, and research resources generated under awards funded by this BAA be made available to the research community and to the public at large. The government reserves the right to identify repositories for submission of data for archive. For additional guidance, refer to the General Submission Instructions, Appendix 2, Section K.

A number of research areas utilize Common Data Elements (CDEs) to facilitate the sharing of data to promote collaboration, accelerate research, and advance knowledge in specific topic areas. In accordance with the White House Office of Science and Technology Policy memorandum, "Increasing Access to the Results of Federally Funded Research," and Executive Order (EO) 13625 and the National Research Action Plan (NRAP) responding to the EO, "Improving Access to Mental Health Services for Veterans, Service Members, and Families" (August 31, 2012), federally funded research is required to be conducted in a manner that promotes public access to scientific data. In cases of psychological health and TBI, use of CDEs is required under the NRAP. The USAMRDC strongly encourages applicants to incorporate CDE measures appropriate to each field of study, such as:

- PhenX Core and Specialty collections, which are available in the Mental Health Research, Substance Abuse and Addiction, and Research Domains Collections of the PhenX Toolkit (https://www.phenxtoolkit.org/index.php) in all studies involving human subjects, as applicable.

- Spinal cord injury research CDEs developed through the collaboration of the International Spinal Cord Society, the American Spinal Injury Association, and the National Institute of Neurological Disorders and Stroke CDE team, as referenced at Spinal Cord Injury | NINDS Common Data Elements (nih.gov).

TBI research data elements must be reported using the National Institute of Neurological Disorders and Stroke (NINDS) TBI CDEs or entered into the Federal Interagency Traumatic Brain Injury Research (FITBIR) data dictionary as new, unique data elements (UDEs). For the most current version of the NINDS TBI CDEs, go to http://www.commondataelements.ninds.nih.gov. Assistance will be available to help the researchers map their study variables to specific CDEs and ensure the formats of the CDEs collected are compatible with the FITBIR Informatics System. Use of the TBI CDEs is required wherever possible in an effort to create standardized definitions and guidelines about the kinds of data to collect and the data collection methods that should be used in clinical studies of TBI. ***Use of UDEs is strongly discouraged and subject to program approval.***

If the project includes the collection of bio-fluids, such as blood, saliva, urine, etc., the PI may be required to include a set of collection variables and patient phenotypic data in order to standardize the quality of bio-fluid studies. The suggested procedures for acquisition, processing, storage, and shipment of bio-fluids can be found in Appendix IV.

For projects involving TBI, PIs may be required to report data to the FITBIR informatics system (https://fitbir.nih.gov/).

For studies that will enroll subjects with psychological health disorders, awardees may be requested to submit data to the National Institute of Mental Health Data Archive (NDA) https://nda.nih.gov/. The NDA is a data repository run by the National Institute of Mental Health (NIMH) that allows researchers studying mental illness to collect and share de-identified information with each other. Such studies may require the inclusion of specific language in the informed consent form which references the NDA (see Appendix V).

OTAs may establish unique data sharing requirements.

II.B.5. Funds Available and Anticipated Number of Awards

The funding amount for this BAA is unspecified, and the number of awards is indeterminate and contingent upon funding availability. Selection of research projects is a highly competitive process and is based on the evaluation of the proposal/application's technical merit, programmatic considerations, and the availability of funds. The quantity of meaningful submissions received normally exceeds the number of awards that the available funding can support. Any funding that is received by the USAMRDC and is appropriate for a research area described within this BAA may be utilized to fund proposals/applications.

II.B.6. Award Amounts and Periods of Performance

There are no specified funding limitations identified for a proposal/application submitted under this BAA. A budget should be commensurate with the nature and complexity of the proposed research. Researchers should submit budgets that include the entire period of performance of the research project. Budgets should include all direct and indirect costs, based on supportable, verifiable estimates. The budget for the full proposal/application should not differ significantly from the Pre-Application Budget Summary Form provided in the pre-proposal/pre-application submission.

Period of performance may differ depending upon the type of funding mechanism awarded under this BAA. For an assistance agreement, the total period of performance may be proposed for up to 4 years in length; additional periods may be considered. For research and development contract awards, the total period of performance may be proposed for up to 5 years in length. For OTAs that utilize the authority within 10 USC 4021 and 4022, the period of performance will be dependent upon each specific award made. Because the nature and scope of each proposed research project will vary, it is anticipated that the size and duration of each award will vary. Start dates will vary, depending on when proposals/applications were submitted and reviewed and the negotiation process. However, no proposal/application submitted under this BAA will be considered for funding after 24 months from the date of submission.

Organizations seeking additional or continuation funding must work with their respective PIs to submit new pre-proposals/pre-applications and be invited to submit full proposals/applications.

Refer to the General Submission Instructions, Section III.A.5, for additional information regarding the Research & Related Budget.

II.B.7. Mechanisms of Support

The USAMRDC executes its extramural research program primarily through the awarding of contracts and assistance agreements (grants and cooperative agreements). The type of instrument used to reflect the business relationship between the organization and the government is at the discretion of the government, in accordance with the Federal Grant and Cooperative Agreement Act of 1977, as amended (31 USC 6301-6308), which provides the legal criteria to select a procurement contract or an assistance agreement. Refer to the General Submission Instructions, Appendix 2, Section D, for additional information.

Proposers awarded a Grant, Cooperative Agreement, Technology Investment Agreement (TIA), or Other Transaction for Research or Prototypes based on their response to this BAA shall follow the applicable rules and regulations governing these various award instruments, but, in all cases, should appropriately identify any potential restrictions on the government's use of any Intellectual Property contemplated under the award instrument in question, refer to Attachment 8: Data and Research Resource Sharing Plan. This includes both noncommercial Items and commercial Items.

II.B.7.a. Procurement Contract: A legal instrument that, consistent with 31 USC 6303, reflects a relationship between the federal government and a state government, local government, or other entity/contractor when the principal purpose of the instrument is to acquire (by purchase, lease, or barter) property or services for the direct benefit or use of the federal government.

Contracts are primarily governed by the following regulations:

a. FAR

b. DFARS

II.B.7.b. Grant: A legal instrument that, consistent with 31 USC 6304, is used to enter into a relationship:

a. The principal purpose is to transfer a thing of value to the recipient to carry out a public purpose of support or stimulation authorized by a law or the United States, rather than to acquire property or services for the federal government's direct benefit or use;

b. In which substantial involvement is not expected between the federal government and the recipient when carrying out the activity contemplated by the grant; and

c. No fee or profit is allowed.

II.B.7.c. Cooperative Agreement: A legal instrument that, consistent with 31 USC 6305, is used to enter into the same kind of relationship as a grant (see definition "grant"), except that substantial involvement (collaboration, participation, or intervention in the research) is expected between the federal government and the recipient when carrying out the activity contemplated by the cooperative agreement. The term does not include "cooperative research and development agreements" as defined in 15 USC 3710a. No fee or profit is allowed.

II.B.7.d. Other Transactions for Research: The USAMRDC will also consider the use of Other Transactions for Research as a vehicle for award under this BAA. In accordance with 10 USC 4021, "Research projects: transactions other than contracts and grants," such other transactions shall not be entered into unless the following conditions are satisfied:

1. To the maximum extent practicable, no other transaction entered into shall provide for research that duplicates research being conducted under existing programs carried out by DOD.

2. The funds provided by the government under another transaction authorization shall not exceed, to the extent that the Secretary of Defense determines practicable, the total amount provided by other parties to the other transaction.

II.B.7.e. Other Transactions for Prototypes: The USAMRDC will also consider the use of Other Transactions for Prototypes as a vehicle for award under this BAA. In accordance with 10 USC 4022, Prototype projects; transactions other than contracts and grants: "No official of an agency shall enter into a transaction (other than a contract, grant, or cooperative agreement) for a prototype project under the authority of 10 USC 4022 unless one of the following conditions is met:

(A) There is at least one nontraditional defense contractor or nonprofit research institution participating to a significant extent in the prototype project.

(B) All significant participants in the transaction other than the Federal Government are small businesses (including small businesses participating in a program described in section 9 of the Small Business Act (15 U.S.C. 638)) or nontraditional defense contractors.

(C) At least one-third of the total cost of the prototype project is to be paid out of funds provided by sources other than the federal government.

(D) The senior procurement executive for the agency determines in writing that exceptional circumstances justify the use of a transaction that provides for innovative business arrangements or structures that would not be feasible or appropriate under a contract, or would provide an opportunity to expand the defense supply base in a manner that would not be practical or feasible under a contract."

In accordance with 10 USC 4022(f), any other transaction for prototypes awarded under this BAA may provide for the award of a follow-on production contract or transaction to the participants in the transaction without the use of competitive procedures.

Additional information can be found in the most current version of the Other Transactions Guide for Prototype Projects at https://www.acq.osd.mil/asda/dpc/cp/index.html.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organizations

Awards are made to eligible organizations, not to individuals. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations. Refer to the General Submission Instructions, Appendix 3, Section B, for general eligibility information.

Note: In accordance with FAR 35.017, Federally Funded Research and Development Centers (FFRDCs) are not eligible to directly receive awards under this BAA. However, teaming arrangements between FFRDCs and eligible organizations are allowed so long as they are permitted under the sponsoring agreement between the federal government and the specific FFRDC.

The USAMRDC is committed to supporting small businesses. Small business, Veteran-owned small business, Service-disabled Veteran-owned small business, HUBZone small business, small disadvantaged business, and woman-owned small business concerns will be given the maximum practical opportunity to participate through subawards on research proposals/applications submitted through this BAA.

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

Proposals/applications for this BAA may only be submitted by extramural organizations. Submissions from intramural DOD organizations to this BAA will be withdrawn. These terms are defined below.

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

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

Proposals/applications from intramural investigators may be submitted extramurally through a research foundation. ***It is permissible, however, for an intramural investigator to be named as a collaborator on a proposal/application submitted through an extramural organization. In this case, the proposal/application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.*** For more information, refer to the General Submission Instructions, Section III.

II.C.1.b. Investigator(s)

Eligible investigators include all individuals, regardless of ethnicity, nationality, or citizenship status, who are employed by or affiliated with an eligible organization.

Investigators are cautioned that awards are made to organizations only, not individuals.

II.C.2. Cost Sharing

Generally, there is no requirement for cost sharing, matching, or cost participation to be eligible for award under this BAA. Cost sharing and matching is not an evaluation factor used under this BAA. Exceptions may exist if the applicant is proposing the use of a TIA, Research OTA, or Prototype OTA as an award instrument. Cost-sharing requirements may be found at 32 CFR 37 for TIAs. Cost-sharing requirements for OTAs are stated in 10 USC 4021 for Research OTAs and 10 USC 4022 for Prototype OTAs.

In addition, if cost sharing is proposed on a grant or cooperative agreement proposal/ application submitted by a nonprofit or institution of higher education, the award will be subject to the restrictions at 2 CFR 200.306. If cost sharing is proposed on a contract proposal/application, the award will be subject to the restrictions at FAR 35.003.

II.C.3. Other

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

Use of the System for Award Management (SAM) and the Federal Awardee Performance and Integrity Information System (FAPIIS): To protect the public interest, the federal government ensures the integrity of federal programs by conducting business with qualified recipients only. The USAMRDC utilizes the Exclusions within the Performance Information functional area of SAM to identify individuals and organizations unqualified to receive federal awards. More information about Exclusions reported in SAM is available at https://www.sam.gov/SAM/. The USAMRDC also reviews and considers information about the applicant in the Office of Management and Budget-designated integrity and performance system, currently FAPIIS, prior

to making an award. Refer to the General Submission Instructions, Appendix 3, for additional information.

Conflict of Interest (COI): All awards must be free of COIs that could bias the research results. Prior to award of a contract, grant, or agreement, applicants will be required to disclose all potential or actual COIs along with a plan to manage them. An award may not be made if it is determined by the Contracting, Grants, or Agreements Officer that COIs cannot be adequately managed. Refer to the General Submission Instructions, Appendix 3, for additional information.

Review of Risk: The following areas may be reviewed in evaluating the risk posed by an applicant: financial stability; quality of management systems and operational controls; history of performance; reports and findings from audits; ability to effectively implement statutory, regulatory, or other requirements imposed on non-federal entities; degree of institutional support; integrity; adequacy of facilities; and conformance with safety and environmental statutes and regulations.

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

Subcontracting Plan: If the resultant award is a contract that exceeds $750,000 and the offeror is other than a small business, the contractor will be required to submit a subcontracting plan for small business and small disadvantaged business concerns, in accordance with FAR 19.704. The subcontracting plan will have to comply with the requirements in FAR 19.704. A mutually agreeable plan will be developed during award negotiation process and incorporated as part of the resultant contract. This requirement is not applicable to assistance agreements or OTAs.

Refer to Section II.H.3, Administrative Actions, for a list of administrative actions that may be taken if a pre-proposal/pre-application or proposal/application does not meet the administrative, eligibility, or ethical requirements defined in this BAA.

II.D. Proposal/Application Submission Information

II.D.1. Where to Obtain the Proposal/Application Submission Package

To obtain the complete Grants.gov proposal/application package (hereinafter, submission package), including all required forms, perform a Grants.gov (https://www.grants.gov/) basic search using the Funding Opportunity Number **HT9425-23-S-BAA1**.

eBRAP (https://ebrap.org) is a secure web-based system that allows PIs to submit their pre-proposals/pre-applications, view and verify extramural full proposals/applications submitted to Grants.gov (https://grants.gov), receive communications from the CDMRP, and submit documentation during award negotiations and throughout the period of performance.

Grants.gov is a federal system required to be utilized by agencies to receive and process extramural grant proposals/applications. Full proposals/applications may only be submitted to Grants.gov after submission of a pre-proposal/pre-application through eBRAP.

Contact information for the eBRAP Help Desk and the Grants.gov Contact Center can be found in Section II.G, Federal Awarding Agency Contacts.

Extramural Submission:

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

II.D.2. Content and Form of Proposal/Application Submission

Submission is a two-step process requiring both ***pre-proposal/pre-application*** (eBRAP.org) and ***full proposal/application*** (Grants.gov) as indicated below. Refer to Table 1, Full Application Guidelines for full proposal/application submission guidelines. ***Note:*** Investigator(s) proposing a clinical trial should refer to Appendix II for a detailed description of the requirements for such a proposal/application.

Pre-Proposal/Pre-Application Submission: Submission of a pre-proposal/pre-application is required and must be submitted through eBRAP (https://eBRAP.org/). If the USAMRDC is interested in receiving a full proposal/application, the PI will be sent an invitation via eBRAP to submit.

The proposal/application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent throughout the entire pre-proposal/pre-application and proposal/application submission process. Inconsistencies may delay proposal/application processing and limit or negate the ability to view, modify, and verify the proposal/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 proposal/application deadline.

Pre-proposals/pre-applications may be submitted at any time prior to the BAA closing date. Pre-proposals/pre-applications should describe specific ideas or projects that pertain to any of the areas described under "Program Description" in this BAA. A pre-proposal/pre-application must include a brief description of the scientific methods and design to address the problem as described below. Brochures or other descriptions of general organizational or individual capabilities will not be accepted as a pre-proposal/pre-application. ***DO NOT include any proprietary information in the pre-proposal/pre-application.***

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

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

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

Note: Proposals/applications for this BAA may only be submitted by extramural organizations. Submissions from intramural DOD organizations to this BAA will be withdrawn.

