I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Defense Medical Research and Development Program (DMRDP)

Joint Program Committee 2 (JPC-2)/Military Infectious Diseases Research Program (MIDRP) and JPC-6/Combat Casualty Care Research Program (CCCRP) Battlefield Wound Management and Infection Research (BWMIR) Award

Intramural Funding Opportunity

Announcement Type: Initial

Funding Opportunity Number: W81XWH-22-DMRDP-BWMIR

Assistance Listing Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), October 20, 2022
- **Application Submission Deadline:** 11:59 p.m. ET, November 16, 2022
- **End of Application Verification Period:** 5:00 p.m. ET, November 21, 2022
- **Peer Review:** January 2023
- **Programmatic Review:** March 2023

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II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

This funding opportunity is intended for intramural applicants only.

- An ***intramural applicant organization*** is defined as a Department of Defense (DOD) laboratory, DOD military treatment facility, and/or DOD activity embedded within a civilian medical center. ***Intramural Submission: An 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.***

- An ***extramural applicant organization*** is defined as all those not included in the definition of intramural investigators, above. Examples of extramural organizations include academic institutions, biotechnology companies, foundations, federal government organizations other than the DOD, and research institutes (e.g., intramural investigators submitting through a research foundation). Submissions from extramural investigators to this funding opportunity announcement will be withdrawn. ***Extramural Submission: An application submitted by a non-DOD organization to Grants.gov.***

Extramural applicants applying through extramural organizations should use the separate funding opportunity announcement that is available through the electronic Biomedical Research Application Portal (eBRAP) at https://eBRAP.org/ under funding opportunity number W81XWH-22-S-DMRDP-BWMIR.

II.A. Program Description

Applications to the Fiscal Year 2022 (FY22) Joint Program Committee 2/Military Infectious Diseases Research Program (JPC-2/MIDRP) and JPC-6/Combat Casualty Care Research Program (CCCRP) Battlefield Wound Management and Infection Research (BWMIR) Award are being solicited for the Defense Health Agency (DHA) J9, Research and Development Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA manages the Defense Health Program (DHP) Research, Development, Test and Evaluation (RDT&E) appropriation. The U.S. Army Medical Research and Development Command (USAMRDC) Congressionally Directed Medical Research Programs (CDMRP) provides DMRDP execution management support for DHP core research program areas, including the JPC-2/MIDRP and JPC-6/CCCRP. This funding opportunity announcement and subsequent awards will be managed and executed by CDMRP on behalf of the JPC-2/MIDRP and JPC-6/CCCRP.

The JPC-2/MIDRP and JPC-6/CCCRP are two of three major research program areas within the DHP. The JPC-2/MIDRP and JPC-6/CCCRP are committees of DOD and non-DOD medical and military technical experts in combat casualty care- and infectious disease-related program areas.

The MIDRP strives to defeat infection by developing solutions to prevent, treat, and diagnose 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 (versus treatment post-infection), is the most cost-effective approach, and reduces casualty rates. Improved diagnosis and treatment of infectious disease casualties is necessary to protect the U.S. Armed Forces. Due to the ever-increasing resistance to currently available treatments, continued countermeasure developments need to be pursued. The vision of the MIDRP wound infections capability area is to conduct basic and applied research leading to the development of rapid identification, prevention, and effective treatment solutions to mitigate complications from multidrug-resistant wound infections in multi-domain operations (MDOs) and during prolonged care. However, without understanding how current standard of care interventions work best to prevent, delay, or treat infection, MIDRP cannot lead and develop new medical countermeasures.

The CCCRP strives to optimize survival and recovery from combat-related injury in current and future operational scenarios. This is accomplished through the development of knowledge and materiel solutions for the acute and early management of combat-related trauma, including point-of-injury, en route, and forward surgical care. Service Members face many threats in hostile fire arenas, whether conducting large-scale mechanized warfare, low-intensity conflicts, or operations other than war. Military casualties may wait for hours before definitive health care can be provided. Furthermore, initial treatment and subsequent evacuation may occur in austere environments characterized by limited supplies and limited diagnostic and life-support equipment, and provision of acute and critical care is labor-intensive and must frequently be provided by non-physician medical personnel. The primary challenge for combat casualty care research is to overcome these limitations by providing biologics, pharmaceuticals, and devices that enhance the capability of first responders to effectively treat casualties as close to the geographic location and time of injury as possible, with a reduced logistical footprint.

The overarching gap in battlefield wound management and infection research is in understanding the complex physiology of combat traumatic wounds to guide researchers and physicians in their efforts to better manage these wounds and limit infection. The DOD seeks to address this gap through refined preclinical and clinical studies to inform clinical practice guidelines aimed at delivering better care for these devastating wounds.

II.A.1. FY22 DMRDP BWMIR Focus Areas

The DMRDP BWMIR Award will support the research and development of materiel and knowledge products to address critical gaps in combat traumatic wound management and control of infection, in operational environments. Specifically, research that supports the understanding of physiological processes of combat-associated traumatic wounds and infections in preclinical and clinical models represents a key priority for the JPC-2/MIDRP and JPC-6/CCCRP. The Focus Areas below broadly describe areas of particular interest for funding under the FY22 DMRDP BWMIR. **To meet the intent of the award mechanism, applications submitted to the FY22 DMRDP BWMIR *must address at least one of the FY22 DMRDP BWMIR Focus Areas* listed below**. Research not aligned to at least one Focus Area will not be considered for funding. Selection of the appropriate FY22 DMRDP BWMIR Focus Area(s) is the responsibility of the applicant.

- Understanding appropriate wound prophylaxis/empiric treatment strategies throughout continuum of care, regardless of injury status, through preclinical and clinical studies to inform clinical practice guidelines for:

    - Managing hemorrhagic shock/super-massive transfusion, traumatic limb ischemia (secondary to vascular disruption or tourniquet use), complex soft tissue injury/blast injury, open fracture, and/or frost bite, including evaluation of antimicrobial dosing and tissue penetration studies.

    - Expanding the understanding of antibiotic use in tissue injury (e.g., systemic versus topical), especially in the context of hemorrhage/resuscitation, blast, and/or delayed evacuation times

- Understanding combat traumatic wound physiology and wound progression through preclinical and clinical studies to inform clinical practice guidelines and standard of care efficacy and gaps.

- Optimizing prolonged care management of penetrating torso injury by developing solutions for prevention/management of deep space infections (e.g., bacterial or fungal) and delays in care of penetrating abdominal injury.

- Development of analysis and decision support tools to guide traumatic combat wound care and casualty management to triage, prevent and/or treat infections. Examples include:

    - Technologies to determine the types of wound infections at risk of progression to complications and sepsis;

    - Tools to evaluate tissue status before devitalization; and

    - Guided triage/intervention techniques to be used by front-line providers at early stages of care.

II.A.2. Award Background

Force strength and lethality are primary missions of the Armed Forces; therefore, operational readiness must include the ability of healthcare providers to render medical treatment to allow maximal return to duty among military Service Members. In the wars in Iraq and Afghanistan, the U.S. military achieved the highest rate of survival from battlefield injuries in history. The wounded-to-killed ratio more than doubled, from 4:1 during last century's world wars, to 10:1 today.[1] Substantial credit for this achievement is due to a 2009 congressional mandate that stated wounded Warfighters should be provided with life-saving care within 60 minutes of injury, a timespan that was previously referred to as the "golden hour." This timeframe was defined by technical and tactical advantages supporting movement of the Warfighter. Current trauma care has shifted away from a specific "golden hour" time frame especially in evolving battlespace

[1]Kotwal RS, Howard JT, Orman JA, et al. 2016. The effect of a golden hour policy on the morbidity and mortality of combat casualties. *JAMA Surgery* 151(1):15-24.

environments. Historically, numerous multi-Service medevac assets, forward surgical teams (Role 2), and combat support hospitals (Role 3) were made available across the battlespace environment enabling rapid transportation of casualties away from the point of injury. Future combat scenarios may require Warfighter operations and movement against peer or near-peer adversaries in large-scale combat operations (i.e., MDOs) where evacuation capabilities are delayed or unavailable. The expanded battle space of competitive and armed conflict as well as medical and casualty care may require support for dispersed and sometimes isolated Forces under difficult conditions such as dense urban, subterranean, maritime, high-altitude, dust storm, extreme environments, and other austere conditions. *Limited access to clinic-based providers and potential restriction on Warfighter movement necessitates the ability to bring effective and efficient life-saving capabilities closer to the point of injury and with the ability to provide prolonged care (greater than 72 hours) where necessary.*

Prolonged care is a critical challenge to combat casualty care and consists of initial damage control efforts in the out-of-hospital or austere environments using limited resources. Effective prolonged care is intended to sustain a critically injured patient until the patient arrives at the next appropriate level of care, while decreasing patient mortality and morbidity. Focusing on wound infection and wound management solutions and strategies addresses multidisciplinary aspects of multimodal therapies and surgical treatment. Advancements will lead to faster recovery, fewer lost duty days, reduced healthcare and training time costs, and reduced mortality caused by pathogens in combat traumatic wounds.

Combat traumatic wound infections in a prolonged care environment are a major risk to Warfighter survivability and their ability to return to battle, posing a significant burden to a Military Health System that has little to no capacity for significant periods of time during MDOs. Research has shown that greater than 30% of all combat wounds become infected.[2] That percentage is expected to rise in a prolonged care environment; hence, integrated interventions provided by Tactical Combat Casualty Care (TCCC) providers at the point of injury are critically important to diminish the occurrence of infection in battlefield wounds.

Trauma care in complex and austere environments is not limited to military contexts. Civilian emergency medical care provided in rural settings or during natural disasters, public health crises, and mass-casualty events draw on lessons learned in battlefield medicine. Solutions addressing medical challenges during combat operations can be integrated into civilian-based practice to minimize the morbidity and mortality of traumatic injuries in any environment to achieve a goal of zero preventable deaths, regardless of environment. The JPC-2/MIDRP and JPC-6/CCCRP expect approaches and technologies developed under the DMRDP BWMIR to improve survivability of injuries sustained in both combat and civilian settings.

II.B. Award Information

The DMRDP BWMIR Award seeks to enhance combat traumatic wound care capabilities throughout the medical continuum of care, which may be complicated by combat operations, limited resources, austere conditions, and/or mass casualty events. The intent of the FY22

[2] Tribble DR, Murray CK, Lloyd BA, et al. 2019. After the Battlefield: Infectious complications among wounded warriors in the Trauma Infectious Disease Outcomes Study. *Mil Med* 184(Suppl 2):18-25.

DMRDP BWMIR Award is to support research that will increase the understanding of complex wound physiology and infection control, in order to support future application and maturation of products, technologies, and clinical practice. Research that advances and/or repurposes existing solutions and has the potential to be broadly applicable is advantageous, but not required. Additionally, submissions may present advances benefiting military health and medicine as well as the general public.

Applicants may leverage existing resources in translational research to address high-impact research ideas or unmet needs to enable the delivery of life-saving care to the Warfighter during prolonged and en route care in austere and combat environments. ***For this award mechanism, the definition of "leveraging" is as follows: carrying out a research project based on existing resources in order to amplify potential gains in knowledge or accelerate technical maturity*.** Research of interest may include knowledge products, i.e., "knowledge resulting from research with the potential to improve individual or public health,"[3] and solutions that can accelerate the introduction of military-relevant health products or technologies into clinical and/or operational use. Projects should take into consideration the varied expertise levels of targeted medical providers, available resources, and the possible diverse environmental conditions in combat situations. Application submissions are encouraged to include characteristics relevant to military use in the pre-hospital, combat operational setting. Submissions that propose solutions to advance civilian trauma care are not precluded, since civilian trauma and trauma care in the military are mutually influential and may be co-occurring in certain situations.

Applications in response to this funding opportunity may *not* be used to support fundamental basic research. For this funding opportunity, basic research is defined as research directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications toward process or products in mind. Applied and preclinical research, including animal studies, that is already supported by substantial preliminary or published data, and is designed to validate clinical translation, is appropriate for this award mechanism.

This funding opportunity may be used to support preclinical research, clinical research, and small-scale clinical trials (e.g., first in human, phase 1/1b). *Phase 2 and phase 3 clinical trials for U.S. Food and Drug Administration (FDA) licensure of drugs and definitive/pivotal testing for device clearance by the FDA will NOT be permitted under this funding opportunity.* **This funding opportunity may *not* be used to support studies requiring an exception from informed consent (EFIC).**

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

[3]Engel CC, Silberglitt R, Chow BG, et al. 2019. Development of a knowledge readiness level framework for medical research. Santa Monica, CA: RAND Corporation, RR-2127-OSD. https://www.rand.org/pubs/research_reports/RR2127.html.

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

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 Code of Federal Regulations, Title 32, Part 219 (32 CFR 219).

The proposed research must be relevant to active-duty Service Members and the American public.

The FY22 DMRDP BWMIR Award has two different funding level options based on the scope of the research proposed. It is the responsibility of the applicant to select the funding level that is most appropriate for the proposed research project. The government reserves the right to fund an application at a lower funding level.

Funding Level 1: Preclinical research studies supported by substantial preliminary or published data. Clinical research and clinical trials are not allowed. Anticipated total costs of Funding Level 1 will not exceed $1.2 million (M).

Funding Level 2: Studies including clinical research or clinical trials supported by substantial preliminary or published data. Research proposed under Funding Level 2 may include some preclinical activities, but must include some aspect of clinical research or a clinical, but must include some aspect of clinical research or a clinical trial. Anticipated total costs of Funding Level 2 will not exceed $2.2M.

For projects proposing a clinical trial or clinical studies:

- *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 Investigational New Drug (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 FY22 DMRDP BWMIR Award 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, 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 FY22 DMRDP BWMIR Award 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.

- If the proposed clinical trial of an investigational product will be conducted at international sites, evidence that an application to the relevant national regulatory agency of the host country(ies) has been submitted or approved must be included in the FY22 DMRDP BWMIR Award application.

- ***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 9, Regulatory Strategy, for further details.

- If a clinical trial is proposed in the DMRDP BWMIR Award application, the trial must be initiated no later than **month 9** of the initial period of performance.

Refer to Section II.D.4, Funding Restrictions, for detailed funding information.

Awards will be made no later than September 30, 2023. For additional information refer to Section II.F.1, Federal Award Notices.

The JPC-2/MIDRP and JPC-6/CCCRP expect to allot approximately $9.39M of FY22 and $7.29M of FY23 DHP RDT&E funds to support approximately 7 to 10 DMRDP BWMIR Award applications. Funding of applications received is contingent upon the availability of federal funds for this program as well as the number of applications received, the quality and merit of the applications as evaluated by scientific and programmatic review, and the requirements of the government. It is anticipated that awards made from this FY22 funding opportunity will be funded with FY22 funds, which will expire for use on September 30, 2028; and FY23 funds, which will expire for use on September 30, 2029. As of the release date of this funding opportunity announcement, the FY23 Defense Appropriations Bill has not been passed and there is no guarantee that any additional funds will be made available to support this program. The funding estimated for this funding opportunity announcement is approximate and subject to realignment. Funding of applications received in response to this funding opportunity announcement is contingent upon the availability of federal funds for this program. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds.

Applications received in response to both the extramural FY22 DMRDP BWMIR broad agency announcement (W81XWH-22-S-DMRDP-BWMIR) and this intramural program announcement will be evaluated and considered for funding together. The government reserves the right to fund any combination of extramural and/or intramural applications.

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), OHARO's 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 OHARO OHRO regulatory review and approval processes following submission of ***all required and complete*** documents to the OHRO. Refer to Appendix IV, 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, a written plan for single IRB review arrangements must be provided at the time of application submission or award negotiation. The lead institution responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements.

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 Landis, S.C., et al., A call for transparent reporting to optimize the predictive value of preclinical research, *Nature* 2012, 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards were written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in research and should be applied consistently across translational studies. Projects that include research on animal models are required to submit Attachment 8, Animal Research Plan, as part of the application package to describe how these standards will be addressed. 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.

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

Research Involving Animals: All research funded by the FY22 DMRDP BWMIR involving new and ongoing research with animals must be reviewed and approved by the USAMRDC OHRO 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 Appendix IV for additional information.

The CDMRP intends that information, data, and research resources generated under awards funded by this program announcement be made available to the research community (which

includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to Appendix V, Section K.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: ***Applications for this program announcement may only be submitted by intramural organizations. Submissions from extramural applicants to this program announcement will be withdrawn.*** Intramural applicants are required to explain how their applications do not overlap with other funded efforts. Applicants from an extramural organization should apply through eBRAP under the funding opportunity number W81XWH-22-S-DMRDP-BWMIR. 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: An 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.***

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

II.C.1.b. Principal Investigator (PI)

Independent investigators at all academic levels (or equivalent) are eligible to be named by the organization as the PI in the application.

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

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

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

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

It is expected that the work funded through this intramural program announcement will be performed by an intramural DOD organization. It is permissible, however, for an extramural investigator to be named as a collaborator in a submission from an intramural investigator. In such cases, the intramural organization will receive all funds and is responsible for executing all necessary awards to collaborating partners through their agency's procedures. Regardless of location, any work that is to be performed by associated non-DOD organizations must be limited to work performed under existing contracts, and resource sharing should be accomplished through Cooperative Research and Development Agreements (CRADAs) or Material Transfer Agreements (MTAs). The government reserves the right to administratively withdraw any application that does not meet these eligibility criteria. ***Applications that require research to be performed by a non-DOD organization under a new service contract will not be considered for funding.***

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.

Refer to Section II.H.1, Administrative Actions, for a list of administrative actions that may be taken if a pre-application or application does not meet the administrative, eligibility, or ethical requirements defined in this program announcement.

II.D. Application and Submission Information

II.D.1. eBRAP

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

eBRAP allows an organization's representatives and PIs to view and modify the full application submissions associated with them and will validate full application files against the specific program announcement requirements. Discrepancies will be noted in an email to the PI and in the "Full Application Files" tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this program announcement.

Contact information for the eBRAP Help Desk can be found in Section II.G, Agency Contacts.

Intramural DOD Submission:

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

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

Submission is a two-step process requiring both ***pre-application*** and ***full application*** through eBRAP (eBRAP.org) as indicated below. The submission process should be started early to avoid missing deadlines. There are no grace periods. Refer to Table 1, Full Application Guidelines for full application submission guidelines.

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

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

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

To begin the pre-application process, first select whether the submitting organization is extramural or intramural, then confirm your selection or cancel. **Incorrect selection of extramural or intramural submission type will delay processing.** ***Note: Applications for this program announcement may only be submitted by intramural DOD organizations.*** Submissions from extramural organizations to this program announcement 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-application components must be submitted by the PI through eBRAP (https://eBRAP.org/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

The applicant organization and associated PI identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the applicant must contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

A change in PI or organization after submission of the 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 CDMRP DMRDP Program Manager.

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

The pre-application consists of the following components, which are organized in eBRAP by separate tabs:

- **Tab 1 – Application Information**

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

- **Tab 2 – Application Contacts**

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

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

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

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

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

  FY22 DMRDP BWMIR Award Programmatic Panel members should not be involved in any pre-application or application. For questions related to panel members and pre-applications or applications, refer to Section II.H.1.c, Withdrawal, or contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

- **Tab 4 – Conflicts of Interest**

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

- **Tab 5 – Pre-Application Files**

  Letter of Intent (LOI) (one-page limit): Provide a brief description of the research to be conducted. Include the focus area under which the application will be submitted as well as intended funding level. LOIs are used for program planning purposes only (e.g., reviewer recruitment) and will not be reviewed during either the peer or programmatic review sessions. An invitation to submit is ***not*** required.

- **Tab 6 – Submit Pre-Application**

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

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

Full application components, which are listed in Table 1 below, must be submitted by the PI through eBRAP.

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

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

Table 1. Full Application Submission Guidelines

Application Package Location
Download application package components for W81XWH-22-DMRDP-BWMIR from eBRAP (https://ebrap.org).
Full Application Package Components
Tab 1 – Summary: Provide a summary of the application information. **Tab 2 – Application Contacts:** This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.
Tab 3 – Full Application Files: Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components: • Attachments • Key Personnel • Budget • Performance Sites **Tab 4 – Application and Budget Data:** Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.
Application Package Submission
Submit package components to eBRAP (https://ebrap.org). **Tab 5 – Submit/Request Approval Full Application:** After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided next to "Enter Your Password Here" and press the "Submit Full Application" button. eBRAP will notify your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official by email. ***Do not password protect any files of the application package, including the Project Narrative.***
Application Verification Period
After eBRAP has processed the full application, the organizational Resource Manager/Comptroller/ Task Area Manager or equivalent Business Official and PI will receive email notification of this status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package may be modified ***with the exception of the Project***

Narrative and Research & Related Budget Form. Your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official should log into eBRAP to review and to approve prior to the application verification deadline.

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

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

For the FY22 DMRDP BWMIR Award program announcement, the eBRAP application package includes the following components, which are organized in eBRAP by separate tabs. **To access these tabs, go to "My Applications" and click on "Start Full Application"** for the log number under which the pre-application was submitted. Page limits are validated as a document is uploaded. ***eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specific below.***

- **Tab 1 – Summary:** Provides a summary of the application information.
- **Tab 2 – Application Contacts:** This tab will be populated by eBRAP. Edit contact information as applicable.
- **Tab 3 – Full Application Files:** Under each Application Component in eBRAP, upload each as an individual PDF file.

    1. **Application Component – Attachments:** Each attachment to the full application components must be uploaded as an individual file in the format specified and in accordance with the formatting guidelines listed in Appendix VI.

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

        - **Attachment 1: Project Narrative (15-page limit for projects that include a clinical trial; 10-page limit for projects without a clinical trial [preclinical and clinical research]): Upload as "ProjectNarrative.pdf".** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

            – **Outline for the Project Narrative:** Describe the proposed project in detail using ***one*** of the two outlines below, depending on whether or not a clinical trial is proposed. Within the Project Narrative describe how the proposed research has

the potential for broadly applicable advances benefiting military health and medicine as well as the general public.