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

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

The applicant organization and associated PI identified in the pre-proposal/pre-application should be the same as those intended for the subsequent proposal/application submission. If any changes are necessary after submission of the pre-proposal/pre-application, the PI must contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507. A change in PI or organization after submission of the pre-proposal/pre-application may be allowed after review of a submitted written appeal (contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507) and at the discretion of the USAMRAA Contracting, Agreements, or Grants Officer.

The pre-proposal/pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Submission Instructions, Section II.B, for additional information on pre-proposal/pre-application submission):

- **Tab 1 – Application Information**

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

- **Tab 2 – Application Contact**

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

  Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 [R&R]), and click on "Add Organizations to this Pre-application." The organization(s) must be either selected from the eBRAP drop-down list or invited in order for the pre-proposal/pre-application to be submitted.

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

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

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

- **Tab 4 – Conflicts of Interest**

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

- **Tab 5 – Required Files**

  Note: No figures, charts, graphs, or other additional material will be accepted during the pre-proposal/pre-application process.

  Provide responses in the appropriate data fields for the following in eBRAP. **EVERY DATA FIELD MUST CONTAIN COMPLETE INFORMATION.** eBRAP will truncate characters exceeding the limit specified for each data field. Enter "none" if there is no information to be included.

  - Problem To Be Studied (4,000 character limit, including spaces).
  - Theoretical Rationale, Scientific Methods, and Design (4,000 character limit, including spaces).
  - Significance and/or Uniqueness of the Proposed Effort (4,000 character limit, including spaces).
  - Military Relevance and Impact (4,000 character limit, including spaces).
  - Brief Description of Research Involving Animals, Human Anatomical Substances and/or Human Subjects (4,000 character limit, including spaces).
  - Plans and Strategy for Translation, Implementation, and/or Commercialization (4,000 character limit, including spaces).

  Upload document(s) as individual PDF file(s). eBRAP will not allow a document to be uploaded in the Required Files tab if the number of pages exceeds the limits specified below.

  - Budget Summary: Upload as "BudgetSummary.pdf". Complete the two-page Pre-application Budget Summary Form (available for download in eBRAP) as instructed.
  - PI and Key Personnel Biographical Sketches (five-page limit per individual): Use boldfaced type or highlight titles of publications relevant to the proposed project. All biographical sketches should be uploaded as a single combined file.

- **Tab 6 – Submit Pre-Application**

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

Pre-Proposal/Pre-Application Screening

USAMRDC scientists and/or contracted, non-governmental subject matter experts will screen pre-proposals/pre-applications for technical merit and programmatic considerations. Based on the screening of the pre-proposal/pre-application, a PI may be invited to submit a full proposal/application.

Notification of Pre-Proposal/Pre-Application Screening Results

Following the pre-proposal/pre-application screening, PIs will be notified as to whether or not they are invited to submit full proposals/applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-proposals/pre-applications. Within 120 calendar days of submission, PIs should receive email notification via eBRAP regarding disposition of their pre-proposals/pre-applications.

II.D.2.b. Step 2: Full Proposal/Application Submission Content

Proposals/applications will not be accepted unless notification of invitation has been received.

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

Each proposal/application submission must include the completed full submission package for this BAA. The full submission package is submitted by the Authorized Organizational Representative through Grants.gov (***https://www.grants.gov/***). See Table 1 below for more specific guidelines.

II.D.2.b.i. Full Proposal/Application Submission Guidelines

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

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

Table 1. Full Proposal/Application Submission Guidelines

Proposal/Application Package Location
Download proposal/application package components for HT9425-23-S-BAA1 from Grants.gov (https://grants.gov) and create a Grants.gov Workspace. Workspace allows online completion of the proposal/application components and routing of the proposal/application package through the applicant organization for review prior to submission.
Full Proposal/Application Package Components
SF424 Research & Related Application for Federal Assistance Form: Refer to the General Submission Instructions, Section III.A.1, for detailed information.
Descriptions of each required file can be found under Full Proposal/Application Submission Components: • Attachments (for submissions **without** clinical trial) • Research & Related Personal Data (for submissions **without** clinical trial) • Research & Related Senior/Key Person Profile (Expanded) (for submissions **without** clinical trial) • Research & Related Budget (for submissions **without** clinical trial) • Project/Performance Site Location(s) Form (for submissions **without** clinical trial) • Research & Related Subaward Budget Attachment(s) Form (for submissions **without** clinical trial) • Attachments (for submissions **with** clinical trial) • Research & Related Personal Data (for submissions **with** clinical trial) • Research & Related Senior/Key Person Profile (Expanded) (for submissions **with** clinical trial) • Research & Related Budget (for submissions **with** clinical trial) • Project/Performance Site Location(s) Form (for submissions **with** clinical trial) • Research & Related Subaward Budget Attachment(s) Form (for submissions **with** clinical trial)

Proposal/Application Package Submission
Create a Grants.gov Workspace. Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission. **Submit a Grants.gov Workspace Package.** A proposal/application may be submitted through Workspace by clicking the "Sign and Submit" button on the "Manage Workspace" page, under the "Forms" tab. Grants.gov recommends submission of the proposal/application package **at least 24-48 hours prior to the BAA closing date** to allow time to correct any potential technical issues that may disrupt the proposal/application submission. ***Note:*** If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated Grants.gov proposal/application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking Identification ***prior to*** the proposal/application submission deadline. ***Do not password protect any files of the application package, including the Project Narrative.*** Proprietary information should only be included if necessary for evaluation of the proposal/ application. Conspicuously and legibly mark any proprietary information that is included in the proposal/application.
Proposal/Application Verification Period
The full proposal/application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the 5-day proposal/application verification period. During the proposal/application verification period, the full proposal/application package may be modified ***with the exception of the Project Narrative and Research & Related Budget Form***.
Further Information
Tracking a Grants.gov Workspace Package. After successfully submitting a Workspace package, a Grants.gov Tracking Number is automatically assigned to the package. The number will be listed on the "Confirmation" page that is generated after submission. Refer to the General Submission Instructions, Section III, for further information regarding Grants.gov requirements.

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

II.D.2.b.ii. Full Proposal/Application Submission Components Without a Clinical Trial

The Grants.gov Workspace submission package includes the following components (refer to the General Submission Instructions, Section III, for additional information on proposal/application submission).

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

Attachments for Proposals/Applications Without a Clinical Trial

Note: Components and attachments for a proposal/application with a clinical trial are provided in Appendix II.

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

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

- **Attachment 1: Project Narrative (15-page limit): Upload as "ProjectNarrative.pdf".** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs (uniform resource locators; web addresses) that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the proposal/application.

  A detailed innovative/state of the art description of the research (relating to the Research Areas of Interest identified in Section II.A and Appendix I) to be undertaken should be submitted. This should include the areas provided below and address their relationship to the state of knowledge in the field and to comparable work in progress elsewhere. Evaluation of the proposed research will be influenced by the adequacy of this information.

  Literature references and curriculum vitae will be shown in separate addenda entries. The following general outline should be followed:

  - Background: Provide a brief statement of ideas and theoretical reasoning behind the proposed study. Describe previous experience most pertinent to this proposal/ application. Cite relevant literature references. Include discussion of any findings (if available) from relevant pilot or preliminary work or any related work underway. For development of devices and technologies, provide an intellectual property plan as part of the supporting documentation.

  - Hypothesis: State the hypothesis to be tested and the expected results. For development of devices and technologies, discuss the technical feasibility of the proposed project including historical background of the problem, previous and current solutions, similar projects previously undertaken, and related development activities.

- Technical Objectives: State concisely the question to be answered by each research objective.

- Project Milestones: Identify timelines for critical events that must be accomplished in order for the project to be successful in terms of cost, schedule, and performance. For development of devices and technologies, discuss the timelines and provide a commercialization strategy/plan for the technology being developed.

- Military Significance: State precisely the estimates as to the immediate and/or long-range usefulness of this study to the U.S. Armed Forces, as distinguished from general advancement of knowledge in medicine.

- Public Purpose: If appropriate, provide a concise, detailed description of how this research project will benefit the general public.

- Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

    - Describe how the proposed research is designed to achieve reproducible and rigorous results, including controls, sample size estimation, randomization, statistical analysis, and data handling.

    - For synthetic chemistry applications, include a clear statement of the rationale for the proposed syntheses. Outline and document the routes to the syntheses.

    - For development of devices and technologies, discuss the engineering/technical design to achieve the project goals demonstrating the feasibility of the proposed product development. Discuss the perceived engineering/design strengths and flaws and recommendations for overcoming/preventing them.

    - For clinical research studies involving human subjects, describe the recruitment plan to include relevant support and justification for sample size, study inclusion criteria, and data collection instruments, as well as access to populations. The proposal/application should describe a plan for data access and sharing. (Access to subjects and data is the sole responsibility of the investigator.) As relevant, describe plans for addressing issues unique to working with military populations.

    - For studies involving human and animal research, provide a statistical and data analysis plan. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Describe the statistical model and data analysis plan with respect to the study objectives as appropriate to the type of study. Specify the approximate number of human subjects that will be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Investigators must develop protocols for research with human subjects and/or human anatomical substances that are specific to the DOD-supported effort outlined in the submitted proposal/application. The research protocol submitted for OHRO review MUST only include those activities funded by the DOD, as referenced in the Statement of Work (SOW). The OHRO will

NOT review protocols submitted for DOD-funded activities if such studies have been added to an ongoing/existing protocol.

- For studies with prospective accrual of human subjects, indicate quarterly enrollment targets. For clinical research studies, further details of clinical research components (including the required strategy for the inclusion of women and minorities appropriate to the objectives of the study) will be required in see Attachment 10: Human Subject Recruitment and Safety Procedures, as applicable.

- For use of human anatomical substances, identify the commercial or organizational source(s) of the material. For cell lines, identify cell line(s) to be used. If human anatomical substances (including cell lines) will be used, specify whether or not identifiable information is accessible to the research team by any means.

- If applicable, indicate time required for submission and/or approval of documents (e.g., IND and IDE) to the FDA or appropriate government regulatory agency.

- For studies involving human subjects, allow at least 2 to 3 months for regulatory review and approval by the USAMRDC OHRO; this does not include the additional time required for local IRB review and approval, as stated above.

- For animal studies, allow at least 2 to 3 months for regulatory review and approval by the USAMRDC Animal Care and Use Review Office; this does not include the additional time required for local Institutional Animal Care and Use Committee review and approval, as stated above.

- Refer to the General Submission Instructions, Appendix 1, for additional regulatory information.

- **Attachment 2: Supporting Documentation: Combine and upload as a single file named "Support.pdf".** Start each document on a new page. If documents are scanned to PDF, the lowest resolution (100 to 150 dpi) should be used. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

  There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested or viewed as an extension of the Project Narrative will result in the removal of those items or may result in administrative withdrawal of the proposal/application.

  - **References Cited:** List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

- **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols.

- **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and existing 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 are now accountable. There is no form for this information.

- **Publications and/or Patent Abstracts:** 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. A letter from each organization involved in the project should be provided. Letters of support not requested in this BAA, such as those from members of Congress, do not impact proposal/application review or funding decisions.

- **Letters of Collaboration (if applicable):** Provide a signed letter from each collaborating individual or organization that demonstrates that the investigator has the support of resources necessary for the proposed work. If an investigator at an intramural organization is named as a collaborator on a proposal/application submitted through an extramural organization, the proposal/application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.

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

- **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 from the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the Associate Chief of Staff for Research and Development (ACOS/R&D) or Clinical Service Chief confirming access to VA patients, resources, and/or VA research space. For VA PIs, if the VA Non-Profit Corporation (NPC) is not identified as the applicant institution for administering the funds, include a letter from the VA ACOS/R&D

confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.

- **Collaboration with Military Facility (if applicable):** *If the project involves collaboration with a Military Facility, special requirements apply.* A DOD researcher, to include collaborating DOD PIs, must obtain a letter from his/her Commanding Officer or Military Facility Director authorizing his/her participation in the research project. This letter must be included with the proposal/application.

- **Joint Sponsorship (if applicable):** Describe present or prospective joint sponsorship of any portion of the program outlined in the proposal/application. In the absence of agreements between/among sponsors for joint support, the proposal/application should be structured so that the research can be carried out without the resources of any other sponsor. If, however, it is desirable to request partial support from another agency, the proposed plan should be stated and the reasons documented. If the plan cannot be formulated at the time the proposal/application is submitted, information should be sent later as an addendum to the proposal/application. Prior approval from both/all agencies must be secured for research to be undertaken under joint sponsorship. Provide letters of support related to recruitment, subject access, and data access plans.

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

  - **Background and Proprietary Information:** All software and data first produced under the award are subject to a federal purpose license. A term of the award requires the recipient to grant the government all necessary and appropriate licenses, which could include licenses to background and proprietary information that have been developed at private expense. Refer to the General Submission Instructions, Appendix 2, Sections C and D, for more information about disclosure of proprietary information.

    Therefore, it is important to disclose/list any intellectual property (software, data, patents, etc.) that will be used in performance of the project or provide a statement that none will be used. If applicable, all proprietary information to be provided to the government should be stated and identified; the applicant should indicate whether a waiver of the federal purpose license will be required.

  - **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 BAA. Demonstrate access to all intellectual property rights necessary for development and commercialization and evidence that the government has the ability to access such products or technologies.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf".** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  The structured technical abstract should be clear and concise and, at a minimum, provide the following information:

  - Background: Provide a brief statement of the ideas and theoretical reasoning behind the proposed work.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
  - Specific Aims: State concisely the specific aims of the study.
  - Study Design: Briefly describe the study design.
  - Relevance: Provide a brief statement explaining the potential relevance of the proposed work to the specific topic area being addressed and its impact on health outcomes.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf".** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Lay abstracts should be written using the outline below. Do not duplicate the technical abstract.

  - Clearly describe the objectives and theoretical reasoning behind the proposed work in a manner readily understood by readers without a background in science or medicine.
  - Clearly describe the problem or question to be addressed and the ultimate applicability and impact of the research.
    - What types of patients will it help and how will it help them? Include the current available statistics to the related injury/condition.
    - What are the potential clinical applications, benefits, and risks?
    - What is the projected timeline it may take to achieve the expected patient-related outcome?
    - Describe how the proposed project will benefit Service Members, Veterans, and/or their family members.

- **Attachment 5: Statement of Work (two-page limit): Upload as "SOW.pdf".** The SOW outlines and establishes the performance expectations and milestones for which the USAMRDC may provide funding. The SOW will be incorporated into the award document and, as such, is subject to release under the Freedom of Information Act. The SOW should identify all collaborating research sites involved in the performance of the research. Suggested SOW formats and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). Recommended strategies for assembling the SOW can be found at https://ebrap.org/eBRAP/public/Program.htm. Refer to either the "***Suggested SOW Strategy Clinical Research***" or "***Suggested SOW Strategy Generic Research***", whichever format is most appropriate for the proposed effort, and use the blank SOW format titled "Suggested SOW Format". The SOW must be in PDF format prior to attaching.

  A series of relatively short statements should be included that comprise the approach to each of the major goals or objectives of the proposed research. The statements should outline the specific tasks, systems, key assessments/techniques, and materials that are reasonable estimates for testing the proposed hypotheses of the study. A timeline should be included that shows the work statements to be accomplished in each year of the award. Any animal use and/or human subjects recruitment should be included. Allow at least 2 to 3 months for the USAMRDC OHARO regulatory review and approval processes for studies involving human subjects and 2 to 3 months for studies involving animal subjects.