Outline for projects <u>without</u> a clinical trial (e.g. Funding Level 1 or Funding Level 2-clinical research only:

- **Background:** Describe the problem, question, or knowledge gap related to at least one of the FY22 DMRDP BWMIR Focus Areas to be addressed by the proposed project. Present the scientific rationale on which the proposed work is based. Provide a critical review and analysis of relevant literature. Describe previous experience most pertinent to the project. Include relevant preliminary data that support proof of concept of the product or a prototype/ preliminary version of the product; these data may be unpublished or from the published literature. Describe any existing resources that the proposed project will leverage. If the project is part of a larger study, articulate the information that establishes a framework for this study. The application must demonstrate logical reasoning and provide a sound scientific rationale for the proposed project.

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

- **Specific Aims:** Concisely explain the project's specific aims. These aims should agree with the primary aims and associated tasks described in the Statement of Work (SOW). If the proposed work is part of a larger study, present only aims that this DOD award would fund. Clearly communicate the objectives/specific aims of the proposed DMRDP BWMIR project.

- **Research Strategy:** Describe the experimental design, methods, and analyses including appropriate controls in sufficient detail for evaluation. Provide a well-developed, well-integrated research strategy that supports the translational feasibility and promise of the approach. Explain how the research strategy will meet the project's goals and milestones within the proposed period of performance(s).

  - Define the specific study outcomes/endpoints and how they will be measured. Address potential problem areas and present alternative methods and approaches.

  - If applicable, describe resources available for the development of sufficient quantities of critical reagents under Good Manufacturing Practice (GMP).

  - If animal studies are proposed, briefly describe the key elements of the study/studies as they relate to the overall project. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and how it is optimal for addressing the study aims and facilitates translation of solutions for the Warfighter. Describe how animal research will be conducted in accordance with the ARRIVE guidelines 2.0

(https://arriveguidelines.org/arrive-guidelines). Further details of research involving animals will be required in Attachment 8, Animal Research Plan, as applicable.

- ❖ If human subjects or human biological samples will be used, briefly describe the study population and include a detailed plan for the recruitment of human subjects or the acquisition of samples. For clinical research, see Attachment 7, Inclusion of Women and Minorities, for the required strategy for the inclusion of women and minorities appropriate to the objectives of the study.

- ❖ For clinical research studies, further details of clinical research components will be required in Attachment 6, Human Subject Recruitment and Safety Procedures for Clinical Research, as applicable.

- **Statistical Plan:** Describe the data management plan. Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, and identification of primary endpoints and secondary endpoints. Describe the data collection instruments (e.g., research questionnaires, assays, assessment measures) that will be used, and to what degree they are appropriate to support the statistical significance of the proposed study. Clearly describe the statistical plan and rationale for the statistical methodology demonstrating that the proposed research is designed to achieve reproducible and rigorous results. Provide a sample size estimate and the method by which it was derived, including power analysis calculation, if applicable. Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA, or international regulatory agency, if applicable.

- **Research Team:** Describe how the background and expertise of the PI and other key personnel demonstrate their understanding of working in military populations or relevant trauma environments. Describe whether the composition of the research or study team is appropriate and complementary.

Outline for projects <u>with</u> a clinical trial. (e.g. Funding Level 2-clinical trial. Note: The Project Narrative is not the formal clinical trial protocol. If recommended for funding, the clinical trial protocol will be requested.):

- **Background:** Describe the problem, question, or knowledge gap related to at least one of the FY22 DMRDP BWMIR Focus Areas to be addressed by the proposed project. Present the scientific rationale on which the proposed work is based. Provide a critical review and analysis of relevant literature. Describe previous experience most pertinent to the project. Importantly, describe the studies showing proof of concept and efficacy in in vivo system(s) that led to the current proposed work. Provide a summary of relevant clinical trials and distinguish how the proposed study differs from

other relevant ongoing or recently completed clinical trials. 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). If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that would be supported with funds from this award. 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. Describe any existing resources that the proposed project will leverage. If the project is part of a larger study, articulate the information that establishes a framework for this study. The application must demonstrate logical reasoning and provide a sound scientific rationale for the proposed project.

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

- **Specific Aims:** Concisely explain the project's specific aims. These aims should agree with the primary aims and associated tasks described in the SOW. If the proposed work is part of a larger study, present only aims that this DOD award would fund. Clearly communicate the objectives/specific aims of the DMRDP BWMIR.

- **Research Strategy (include only if laboratory research studies are proposed as a component of the application):**

  - Describe the laboratory research studies that will be performed under this award and how they are ***clearly linked*** to the clinical trial.

  - Describe the experimental design and methodology, including reagents, assay validation, statistical analysis, potential pitfalls, and alternative approaches. Where relevant, describe the availability of, and access to, necessary data and/or critical reagents (e.g., therapeutic molecules, human samples) necessary for the proposed research. If applicable, describe resources available for the development of sufficient quantities of critical reagents under GMP.

  - Provide a well-developed, well-integrated research strategy that supports the translational feasibility and promise of the approach. Address potential problem areas and present alternative methods and approaches. Define the specific study outcomes/endpoints and how they will be measured.

  - Define the specific study outcomes/endpoints and how they will be measured.

- **Clinical Trial *(only small-scale [first in human, phase 1/1b] clinical trials are allowed)*:** Provide detailed plans for initiating, conducting, and completing the clinical trial during the period of performance. If the clinical trial is proposed in the DMRDP BWMIR Award application, the trial must be initiated no later than **month 9** of the initial period of performance. As appropriate, outline a plan for obtaining IND/IDE status (or other FDA approvals). Describe the type of clinical trial to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate. Explain how the research strategy will meet the project's goals and milestones within the proposed period of performance(s).

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

  - ❖ Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.

  - ❖ Describe the availability of, and access to, critical reagents (e.g., therapeutic molecules) necessary for the clinical trial.

  - ❖ Describe how the clinical trial will inform the correlative clinical research, if applicable.

  - ❖ 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). Provide information on the availability of, and access to, sufficient subjects to meet accrual goals for the clinical trial.

  - ❖ Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers). See Attachment 7, Inclusion of Women and Minorities, for the required strategy for the inclusion of women and minorities appropriate to the objectives of the study.

  - ❖ Further details of clinical trial components will be required in Attachment 6, Human Subject Recruitment and Safety Procedures for Clinical Research, as applicable.

- **Statistical Plan:** Describe the data management plan. Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, and identification of primary endpoints and secondary endpoints. Specify the number of human subjects that will be enrolled. If multiple 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. Describe the data collection instruments (e.g., research questionnaires, assays, assessment measures) that will be used, and to what degree they are appropriate to support the statistical significance of the proposed study. Clearly describe the statistical plan and rationale for the statistical methodology demonstrating that the proposed research is designed to achieve reproducible and rigorous results. Provide a sample size estimate and the method by which it was derived, including power analysis calculation, if applicable. Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA, or international regulatory agency, if applicable.

- **Clinical Team:** Describe how the background and expertise of the PI and other key personnel demonstrate their understanding of working in military populations or relevant trauma environments. Describe whether the composition of the research or study team is appropriate and complementary. If prospective clinical studies are included, the PI or research team must demonstrate appropriate expertise in conducting clinical studies.

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

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

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

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

  - **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present government award under which the facilities or equipment items are now accountable. There is no form for this information.

- **Publications and/or Patents:** Include a list of relevant publication URLs and/or patent abstracts. If articles are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.

- **Letters of Organizational Support:** Provide a letter (or letters, if applicable) signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the program announcement, such as those from members of Congress, do not impact application review or funding decisions.

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

- **Letters of Commitment (if applicable, 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.

- **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 DMRDP BWMIR Award are subject to a federal purpose license. A term of the DMRDP BWMIR 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 Appendix V, 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:** Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Data and Research Resources Sharing Plan:** Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to Appendix V, Section K, for more information about the CDMRP expectations for making data and research resources publicly available.

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

- **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.

- **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.

  Programmatic reviewers rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

  The technical abstract should include the following elements:

  - **Background:** Describe the idea and rationale behind the proposed work.

  - **Objective/Hypothesis:** State the objective to be reached/hypothesis to be tested. Provide evidence or rationale that supports the hypothesis(es)/objective(s).

  - **Specific Aims:** State concisely the specific aims of the study.

  - **Study Design:** Briefly describe the study design, including appropriate controls. For studies enrolling human subjects, describe the population and enrollment targets. For animal studies, include a description of the animal model.

- **Impact and Translation:** Identify the FY22 DMRDP BWMIR Focus Area(s) that the research addresses. Indicate how the proposed work will lead to improvements in prevention and care of combat traumatic wound injuries and/or anticipated changes in clinical practice guidelines.

- **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.

  - Describe the objectives and rationale for the research in a manner that will be readily understood by readers without a background in science or medicine.
  - Identify the FY22 DMRDP BWMIR Focus Area(s) to be addressed.
  - Describe the potential research and clinical applications, benefit, and risks.
  - Describe the projected timeline to achieve any potential patient-related outcomes.
  - Describe how the proposed project will benefit Service Members and/or the American public.

- **Attachment 5: Statement of Work (six-page limit if a clinical trial is proposed; three-page limit if no clinical trial is proposed): Upload as "SOW.pdf".** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). Recommended strategies for assembling the SOW can be found at https://ebrap.org/eBRAP/public/Program.htm.

  For the DMRDP BWMIR mechanism, refer to the **"*Suggested SOW Strategy Generic Research*"** document for Funding Level 1 or the ***"Suggested SOW Strategy Clinical Research"*** for Funding Level 2, and use the blank SOW format titled "Suggested SOW Format". The SOW must be in PDF format prior to attaching.

- **Attachment 6: 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 for Clinical Research 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 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 Appendix IV, 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.

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

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

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

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

- **Description of the Informed Consent Process:** Specifically describe the plan for obtaining informed consent from human subjects. ***This funding opportunity announcement may not be used to support studies requiring EFIC.***

  - 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 local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. ***Note:*** In compliance with 10 USC 980 (https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf), the application must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical study. If applicable, refer to Appendix IV, 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 local IRB to identify the conditions necessary for obtaining assent.

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

– **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is exposed to as a result of participation in the clinical 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:**
  - 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: Inclusion of Women and Minorities (required for applications that propose clinical research, including clinical trials; four-page limit): Upload as "Inclusion.pdf".** Describe the strategy for the inclusion of women and minorities appropriate to the objectives of the study, including a description of the composition of the proposed study population in terms of sex/gender, race, and ethnicity, and an accompanying rationale for the selection of subjects. Provide an anticipated enrollment table(s) for the inclusion of women and minorities appropriate to the objectives of the study with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The Public Health Service (PHS) Inclusion Enrollment Report is a three-page fillable PDF form, which can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

- **Attachment 8: Animal Research Plan (if applicable; required for all studies utilizing animals; five-page limit): Upload as "AnimRschPln.pdf".** When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be submitted to the IACUC as the Animal Research Plan. In accordance with the ARRIVE guidelines 2.0 (https://arriveguidelines.org/arrive-guidelines), the Animal Research Plan should address the following points for each proposed animal study:

  - Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.

  - For studies using non-gyrencephalic (lissencephalic) animal models of traumatic brain injury (TBI), include justification for their use.

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

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

  - Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.

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

  - 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.

- **Attachment 9: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page, combine, and upload as a single file named "Regulatory.pdf".** Address the following items and provide supporting documentation as applicable. Evidence of IND or IDE application submission or authorization without clinical hold status must be included in the FY22 DMRDP BWMIR Award application.

  - State the product/intervention name.