- **Attachment 6: Impact/Outcomes Statement (one-page limit): Upload as "Impact.pdf".** Explain the potential impact of the research in the field, the significance of this impact, and when it can be anticipated. Explain how the results of this research are expected to impact the intended beneficiaries. Describe how the anticipated outcomes could be implanted in a dual-use capacity to address the healthcare needs of military Service Members, Veterans, and/or their beneficiaries, as well as the civilian population, as appropriate.

- **Attachment 7: Military Relevance Statement (one-page limit): Upload as "MilRel.pdf".**

  - Describe how the proposed study is responsive to the healthcare needs of military Service Members, Veterans, and/or beneficiaries. Provide information about the incidence and/or prevalence of the disease or condition in the general population as well as in military Service Members, Veterans, and/or beneficiaries.

  - If active-duty military, military families, and/or Veteran population(s) will be used in the proposed research project, describe the population(s) and the appropriateness of the population(s) for the proposed study. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Service Members, Veterans, and/or beneficiaries).

  - As applicable, show how the proposed research project aligns with DOD and VA areas of research interests. Provide a description of how the knowledge or technology

gained from the research could be implemented in a dual-use capacity to benefit the civilian population and address a military need, as appropriate.

- **Attachment 8: Data and Research Resource Sharing Plan (one-page limit):** ***All data must be shared while ensuring appropriate protection of information.*** **Upload as "Sharing.pdf".** Describe how unique and/or final research data will be shared with the research community, along with any resulting research resources. This includes cases where pre-existing data or research resources will be utilized and/or modified during the course of the proposed project. If there are limitations associated with a pre-existing agreement for the original data or research resources that preclude subsequent sharing, the applicant should explain this in the data and/or research resource sharing plan.

  Refer to the General Submission Instructions, Appendix 2, Section K, for additional information.

- **Attachment 9: Post-Award Transition Plan (two-page limit): Upload as "Transition.pdf".** Describe the methods and strategies proposed to move the anticipated research outcomes to the next phase of development or clinical application (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. Applicants are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The post-award transition plan should include the components listed below:

  - The project's anticipated research outcomes including knowledge products, clinical products for development, etc.

  - Using Appendix VI as a guide, describe the maturity of the product and provide the current and projected research technology or knowledge readiness level (as appropriate) at the end of the proposed project or knowledge outcome.

  - A description of the scientific or technical requirements needed to advance the research findings. Include steps necessary for FDA regulatory approval for the planning indication, and compliance with Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP), and Good Clinical Practice (GCP) guidelines as appropriate.

  - A timeline with defined milestones and deliverables describing the expected post-award progress of the results toward the next phase of development and eventual clinical impact.

  - An assessment of the opportunities available and potential barriers that would impact the progress of commercializing and/or translating the study results into clinical practice.

  - A plan for management of intellectual property.

- Details of the funding strategy to transition to the next level of investigation, development, and/or commercialization (e.g., partners, internal/external funding opportunities to be applied for).

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

- A plan to distribute the findings or intervention to the civilian and/or military communities.

- **Attachment 10: Human Subject Recruitment and Safety Procedures for Clinical Research (no page limit), if applicable; required for all studies recruiting human subjects: Upload as "HumSubProc.pdf".** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below, where applicable.

  Applicants and collaborating organizations may not use, employ, or subcontract for the use of any human participants, including the use of human anatomical substances, human data, and/or human cadavers until applicable regulatory documents are reviewed and approved by the USAMRDC OHARO to ensure that DOD regulations have been met.

  - **Study Population:** Describe the availability of the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Provide a table of anticipated enrollment counts at each study site. Demonstrate that the research team has access to the proposed study population at each site, and describe the efforts that will be made to achieve accrual goals. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical studies (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention. Identify ongoing clinical studies that may compete for the same patient population and how they may impact enrollment progress. 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 clinical research proposing to include military personnel, refer to the General Submission Instructions, Appendix 1, for more information.***

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

  - **Women and Minorities in the Study:** Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRDC. This policy is intended to promote

equity both in assuming the burdens and in receiving the benefits of human subjects research. Describe the strategy for the inclusion of women and minorities 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 a planned enrollment table(s) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The Public Health Service (PHS) Inclusion Enrollment Report, Policy on Inclusion of Women and Minorities, and Frequently Asked Questions for the policy may be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

- **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, healthcare provider identification of potential subjects, recruitment databases, advertising).

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

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

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

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

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

  - 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 or not the potential human subject will be allowed to discuss the study with anyone before making a decision.

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

- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The performance site's IRB office 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 study. If applicable, please refer to the General Submission Instructions, Appendix 1, for more information.

- ***Assent:*** If minors or other populations that cannot provide informed consent are included in the proposed clinical study, 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 IRB office to identify the conditions necessary for obtaining assent.

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

– **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 study. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:**

  - Appropriate to the study's level of rise, describe how safety monitoring and reporting to the IRB and FDA (if applicable) will be managed and conducted.

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

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

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

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

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

- **Attachment 11: Data Management (no page limit), if applicable; required for all studies recruiting human subjects: Upload as "Data_Manage.pdf".** The Data Management attachment should include the components listed below.

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

    - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.

    - **Confidentiality:**

      - ❖ Explain measures taken to protect the privacy of human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.

      - ❖ Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DOD are eligible to review study records.

      - ❖ Address requirements for reporting sensitive information to state or local authorities.

    - **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time the data will be stored. Describe the proposed database, how it will be developed and validated, and its

capability to safeguard and maintain the integrity of the data. Describe the database lock process. For FDA-regulated studies, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.

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

- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, including results from any screening or diagnostic tests performed as part of the study.

– **Laboratory Evaluations:**

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

- **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).

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

- **Laboratories 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 12: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** ***(Attachment 12 is required for human subjects studies using an investigational drug or device.)*** Provide the information requested below and provide supporting documentation as applicable.

– State the product/intervention name.

For products/interventions that do not require regulation by the FDA or an international regulatory agency:

- Explain why the product/intervention is exempt from FDA oversight. Provide evidence that the proposed study does not require regulation by the FDA. If the proposed study will be conducted at international sites, provide equivalent information relevant to the host country(ies) regulatory requirements.

For products/interventions that require regulation by the FDA and/or an international regulatory agency:

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

- If the product is marketed in the United States, state the product label indication. State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population. Indicate whether the proposed research involves a change that increases the risks associated with using the product. State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).

- If the product is not currently FDA-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification. Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.

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

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

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

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

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

- Describe the overall regulatory strategy and product development plan that will support the planned product indication/label. Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of FDA meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.

- **Attachment 13: Representations: 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 Submission Instructions, Appendix 5, Section B, Representations.

- **Attachment 14: Suggested Collaborating DOD Military Facility Budget Format, *if applicable*: Upload as "MFBudget.pdf".** If a Military Facility (MHS facility, research laboratory, medical treatment facility, dental treatment facility, or a DOD activity embedded within a civilian medical center) will be a collaborator in performance of the project, complete a separate budget using, "Suggested Collaborating DOD Military Facility Budget Format," available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm), including a budget justification for each Military Facility as instructed. The costs per year should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Submission Instructions, Section III.A.8, for detailed information.

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

Research & Related Personal Data: Refer to the General Submission Instructions, Section III.A.3, for detailed information.

Research & Related Senior/Key Person Profile (Expanded): Refer to the General Submission Instructions, Section III.A.4, for detailed information.

- PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf". The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The National Institutes of Health (NIH) Biographical Sketch may also be used. All biographical sketches should be submitted in uneditable PDF format.

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

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

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

Research & Related Budget: Refer to the General Submission Instructions, Section III.A.5, for detailed information.

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

Project/Performance Site Location(s) Form: Refer to the General Submission Instructions, Section III.A.6, for detailed information.

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

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

Note: Proposals/applications from **federal agencies** must include in their budget justifications a **Federal Financial Plan**. Proposals/applications from organizations that include **collaborations with DOD Military Facilities** must comply with special requirements. Refer to the General Submission Instructions, Section III.A.5, Research & Related Budget, for detailed information.

Intramural DOD Collaborator(s): Complete the Suggested Collaborating DOD Military Facility Budget Format and upload to Grants.gov attachment form as Attachment 14. (Refer to the General Application Instructions, Section IV.A.4, for detailed information.) Each Intramural DOD Collaborator should include costs per year on the Grants.gov Research & Related Budget Form under subaward costs.

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

The applicant organization must be registered as an entity in SAM (https://www.sam.gov/SAM/) and receive confirmation of an "Active" status before submitting a proposal/application through Grants.gov. As published in the Federal Register, July 10, 2019, (https://www.federalregister.gov/documents/2019/07/10/2019-14665/unique-entity-id-standard-for-awards-management), the UEI for awards management generated through SAM will be used instead of the Data Universal Numbering System (DUNS) number as of April 2022. ***All federal awards including, but not limited to, contracts, grants, and cooperative agreements will use the UEI.*** USAMRDC will transition to use of the UEI beginning with FY22 announcements and utilize the latest SF424, which includes the UEI. The DUNS will no longer be accepted. Applicant organizations will not go to a third-party website to obtain an identifier. During the transition, your SAM registration will automatically be assigned a new UEI displayed in SAM. (For more information, visit the General Services Administration: https://www.gsa.gov/about-us/organization/federal-acquisition-service/office-of-systems-management/integrated-award-environment-iae/iae-systems-information-kit/unique-entity-identifier-update.) Current SAM.gov registrants are assigned their UEI and can view it within SAM.gov. ***Authorized Organizational Representatives with existing eBRAP accounts should update their organizational profile to include the UEI prior to submission of the full application to Grant.gov (see Section II.D.4, Submission Dates and Times below).*** Refer to the General Submission Instructions, Section III, for further information regarding Grants.gov requirements.

II.D.4. Submission Dates and Times

This is a continuously open announcement through September 30, 2027; therefore, reviews occur throughout the year. Pre-proposals/pre-applications may be submitted at any time throughout the 5-year period from the BAA release date to the BAA closing date (noted in Section I). An invited full proposal/application should be submitted within 90 days of the PI's receipt of an invitation to submit. No pre-proposal/pre-application or full proposal/application may be submitted under this BAA after September 30, 2027, 11:59 p.m. Eastern Time. If an invited proposal/application is not submitted by September 30, 2027, 11:59 p.m. Eastern Time, the applicant must wait for the next available opportunity for submission, i.e., the release of the FY28 BAA (to be posted to Grants.gov October 1, 2027). No proposal/application received under this BAA will be considered for funding after 24 months from the date of submission.

Applicant Verification of Full Proposal/Application Submission in eBRAP

eBRAP allows an organization's representatives and PIs to view and modify the full proposal/application submissions associated with them. Following retrieval and processing of the full proposal/application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the full proposal/application submission. eBRAP will validate full proposal/application files against the BAA requirements, and discrepancies will be noted in an email to the PI and in the "Full Application Files" tab in eBRAP. eBRAP does not confirm the accuracy of file content. Proposal/application viewing, modification, and verification in eBRAP are strongly recommended, but not required. It is the applicant's responsibility to review all proposal/application components and ensure proper ordering as specified in the BAA. ***If either the Project Narrative or the budget fails eBRAP***

validation or needs to be modified, an updated full proposal/application package must be submitted. Other proposal/application components may be changed until the end of the proposal/application verification period. Verify that subaward budget(s) and budget justification forms are present in eBRAP during the proposal/application verification period. If these components are missing, upload them to eBRAP before the end of the proposal/application verification period. After the end of the proposal/application verification period, the full proposal/application cannot be modified.

The full proposal/application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the 5-day proposal/application verification period. During the proposal/application verification period, the full proposal/application package, ***with the exception of the Project Narrative and Budget Form***, may be modified.

II.D.5. Intergovernmental Review

This BAA is not subject to EO 12372, "Intergovernmental Review of Federal Programs." The EO provides for state and local government coordination and review of proposed federal financial assistance and direct federal development. The EO allows each state to designate an entity to perform this function. This coordination and review is not required under this BAA.

II.D.6. Funding Restrictions

There are no specified funding limitations identified for a proposal/application submitted under this BAA. Refer to the General Submission Instructions, Section III.A.5, "Research & Related Budget," for discussion of allowable costs, including pre-award costs and collaborations with Military Facilities.

II.D.7. Other Submission Requirements

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

II.E. Proposal/Application Review and Selection Information

II.E.1. Criteria for Research Proposals/Applications Without a Clinical Trial

II.E.1.a. Peer and Programmatic Review

1. **Peer Review:** To determine technical merit, all proposals/applications will be evaluated according to the following scored criteria, which are listed in descending order of importance:

    - **Research Objectives:**

        - The degree to which the stated objectives are clear, valid, and logical.

        - For development of devices and technologies, the degree to which the performance objectives are feasible; the proposed effort demonstrates familiarity with the historical

background of the problem and previous/current solutions; and the awareness of similar projects previously undertaken and related development activities.

- The extent to which the proposed research project demonstrates an innovative approach and relates to the Research Areas of Interest identified in Section II.A and Appendix I.

- **Scientific Design Excellence:**
  - The degree to which proposed plans, methods, techniques, and procedures are feasible, clear, valid, adequately referenced, and state of the art; the merit of the statistical features of the study; and the extent to which literature searches were used to document the strengths of the proposed project.
  - For development of devices and technologies, the feasibility of the proposed product/technology development plan; how well the engineering/technical design is likely to achieve the goals indicated; adequacy of the engineering/design solutions; and how well the perceived engineering/design strengths and flaws are addressed.
  - How well the proposed research is designed to achieve reproducible and rigorous results, including controls, sample size estimation, randomization, statistical analysis, and data handling.
  - How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable. To what degree the data collection instruments, if applicable, are appropriate to the proposed study.

- **Impact/Outcomes**
  - How well the potential impact of the research in the field, the significance of this impact, and when the impact can be anticipated are demonstrated.
  - The degree to which the results of this research are expected to impact the intended beneficiaries.
  - To what degree the anticipated outcomes could be implemented in a dual-use capacity to address the healthcare needs of military Service Members, Veterans, and/or their beneficiaries and to benefit the civilian population, if applicable.
  - How well the intervention addresses the clinical needs and how it compares with currently available interventions and/or standards of care.

- **Recruitment, Accrual, and Feasibility (for studies recruiting human subjects)**
  - How well the availability of human subjects for the clinical research and the prospect of their participation is addressed.
  - Whether access to the proposed human subjects population is demonstrated.

- To what degree the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.

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

- For clinical research studies, how well the proposal/application describes a plan to recruit subjects, including description of the inclusion and randomization criteria and whether the exclusion criteria are justified.

- **Ethical Considerations (for studies recruiting human subjects)**

  - How well the evidence shows that procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.

  - Whether the level of risk to human subjects is minimized and clearly communicated through informed consent.

  - How well safeguards are described and suitable for vulnerable populations.

  - The degree to which confidentiality and/or privacy issues are appropriately considered.

- **Transition Plan**

  - How well the proposal/application demonstrates feasible methods and strategies to move the project's findings to the next phase of development or clinical application.

  - Whether the proposal/application appropriately addresses available opportunities and potential barriers that could impact the progress of commercializing and/or translating the study results to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into clinical practice, and/or approval by the FDA) are achievable.

  - Whether the timeline for expected post-award progress is reasonable and contains appropriate milestones and deliverables for advancing the study results toward clinical impact.

  - Whether the funding strategy described to bring the anticipated research outcomes to the next level of development is reasonable and realistic.

  - To what degree the proposed collaborations and other resources for providing continuity of development are established and/or achievable.

  - How well the plan is described for distribution of the findings or intervention to the civilian and/or military communities.

- How well the proposal/application identifies intellectual property ownership, describes any appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this BAA.

- Whether the applicant has demonstrated that they have access to all intellectual property rights necessary for development and commercialization and evidence that the government has the ability to access such products or technologies.

- To what degree the intellectual and material property plan is appropriate and demonstrates cooperating institutions' willingness and ability to resolve intellectual and material property issues.

- **PI and Key Personnel Qualifications:** How well the qualifications, capabilities, and experience of the proposed PI and other key personnel demonstrate that the proposed staff has the knowledge, technical expertise, and management skills to achieve the proposed objectives as well as the time available for the percentage of efforts indicated for the project.

- **Facilities and Resources:** How well the proposed facilities and equipment, population resources, or unique combinations of these, demonstrate that the organization has the necessary facilities and resources required for accomplishing the proposed objectives.

- **Budget:** The degree to which the budget reflects the actual needs of the proposed work and is thoroughly detailed and fully justified so that the government can evaluate and determine the costs to be allocable, allowable and reasonable, and commensurate with the complexity and nature of the research proposed.

2. **Programmatic Review:** To make funding recommendations, the following criteria will be used by programmatic reviewers:

   - Scientific peer review results

   - Adherence to the intent of the award mechanism

   - Program portfolio composition and priorities

   - Relative military benefit

   - Relative innovation, impact, and translatability

   Note: Military-relevant research must be responsive to the healthcare needs of the Armed Forces, family members of the Armed Forces, and the U.S. Veteran population. Proposals/ applications must address a military-relevant health problem responsive to one of the Research Areas of Interest identified in Section II.A and Appendix I.

II.E.2. Proposal/Application Selection Process

All invited proposals/applications are evaluated by USAMRDC scientists, and/or contracted, non-governmental subject matter experts, other federal agency representatives, clinicians, consumers, or combinations thereof, using a two-tier review process. The first tier is peer review of proposals/applications against established criteria to determine technical merit, where each proposal/application is assessed for its own merit, independent of other proposals/applications. The second tier is programmatic review, a comparison-based process in which proposals/applications with high scientific and technical merit are further evaluated for relevance to the mission of the USAMRDC and its programs. Additional information about the two-tier process used by the CDMRP can be found at https://cdmrp.health.mil/about/2tierRevProcess.

All USAMRDC review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement declaring that proposal/application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's proposal/application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party by military personnel or employee of the federal government is a crime in accordance with 18 USC 1905.

After the two-tier evaluation, proposals/applications recommended for funding may be prioritized. A prioritized listing of alternates (deferred decisions) may also be prepared, when warranted. Subsequent awards depend upon the availability of funds and fulfillment of requirements and priorities determined to exist at the time of award. In some cases, funding priorities may change as certain scientific tasks are addressed and new mission assignments arise.

If selected for funding, the award may also be dependent on the organization providing adequate additional regulatory documentation, such as human subjects/anatomical substances/use of cadavers protocols and approvals, animal subjects protocols and approvals, and environmental information. The award may also be dependent on additional supporting administrative and budgetary information.

II.E.3. Integrity and Performance Information

Prior to making an 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 FAPIIS.

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

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

II.E.4. Notification of Proposal/Application Review Results

Each PI and organization will receive email notification via eBRAP of the proposal/application status. Notifications should be sent within 180 calendar days of submission. Each PI will receive a peer review summary statement on the strengths and weaknesses of the proposal/application.

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

The PI should receive disposition regarding the full proposal/application via an email from eBRAP within 180 days of submission. **A recommended for funding notification is NOT an authorization to begin performance nor a guarantee of an award.** If selected for funding, a representative from the USAMRAA will contact the Business Official authorized to negotiate on behalf of the PI's organization.

The awarding agency will be the USAMRAA. The USAMRAA Contracting, Agreements, and Grants Officers are the only individuals authorized to obligate funds and bind the federal government.

Authorization to begin performance will be received via an award document (contract, grant, or cooperative agreement, as applicable) signed by the USAMRAA Contracting, Agreements, or Grants Officer. No commitment on the part of the government should be inferred from discussions with any other individual.

Awards will be made at any time throughout the year and are contingent upon availability of funding, adequacy of supporting documentation submitted, fulfillment of requirements, and completion of successful negotiations. No proposal/application submitted under this BAA will be considered for funding after 24 months from the date of submission to Grants.gov. Refer to the General Submission Instructions, Appendix 2, Section D, Award Notices, for additional information.

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 BAA. Refer to the full text of the USAMRAA General Research Terms and Conditions for Institutions of Higher Education, Hospitals, and Non-Profit Organizations and the USAMRAA General Research Terms and Conditions for For-Profit Organizations available at https://www.usamraa.health.mil/Pages/Resources.aspx for further information.

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

Refer to the General Submission Instructions, Appendix 2, Sections L and M, for general information on changes to PIs and organizational transfers.

II.F.2. Administrative and National Policy Requirements

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

Applicable requirements in the FAR, found in 48 CFR, Chapter 1 and DFARS, found in 48 CFR, Chapter 2, apply to contracts resulting from this BAA.

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

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

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

New Requirement: Certification Regarding Disclosure of Funding Sources. The proposing entity must comply with Section 223(a) of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021, which requires that the PI, Partnering PIs (if applicable), and all key personnel:

- Certify that the current and pending support provided on the application is current, accurate, and complete;
- Agree to update such disclosure at the request of the agency prior to the award of support and at any subsequent time the agency determines appropriate during the term of the award; and
- Have been made aware of the requirements under Section 223(a)(1) of this Act.

False, fictitious, or fraudulent statements or claims may result in criminal, civil, or administrative penalties (18 USC 1001).

II.F.3. Reporting Requirements

Refer to the General Submission Instructions, Appendix 2, Section A, for general information on reporting requirements. ***If there are technical reporting requirement delinquencies for any existing USAMRAA-sponsored awards at the applicant organization, no new awards will be issued to the applicant organization until all delinquent reports have been submitted.***

Technical/scientific reporting requirements may include:

- Quarterly and/or annual progress reports
- Final progress report
- In-progress reviews
- Quad charts: The Quad Chart template is a one-page Word document or PowerPoint file that must be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm and completed for submission and application.
- PHS Inclusion Enrollment Reporting Requirement (only required for clinical research studies): Enrollment reporting on the basis of sex/gender, race, and ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP.

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

Awards resulting from this BAA 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 FAPIIS about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a federal award. These recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Submission Instructions, Appendix 5, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

Questions related to BAA content or submission requirements as well as questions related to the submission of the pre-proposal/pre-application through eBRAP should be directed to the eBRAP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern Time. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

Questions related to full proposal/application submission through the Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. federal holidays). Note that the eBRAP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726 (International: 1-606-545-5035)

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the BAA or by responding to the prompt provided by Grants.gov when first downloading the submission package. If the submission package is updated or changed, the original version of the submission package may not be accepted by Grants.gov.

II.H. Other Information

II.H.1. Contractor/Recipient Qualification

Refer to the General Submission Instructions, Appendix 3, for general information on required qualifications.

In addition to other information provided herein, by submitting a proposal/application and accepting an award, the organization is: (1) certifying that the investigators' credentials have been examined and (2) verifying that the investigators are qualified to conduct the proposed study and to use humans and/or animals as research subjects, if proposed. Investigators include all individuals, regardless of ethnicity, nationality, or citizenship status, who are employed by, or affiliated with, an eligible organization.

Should the PI of a funded project leave the award organization, both the PI and organization must contact the USAMRAA as soon as possible to discuss options for continued support of the research project. Every effort should be made to notify the USAMRAA prior to the PI leaving the organization.

II.H.2. Proprietary Information

Do not include any proprietary information in the pre-proposal/pre-application. Proprietary information should ***only be included*** in the full proposal/application ***if necessary for evaluation purposes.*** Abstracts of all funded proposals/applications will be posted publicly. ***Therefore, do not include proprietary information in the abstracts.***

Conspicuously and legibly, mark any proprietary information that is included in the full proposal/application. Identify any proprietary information to be provided to the government and indicate whether the applicant will request a waiver of government purpose rights.

II.H.3. Administrative Actions

After receipt of proposals/applications, the following administrative actions may occur:

II.H.3.a. Rejection

The following will result in administrative rejection of the proposal/application:

- Project Narrative exceeds the page limit.

- Project Narrative is missing.
- Budget Form contains only zeros.
- Full proposal/application submission in the absence of an invitation.

For proposals/applications recruiting human subjects without clinical trials:

- Attachment 10, Human Subject Recruitment and Safety Procedures, is missing.
- Attachment 11, Data Management, is missing.

For proposals/applications with clinical trials:

- Attachment 6, Human Subject Recruitment and Safety Procedures, is missing.
- Attachment 7, Intervention, is missing.
- Attachment 8, Data Management, is missing
- Attachment 13, Regulatory Strategy, is missing

II.H.3.b. Modification

- Pages exceeding the specific limits may be removed prior to review for all documents other than the Project Narrative.
- Documents not requested may be removed.
- Following proposal/application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the proposal/application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed above in Section II.H.3.a, Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the 5-day proposal/application verification period; otherwise, the proposal/application will be reviewed as submitted. If either the Project Narrative exceeds the page limit or the Budget Form contains only zeros, an updated Grants.gov submission package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking Identification.

II.H.3.c. Withdrawal

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

- The proposal/application fails to conform to this BAA description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

- Federal agency personnel involved in the review process and/or with making funding recommendations are named as being involved in the research proposed or found to have assisted in the pre-proposal/pre-application or proposal/application processes, including, but not limited to, concept design, proposal/application development, budget preparation, and the development of any supporting documentation. ***If formal collaboration with Military Facility personnel is planned (i.e., included in the proposal/application in performance of the research), this prohibition is not applicable. However, these Military Facility personnel are prohibited from being involved in the review process and/or with making funding recommendations.***

- Inclusion of any employee of USAMRDC review contractors in pre-proposal/pre-applications or full proposals/applications for funding without adequate plans to manage COIs. Refer to General Submission Instructions, Appendix 3, Section D, for detailed information.

- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.

- The full proposal/application does not propose the same research project as described in the pre-proposal/pre-application.

- The full proposal/application budget differs significantly from the budget included in the pre-proposal/pre-application.

- Proposed research of work that has been funded, or selected for funding, through another mechanism may result in withdrawal.

- The proposal/application requiring IND/IDE (or international equivalent) does not include documentation of submission in the Regulatory Strategy (Attachment 12 for proposals/applications without clinical trials; Attachment 13 for proposals/applications with clinical trials).

II.H.3.d. Withhold

Proposals/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 Contracting, Agreements, or Grants Officer for a determination of the final disposition of the proposal/application.

II.I. Checklist for Research Proposal/Application Submission Without a Clinical Trial

Grants.gov Application Components	Upload Order	Action	Completed
SF424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf"	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf"	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf"	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf"	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf"	
	6	Impact/Outcomes Statement: Upload as Attachment 6 with file name "Impact.pdf"	
	7	Military Relevance Statement: Upload as Attachment 7 with file name "MilRel.pdf"	
	8	Data and Research Resource Sharing Plan: Upload as Attachment 8 with file name "Sharing.pdf"	
	9	Post-Award Transition Plan: Upload as Attachment 9 with file name "Transition.pdf"	
	10	Human Subject Recruitment and Safety Procedures: Upload as Attachment 10 with file name "HumSubProc.pdf" if applicable	
	11	Data Management: Upload as Attachment 11 with file name "Data_Manage.pdf" if applicable	
	12	Regulatory Strategy: Upload as Attachment 12 with file name "Regulatory.pdf" if applicable	
	13	Representations: Upload as Attachment 13 with the file name "RequiredReps.pdf"	
	14	Suggested Collaborating DOD Military Facility Budget Format: Upload as Attachment 14 with file name "MFBudget.pdf" if applicable	
Research & Related Personal Data		Complete form as instructed.	

Grants.gov Application Components	Upload Order	Action	Completed
Research & Related Senior/Key Person Profile (Expanded)		Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
		Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
		Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
		Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
Research & Related Subaward Budget Attachment(s) Form		Complete form as instructed.	

APPENDIX I: RESEARCH AREAS OF INTEREST

I. Military Infectious Diseases Research Program

Research and development of solutions for the prevention, treatment, and diagnosis of infectious diseases

- **Prophylactics:** The MIDRP supports the development of solutions to prevent infectious disease threats to eliminate their impacts on operational readiness for the U.S. military. Prevention is the most desirable infectious disease countermeasure because it prevents disease from occurring (vs. treatment post-infection), is the most cost-effective approach, and reduces unit loss rate. The MIDRP supports discovery, optimization, development of animal models, efficacy testing *in vitro*, efficacy and safety testing in validated preclinical animal models, cGMP manufacture, safety and efficacy testing in clinical trials of novel prophylactics for the following:
    - Endemic diarrheal diseases
    - Combat wound infections (from complex traumatic penetrating injuries) and/or associated sepsis
    - Dengue fever
    - HIV
    - Emerging infectious diseases
    - Pathogen agnostic and/or broad spectrum prophylactics targeting diseases/pathogens listed above
- **Treatments:** The MIDRP supports the development of solutions to treat infectious disease threats to eliminate their impacts on operational readiness. Improved treatment solutions for infectious disease casualties are necessary to return Warfighters to competition. The MIDRP supports discovery, optimization, development of animal models, efficacy testing *in vitro*, efficacy and safety testing in validated preclinical animal models, current GMP (cGMP) manufacture, safety and efficacy testing in clinical trials of novel treatments for the following:
    - Combat wound infections (from complex traumatic penetrating injuries) and/or associated sepsis
    - Dengue fever
    - Hantavirus
    - Emerging infectious diseases

- Pathogen agnostic and/or broad spectrum treatments targeting diseases/pathogens listed above

- **Diagnostics:** The MIDRP supports the development of improved predictive solutions to diagnose infectious disease threats to eliminate their impacts on operational readiness. Improved predictive diagnostic solutions for infectious disease casualties are necessary to accurately inform treatment decisions, and ultimately return Warfighters to competition. The MIDRP supports the identification of targets for diagnostic assay design, optimization of assays on selected platforms, validation and testing of diagnostic assays and platforms for the following:

  - Diagnostics for the pre-symptomatic/early symptomatic detection of wound infections and/or sepsis in far forward austere environments

  - Diagnostics for the pre-symptomatic/early symptomatic detection of bacterial and/or viral infections in far forward austere environments

II. Combat Casualty Care Research Program

A. Research and development of technologies to stop blood loss, resuscitate the casualty, and limit the immediate, short-, and long-term deleterious consequences of severe hemorrhage: Research focused on the pre-hospital setting including point of injury and scenarios in which a casualty cannot be transported through traditional levels of care (i.e., prolonged care) are of high interest. Included in this area of interest are diagnostics and therapeutics to predict, diagnose, prevent, and treat coagulopathy of trauma and non-invasive or minimally invasive sensors to detect and warn of impending vascular collapse and/or significant tissue damage due to perfusion deficits. Examples of specific products include local and systemic hemostatic agents or devices (intracavitary, junctional or endovascular) for control of vascular disruption and subsequent compressible and non-compressible hemorrhage, treatments to sustain or enhance oxygen delivery and perfusion of vital tissues and organs, and equipment, procedures, and blood product or other fluids and adjuncts for effective resuscitation. Also of interest are the improved preservation, storage, transportability, and processing of red blood cells, platelets and plasma, and other blood or blood-like substitutes.