  - If applicable, state how many months into the award the anticipated clinical trial would be initiated after the award begins, taking into account any required advanced preclinical work (e.g., GMP production, pharmacokinetics, and toxicity testing) and/or clinical trial preparation (IRB and DOD OHRO approval).

*Clinical trials proposed in the DMRDP BWMIR Award application must be initiated no later than **month 9** of the initial period of performance*.

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

– For investigator-sponsored regulatory exemptions (e.g., IND, IDE) provide evidence of institutional support. Provide evidence that the clinical trial does not require regulation by the FDA. If the clinical trial will be conducted at international sites, provide equivalent information relevant to the host country(ies) regulatory requirements. No further information for this attachment is required.

For products 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 in the DMRDP BWMIR Award application period of performance, evidence of the IND or IDE application submission or authorization without clinical hold status must be included in the 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 trial. ***Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission.*** If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold). If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of

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

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

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

- 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, Good Laboratory Practice (GLP), and Good Clinical Practice (GCP) guidelines.

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

- If a drug is to be used in the proposed clinical trial, 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).

- If a device is to be used in the proposed clinical trial, indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for the conduct of the clinical trial.

- If the clinical trial involves the use of a drug that has not been approved by the FDA for the proposed investigational use, then an IND application to the FDA that meets all requirements under 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 is not required. If the investigational product is a device, then an 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 from the IRB of record or the FDA if an IDE is not required or if the device qualifies for an abbreviated IDE. The government reserves the right to withhold or withdraw funding if an IND or IDE is necessary to conduct the clinical trial during the Option period but has not been obtained within 6 months of the award date.

- **Attachment 10: Transition Plan (three-page limit): Upload as "Transition.pdf".**

  Describe the methods and strategies proposed to enable the product or knowledge outcomes to move to the next phase of development (e.g., clinical trials, partnership with DOD advanced developers, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Estimate the target technology readiness level/knowledge readiness level (TRL/KRL) upon completion of the proposed research (Appendix III). For clinical trials, demonstrate how the proposed product is currently at a minimum of TRL4. 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, DOD advanced developers, and/or other funding agencies to facilitate moving the product into the next phase of development. The transition plan should include the components listed below.

  – Details of the funding strategy to transition the product(s) to the next level of development and/or commercialization (e.g., specific potential industry partners, specific funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.

  – A brief schedule and milestones for transitioning the product(s) to the next phase of development (e.g., next-phase clinical trials, transition to industry, delivery to the civilian and/or military market, incorporation into clinical practice, and/or approval by the FDA).

  – For applications that ***do not*** propose a clinical trial, describe the current and planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication (e.g., Target Product Profile). Describe in detail the FDA regulatory strategy, including the number and types of studies proposed to reach approval, licensure, or clearance; the types of FDA meetings to be held; the submission filing strategy; and considerations for compliance with GMP, GLP, and GCP guidelines, if appropriate. For clinical trials, see Attachment 9 for the required regulatory strategy appropriate to the objectives of the study.

  – For knowledge products, a description of collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications.

  – 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.

- If prior federally funded Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) data supports the proposed development effort, describe the connection between the prior SBIR/STTR and the current project and explain all active SBIR/STTR data rights.

- A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 11: Impact and Military Benefit Statement (two-page limit): Upload as "Impact.pdf".** The Impact Statement should be written with a broad audience in mind, including readers without a background in science or medicine.

  - **Short-Term Impact:** Describe the anticipated short-term outcome(s) that will have the potential to optimize survival and recovery from combat traumatic wounds in austere environments and when access to definitive medical care is delayed or unavailable.

  - **Long-Term Impact:** Describe the anticipated research outcomes or long-term vision that will impact the development of medical solutions for Service Members and the public. Describe how the proposed materiel or knowledge product represents an improvement to currently available pharmacologic agents, devices, or clinical guidance (as applicable).

  - **Military Benefit:** Describe how the proposed research can be applied in far-forward roles of care (e.g., combat, at the point of injury, en route) and other operational environments to optimize survival and recover during future MDOs.

  - **Public Purpose:** Concisely describe how this research can benefit the general public.

  - **Challenges:** Describe potential issues that might limit the impact of the proposed research and strategies that may be employed to overcome those issues.

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

2. **Application Component - Research & Related Personal Data:** This form will be used by DOD as the source of demographic information, such as gender, race, ethnicity, and disability information, for the Project Director (PD)/PI and all other persons identified as Co-PD(s)/Co-PI(s).

   Each application must include this form with the name fields of the PD/PI and any Co-PD(s)/Co-PI(s) completed; however, provision of the demographic information in the form is voluntary. If completing the form for multiple individuals, each Co-PD/Co-PI can be added by selecting the "Next Person" button. The demographic information, if provided, will be used for statistical purposes only and will not be made available to

merit reviewers. Applicants who do not wish to provide some or all of the information should check or select the "Do not wish to provide" option.

Upload the Research & Related Personal Data Form as "PersonalData_LastName.pdf" under the Key Personnel Application Components.

3. **Application Component - Research & Related Senior/Key Person Profile:** Each attachment must be uploaded as an individual PDF file unless otherwise stated. The Biographical Sketches and the Previous/Current/Pending Support for the PI and Key Personnel may be either attached to the Research & Related Senior/Key Person Profile (Expanded) Form or uploaded as individual files in the "Key Personnel" Application Component.

    - **Research & Related Senior/Key Person Profile (Expanded):** The Degree Type and Degree Year fields on the Research and Related Senior/Key Person Profile (Expanded) will be used by the DOD as the source for career information. In addition to the required fields on the form, applicants must complete these two fields for all individuals that are identified as having the project role of PD/PI or Co-PD/Co-PI on the form. Additional senior/key persons can be added by selecting the "Next Person" button. Upload the Research & Related Senior/Key Person Profile (Expanded) as "KeyPersonnel_LastName.pdf" under the Key Personnel Application Components.

    Include the requested information for each person who will contribute significantly to the proposed research project.

    - PI Biographical Sketch (six-page limit): Upload as "Biosketch_LastName.pdf" where "LastName is the last name of the PI. The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. Use of this document is optional. The National Institutes of Health (NIH) Biographical Sketch may also be used. Each biographical sketch must be in PDF format prior to attachment.

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

    - Key Personnel Biographical Sketches (six-page limit each): Upload as "Biosketch_LastName.pdf" where "LastName" is the last name of the respective individual.

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

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 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).

4. **Application Component – Budget Form:** Use the Suggested DOD Military Facility Budget Format available for download on the eBRAP "Funding Opportunities & Forms" web page https://ebrap.org/eBRAP/public/Program.htm). Refer to Appendix VII for detailed information on completing this form.

    - Upload the Suggested DOD Military Facility Budget Format as "MFBudget.pdf".

    - Budget Justification (no page limit): Upload as "BudgetJustification.pdf". The budget justification must include a Federal Agency Financial Plan, as described in Appendix VII. 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.

    - Subaward Budget: Include all Subaward budgets. Describe in detail funding arrangements with extramural partners (if applicable). For each subaward (intramural or extramural), complete a separate detailed budget using the Suggested DOD Collaborating Military Facility Budget Format including a budget justification for each subaward in accordance with the instructions listed above. Title each individual subaward "Budget" or "Budget Justification," with the name of the subawardee/subrecipient organization.

5. **Application Component – Project/Performance Site Location(s) Form:** Indicate the primary site where the work will be performed. If a portion of the work will be performed at any other site(s), include the name and address for each collaborating location in the data fields provided. Add more sites as necessary using the "Next Site" button. If more than eight performance site locations are proposed, provide the requested information in a separate file and attach it to this form. Each additional research site requesting funds will require a subaward budget.

- **Tab 4 – Application and Budget Data**

  Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.

- **Tab 5 – Submit/Request Approval of the Full Application**

  Once all components have been uploaded and prior to the full application submission deadline, enter your password in the space provided next to "Enter Your Password Here" and press the "Submit Full Application" button. eBRAP will validate files against the program announcement requirements, and discrepancies will be noted. If no discrepancies are noted, press the "Confirm Submission" button to complete the application submission. eBRAP will notify your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official by email to log into eBRAP to review and approve the full application package prior to the approval deadline.

II.D.3. Submission Dates and Times

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

Applicant Verification of Full Application Submission in eBRAP

eBRAP allows an organization's representatives and PIs to view and modify the full application submissions associated with them. Following retrieval and processing of the full application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the full application submission. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in an email to the PI and in the "Full Application Files" tab in eBRAP. eBRAP does not confirm the accuracy of file content. Application viewing, modification, and verification in eBRAP are strongly recommended, but not required. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the program announcement. ***If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the application submission deadline. The Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline.*** Other application components may be changed until the end of the application verification period. Verify that subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

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

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

II.D.4. Funding Restrictions

The requested funding level should be aligned with the scope of the research proposed and the funding level descriptions. The government reserves the right to fund an application at a lower funding level.

Funding Level 1:

- The maximum period of performance is **3** years.
- The anticipated total costs (direct and indirect) budgeted for the entire period of performance will not exceed **$1.2M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **$1.2M** total costs or using an indirect rate exceeding the organization's negotiated rate.

Funding Level 2:

- The maximum period of performance is **4** years.
- The allowable range of total costs (direct and indirect) budgeted for the entire period of performance is **$2.2M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **$2.2M** total costs or using an indirect rate exceeding the organization's negotiated rate.

For Both Funding Levels:

- All direct and indirect costs of any subaward or contract must be included in the total direct costs of the primary award.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum (3 years for Funding Level 1; 4 years for Funding Level 2).

For this award mechanism, direct costs must be requested for:

- Travel costs for the PI to present project information or disseminate project results at a DOD-sponsored meeting (e.g., progress review meeting or Military Heath System Research Symposium) in year 2 of the award. For planning purposes, it should be assumed that the meeting will be held in the Central Florida Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all inclusive):

- Special purpose equipment

- Travel in support of multidisciplinary collaborations
- Travel costs for one investigator to travel to one scientific/technical meeting per year in addition to the required meeting described above. The intent of travel costs to scientific/ technical meetings is to present project information or disseminate project results from the DMRDP BWMIR Award.

Must not be requested for:

- Equipment (other than special purpose equipment)
- Tuition

Funding to intramural DOD and other federal agencies will be managed through a direct funds transfer. Participating intramural sites receiving direct funds are responsible for coordinating through their agency's procedures the use of contractual or assistance funding awards or other appropriate agreements to support extramural collaborators. It is the responsibility of intramural research site to ensure intramural funds are obligated by the deadlines associated with the fiscal year of funds. Regardless of location, any work that is to be performed through an intramural investigator must be limited to work performed under existing support vehicles, and resource sharing should be accomplished through Cooperative Research and Development Agreements or Material Transfer Agreements. The government reserves the right to administratively withdraw any application that does not meet these eligibility criteria. ***Applications that require research at intramural sites to be performed by a non-DOD organization under a new support vehicles will not be considered for funding.*** Refer to Appendix VII for budget regulations and instructions for the Research & Related Budget. ***For federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Appendix VII.***

II.D.5. Other Submission Requirements

Refer to Appendix VI for detailed formatting guidelines.

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

To determine technical merit, all applications will be evaluated according to the following **scored criteria**, of which are listed in decreasing order of importance.