B. Research and development of technologies to diagnose and to limit the immediate, short-, and long-term impairments that follow TBI: Knowledge and materiel solutions that seek to improve the far-forward capabilities of military diagnostic, characterization and treatment for the spectrum of TBI severities. Objective diagnosis and treatment of brain injury are recognized as high priorities. Research objectives in this area includes (but is not limited to):

- Developing life-saving resuscitation interventions for TBI and polytrauma/complex injury.

- Fielding point-of-injury therapeutic interventions to mitigate secondary effects of brain injury.

- Enabling far-forward, rapid diagnostic capabilities to diagnose and monitor TBI in a prolonged care environment, with an emphasis on non- or minimally-invasive technologies.

- Developing monitoring and recording technologies for management and maintenance of TBI in a prolonged care environment.

C. Research and development of technologies to diagnose and reduce acute secondary organ damage: Secondary damage to organs frequently occurs after severe trauma and resuscitation. The CCCRP is interested in materiel and/or devices that can reduce acute secondary organ damage such as ischemia/reperfusion injury, cell death, general organ failure, and secondary brain damage. Technologies to sustain or support single- and multiple-organ injury and failure are also of interest to the CCCRP. These objectives include methods to reduce cellular demand for oxygen and metabolic substrates and therapeutics to modulate the immune response to traumatic injury as well as single- and multiple-organ support or replacement technologies (extracorporeal). In addition, the utilities of these modalities during (and the effects of longer distance) en route care on the critically injured casualty are also of interest.

D. Research and development into the delivery of care during transport: An important element of combat casualty care is the transport of patients from the initial point of injury and throughout the continuum of care. Accordingly, the CCCRP is interested in improving and maintaining optimal clinical outcomes for en route care. Identifying feasible ways to mitigate the stresses of flight and/or transport (such as hypobaria, hypoxia, vibration, and g-forces) in an austere/constrained environment and the impact on clinical outcomes (such as healing rates, pain, infection rates, etc.) are particularly important. Additionally, establishing either timeframes or ways to measure the appropriate time to transport patients with critical injuries (including neurotrauma, burns, lung injuries, and musculoskeletal injuries) is a critical element to improving outcomes. Solutions that improve the capacity and capability of en route care delivery, including development of autonomous care and critical care solutions will be considered. Particular challenges of prolonged transport of critically injured patients requiring ongoing resuscitation and evacuation of large numbers of casualties are of particular interest.

E. Research, development, and translation into clinical practice of novel/optimized treatments for severe burn injuries: Safe and effective therapies and technologies are needed to provide early, life-saving burn fluid resuscitation, and early/ongoing care for severe burn skin (and underlying tissue) wounds as well as burn inhalation injury across the continuum of care. Prioritized approaches will be amenable for use by non-specialist care givers, logistically practicable in austere environments, and simplified for self- and buddy-aid where feasible. Burn injury management strategies of highest interest will advance the standard of care available to stabilize burn casualties close to the point of injury, potentially during prolonged delay of evacuation to definitive care by burn specialists, with additional consideration for utility in mass casualty events. Advanced solutions are sought to: prevent burn wound conversion; stabilize burn wounds and promote/accelerate healing; reduce the need for grafting; optimize burn fluid resuscitation, with limited fluid volumes, non-invasive routes of fluid administration, and treatment automation; treat inhalation injury; preclude

and/or mitigate complications of burn injury (e.g., dysregulated inflammatory and immune physiology, burn wound infection; burn sepsis/shock). Solutions to enhance both burn treatment capability at all echelons of care and burn casualty capacity especially in the prehospital environment are of interest. Decision support tools to objectively predict the ability of burn casualties to safely return to duty are needed. Development of model systems to characterize burn injuries caused by emerging weapons and to evaluate potential therapies/therapeutics is also a priority.

F. Pain Management: The primary interest of the Pain Management program area is management of acute pain associated with traumatic or combat-related injuries, with a secondary interest in early interventions to prevent pain chronification. The CCCRP's specific needs include development of alternative interventions to current opioid analgesics administered on the battlefield and in resource-limited environment by the medic/corpsman; pain management strategies that promote military readiness (including treatments with limited side effects, e.g., no effect on respiration or cognitive function); treatments for the variety of pain etiologies resulting from polytrauma; understanding and treatments for comorbid physical and mental health factors that impact pain; development of strategies for identifying and addressing biopsychosocial aspects of pain; solutions for pain management under prolonged care conditions; chronic pain treatment; and pain chronification prevention. Field expedient regional analgesia solutions will also be considered.

G. Regenerative Medicine: Regenerative medicine involves the use of innovative technologies such as scaffolds and tissue engineering, growth factors, and cell-based treatments to restore Service Members who have suffered combat-related injuries. Research topics of particular interest include those directed toward the use of regenerative medicine-based technologies to provide early field solutions for tissue coverage and would healing, blood product production, hemostatis, volumetric muscle loss and vascular defects.

H. Autonomous Care and Evacuation / Medical Assist Support Technologies (MAST), is focused on increasing capabilities to support dispersed operations in a MDO environment that includes not only typical military fighting capabilities of the physical domains, but also greater emphasis on space, cyberspace, and other contested areas such as the information environment, and the cognitive dimension of warfare. MAST consists of two program areas of medical robotics and autonomous medical systems, and virtual health.

- Medical Robotics and Autonomous Systems (MED-RAS): research, design, and prototype future medical robotic, autonomous/unmanned medical capabilities to deliver high-quality care in far-forward/dispersed operations in support of disruptive approaches to complex environments.

- Virtual Health: future Virtual Health enterprise process architectures, telemedicine, telementoring, decision-support and adaptive approaches for delivery of care, intelligent data driven decision aides, and integrated physical solutions capable of supporting prolonged field care and dispersed operations in conditions with limited or lacking traditional field communications.

I. Medical Countermeasures (MCMs) for Acute Radiation Exposure: Radiation MCMs include radioprotectants (pre-exposure) and mitigators and therapeutics (post-exposure). Both categories of MCMs are focused on preventing or treating the effects of acute radiation exposure, including the resultant development of acute radiation syndrome (ARS). The focus area examines ARS resulting from exposure to ionizing radiation from radioactive sources or a nuclear detonation, including low linear energy transfer (LET) sources (gamma and X-rays) and high LET sources (neutrons). Research objectives include, but are not limited to, identifying mechanisms of action, obtaining efficacy and safety data in animal models for MCMs for ARS, and demonstrating improved survivability following high doses of radiation with treatment either before exposure or within 24 hours after exposure. Research in biodosimetry in support of MCM development may also be considered.

J. Combined Injury: Solutions that address medical specific alterations in medical care including diagnosis, triage, prognostication and treatment for warfighters that incur combined injury from polytrauma and/or burn with chemical, biological, radiologic/nuclear injury.

III. Military Operational Medicine Research Program

A. Injury Prevention and Treatment: This area of research addresses the requirement to provide the biomedical basis for countermeasures and scalable strategies that prevent and treat Service Member injuries and performance decrements occurring in training and operational (including close combat) environments, optimize diagnosis, treatment, rehabilitation, and reintegration following service-related neuromusculoskeletal injury, decrease attrition and medical cost, minimize personal impact to the Service Member, accelerate recovery and promote, optimize, and enhance readiness. The primary needs of the Injury Prevention and Treatment portfolio are developing and validating RTD physical performance standards following neuromusculoskeletal injury; developing and validating rehabilitation strategies and technologies for neuromusculoskeletal injury and associated polymorbidities, including optimal timing, dose, frequency, and intensity; treating common acute injuries and repetitive overuse injuries that affect readiness; developing and validating diagnosis, treatment and rehabilitation interventions at or near the point of injury; providing solutions to repair, reconstruct, or regenerate tissue lost or damaged due to traumatic injury; optimizing limb trauma/limb loss rehabilitation and prosthetic/orthotic management; understanding the physiological impact of exposure to repetitive low-level blast in order to validate military safety standards and health hazard assessment prediction tools to prevent brain, sensory, and lung injury; understanding effectiveness of personal protective equipment for blast, blunt, accelerative and emerging directed energy threats; understanding the bioeffects from exposure to emerging directed energy threats (e.g., laser, microwave, and radiofrequency waves); understanding the physiology of injury and repair mechanisms and their interrelationships with both modifiable and non-modifiable factors (e.g., environment, nutrition, sleep, stress, situational and cognitive awareness, genetics, sex, age) to promote effective interventions; providing validated injury criteria with animal models and postmortem human subject against blunt and ballistic threats to inform helmet and body armor developments; developing injury thresholds against directed energy threats; developing interventions and validated tools to mitigate neuromusculoskeletal injury risk while optimizing and enhancing Service member performance (individual and group) in

complex military systems. Research needs also encompass identification and validation of cognitive/brain health factors that impact physical performance. Finally, "omics"-level efforts, genetic indicators, and other confounders that identify individual strengths/ vulnerabilities to injury, treatment, rehabilitation, and performance are important to guide training and operational strategies that maximize readiness and lethality. Development goals include decision aids, biomedical guidance, assessment techniques, and validated metrics (including biomarkers). Coordination with medical DOD laboratories such as the U.S. Army Aeromedical Research Laboratory and Walter Reed Army Institute of Research, other DOD Military Treatment Facilities, other DOD services (Navy, Marines, Air Force), and academia/universities and support of the U.S. Army Training and Doctrine Command, Center for Initial Military Training and U.S. Army Forces Command (including the Holistic Health and Fitness (H2F) System) is highly encouraged. For neurosensory injury-related areas, the goal is to repair, restore, monitor, preserve, and maintain sensory system (e.g., vision, hearing, balance) function after operational threats (including but not limited to directed energy exposure). Seeking research efforts to develop innovative strategies and technologies that may include medical devices, pharmaceuticals, rehabilitation strategies, and regenerative medicine-based approaches, to assess, diagnose, treat, restore, and preserve spared tissue and function, and/or rehabilitate patients due to sensory injury.

B. Psychological Health and Resilience: The Psychological Health and Resilience research program area is interested in research that is aimed at optimizing Service Member, Unit, and Family psychological health, readiness, and resilience; maximizing the Force's readiness through prevention and early objective psychological health screening, and optimizing the treatment of psychological injuries/illnesses, their comorbidities, and subtypes to achieve remission and rapid return to duty (RTD). This program area aims to decrease the incidence and functional impact of behavioral health disorders such as PTSD, adjustment disorders, depression and anxiety disorders, prevent suicides and suicide attempts, and reduce risk behaviors (e.g., substance abuse, anger/aggression, sexual harassment and assault, and interpersonal workplace and domestic violence within the military). It focuses on the development and validation of effective training and prevention interventions, screening and assessment strategies, treatment and rehabilitation interventions, and enhanced translation, implementation, and uptake of evidence-based psychological health strategies and treatments in the MHS that address the psychological health topic areas. Research areas of particular interest include: effective solutions to sustain and/or restore the mental health, well-being, and resilience of healthcare personnel, particularly those providing high-stress, traumatic, or psychological healthcare to Service Members and families; studies to elucidate objective markers predicting treatment response in PTSD samples or complex/comorbid behavioral health populations; studies addressing comorbidities of psychiatric diagnoses (e.g., PTSD, mood disorders, and adjustment disorders) including, but not limited to concussion, alcohol, and other drug abuse, sleep disturbance/insomnia, suicidality, interpersonal violence, and interpersonal psychosocial factors); research focused on designing and testing pharmacological and non-pharmacological interventions or solutions to prevent acute stress reactions and/or mitigate risk of PTSD development immediately after exposure to trauma; establishing validated objective RTD standards following psychological injury. Research focused on community/systems-level health psychology approaches appropriate for military populations and culture is of interest. Additionally, MOMRP accepts applications focused on implementing effective suicide prevention interventions (both clinical and community-based

interventions); research on effective post-treatment discharge care and follow-up for suicide; research on technology based interventions for suicide prevention. Additional psychological health areas of interest include military-related grief, guilt, or loss issues; moral injury; interdisciplinary and universal prevention and life-skills training strategies to mitigate negative psychological health trajectories; and reduction of stigma and other barriers to psychological healthcare-seeking. The MOMRP has interest in understanding and addressing psychosocial/psychological health challenges unique to military culture, military families, women Service Members, Reserve and Guard, and lesbian, gay, bisexual, and transgender Service Members. Proposals/applications that incorporate and evaluate leveraging of technology (e.g., telemedicine, remote monitoring, biosensors, advance immunologic testing, and health information technologies) and leverage existing resources (to include mining/use of medical record data) and infrastructure to support psychological risk prevention and management, lifecycle logistics, and sustainability are encouraged. Also of interest are rigorous studies on complementary and integrative health (CIH) approaches spanning mind/body, movement, natural products, non-Western medicine approaches and spiritual practices, along with validation studies of CIH therapies. Research topics of particular interest include those directed at evaluating efficacy of cognitive training approaches to promote resilience and prevent/mitigate acute negative responses to psychological trauma and promote readiness; and the development of a systematically applied set of therapeutic services designed to mitigate psychological disorders by changing unhelpful thought patterns and unhealthy behaviors, reducing emotional distress, and restoring function and quality of life.

C. **Physiological Health and Performance:** This area of research develops biomedical countermeasures to sustain Service Member health and operational effectiveness. It informs military policy, training, Clinical Practice Guidelines (CPG), and the development of materiel solutions to establish, sustain, optimize, and monitor Service Member health, physiological factors of resilience, and cognitive and physical performance throughout the military lifecycle, including training, deployment, reset, and injury recovery cycles. This research area aims to prevent or mitigate the negative effects of operational and training stressors on the readiness, performance, and fitness of Service Members, as well as safely and ethically enhance performance with evidence-based biomedical and materiel personalized strategies based on a systems medicine approach. Studies may include, but are not limited to, those that investigate the use of dietary supplements and nutritional and behavioral interventions to mitigate threats to readiness, operational health, and performance. Research also aims to develop healthy sleep and fatigue management strategies, strategies that exploit individual differences in sleep loss resilience, and strategies that promote individualized resilience to various operational stressors and injuries. Physiological health and performance research also encompasses work focusing on cognitive performance. Basic, applied, and advanced research studies utilizing technologies and strategies to monitor and promote Service Member and family readiness and health to support the Army Surgeon General's Performance Triad also fall under this research area.

D. **Environmental Health and Protection:** This area of research includes assessment and sustainment of health, force readiness, protection, and the operational effectiveness of Service Members exposed to harsh operational environments including altitude, cold/Arctic, heat, undersea, and exposures to environmental toxicant health hazards in the dense urban

and enclosed spaces, and/or a combination of multi-environmental stressors. Studies proposed may include, but are not limited to, methods for effective monitoring of environmental exposures in individuals and populations and assessment of health risks following exposures to environmental stressors. This research also includes development of policy, training, mission planning/management tools, knowledge and materiel solutions, physiological status monitoring systems (to include use of existing/COTS wearable technologies), interventions, and reset solutions to sustain Service Member readiness, and health and operational effectiveness to environmental stressors encountered during extreme training or operations. In addition, research identifies biomarkers of exposure, dosimetry, and risk management to environmental health hazards, neurological and physical assessment tools for optimizing performance of the Service Member exposed to extreme operational environments, biomarkers of complex exposures, and health effects in support of military operational requirements. Research also focuses on developing wearable solutions that are small size, low weight, small cube, and have minimal power requirements for real-time physiological status monitoring in extreme training and operational environments.

IV. Medical Biological Defense Research Program

A. Viral, Toxin, and Bacterial Studies

- Identification and characterization of organisms and toxins. Molecular antigenic analysis; development of diagnostic assays; studies on structure and function that are related to mechanisms of action, binding, internalization, and interaction with the immune system and neutralizing antibodies; investigation of pathogenesis and immunology that will inform and enable decisions regarding the optimal approach to disease prevention and control. Specific long-term goals include development of physiological support methodologies, diagnostic tests, rational prevention and control strategies, and improvement of existing products.

- Vaccine development, with emphasis on protection from aerosolized agents, molecular approaches for development of vaccines, measurement of relevant cellular and humoral protective immune responses, and expression or production of protective antigens using recombinant technology. Development of vaccines for specific toxins and disease agents involving the generation, selection, and characterization of attenuated strains or inactivated purified antigen preparations, to include polyvalent vaccines that are more broadly effective. Safer means of passive immunization such as production of human monoclonal or modified antibodies that are de-speciated are also of interest. Identification of surrogate markers of protection for the agents identified above and development of assays to assess such protection are needed.

- Development of improved methods for delivery of vaccines, including adjuvants, nucleic acid vaccines, methods for oral or nasal immunization with inactivated, live, and subunit antigens; sustained release formulations; and development of methods for delivery of antigens for specific induction of mucosal immunity and development of methods to enhance appropriate immune responses to include co-delivery of cytokines.

- Preparation of research quantities of highly purified and characterized toxins as well as studies on basic chemistry, mechanisms of action, metabolism, and excretion.

B. Drug Development: Development, synthesis, and testing of compounds that possess antiviral, antibacterial, immunomodulatory, or antitoxin activities, with emphasis on compounds that provide broad, non-specific protection against viruses, bacteria, and toxins as described above. Studies of their pharmacokinetics and other measurements relevant to more effective drug use are also of interest, as is the development of lead compound(s) that are potent, active-site inhibitors that may include combinatorial-derived organic molecules and/or rationally designed transition-state substrate analogs. Testing for potency is required. Approaches that will be considered include, but are not limited to, computational chemistry, combinatorial organic synthesis, high-throughput in vitro screening, and x-ray analysis of ligand-toxin co-crystals.

Research areas of interest include:

- Discovery of novel or unique biochemical elements or compounds with antiviral, antibacterial, or antitoxin activity against biological organisms.

- Development of testing models for evaluation of compounds effective against toxins of several classes, including pre- and post-synaptic toxins, membrane-damaging toxins, and toxins that inhibit protein synthesis and others.

- Mechanism of action studies of immunomodulators, including characterization of effector cells (lymphocytes, macrophages), effector mechanisms, ancillary effects on other cells of the immune system, and production and characterization of cytokines released as a consequence of immunomodulation.

- Development of novel treatments to reverse paralysis in nerve terminals exposed to botulinum neurotoxin (BoNT) serotypes A, B, E, or F, with emphasis on the following objectives: (a) development of clinically feasible treatments to block the catalytic activity of the BoNT light chain; (b) treatments to accelerate recovery from paralysis-induced atrophy by targeting skeletal muscle regenerative pathways; and (c) identification and development of novel chemical scaffolds for small molecule inhibitors of the catalytic activity of the light chain of BoNT serotype A. While there may be limited funds available for development of promising approaches, this effort is predominantly focused on the accelerated development of clinically viable treatments with existing efficacy data.

C. Identification, Diagnosis, and other Medical Interventions: The investigation and evaluation of sensitive and specific methods of identifying and diagnosing both antigens and antibodies of viruses, bacteria, and rickettsia in biological materials. Development of sensitive and specific immunologic, chemical, or biological assays for the rapid (within minutes) and reliable (1) diagnoses of acute diseases due to agents of potential biological threat and (2) identification of toxins or their metabolites in biological samples. Assay may include antigen, antibody, or metabolite detection or the use of nucleic acid probes or synthetic antigens. In addition, there is interest in the development of rapid identification and

diagnostic methods for the assay of toxins, metabolites, and analogs in clinical specimens. Finally, the program is interested in any other medical interventions, techniques and treatments that show promise in supporting survival and/or recovery of biological or toxin-exposed casualties.

D. Biosurveillance (BSV): The process of gathering, integrating, analyzing, and communicating a range of information that relates to health threats for people, animals, and plants to help inform decisions and provide for increased global health security. The Joint Biosurveillance Common Framework (JBCF) will be the first materiel solution and provides a single enterprise environment that supports collaboration, data sharing, and coordination between/among multiple BSV stakeholders. The JBCF and future BSV applications, tools, and devices will provide a conduit between the medical, physical, and operational communities. This topic includes:

- Algorithms for rapid identification of baseline deviation; novel/unknown pathogens, naturally occurring versus intentional release.
- Models to predict the likelihood of an outbreak, forecast the associated epidemic curves and impacts of interventions, and update forecast based on field (and simulated) data.
- Applications to engage citizens via social media, crowd sourcing, gaming, etc.

In addition, two specific topics currently of interest are:

- Next-generation analytic capabilities for BSV: The objective is to develop next-generation methodologies to enhance analytic capabilities in the detect-identify-respond timeline for a bioevent. Research should be exploratory, with a low-technology readiness level, and should address long-term challenges in threat surveillance. Efforts should significantly contribute to the current body of knowledge and lead to new concepts for technology application that may have impact on future BSV analytic capabilities.
- Biosurveillance Ecosystem (BSVE) Analytics 2.0: The objective is to ensure state of the art technologies are made rapidly accessible through the BSVE. This topic seeks to develop analytic applications to synthesize and interrogate multiple sources of data to provide high confidence in the prediction, early warning, and forecasting (inclusive of mitigation strategies) of disease events. Metrics shall be devised such that successful utilization of these analytic tools will result in a measurable impact on the bioevent timeline. Efforts in this area should result in flexible, extensible, and sustainable analytics and models that are designed to plug into the BSVE as à-la-carte services rather than as standalone capabilities.

V. Medical Chemical Defense Research Program

- Characterizing the mechanisms of vesicant agent pathophysiology to identify medical countermeasures against vesicant agents.
- Developing innovative models of the pathophysiology of vesicant agent injury.

- Identifying and/or evaluating innovative candidate medical countermeasures against vesicant agents.
- Identifying, exploring, and developing innovative clinical diagnostic, prognostic, and management approaches to vesicant agent casualties.
- Characterizing the ocular lesions associated with vesicant agent exposures; developing treatments to ameliorate these injuries.
- Characterizing the mechanisms of nerve agent-induced seizures and resulting pathophysiology to identify medical countermeasures against nerve agent-induced seizures.
- Identifying, synthesizing, and/or evaluating innovative candidate medical countermeasures against nerve agent-induced seizures.
- Developing innovative models of the pathophysiology of nerve agent-induced seizures.
- Developing catalytic and/or stoichiometric chemical warfare agent scavengers from biological molecules (e.g., antibodies and enzymes) that provide protection against nerve agent incapacitation and lethality for extended periods following their administration.
- Developing innovative models for evaluation of chemical warfare agent scavengers.
- Identifying, expressing, synthesizing, and/or evaluating biotechnologically derived or pharmaceutically based scavengers as candidate medical countermeasures against chemical warfare agents.
- Developing and evaluating custom-synthesized pharmaceuticals based on a detailed understanding of the pathophysiology and mechanisms of action of the chemical warfare agent structure and the function of the intended target molecule.
- Developing catalytic and/or stoichiometric additives for use in skin protectants, or decontaminants, to protect against chemical warfare agents, especially vesicant and nerve agents.
- Developing innovative models for evaluation of catalytic and/or stoichiometric additives in skin protectants or decontaminants.
- Developing candidate formulations for skin protectants or decontaminants containing catalytic and/or stoichiometric additives and evaluating these formulations against chemical warfare agents.
- Characterizing the pathophysiology and natural progression of chemical warfare agent-induced damage to human tissues.
- Developing and validating innovative techniques for rapid and accurate analysis of human tissues and body fluids for detection of chemical warfare agent exposures.

- Characterizing the effects of long-term or chronic exposures to chemical warfare agents and/or medical countermeasures to these agents.

- Identifying, exploring, and developing innovative clinical diagnostic, prognostic, and management approaches to nerve agent casualties.

- Developing and validating field-usable procedures for diagnosis, prognosis, and treatment of chemical warfare agent casualties under both field and laboratory conditions.

- Addressing the unique challenges of combined injuries due to both physical trauma from kinetic weapons and exposure to chemical agents. See also, Section II.A.2, Combat Casualty Care Research Program, and Appendix I.II, when research focus is on survival from conventional injuries in a contaminated environment.

APPENDIX II: CLINICAL TRIALS

I. Important Aspects of Clinical Trials

A clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. ***NOTE:*** FDA-regulated clinical investigation is always a clinical trial, but not all clinical trials are FDA clinical investigations.

If the proposed clinical trial involves the use of a drug that has not been approved by the FDA for the proposed investigational use, then an IND application to the FDA that meets all requirements under 21 CFR 312 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the FDA if an IND application is not required. ***If an IND application is required, evidence that an IND application has been submitted or IND authorization without clinical hold status has been secured must be included in the proposal/application.*** The IND application should be specific for the product (i.e., the product should not represent a derivative or alternate version of the investigational agent described in the IND application) and indication to be tested in the proposed clinical trial. For more information on IND applications, the FDA has provided guidance at https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application.

If the investigational product is a device, and will be assessed under a Significant Risk (SR) Device Study, then an Investigational Device Exemption (IDE) application to the FDA that meets all requirements under 21 CFR 812 may be required. It is the responsibility of the applicant to provide evidence if an IDE application is not required or the device qualifies for an abbreviated IDE application. ***If an IDE application is required, evidence that an IDE application submission or IDE authorization without clinical hold status has been secured must be included in the proposal/application.*** The IDE application should be specific for the device (i.e., should not represent a derivative or modified version of the device described in the IDE application) and indication to be tested in the proposed clinical trial. For more information on IDE applications, the FDA has provided guidance at https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/investigational-device-exemption-ide.

If an IND or IDE is required for the work proposed, the IND/IDE application must be submitted to the FDA prior to submission of the full proposal/application. The government reserves the right to withhold or withdraw funding if an IND or SR IDE is necessary to conduct the proposed study but has not been obtained within 6 months of the award date.

The following are important aspects of submissions proposing a clinical trial:

- **Clinical Trial Start Date:** The proposed clinical trial is expected to begin no later than 12 months after the award date.

- **Preliminary data are required:** Inclusion of preliminary data relevant to the proposed clinical trial is required. The proposed clinical trial must be based on sound scientific

rationale that is established through logical reasoning and critical review and analysis of the literature and/or laboratory/preclinical evidence.

- **Study Population:** The application should demonstrate the availability of and access to a suitable patient population that will support a meaningful outcome for the study. The application should include a discussion of how accrual goals will be achieved, as well as the strategy for inclusion of women and minorities in the clinical trial appropriate to the objectives of the study. The application should demonstrate how the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?).

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

- **Personnel and Environment:** The application should demonstrate the study team's expertise and experience in all aspects of conducting clinical trials, including appropriate statistical analysis, knowledge of FDA processes (if applicable), and data management. The application should include a study coordinator(s) who will guide the clinical protocol through the local Institutional Review Board (IRB) of record and other federal agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual. The application should show strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312), Subpart D, are fulfilled.

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

Funded trials are required to post a copy of the IRB-approved informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to file the study in the National Institutes of Health, National Library of Medicine clinical trials registry, www.clinicaltrials.gov. Refer to the General Submission Instructions, Appendix 1, Section C, for further details.

Multi-Institutional Clinical Trials: If the proposed clinical trial is multi-institutional, plans for the multi-institutional structure governing the research protocol(s) should be outlined in Attachment 9: Study Personnel and Organization. The lead organization responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements. In accordance with 32 CFR 219.114, a single IRB pathway is required for any U.S.-based research sites. The IRB-approved

master protocol and consent form must be reviewed by the OHRO prior to distribution to the additional sites for IRB review. Communication and data and specimen management among the collaborating institutions should be included in the appropriate sections of the proposal/application. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials. PIs are encouraged to integrate with existing DOD or other government-funded clinical trial networks if appropriate.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DOD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRDC OHARO, OHRO, prior to research implementation. This administrative review requirement is in addition to the local IRB or EC review. Local IRB/EC approval at the time of submission is ***not*** required. Allow up to 3 months to complete the OHRO regulatory review and approval process following submission of ***all required and complete*** documents to the OHRO. Refer to the General Application Instructions, Appendix 1, and the Human Research Protections Office Resources and Overview document available on the electronic Biomedical Research Application Portal (eBRAP) "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

II. Full Proposal/Application Submission Components for Studies With a Clinical Trial

The Grants.gov submission package includes the following components (refer to the General Submission Instructions, Section III, for additional information on proposal/application submission):

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

Attachments for Proposals/Applications With a Clinical Trial

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

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

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

rejection of the entire application. If recommended for funding, the clinical trial protocol will be requested.

- **Attachment 1: Project Narrative (20-page limit): Upload as "ProjectNarrative.pdf".** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

  Describe the proposed project in detail using the outline below.

  - **Background:** Describe in detail the rationale for the study. Provide a literature review and describe the preliminary studies and/or preclinical data that led to the development of the proposed clinical trial. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. Include a discussion of any current clinical use of the intervention under investigation and/or details of its study in clinical trials for other indications (as applicable). The Background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

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

  - **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses. The aims should agree with the primary aims and associated tasks described in the SOW.

  - **Study Design:** Describe the type of study to be performed (e.g., treatment, prevention, diagnostic), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to show a clear course of action. Describe the type of study to be performed (e.g., treatment, prevention, diagnostic), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to show a clear course of action.

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

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

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

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

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

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

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

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

- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study and all proposed correlative studies. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study. For phase 3 clinical trials, describe plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity as appropriate for the scientific goals of the study. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.

- **Attachment 2: Supporting Documentation: Combine and upload as a single file named "Support.pdf".** Start each document on a new page. If documents are scanned to PDF, the lowest resolution (100 to 150 dpi) should be used. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

  There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested or viewed as an extension of the Project Narrative will result in the removal of those items or may result in administrative withdrawal of the proposal/application.

- **References Cited:** List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

- **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols.

- **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and existing 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 are now accountable. There is no form for this information.

- **Publications and/or Patent Abstracts:** 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. A letter from each organization involved in the project should be provided. Letters of support not requested in this BAA, such as those from members of Congress, do not impact proposal/application review or funding decisions.

- **Letters of Collaboration (if applicable):** Provide a signed letter from each collaborating individual or organization that demonstrates that the investigator has the support of resources necessary for the proposed work. If an investigator at an intramural organization is named as a collaborator on a proposal/application submitted through an extramural organization, the proposal/application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.

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

- **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 from the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the ACOS/R&D or Clinical Service Chief confirming access to VA patients, resources, and/or VA research space. For VA PIs, if the VA NPC is not identified as the applicant institution for administering the funds, include a letter from the VA ACOS/R&D confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.