- **Research Strategy and Feasibility**
    - How well the scientific rationale supports the project and its translational feasibility as demonstrated by a critical review and analysis of published literature, logical reasoning, and preliminary data, if applicable.

- How well the hypothesis, objectives, specific aims, experimental design, methods, and analyses are developed.
- How well the application describes study outcomes/endpoints and how they will be measured.
- How well the application acknowledges potential problem areas and addresses alternative methods and approaches.
- How well the animal study is (or studies are) designed to achieve the objectives, including the choice of model and endpoints/outcome measures to be used, and facilitate development of solutions for the Warfighter (if applicable).
- How well the applicant demonstrates access to the relevant study resources, necessary data, and/or critical reagents (e.g., therapeutic molecules, human samples).
- For research conducted with human subjects (clinical research and clinical trials), how well the application demonstrates the availability of, and access to, the appropriate patient populations(s), as well as the ability to accrue a sufficient number of subjects.
- For research conducted with human subjects (clinical research and clinical trials), to what extent the strategy for the inclusion of women and minorities and distribution of proposed enrollment are appropriate for the proposed clinical research.
- To what extent the intellectual and material property plan is appropriate (if applicable).
- To what extent the research can be completed within the proposed period of performance.

- **Clinical Trial Strategy *(for applications that include a clinical trial)***
  - To what extent the type of clinical trial (e.g., prospective, randomized, controlled) proposed is appropriate to meet the project's objectives.
  - To what extent the clinical trial is designed with appropriate study variables, controls, and endpoint.
  - How well the application sufficiently demonstrates the clinical trial can be initiated by **month 9** of the award.
  - How well potential challenges and alternative strategies are appropriately identified.
- **Impact**
  - To what extent the short-term outcome(s) of the proposed research has the potential to optimize survival and recovery from combat related or trauma-induced injury in austere environments when access to definitive medical care is delayed or unavailable.

- To what extent the anticipated research outcome(s) or long-term vision of the proposed research may impact the development of medical solutions for Service Members and the public.

- To what degree the proposed materiel or knowledge product represents an improvement to currently available pharmacologic agents, devices, or clinical guidance (as applicable).

- **Regulatory Strategy and Transition Plan**

  - How the regulatory strategy and the development plan to support the proposed product label are appropriate and well-described (if applicable).

  - As appropriate, whether the application includes documentation that the study is exempt from FDA or other international agency regulation, or that the IND or IDE application and/or international equivalent has been submitted to the FDA and/or relevant international regulatory agency or authorized without clinical hold status.

  - For clinical trials, how well the documentation provided supports the feasibility of acquiring an active IND or IDE and/or international equivalent covering the proposed trial (if applicable).

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

  - For clinical trials, whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.

  - Whether the identified next level of development and/or plan for commercialization is realistic (if applicable).

  - Whether the proposed target TRL or KRL is realistic and appropriate.

  - Whether the schedule and milestones for bringing the anticipated product(s) to the next level of development (clinical trials, transition to industry, delivery to the military or civilian market, incorporation into clinical practice, or approval by the FDA) are achievable.

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

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

  - Whether the proposed collaborations and other resources for providing continuity of development of knowledge products, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient

brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications are established and/or achievable (if applicable).

- **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.
    - How well the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
    - For clinical trials, whether the population selected to participate in the trial stands to benefit from the knowledge gained.
    - To what degree privacy issues are appropriately considered.
    - To what degree the processes for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
- **Statistical and Data Analysis Plan**
    - 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 adequate the statistical plan, including sample size projections and power analysis, is for achieving the study objectives and is appropriate to type and phase of study.
    - How well the application identifies sampling methods to gain a representative sample from the population(s) of interest (if applicable).
    - To what degree the research data collection instruments, are appropriate to support statistical significance of the proposed study.
- **Research Team**
    - To what degree the background, experience, and expertise of the PI and other key personnel demonstrate their ability to perform the proposed work.
    - To what degree the levels of effort by the PI and other key personnel are appropriate to ensuring the successful conduct of the project.
    - How the PI’s record of accomplishment demonstrates their ability to accomplish the proposed work.
- **Environment**
    - How the scientific environment is appropriate for the proposed research.

- How the quality and extent of organizational support are appropriate for the proposed research.

- How the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).

In addition, the following **unscored criteria** will also contribute to the overall evaluation of the application:

- **Budget**

  - Whether the **total** costs exceed the allowable total costs as published in the program announcement.

  - Whether the budget is appropriate for the proposed research.

- **Application Presentation**

  - To what extent the writing, clarity, and presentation of the application components influence the review.

II.E.1.b. Programmatic Review

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

- Ratings and evaluations of the peer reviewers

- Relevance to the mission of the DHP and FY22 DMRDP, as evidenced by the following:

  - Adherence to the intent of the award mechanism

  - Program portfolio composition

  - Relevance to military health

  - Relative impact and translatability

II.E.2. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding General, USAMRDC. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various***

factors as described in Section II.E.1.b, Programmatic Review. Additional information about the two-tier process used by the CDMRP can be found at https://cdmrp.health.mil/about/2tierRevProcess. An information paper describing the funding recommendations and review process for the DMRDP BWMIR will be provided to the PI and posted on the CDMRP website.

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

II.E.3. Integrity and Performance Information

Prior to making an assistance agreement award where the federal share is expected to exceed the simplified acquisition threshold, as defined in 2 CFR 200.1, 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 may review FAPIIS, accessible through SAM, and submit comments to FAPIIS on any information about the organization that a federal awarding agency previously entered and is currently available in FAPIIS.

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

II.E.3. Anticipated Announcement and Federal Award Dates

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

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Awards supported with FY22 funds are anticipated to be made no later than September 30, 2023. Refer to Appendix V for additional award administration information.

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

Federal Government Organizations: Funding made to federal government organizations (to include intramural DOD organizations) will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Funds will be transferred to organizations, not to individual PIs. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

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

The organizational transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the CDMRP DMRDP Program Manager.

Unless otherwise restricted, changes in PI or organization will be allowed at the discretion of the CDMRP DMRDP Program Manager, provided the intent of the award mechanism is met.

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

Refer to Appendix V, Section B, for general information on PI or organization changes.

II.F.2. Reporting

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

Annual progress reports and quad charts, as well as annual and final progress reports may be required. The Award Terms and Conditions will specify if more frequent reporting is required.

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the first annual report. Use the one-page template "Award Expiration Transition Plan," available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) under the "Progress Report Formats" section. The Award Expiration Transition Plan must outline if and how the research

supported by this award will progress and must include source(s) of funding, either known or pending.

PHS Inclusion Enrollment Reporting Requirement ***(only required for clinical research studies)***: Enrollment on the basis of sex/gender, race, and/or ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP.

Awards resulting from this program announcement may entail additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have federal contract, grant, and cooperative agreement awards with a cumulative total value greater than $10M are required to provide information to 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.

II.G. Agency Contacts

II.G.1. eBRAP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

II.H. Other Information

II.H.1. Administrative Actions

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

II.H.1.a. Rejection

The following will result in administrative rejection of the pre-application:

- Pre-Application (LOI) was not submitted

The following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.

- Budget is missing.

For applications involving animal research:

- Attachment 8, Animal Research Plan, is missing.

For applications recruiting human subjects:

- Attachment 6, Human Subject Recruitment and Safety Procedures for Clinical Research is missing.
- Attachment 7, Inclusion of Women and Minorities, is missing.

For applications proposing clinical trials:

- Attachment 9, Regulatory Strategy, is missing.

II.H.1.b. Modification

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

II.H.1.c. Withdrawal

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

- An FY22 DMRDP BWMIR Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. ***A list of the FY22 DMRDP BWMIR Programmatic Panel members can be found at https://cdmrp.health.mil/dmrdp/panels/bwmirapanel22.***
- The application fails to conform to this program announcement description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY22, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.health.mil/about/2tierRevProcess). Applications that include names of personnel from either of these companies may be administratively withdrawn.

- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications submitted by an intramural DOD organization as the contracting organization.
- The invited application proposes a different research project than that described in the pre-application.
- The application does not address at least one of the FY22 DMRDP BWMIR Focus Areas.
- The proposed research includes a phase 2 or phase 3 clinical trial.
- The application requiring IND/IDE (or international equivalent) during the period of performance does not include documentation of submission or authorization without clinical hold status in the Regulatory Strategy (Attachment 9).
- The application involves research at intramural sites to be performed by a non-DOD organization under a new support vehicle.

II.H.1.d. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be required to provide the findings of the investigation to the CDMRP for a determination of the final disposition of the application.

II.H.2. Application Submission Checklist

Application Components	Action	Completed
Summary (Tab 1) and Application Contacts (Tab 2)	Complete tabs as instructed	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf"	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf"	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf"	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf"	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf"	
	Human Subject Recruitment and Safety Procedures for Clinical Research: Upload as Attachment 6 with file name "HumSubProc.pdf" if applicable	
	Inclusion of Women and Minorities: Upload as Attachment 7 with file name "Inclusion.pdf" if applicable	
	Animal Research Plan: Upload as Attachment 8 with file name "AnimRschPln.pdf" if applicable	
	Regulatory Strategy: Upload as Attachment 9 with file name "Regulatory.pdf" if applicable	
	Transition Plan: Upload as Attachment 10 with file name "Transition.pdf"	
	Impact and Military Benefit Statement: Upload as Attachment 11 with file name "Impact.pdf"	
Research & Related Personal Data	Complete form as instructed	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field	
	Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field	

Application Components	Action	Completed
	Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field	
Budget	Suggested DOD Military Budget Format, including justification	
Project/Performance Site Location(s) Form	Complete form as instructed	
Research & Related Subaward Budget Attachment(s) Form, if applicable	Complete form as instructed	

APPENDIX I: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
ACURO	Animal Care and Use Review Office
ARRIVE	Animal Research: Reporting *In Vivo* Experiments
AVI	Audio Video Interleave
BWMIR	Battlefield Wound Management and Infection Research
CCCRP	Combat Casualty Care Research Program
CDC	Centers for Disease Control and Prevention
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
COI	Conflict of Interest
CRADA	Cooperative Research and Development Agreement
DA PAM	Department of the Army Pamphlet
DFARS	Defense Federal Acquisition Regulation Supplement
DHP	Defense Health Program
DMRDP	Defense Medical Research and Development Program
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
DoDI	Department of Defense Instruction
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
EFIC	Exception from Informed Consent
ET	Eastern Time
FAD	Funding Authorization Document
FAPIIS	Federal Awardee Performance and Integrity Information System
FAR	Federal Acquisition Regulation
FDA	U.S. Food and Drug Administration
FITBIR	Federal Interagency Traumatic Brain Injury Research
FOIA	Freedom of Information Act
FWA	Federalwide Assurance
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HIPAA	Health Insurance Portability and Accountability Act
IACUC	Institutional Animal Care and Use Committee
IDE	Investigational Device Exemption

IND	Investigational New Drug
IRB	Institutional Review Board
IRP	Inquiry Review Process
JPC	Joint Program Committee
KP	Knowledge Product
KRL	Knowledge Readiness Level
LAR	Legally Authorized Representative
LOI	Letter of Intent
M	Million
MB	Megabytes
MDO	Multi-Domain Operation
MIPR	Military Interdepartmental Purchase Request
MPEG	Moving Picture Experts Group
MTA	Material Transfer Agreement
NIH	National Institutes of Health
NPC	Non-Profit Corporation
OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
OHARO	Office of Human and Animal Research Oversight
OHRO	Office of Human Research Oversight
ORCID	Open Researcher and Contributor ID, Inc.
PD	Project Director
PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
PII	Personally Identifiable Information
RDT&E	Research, Development, Test and Evaluation
SAM	System for Award Management
SF	Standard Form
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
TBI	Traumatic Brain Injury
TCCC	Tactical Combat Casualty Care
TIFF	Tagged Image File Format
TRA	Technology Readiness Assessment
TRL	Technology Readiness Level
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command

USC	United States Code
VA	Department of Veterans Affairs
WAV	Waveform Audio

APPENDIX II: DOD AND VA WEBSITES

Applicants are encouraged to integrate and/or align their research projects with DOD and/or VA research laboratories and programs. Collaboration with DOD and/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/

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

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

Defense Health Agency
https://health.mil/dha

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

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

Military Health System Research Symposium
https://mhsrs.amedd.army.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/sites/nmcphc/Pages/Home.aspx

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

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

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

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

U.S. Army Sharp, Ready and Resilient Directorate
https://www.armyresilience.army.mil/

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

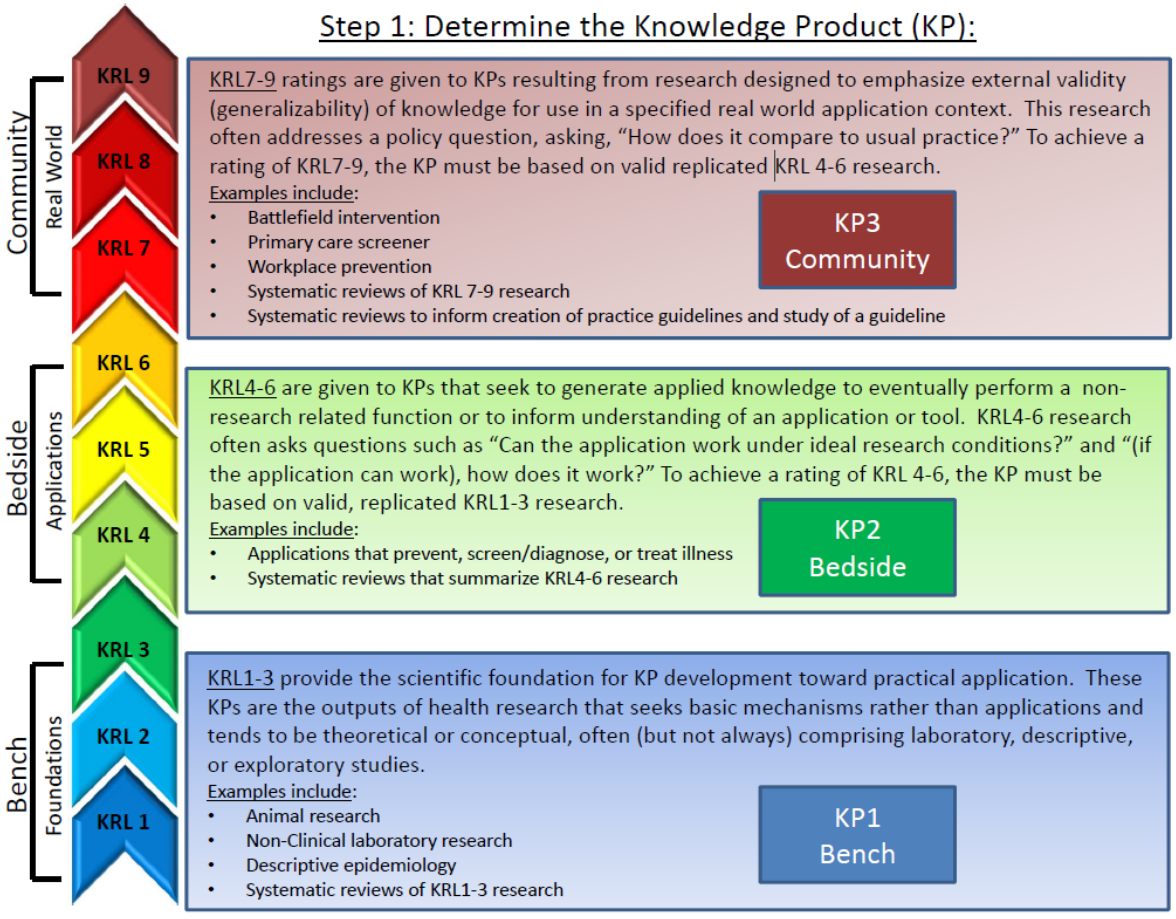
U.S. Naval Research Laboratory
https://www.nrl.navy.mil

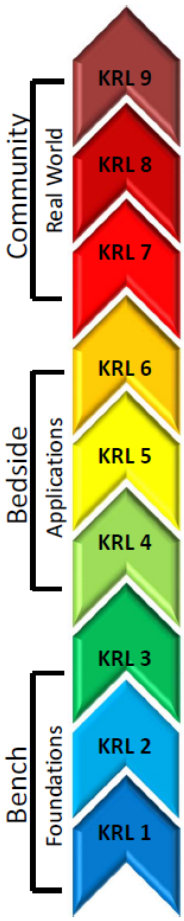
Walter Reed Army Institute of Research
https://www.wrair.army.mil/

APPENDIX III: TECHNOLOGY READINESS LEVELS AND KNOWLEDGE READINESS LEVELS

Technology Readiness Levels: TRLs are used to categorize the product maturity of materiel solutions. The DOD's 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 that 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: The scientific maturity of knowledge products resulting from biomedical research is not assessed in the same manner as that of materiel solutions. At the request of the USAMRDC, 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.





Step 2: Determine the Knowledge Readiness Level (KRL)

KRL9 research replicates or reviews well-designed KRL7 and KRL8 studies (e.g., cost analyses to achieve desired effect; comparative effectiveness studies to aid context specific policy development or intervention decisions; systematic review to estimate effect size with average participants in a real world context, assess **"Does the application work?"** in a context, or determine for which participants or time period the application works in an identified context.)

KRL8 research expands on or replicates KRL7 studies to directly assess "Does the application work in the context of interest?" It uses valid designs with emphasis on external validity (generalizability) for an intended context. (e.g., multi-site to obtain average effects; generalizable analyses of real world, (e.g., administrative) data; usual or standard care (not placebo or contact time) controls; and average (not ideal) participants.)

KRL7 research comprises early studies adapting applications supported by KRL4-6 research for use in a military health context. (e.g., adaptation from a longer screener, feasibility and standardization for post-deployment use of a brief screener; initial multi-modal tests of combined KRL4-6 supported interventions to achieve improved outcomes in primary care; adaptation and initial study in military mental health settings of KRL4-6 support therapy for PTSD; adaptation and initial study of KRL4-6 supported protective gear for preventing TBI during deployment.)

KRL6 research replicates well-designed KRL5 studies. It adds nuance to answers from completed studies (e.g., not just "Can it work" and "How," but also "For whom," "Under what conditions," or "With what frequency?") It validates hypotheses that may suggest important application contexts (e.g., battlefield, primary care, emergency rooms, post-deployment screening). It includes systematic reviews of KRL4-5 studies to address "Can it work?" and "How?" questions.

KRL5 research tests *a priori* (pre-specified) hypotheses using rigorous scientific designs (e.g., RCTs for intervention efficacy) to directly assess "Can it work" and "If so, how?" It expands on or replicates a KRL4 finding and/or improves on the design of one or more KRL4 studies.

KRL4 research generates initial knowledge regarding a human health-related application or use. KRL4 findings require subsequent replication (e.g., descriptive human epidemiology or preliminary human studies, human studies that test a clinical hypotheses, pilot tests of an intervention, screening or diagnostic tool, and development of instrumentation needed to test an intended application (e.g., outcome measure).

KRL3 research validates hypotheses and hints at future applications, research that replicates or systematically reviews well-designed KRL1-2 studies or theory, descriptive studies, particularly involving animal research (e.g., tool for prediction, prognosis, screening, diagnosis, treatment, prevention)

KRL2 research expands on or replicates a KRL1 finding, including systematic review of KRL1 studies to formulate a theoretical model (e.g., animal studies that test a hypothesis or are the first true experiment on a nascent theory and human studies not based on animal study findings that are descriptive or hypothesis generating.

KRL1 research generates initial or very early scientific knowledge without regard to or indication of a specific health use. Its purpose is inferential, with the intention to generalize. Its findings require replication. (e.g., descriptive animal studies, or those that are hypothesis generating rather than hypothesis testing.)

APPENDIX IV: REGULATORY REQUIREMENTS

A. Safety and Environmental Requirements

Based on changes to DOD compliance requirements (Department of the Army Pamphlet [DA PAM] 385-69, DA PAM 385-10, 32 CFR 651, September 6, 2012), provisions previously required for Safety and Environmental Compliance have been removed. However, in certain instances, compliance review may require submission of additional documentation prior to the awarding of any assistance agreement. Such instances may include use of Army-provided infectious agents or toxins, Biological Select Agents or Toxins, specific chemical agent(s), or pesticides outside of an established laboratory. The USAMRDC Office of Surety and Environment will identify any need for compliance review, and documents must be submitted upon request.

Additional information is available at https://mrdc.health.mil/index.cfm/resources/researcher_resources/safety.

B. Research Protections Review Requirements

The USAMRDC OHARO ensures that research conducted, contracted, sponsored, supported, or managed by the DOD and involving human subjects, human anatomical substances, human data, human cadavers, or animals is conducted in accordance with federal, DOD, Army, USAMRDC, and international regulatory requirements.

All DOD-funded research involving new and ongoing research with animals must be reviewed and approved by the USAMRDC OHARO ACURO, in addition to the local IACUC of record. The ACURO must review and approve all animal use prior to the start of working with animals, including amendments to ongoing projects.

All DOD-funded research involving new and ongoing research with human anatomical substances, human subjects, human data, 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.

PIs and applicant organizations **may not commence performance** of research involving the above, **or expend funding** on such efforts, until regulatory documents are submitted and approved by the USAMRDC OHARO to ensure that DOD regulations are met. All expectations described below are consistent with DoD Instruction (DoDI) 3216.01, "Use of Animals in DoD Programs," and DoDI 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and -Supported Research."

Additional information is available at https://mrdc.health.mil/index.cfm/collaborate/research_protections.

1. Research Involving Animal Use

The ACURO must review and approve all animal use funded by the award prior to the start of working with animals, including amendments to ongoing projects. IACUC approval at the

time of submission is not required. Specific documents relating to the use of animals in the proposed research will be requested if the application is selected for funding. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." For guidance, visit the ACURO website at https://mrdc.health.mil/index.cfm/collaborate/research_protections/acuro. ***Allow at least 3 to 4 months for regulatory review and approval processes for animal studies.***

For additional information, send questions via email to ACURO (usarmy.detrick.medcom-usamrdc.other.acuro@health.mil).

2. Research Involving Human Subjects

The OHRO ensures that DOD-supported research complies with specific laws, regulations, and requirements governing human subjects research. 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. Studies taking place in international settings may require additional time for completion of OHARO OHRO reviews.