- **Collaboration with Military Facility (if applicable):** *If the project involves collaboration with a Military Facility, special requirements apply.* A DOD researcher, to include collaborating DOD PIs, must obtain a letter from his/her Commanding Officer or Military Facility Director authorizing his/her participation in the research project. This letter must be included with the proposal/application.

- **Joint Sponsorship (if applicable):** Describe present or prospective joint sponsorship of any portion of the program outlined in the proposal/application. In the absence of agreements between/among sponsors for joint support, the proposal/application should be structured so that the research can be carried out without the resources of any other sponsor. If, however, it is desirable to request partial support from another agency, the proposed plan should be stated and the reasons documented. If the plan cannot be formulated at the time the proposal/application is submitted, information should be sent later as an addendum to the proposal/application. Prior approval from both/all agencies must be secured for research to be undertaken under joint sponsorship. Provide letters of support related to recruitment, subject access, and data access plans.

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

  - **Background and Proprietary Information:** All software and data first produced under the award are subject to a federal purpose license. A term of the award requires the recipient to grant the government all necessary and appropriate licenses, which could include licenses to background and proprietary information that have been developed at private expense. Refer to the General Submission Instructions, Appendix 2, Sections C and D, for more information about disclosure of proprietary information.

    Therefore, it is important to disclose/list any intellectual property (software, data, patents, etc.) that will be used in performance of the project or provide a statement that none will be used. If applicable, all proprietary information to be provided to the government should be stated and identified; the applicant should indicate whether a waiver of the federal purpose license will be required.

  - **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

BAA. Demonstrate access to all intellectual property rights necessary for development and commercialization and evidence that the government has the ability to access such products or technologies.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf".** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  The structured technical abstract should be clear and concise and, at a minimum, provide the following information:

  - Background: Provide a brief statement of the ideas and theoretical reasoning behind the proposed work.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
  - Specific Aims: State concisely the specific aims of the study.
  - Study Design: Briefly describe the study design.
  - Relevance: Provide a brief statement explaining the potential relevance of the proposed work to the specific topic area being addressed and its impact on health outcomes.
  - Clinical Impact: Briefly describe how the proposed project will have an impact on research and patient care.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf".** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Lay abstracts should be written using the outline below. Do not duplicate the technical abstract.

  - Clearly describe the objectives and theoretical reasoning behind the proposed work in a manner readily understood by readers without a background in science or medicine.
  - Clearly describe the problem or question to be addressed and the ultimate applicability and impact of the research.
    - What types of patients will it help, and how will it help them? Include the current available statistics to the related injury/condition.

- What are the potential clinical applications, benefits, and risks?
- What is the projected timeline it may take to achieve the expected patient-related outcome?
- Describe how the proposed project will benefit Service Members, Veterans, and/or their family members.

- **Attachment 5: Statement of Work (three-page limit): Upload as "SOW.pdf".** The SOW outlines and establishes the performance expectations and milestones for which the USAMRDC may provide funding. The SOW will be incorporated into the award document and, as such, is subject to release under the Freedom of Information Act. The SOW should identify all collaborating research sites involved in the performance of the research. Suggested SOW formats and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). Recommended strategies for assembling the SOW can be found at https://ebrap.org/eBRAP/public/Program.htm. Refer to the "***Suggested SOW Strategy Clinical Research***", and use the blank SOW format titled "Suggested SOW Format". The SOW must be in PDF format prior to attaching.

  A series of relatively short statements should be included that comprise the approach to each of the major goals or objectives of the proposed research. The statements should outline the specific tasks, systems, key assessments/techniques, and materials that are reasonable estimates for testing the proposed hypotheses of the study. A timeline should be included that shows the work statements to be accomplished in each year of the award. Any animal use and/or human subjects recruitment should be included. Allow at least 2 to 3 months for the USAMRDC OHARO regulatory review and approval processes for studies involving human subjects and 2 to 3 months for studies involving animal subjects.

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

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

  Applicants and collaborating organizations may not use, employ, or subcontract for the use of any human participants, including the use of human anatomical substances, human data, and/or human cadavers until applicable regulatory documents are reviewed and approved by the USAMRDC OHARO to ensure that DOD regulations have been met.

  - **Study Population:** Describe the availability of the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Provide a table of anticipated enrollment counts at each study site. Demonstrate that the research team

has access to the proposed study population at each site, and describe the efforts that will be made to achieve accrual goals. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical studies (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention. Identify ongoing clinical studies that may compete for the same patient population and how they may impact enrollment progress. 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 clinical research proposing to include military personnel, refer to the General Submission Instructions, Appendix 1, for more information.***

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

- **Women and Minorities in the Study:** Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRDC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Describe the strategy for the inclusion of women and minorities 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 a planned enrollment table(s) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The PHS Inclusion Enrollment Report, Policy on Inclusion of Women and Minorities, and Frequently Asked Questions for the policy may be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

- **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, healthcare provider identification of potential subjects, recruitment databases, advertising).

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

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

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

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

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

  - 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 or not the potential human subject will be allowed to discuss the study with anyone before making a decision.

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

  - Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The performance site's IRB office 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 study. If applicable, please refer to the General Submission Instructions, Appendix 1, for more information.

  - ***Assent:*** If minors or other populations that cannot provide informed consent are included in the proposed clinical study, 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 IRB office to identify the conditions necessary for obtaining assent.

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

- **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 study. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

  - **Risk management and emergency response:**

    - Appropriate to the study's level of rise, describe how safety monitoring and reporting to the IRB and FDA (if applicable) will be managed and conducted.

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

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

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

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

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

- **Attachment 7: Intervention (no page limit): Upload as "Intervention.pdf".** The Intervention attachment should include the components listed below.

  - **Description of the Intervention:** Identify the intervention to be tested and describe the particular outcomes. Describe how the intervention addresses the clinical needs and how it compares with currently available interventions and/or standards of care. As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should

include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for the conduct of the clinical trial.

Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety and stability (as appropriate) of the intervention. Describe measures to ensure consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions).

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

- **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 8: Data Management (no page limit): Upload as "Data_Manage.pdf".** Describe the data management plan in accordance with DoD Instructions 3200.12, Enclosure 3, Section 3.c. Also, refer to General Submission Instructions, Section III, A.2, "Attachments Form, Attachment 2, Supporting Documentation," for more detailed information. The Data Management attachment should include the components listed below.

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

    - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.

    - **Confidentiality:**

      - Explain measures taken to protect the privacy of human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.

- ❖ Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DOD are eligible to review study records.

- ❖ Address requirements for reporting sensitive information to state or local authorities.

- **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time the data will be stored. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process. For FDA-regulated studies, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.

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

- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, including results from any screening or diagnostic tests performed as part of the study.

– **Laboratory Evaluations:**

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

- **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).

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

- **Laboratories 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

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

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

  - **Study Personnel Description:** Briefly describe the composition of the study team, including roles of the individuals listed in the organizational chart on the project. Study coordinator(s) should be included. Describe how the levels of effort for each individual are appropriate to successfully support the proposed research. Describe relevant background and qualifications that demonstrate appropriate expertise to accomplish the proposed work, including previous interactions with the FDA, if applicable.

  - **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial involves more than one institution, clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions. Provide a regulatory submission plan for the master protocol and master consent form by the lead institution. If the research involves more than one institution, a single IRB/EC review for all U.S.-based research sites institutions located in the United States. If applicable, describe how communication and data transfer between/among the collaborating institutions will occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.

- **Attachment 10: Research Data Collection Instruments, if applicable (no page limit): Upload as "Data_Collection.pdf".** The Research Data Collection Instruments attachment should include a copy of the most recent version of questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable. If the adaptation results in a deviation from validated instruments, please justify.

- **Attachment 11: Impact and Relevance to Military Health Statement (three-page limit): Upload as "Impact.pdf".**

  - Identify the volunteer population(s) that will participate in the proposed intervention, describe how they represent the target population that would benefit from the intervention, and describe the potential impact of the proposed clinical trial on the outcomes of individuals with the targeted disease or condition.

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

  - ***Describe the long-term impact:*** Explain the long-range vision for implementation of the intervention in the clinic or field, and describe the anticipated long-term benefits for the targeted population including how they may impact patient care and/or quality of life.

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

  - Describe any potential issues that might limit the impact of the proposed clinical trial and strategies that may be employed to overcome those issues.

  - Describe how the intervention represents an improvement over currently available interventions and/or standards of care.

  - Describe how the proposed study is responsive to the healthcare needs of military Service Members, Veterans, and/or beneficiaries. Provide information about the incidence and/or prevalence of the disease or condition in the general population as well as in military Service Members, Veterans, and/or beneficiaries.

  - If active-duty military, military families, and/or Veteran population(s) will be used in the proposed research project, describe the population(s) and the appropriateness of the population(s) for the proposed study. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Service Members, Veterans, and/or beneficiaries).

  - If applicable, show how the proposed research project aligns with DOD and VA areas of research interests. Provide a description of how the knowledge or technology gained from the research could be implemented in a dual-use capacity to benefit the civilian population and address a military need, as appropriate.

- **Attachment 12: Post-Award Transition Plan (two-page limit): Upload as "Transition.pdf".** Describe/discuss the methods and strategies proposed to move the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product

into the next phase of development. The post-award transition plan should include the components listed below.

- The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication. Describe in detail the FDA regulatory strategy, to include considerations for compliance with GMP, GLP, and GCP (if appropriate).
- Using Appendix VI as a guide, describe the maturity of the product and provide the current and projected research technology or knowledge readiness level (as appropriate) at the end of the proposed project or knowledge outcome.
- A description of the scientific or technical requirements needed to advance the research findings. Include steps necessary for FDA regulatory approval for the planning indication, and compliance with GMP, GLP, and GCP guidelines as appropriate.
- Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., partners, internal/external funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.
- For Knowledge Products, a description of collaborations and other resources that will be used to provide continuity of development including proposed development or modification of CPG and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. A "Knowledge Product" is a non-materiel product that addresses an identified need, topic area, or capability gap, is based on current evidence and research, aims to transition into medical practice, training, tools, or to support materiel solutions (systems to develop, acquire, provide, and sustain medical solutions and capabilities), and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.
- A timeline with defined milestones and deliverables describing the expected post-award progress of the results toward the next phase of development and eventual clinical impact.
- Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the government's ability to access such products or technologies in the future.
- A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 13: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** Provide the information requested below and provide supporting documentation as applicable.

Clinical trials must be initiated no later than 12 months after the award date. ***Note: The government reserves the right to withhold or withdraw funding if an IND or IDE is necessary to conduct the clinical trial but has not been obtained within 6 months of the award date.***

- State the product/intervention name.

For products/interventions that do not require regulation by the FDA or an international regulatory agency:

- Explain why the product/intervention is exempt from FDA oversight. Provide evidence that the proposed study does not require regulation by the FDA. If the proposed study will be conducted at international sites, provide equivalent information relevant to the host country(ies) regulatory requirements.

For products/interventions that require regulation by the FDA and/or an international regulatory agency:

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

- If the product is marketed in the United States, state the product label indication. State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population. Indicate whether the proposed research involves a change that increases the risks associated with using the product. State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).

- If the product is not currently FDA-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification. Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.

- **If an IND or IDE is required for the work proposed, the IND/IDE application must be submitted to the FDA prior to submission of the full proposal/application.** The IND or IDE should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed pilot clinical trial. Provide the date of submission, the application number, and existing copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold). If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency

meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.

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

- If an active IND or IDE for the investigational product is in effect, but the amendment is needed to include the proposed study, describe the type and nature of the amendments(s) ***and provide evidence of the submission within the proposal/application***. Indicate whether the amendment increases the risk of the intervention.

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

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

- Describe the overall regulatory strategy and product development plan that will support the planned product indication or product label change (if applicable). Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of FDA meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines. Identify and address the impact of intellectual property issues on product development and subsequent government access to products supported by this BAA.

- **Attachment 14: Representations: 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 Submission Instructions, Appendix 5, Section B, Representations.

- **Attachment 15: Suggested Collaborating DOD Military Facility Budget Format, if applicable: Upload as "MFBudget.pdf".** If a Military Facility (MHS facility, research laboratory, medical treatment facility, dental treatment facility, or a DOD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete a separate budget using "Suggested Collaborating DOD Military Facility Budget Format," available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm), including a budget justification, for each Military Facility as instructed. The costs per year should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Submission Instructions, Section III.A.8., for detailed information.

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

Research & Related Personal Data: Refer to the General Submission Instructions, Section III.A.3, for detailed information.

Research & Related Senior/Key Person Profile (Expanded): Refer to the General Submission Instructions, Section III.A.4, for detailed information.

- PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The National Institutes of Health (NIH) Biographical Sketch may also be used. All biographical sketches should be submitted in uneditable PDF format.

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

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

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

Research & Related Budget: Refer to the General Submission Instructions, Section III.A.5, for detailed information.

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

Project/Performance Site Location(s) Form: Refer to the General Submission Instructions, Section III.A.6, for detailed information.

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

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

Note: Proposals/applications from **federal agencies** must include in their budget justifications a **Federal Financial Plan**. Proposals/applications from organizations that include **collaborations with DOD Military Facilities** must comply with special requirements. Refer to the General Submission Instructions, Section III.A.5, "Research & Related Budget," for detailed information.

Intramural DOD Collaborator(s): Complete the Suggested Collaborating DOD Military Facility Budget Format and upload to Grants.gov attachment form as Attachment 15. (Refer to the General Application Instructions, Section IV.A.4, for detailed information.) Each Intramural DOD Collaborator should include costs per year on the Grants.gov Research & Related Budget Form under subaward costs.

III. Review Criteria for Research Proposals/Applications With a Clinical Trial

Peer Review: To determine technical merit, all proposals/applications will be evaluated according to the following scored criteria, which are listed in descending order of importance:

- **Clinical Impact**
    - How relevant the anticipated outcomes of the proposed clinical trial are to the targeted population.
    - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
    - How the potential outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals.
    - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
- **Research Strategy**
    - How well the scientific rationale for testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/ preclinical evidence.
    - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective.
    - How well the inclusion and randomization criteria meet the needs of the proposed clinical trial.
    - How well the exclusion criteria are justified.

- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.

- To what degree the data collection instruments, if applicable, are appropriate to the proposed study.

- **Statistical Plan**

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

  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.

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

- **Intervention**

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

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

  - How the intervention compares with currently available interventions and/or standards of care.

  - To what degree preclinical and/or clinical evidence supporting the safety of the intervention is provided.

  - Whether a member of the study team holds the IND/IDE for the indication proposed or whether the timeline proposed for obtaining the IND/IDE is appropriate (if applicable).

  - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.

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

  - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).

- **Recruitment, Accrual, and Feasibility**

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

- Whether access to the proposed human subjects population is demonstrated.
- The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
- How well the proposal/application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
- To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?).

- **Ethical Considerations**
  - How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
  - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
  - To what degree confidentiality and privacy issues are appropriately considered.
  - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Personnel and Communication**
  - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
  - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
  - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
  - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.

- **Transition Plan and Regulatory Strategy**
  - Whether the identified next level of development and/or commercialization is realistic.
  - Whether the application appropriately addresses available opportunities and potential barriers that could impact the progress of commercializing and/or translating the study

results into clinical practice to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into clinical practice, and/or approval by the FDA) are achievable.

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

- How the regulatory strategy and development plan to support a product label change, if applicable, is appropriate and well described.

- Whether the proposed collaborations and other resources for providing continuity of development, including proposed development or modification of CPG and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications are established and/or achievable.

- Whether the timeline for expected post-award progress is reasonable and contains appropriate milestones and deliverables for advancing the study results toward clinical impact.

- Whether the potential risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.

- How well the proposal/application identifies intellectual property ownership, describes any appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this BAA.

- Whether the applicant has demonstrated that they have access to all intellectual property rights necessary for development and commercialization and evidence that the government has the ability to access such products or technologies.

- **Budget**

  - Whether the budget is appropriate for the proposed research.

- **Environment**

  - To what degree the scientific environment, clinical setting, and accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).

  - Whether there is evidence for appropriate institutional commitment from each participating institution.

  - If applicable, to what degree the intellectual and material property plan is appropriate.

Programmatic Review: To make funding recommendations, the following criteria will be used by programmatic reviewers:

- Scientific peer review results
- Adherence to the intent of the award mechanism
- Program portfolio composition and priorities
- Relative military benefit
- Relative innovation, impact, and translatability

Note: Military-relevant research must be responsive to the healthcare needs of the Armed Forces, family members of the Armed Forces, and the U.S. Veteran population. Proposals/ applications must address a military-relevant health problem responsive to one of the Research Areas of Interest identified in Section II.A and Appendix I.

IV. Checklist for Research Proposal/Application Submission With a Clinical Trial

Application Components	Action	Completed
SF424 (R&R) Application for Federal Assistance	Complete form as instructed.	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf"	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf"	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf"	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf"	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf"	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 6 with file name "HumSubProc.pdf"	
	Intervention: Upload as Attachment 7 with file name "Intervention.pdf"	
	Data Management: Upload as Attachment 8 with file name "Data_Manage.pdf"	
	Study Personnel and Organization: Upload as Attachment 9 with file name "Personnel.pdf"	
	Research Data Collection Instruments: Upload as Attachment 10 with file name "Data_Collection.pdf," if applicable	
	Impact and Relevance to Military Health Statement: Upload as Attachment 11 with file name "Impact.pdf"	
	Post-Award Transition Plan: Upload as Attachment 12 with file name "Transition.pdf"	
	Regulatory Strategy: Upload as Attachment 13 with file name "Regulatory.pdf"	
	Representations: Upload as Attachment 14 with file name "RequiredReps.pdf"	
	DOD Military Budget Form(s): Upload as Attachment 15 with file name "MFBudget.pdf" if applicable	
Research & Related Personal Data	Complete form as instructed.	

Application Components	Action	Completed
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
	Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
Research & Related Subaward Budget Attachment(s) Form, if applicable	Complete form as instructed.	

APPENDIX III: DOD AND VA WEBSITES

PIs are encouraged to integrate and/or align their research projects with DOD and/or VA research laboratories and programs. Collaboration with DOD or VA investigators is also encouraged. Below is a list of websites that may be useful in identifying additional information about DOD and VA areas of research interest, ongoing research, or potential opportunities for collaboration.

Air Force Office of Scientific Research
https://www.afrl.af.mil/AFOSR/

Air Force Research Laboratory
https://www.afrl.af.mil

Armed Forces Radiobiology Research Institute
https://afrri.usuhs.edu/home

Combat Casualty Care Research Program
https://cccrp.health.mil/Pages/default.aspx

Congressionally Directed Medical Research Programs
https://cdmrp.health.mil

Defense Advanced Research Projects Agency
https://www.darpa.mil/

Defense Health Agency
https://health.mil/About-MHS/OASDHA/Defense-Health-Agency

Defense Technical Information Center
https://www.dtic.mil

Defense Threat Reduction Agency
https://www.dtra.mil/

Military Health System Research Symposium
https://mhsrs.health.mil/SitePages/Home.aspx

Military Infectious Diseases Research Program
https://midrp.health.mil/

Military Operational Medicine Research Program
https://momrp.health.mil/

Naval Health Research Center
https://www.med.navy.mil/Naval-Medical-Research-Center/R-D-Commands/Naval-Health-Research-Center/

Navy Bureau of Medicine and Surgery
https://www.med.navy.mil/

Naval Medical Research Center
https://www.med.navy.mil/Naval-Medical-Research-Center/

Navy and Marine Corps Public Health Center
https://www.med.navy.mil/Navy-Marine-Corps-Public-Health-Center/Pages/Home/

Office of Naval Research
https://www.nre.navy.mil/

Office of the Under Secretary of Defense for Acquisition, Technology and Logistics
https://www.acq.osd.mil/

Telemedicine and Advanced Technology Research Center
https://www.tatrc.org/www/

Uniformed Services University of the Health Sciences
https://www.usuhs.edu/research

U.S. Air Force 59th Medical Wing
https://www.59mdw.af.mil

U.S. Army Aeromedical Research Laboratory
https://usaarl.health.mil/

U.S. Army Combat Capabilities Development Command
https://www.army.mil/devcom

U.S. Army Institute of Surgical Research
https://usaisr.health.mil/

U.S. Army Medical Research and Development Command
https://mrdc.health.mil/

U.S. Army Medical Research Institute of Infectious Diseases
https://usamriid.health.mil/

U.S. Army Research Institute of Environmental Medicine
https://usariem.health.mil/

U.S. Army Research Institute for Behavioral and Social Sciences
https://ari.altess.army.mil/

U.S. Army Research Laboratory
https://www.arl.army.mil

U.S. Army Sharp, Ready & Resilient Directorate
https://www.armyresilience.army.mil/sharp/index.html

U.S. Department of Defense Blast Injury Research Program
https://blastinjuryresearch.health.mil/

U.S. Department of Veterans Affairs, Office of Research and Development
https://www.research.va.gov

U.S. Naval Research Laboratory
https://www.nrl.navy.mil

Walter Reed Army Institute of Research
https://www.wrair.army.mil/

APPENDIX IV: PROCEDURES FOR ACQUISITION, PROCESSING, STORAGE, AND SHIPMENT OF BIO-FLUIDS

The following pre-analytical variables should be recorded when collecting bio-fluids:

- Time of sample collection
- Time of sample freezing and the interval between collection and freezing
- Temperature of freeze
- Needle size and type (21 G preferred)
- Tube collection order
- Tube labels
- Centrifugation parameters
- Handling, shipping, and storage temperature
- Tube handling
- Small aliquot size
- Sample storage quality control

The following subject characteristics should be recorded when collecting bio-fluids:

- Fasting and diet
- Therapy
- Time of day
- Physical activity
- Acute state (rested?)
- Body position

APPENDIX V: NATIONAL INSTITUTE OF MENTAL HEALTH DATA ARCHIVE — INFORMED CONSENT

Psychological Health, Human Subjects Studies
Informed Consent and Data Repository

Data from this study may be submitted to the NDA. NDA is a data repository run by the NIMH that allows researchers studying mental illness to collect and share deidentified information with each other. A data repository is a large database where information from many studies is stored and managed. Deidentified information means that all personal information about research participants such as name, address, and phone number is removed and replaced with a code number. With an easier way to share, researchers hope to learn new and important things about mental illnesses more quickly than before.

During and after the study, the researchers will send deidentified information about your health and behavior and in some cases, your genetic information, to NDA. Other researchers nationwide can then file an application with the NIMH to obtain access to your deidentified study data for research purposes. Experts at the NIMH who know how to protect health and science information will look at every request carefully to minimize risks to your privacy.

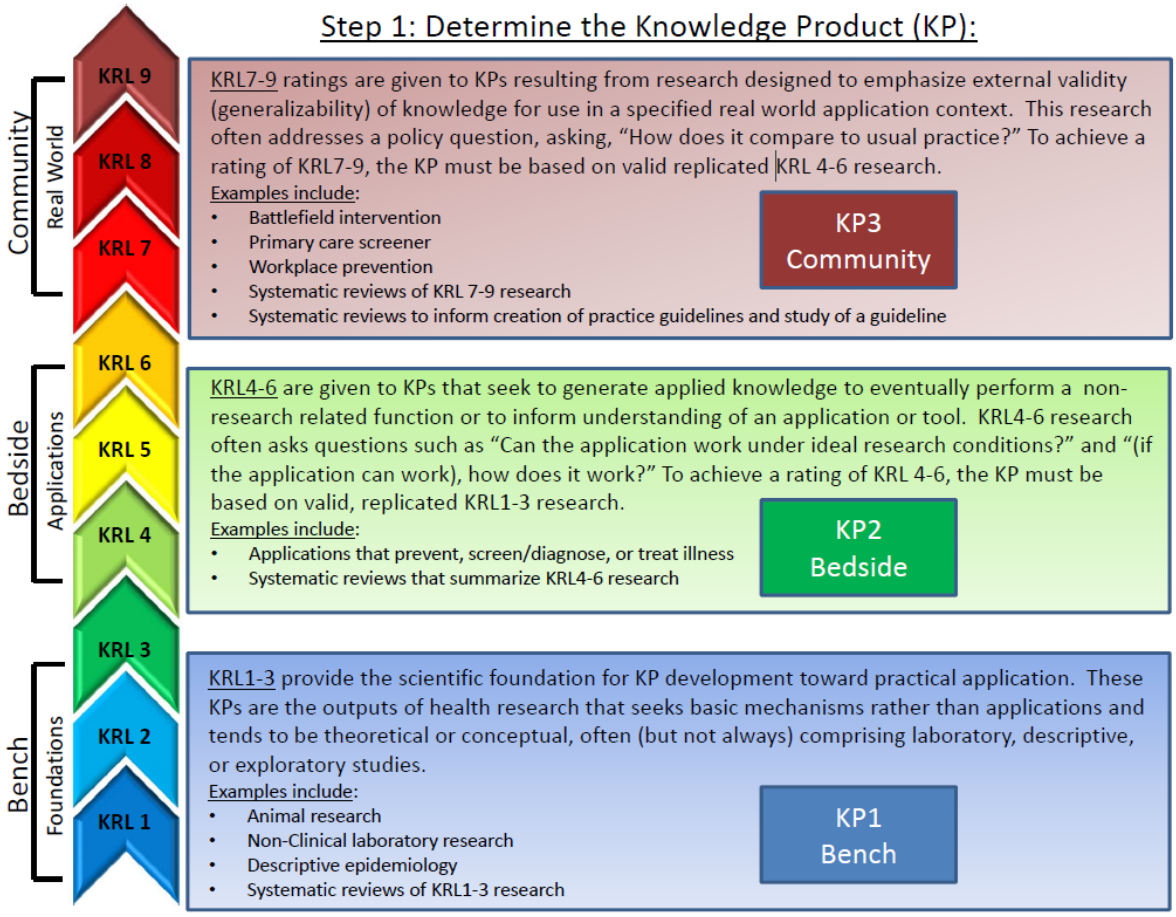
You may not benefit directly from allowing your information to be shared with NDA. The information provided to NDA may help researchers around the world treat future children and adults with mental illnesses so that they have better outcomes. NIMH will also report to Congress and on its website about the different studies that researchers are conducting using NDA data. However, you will not be contacted directly about the data you contributed to NDA.

You may decide now or later that you do not want to share your information using NDA. If so, contact the researchers who conducted this study, and they will tell NDA, which can stop sharing the research information. However, NDA cannot take back information that was shared before you changed your mind. If you would like more information about NDA, this is available on-line at https://nda.nih.gov/.

APPENDIX VI: TECHNOLOGY READINESS LEVELS AND KNOWLEDGE READINESS LEVELS

Technology Readiness Levels (TRLs): TRLs are used to categorize the product maturity of materiel solutions. The DOD Technology Readiness Assessment (TRA) Deskbook, is a reference for systematic assessment of technical maturity of relevant materiel solutions. For biomedical applications, Biomedical TRL definitions and descriptions have been developed which account for regulatory context for technology maturity and *intended context of use*. Information on Biomedical TRLs can be found in Appendix E of the DOD TRA Deskbook (July 2009, https://apps.dtic.mil/docs/citations/ADA524200).

Knowledge Readiness Levels (KRLs): The scientific maturity of knowledge products resulting from biomedical research are not assessed in the same manner as materiel solutions. At the request of the U.S. Army Medical Research and Development Command, the Rand Corporation developed and released a framework to assess the relative scientific maturity of knowledge products. This process is described in a 2019 Rand Corporation Report (https://www.rand.org/pubs/research_reports/RR2127.html). The figures below represent a quick reference guide for assessing KRLs for knowledge products.



APPENDIX VII: ACRONYMS AND ABBREVIATIONS

ACOS/R&D	Associate Chief of Staff for Research and Development
ARRIVE	Animal Research: Reporting *In Vivo* Experiments
ARS	Acute Radiation Syndrome
BAA	Broad Agency Announcement
BoNT	Botulinum Neurotoxin
BSV	Biosurveillance
BSVE	Biosurveillance Ecosystem
CCCRP	Combat Casualty Care Research Program
CDE	Common Data Element
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
cGMP	Current Good Manufacturing Practices
CIH	Complementary and Integrative Health
CPG	Clinical Practice Guidelines
CFR	Code of Federal Regulations
COI	Conflict of Interest
DFARS	Defense Federal Acquisition Regulation Supplement
DOD	Department of Defense
DoDAF	Department of Defense Architecture Framework
DoDEA	Department of Defense Education Activity
DoDGARs	Department of Defense Grant and Agreement Regulations
DoDI	Department of Defense Instruction
DTRA	Defense Threat Reduction Agency
eBRAP	electronic Biomedical Research Application Portal
EC	Ethics Committee
EO	Executive Order
FAPIIS	Federal Awardee Performance and Integrity Information System
FAR	Federal Acquisition Regulation
FDA	U.S. Food and Drug Administration
FFRDC	Federally Funded Research and Development Center
FITBIR	Federal Interagency Traumatic Brain Injury Research
FY	Fiscal Year
GA	Tabun
GB	Sarin
GD	Soman
GCP	Good Clinical Practices

GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
IT	Information Technology
JBCF	Joint Biosurveillance Common Framework
JSTO-CBD	Joint Science and Technology Office for Chemical and Biological Defense
KRL	Knowledge Readiness Level
LAR	Legally Authorized Representative
LET	Linear Energy Transfer
MBDRP	Medical Biological Defense Research Program
MCDRP	Medical Chemical Defense Research Program
MCM	Medical Countermeasure
MDO	Multi-Domain Operations
MHS	Military Health System
MIDRP	Military Infectious Diseases Research Program
MOMRP	Military Operational Medicine Research Program
NATO	North Atlantic Treaty Organization
NDA	National Institute of Mental Health Data Archive
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NPC	Non-Profit Corporation
NRAP	National Research Action Plan
OHRO	Office of Human Research Oversight (previously, Human Research Protection Office [HRPO])
OHARO	Office of Human and Animal Research Oversight (previously, Office of Research Protections [ORP])
PI	Principal Investigator
PTSD	Post-Traumatic Stress Disorder
RTD	Return to Duty
SAM	System for Award Management
SBIR	Small Business Innovation Research
SOW	Statement of Work
S&T	Science and Technology
STEM	Science, Technology, Engineering, or Mathematics
TBI	Traumatic Brain Injury

TRA	Technology Readiness Assessment
TRL	Technology Readiness Level
UDE	Unique Data Element
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
USASOC	U.S. Army Special Operations Command
USC	United States Code
VA	Department of Veterans Affairs