NOTE: The protocol submitted for OHRO review must include only those activities funded by the DOD, as referenced in the approved SOW. If the DOD-funded activities have been added to an ongoing/existing protocol that is not DOD-funded, OHRO will require the PI to write a stand-alone protocol that is limited to those activities supported under the DOD award.

Effective January 20, 2020, The Revised Common Rule (i.e., the 2018 Requirements) at 45 CFR 46.114(b) requires that all institutions located in the United States that are engaged in cooperative research conducted or supported by a Common Rule department or agency rely upon approval by a single IRB for the portion of the research that is conducted in the United States. These provisions apply to DOD-funded research. Applicants must provide a written plan for single IRB review arrangements at the time of application submission or award negotiation.

Questions regarding applicable human subjects protection regulations, policies, and guidance should be directed to the local IRB or the OHARO OHRO (usarmy.detrick.medcom-usamrdc.other.hrpo@health.mil). For in-depth information and to access OHRO protocol submission forms, refer to the OHARO OHRO website (https://mrdc.health.mil/index.cfm/collaborate/research_protections/hrpo). Key requirements found in the OHARO OHRO guidance document, "Information for Investigators – Human Subjects Research" include:

- **Assurance of Compliance:** Each institution engaged in non-exempt human subjects research must have a current DHHS Office for Human Research Protection Federalwide Assurance (FWA) or DOD Assurance.

- **Training:** Personnel involved in human subjects research must have completed appropriate training in the protection of human subjects per institutional requirements.

Documentation confirming completion of appropriate training will be required during the OHARO OHRO review process.

- **Informed Consent Form:** The following must appear in the consent form:
    - A statement that the DOD is providing funding for the study.
    - A statement that representatives of the DOD are authorized to review research records.
    - In the event that Health Insurance Portability and Accountability Act (HIPAA) authorization is required, the DOD must be listed as one of the parties to whom private health information may be disclosed.
- **Access to DOD-Affiliated Personnel for Research:** See the guidance document, "A Primer for Conducting Department of Defense (DOD) Funded Human Research With Military Populations," at https://mrdc.health.mil/assets/docs/orp/Conducting_Research_Military_Pop_DoD_May_2021.pdf.
- **10 USC 980 Waiver:** If the applicant proposes to conduct a trauma clinical trial or other planned emergency research subject to the requirements for exception from advanced informed consent under 21 CFR 50.24, the applicant should plan for 3-6 months of additional time for the OHARO OHRO to review the submission and request a waiver of 10 USC 980 from the Secretary of the Army or the DOD Office of Human Research Protections.

3. Research Involving the Secondary Use of Data/Specimens

Research involving the use of human data and/or specimens not otherwise subject to institutional review requires a determination letter (e.g., stating that the project does not constitute "human subjects research" or can be considered "exempt human subjects research") from the PI's human subjects protection office as well as a concurrence from the OHARO OHRO.

All USAMRDC-supported research involving the secondary use of human data, human biospecimens (hereafter referred to as data/specimens) must be reviewed for compliance with federal and DOD human subjects protection requirements and approved by the OHARO OHRO prior to implementation. For additional guidance and instructions on OHARO OHRO review of DOD-funded research activities involving access, use, and analysis of data/specimens, see the guidance document, "Information for Investigators – Research with Data/Specimens," found at https://mrdc.health.mil/assets/docs/orp/Investigator_Guidance_on_HRPO_Review_of_Use_of_Data_Specimens.pdf

NOTE: The protocol submitted for OHRO review must include only those activities funded by the DOD, as referenced in the SOW. If the DOD-funded activities have been added to an ongoing/existing protocol that is not DOD-funded, OHRO will require the PI to write a stand-alone protocol that is limited to those activities supported under the DOD award.

4. Additional Information/Requirements

Site Visits: The USAMRDC OHARO OHRO conducts site visits as part of its responsibility for compliance oversight.

Accurate and complete study records must be maintained and made available to representatives of USAMRDC as a part of their responsibility to protect human subjects in research. Research records must be stored in a confidential manner so as to protect the confidentiality of subject information.

Protocol Submission Format: The OHARO OHRO accepts protocol submissions in the format required by the local IRB. The IRB protocol application, if separate from the protocol itself, should be included with protocol submissions.

Research Involving the Use of U.S. Food and Drug Administration-Regulated Products (i.e., drugs, devices, in vitro diagnostics) in which the focus of the study is on the safety or effectiveness of the product requires IRB review in accordance with 21 CFR 50 and 21 CFR 56.

Clinical Trial Registry: PIs are required to register applicable clinical trials individually on https://clinicaltrials.gov/ using a Secondary Protocol ID number designation of "CDMRP-eBRAP Log Number" (e.g., CDMRP-PC22####). If several protocols exist under the same application, the Secondary Protocol ID number must be designated "CDMRP-eBRAP Log Number-A, B, C, etc." (e.g., CDMRP-PC22####-A). Clinical trials must be registered prior to enrollment of the first patient. All trials that meet the definition on the NIH database (see https://prsinfo.clinicaltrials.gov/, click on "Support Materials (including data element definitions)") are required to register. Failure to do so may result in a civil monetary penalty and/or the withholding or recovery of grant funds as per U.S. Public Law 110-85. PIs conducting phase 3 clinical trials shall submit results of analyses of group differences on the basis of sex/gender, race, and/or ethnicity to clinicaltrials.gov at the time of final report submission. If final analyses of sex/gender and race/ethnicity are not available at the time of the final technical report, a justification and plan ensuring completion and reporting of the analyses must be submitted to USAMRAA.

Research Involving Recombinant DNA: The recipient must assure that all work involving the use of recombinant DNA will be in compliance with guidance provided at Biosafety and Recombinant DNA Policy – Office of Science Policy (nih.gov).

5. Use of Human Cadavers or Human Anatomical Substances Obtained from Human Cadavers

RDT&E, education, or training activities involving human cadavers or human anatomical substances obtained from cadavers (postmortem samples) shall not begin until the USAMRDC OHARO grants approval in accordance with the Army Policy for Use of Human Cadavers for RDT&E, Education, or Training (https://mrdc.health.mil/assets/docs/orp/Army_Policy_for_Use_of_Human_Cadavers.pdf). The USAMRDC OHARO is the Action Office for this Army policy. **Additional requirements apply to activities involving exposure of cadavers to impacts, blasts, ballistics testing, crash testing, and other destructive forces.**

Award recipients must coordinate with the supporting/funding Army organization to ensure that proper approvals are obtained. Specific requirements for submission and review of RDT&E, education, and training involving cadavers and postmortem specimens can be found at https://mrdc.health.mil/index.cfm/collaborate/research_protections.

Written approvals to begin the activity will be issued under separate notification to the recipient. Questions regarding submission of human cadaver research for USAMRDC OHARO review and approval should be directed to the OHARO at usarmy.detrick.medcom-usamrdc.other.hrpo@health.mil.

C. Use of DOD or VA Resources:

If the proposed research involves access to active-duty military patient populations and/or DOD resources or databases, the application must describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research. Access to the target active-duty military patient population(s) and/or DOD resource(s) or database(s) should be confirmed by including a letter of support, signed by the lowest-ranking person with approval authority.

If the proposed research involves access to VA patient populations, VA study resources and databases, and/or VA research space and equipment, VA PIs/Co-PIs must have a plan for obtaining and maintaining access throughout the proposed research. Access to VA patients, resources, and/or VA research space should be confirmed by including 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. If appropriate, the application should identify the VA-affiliated NPC as the applicant institution for VA PIs. If the VA NPC is not identified as the applicant institution for administering the funds, the application should 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.

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 access cannot be confirmed at the time of application submission, 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).

APPENDIX V: REPORTING REQUIREMENTS AND ADMINISTRATIVE INFORMATION

A. Reporting Requirements for Awards

The government requires periodic reports to be submitted to continue the research and funding through the entire period of performance. Specific reports required by the government will be described in each award and may include:

- Technical/Scientific:
    - In addition to annual progress reports, the Terms and Conditions of the award will indicate any additional reporting required.
    - Final technical/progress report
    - Quad Chart: 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 as an attachment to a standard post-award progress report under Special Reporting Requirements if required by the terms and conditions of the award.
    - USAMRDC research progress reporting requirements and instructions can be found at https://mrdc.health.mil/index.cfm/resources/researcher_resources/reporting/training.
- Fiscal (SF425 "Federal Financial Report"):
    - Quarterly and/or annual reports
    - Final report
- Regulatory:
    - Research Involving Human Subjects: For DOD awards that include funding to support research with human subjects, the USAMRDC's OHRO requires submission of institutional continuing review reports and study event reports. Instructions are found at https://mrdc.health.mil/index.cfm/collaborate/research_protections/hrpo.
    - The USAMRDC's OHRO will no longer require submission of local IRB annual continuing review materials for studies that no longer require continuing review under the 2018 Revised Common Rule (49 CFR Part 11).
    - Research Involving Animals: For DOD awards that include funding to support animal studies, staff from the USAMRDC's ACURO will contact the PI regarding submission requirements and deadlines. Questions related to ACURO review and approval should be directed to the ACURO central email account at usarmy.detrick.medcom-usamrdc.other.acuro@health.mil.

- PHS Inclusion Enrollment Report: This is used to report the sex/gender, race, and ethnicity of study participants that will be enrolled in the clinical research (both planned and actual). The PHS Inclusion Enrollment Report format is a fillable PDF form that may be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm and completed for submission with the application.

B. Post-Award Organization and Principal Investigator Changes

Transfer of Award to New Organization: Unless restricted by the specific program announcement, a change in organizational affiliation will be considered on a case-by-case basis by the USAMRAA Grants Officer. If approved, the PI's original organization will be required to agree to relinquish the award. The new organization will be required to resubmit the entire application on behalf of the PI, including regulatory documentation. Extended times for transfer may put the award funding at risk. A transfer will not, unless under extraordinary circumstances, be allowed for any organization that includes a study site/clinical trial at its location. Organization transfers are not allowed in the last year of the performance period.

Change in Principal Investigator: Unless otherwise restricted, changes in PI will be allowed at the discretion of the USAMRAA Grants Officer, provided that the intent of the award mechanism is met.

C. Disclosure of Proprietary or Confidential Information

Do not include proprietary or confidential information in a pre-application or abstract. Proprietary information should only be included in a full application if necessary for evaluation.

Evaluators must agree that proprietary or confidential information in the application will be used for evaluation purposes only and will not be further disclosed or used. All applications may be subject to public release under the Freedom of Information Act (FOIA).

Applications for funded projects will be subject to public release under the FOIA to the extent that they are incorporated in an award document; applications that are not selected for funding will not be subject to public release.

D. Marking of Proprietary or Confidential Information

Conspicuously and legibly mark any proprietary or confidential information that is included in the application.

E. Inquiry Review Process (IRP)

Although not required by law or acquisition regulation, CDMRP offers a courtesy to all applicants in an effort to maintain high integrity in its review processes. If an application is not recommended for funding and a factual or procedural error is believed to have occurred during the review of the application, the organization or PI may submit an inquiry within 15 business days after the notification email is sent. Inquiries submitted after 15 business days will not be considered.

The inquiry must specifically address a factual or procedural error that is believed to have occurred during review of the application, as defined below:

- **Factual error:** An error in the review (peer or programmatic) that is restricted to, or based on, fact. Differences of opinion between reviewers or between reviewer(s) and an applicant are not factual errors.

- **Procedural error:** An error in the review (peer or programmatic) that is restricted to review process adherence. Review process did not follow the procedures as outlined in the program announcement describing peer and programmatic review (e.g., documents requested in the program announcement and submitted with the original application were left out of the peer or programmatic review package).

Inquiries should be submitted through the CDMRP Help Desk at help@eBRAP.org. An inquiry review panel consisting of CDMRP staff will determine whether an error occurred in either peer or programmatic review and, if so, recommend corrective action where appropriate. The determination of an error in the review process is not a guarantee of funding. The final determination of the IRP and the funding decision are not subject to appeal. Questions related to the IRP prior to or after submitting an inquiry should be directed to the CDMRP Help Desk at help@eBRAP.org.

F. Information Service

Applicants may use the technical reference facilities of the U.S. Department of Commerce National Technical Information Service (https://www.ntis.gov) and/or the Defense Technical Information Center (DTIC) (https://discover.dtic.mil) to obtain information about existing research to avoid duplication of scientific and engineering effort.

G. Freedom of Information Act Requests

The FOIA (5 USC 552) provides a statutory basis for public access to official government records. The definition of "records" includes documentation received by the government in connection with the transaction of public business. Records must be made available to any person requesting them unless the records fall under one of nine exceptions to the Act (www.usdoj.gov/oip/index.html).

When a FOIA request asks for information contained in a successful application that has been incorporated into an award document, the submitter will be contacted and given an opportunity to object to the release of all or part of the information that was incorporated. A valid legal basis must accompany each objection to release. Each objection will be evaluated by USAMRDC in making its final determination concerning which information is or is not releasable. If information requested is releasable, the submitter will be given notice of USAMRDC's intent to release and will be provided a reasonable opportunity to assert available action.

H. Information Release

A recipient of an award will be required to agree to the release of information pertaining to the research and development supported by the federal agency. "Information" includes but is not limited to news releases, articles, manuscripts, brochures, advertisements, still and motion pictures, speeches, trade association meetings, and symposia. Certain research topics may require prior approval by the contracting officer prior to publishing, reference DFARS 252.204-7000.

The following statements must be included in all information releases:

(1) All releases shall identify the award number and include a statement acknowledging the federal sponsoring agency. The release shall also contain a statement that the opinions, interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the DOD. The requirement with specific language will be included in the award notice. Below is an example:

"This work was supported by the Office of the Assistant Secretary of Defense for Health Affairs and the Defense Health Agency J9, Research and Development Directorate, or the U.S. Army Medical Research Acquisition Activity at the U.S. Army Medical Research and Development Command, in the amount of (*insert total costs*), through the (*insert program name*) under Award No. (HT9425-23-1-XXXX). Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense."

(2) "In conducting research using animals, the investigator(s) adheres to the laws of the United States and regulations of the Department of Agriculture." Include required assurances, approvals, documents and information specified on the ACURO website. (https://mrdc.health.mil/index.cfm/collaborate/research_protections/acuro).

(3) "In the conduct of research utilizing recombinant DNA, the investigator adhered to NIH Guidelines for research involving recombinant DNA molecules." (https://www.nih.gov/)

(4) "In the conduct of research involving hazardous organisms or toxins, the investigator adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories." (https://www.cdc.gov/safelabs/resources-tools.html)

Failure to include the above statements and adhere to the above regulations, when required, may result in loss of funding.

I. Contracted Fundamental Research

Any awards to universities or industry and funded by Basic Research funds (6.1), or to universities for on-campus research and funded by Applied Research funds (6.2), meet the DOD definition of "Contracted Fundamental Research." The results of this research are to be unrestricted to the maximum extent possible. The research shall not be considered fundamental in those rare and exceptional circumstances where the effort presents a high likelihood of disclosing performance characteristics of military systems or manufacturing technologies that

are unique and critical to defense, and where agreement on restrictions have been recorded in the award.

J. Sharing of Application Information

The USAMRDC shares application information with other federal funding agencies (e.g., NIH, National Science Foundation, VA) to inform funding priorities and decisions, and to increase transparency. In addition, award data are made available to the public through the CDMRP website and to other organizations such as the International Cancer Research Partnership. By sharing and leveraging this information, duplication of effort can be avoided, allowing for the support of more investigators with federal funds. The CDMRP believes that such sharing allows for a more expeditious translation of research results into knowledge, products, and procedures to improve human health. Updates on CDMRP-funded awards including awardee information and published results are shared on DTIC.

K. Sharing of Data and Research Resources

The CDMRP intends that information, data, and research resources generated under awards funded by the program announcement be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large.

Data and research resources generated by funded research should be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public. The expectations for sharing of data and research resources apply to all types of research funded by the program announcement. This includes all data and research resources generated during the project's period of performance as annotated in the assistance agreement:

- **Unique Data** are defined as data that cannot be readily replicated. Examples of unique data include large research data collections that are expensive to replicate; studies of unique populations, such as patients to whom access is not widely available; studies conducted at unique times, such as during military conflict; studies of rare phenomena, such as rare diseases. (Adapted from https://sharing.nih.gov/data-management-and-sharing-policy/sharing-scientific-data.)

- **Final Research Data** are defined as recorded factual material commonly accepted in the scientific community as necessary to document and support research findings. These are not the summary statistics or tables; rather, final research data are the data on which summary statistics and tables are based. Final research data do not include laboratory notes or notebooks, partial datasets, preliminary analyses, drafts of scientific papers, plans for future research, peer review reports, communications with colleagues, or physical objects, such as gels or laboratory specimens. (Adapted from https://sharing.nih.gov/data-management-and-sharing-policy/sharing-scientific-data.)

- **Research Resources** include, but are not limited to, the full range of tools that scientists and technicians use in the laboratory, such as cell lines, antibodies, reagents, animal models, growth factors, combinatorial chemistry, DNA libraries, clones and cloning tools, methods, laboratory equipment and machines. (Adapted from https://sharing.nih.gov/other-sharing-policies/research-tools-policy.)

Data and research resources generated from CDMRP-funded research should be made as widely available as possible while safeguarding the privacy of participants and protecting confidential and proprietary data and third-party intellectual property.

By sharing and leveraging data and research resources, duplication of effort can be avoided, allowing for the support of more investigators with federal funds. The USAMRDC believes that such sharing allows for a more expeditious translation of research results into knowledge, products, and procedures to improve human health. Depending on the program announcement, the PI may be required to participate in the following:

- Traumatic Brain Injury: If the project includes TBI research, the PI may be required to make TBI data generated via an award available to the research community by depositing de-identified research data into the Federal Interagency TBI Research (FITBIR) Informatics System (https://fitbir.nih.gov).

- Clinical Trials: If the project includes a clinical trial(s), the PI may be required to register the clinical trial(s) individually on the registry and database ClinicalTrials.gov (https://www.clinicaltrials.gov/).

For additional information on CDMRP's expectations and policies for data sharing, refer to "Policy on Sharing Data & Research Resources," available on eBRAP under Resources and Reference Material at https://ebrap.org/eBRAP/public/Program.htm. For unique data-sharing guidelines and requirements, refer to the instructions in the specific program announcement.

L. Property/Equipment

Unless otherwise specified in the award, the title to equipment or other tangible property acquired with government funds will vest in institutions of higher education or with non-profit organizations whose primary purpose is conducting scientific research. Normally, the title will vest in the recipient if vesting will facilitate scientific research performed by the organization for the government. Title to equipment or other tangible property acquired by for-profit organizations will conditionally vest in the organization subject to the requirements of the DoDGARs, Part 34.21. However, if the award is subsequently transferred to a new organization, the DOD reserves the right to require the transfer of equipment acquired with the award funds to the federal government or to an eligible third party.

M. Title to Inventions and Patents

In accordance with the Bayh-Dole Act (35 USC 200 et seq.), the recipient and collaborators may elect to retain title to their subject inventions, subject to meeting the reporting and patent filing requirements and retained rights to the U.S. government. The U.S. government shall, at a minimum, retain non-exclusive rights for the use of such inventions. Instructions in the assistance agreement concerning subject inventions must be followed.

APPENDIX VI: FORMATTING GUIDELINES

All pre-application and application documents must be legible and should conform to the formatting guidelines described below. The font size, spacing, page size, and margins may differ among the word processing, PDF, and printed versions. These guidelines apply to the document properties of the electronic version of the PDF file(s) as viewed on a computer screen.

- **Document Format:** Each attachment to the full application forms must be uploaded as an individual file in the format specified in the program announcement. All contributors to the application must use matching compatible versions of Adobe software for all PDF documents when editing and preparing application components. The use of different software versions will result in corruption of the submitted file.
- **Font Size:** 12 point, not condensed.
- **Font Type:** Times New Roman.
- **Spacing:** Single space or no more than six lines of type within a vertical inch (2.54 cm).
- **Page Size:** No larger than 8.5 inches x 11.0 inches (21.59 cm x 27.94 cm).
- **Margins:** At least 0.5 inch (1.27 cm) in all directions.
- **Print Area:** 7.5 inches x 10.0 inches (19.05 cm x 25.40 cm).
- **Color, High-Resolution, and Multimedia Objects:** Project narratives and pre-application files may include color, high-resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files; however, these objects should not exceed 15 seconds in length and a size of 10 MB. Photographs and illustrations must be submitted in JPEG format; bitmap and TIFF formats are not allowed. Please note that these types of objects are not allowed in the technical and public abstracts.
- **Scanning Resolution:** 100 to 150 dots per inch.
- **Internet URLs:** URLs, or web addresses, directing reviewers to websites that contain additional information about the proposed research are not allowed in the application or its components. Inclusion of such URLs may be perceived as an attempt to gain an unfair competitive advantage. However, links to publications referenced in the application are encouraged.
- **Language:** All documents must be submitted in English, unless otherwise specified in the program announcement (e.g., foreign transcripts submitted with English translations).
- **Headers and Footers:** Should not be used. Pre-existing headers and footers on required forms are allowed.
- **Page Numbering:** Should not be used.

- **Recommended Attachment Size:** Individual attachments should be no larger than 20 MB. ***If the file size for the entire Grants.gov submission package will or may exceed 200 MB, applicants should contact the Grants.gov Contact Center (***support@grants.gov***) for written confirmation that the file will be accepted or for other guidance.***

APPENDIX VII: BUDGET INSTRUCTIONS

An estimate of the total proposed research project cost, with a breakdown of all cost categories for each year, must be submitted on the Suggested DOD Military Budget Format and Justification form. For limits on funding amounts, types of costs, and period of performance, refer to Section II.D.4, Funding Restrictions. No budget will be approved by the government exceeding the cost limit stated in this funding opportunity announcement. The budget and budget justification should include sufficient detail for the government to determine whether the proposed costs are allowable, allocable, and reasonable for the proposed research.

The PI's name, eBRAP Log number, and period of performance fields should be entered at the top of the Suggested DOD Military Budget Format.

DOD Civilian and Military Personnel: Personnel involved in the project should be listed in this section; however, this award is not intended to provide salary support for any federal employee, as those costs were to have been included in infrastructure costs. If salary support is requested, sufficient justification must be provided in the budget justification section.

- **Name:** Beginning with the PI, list all participants who will be involved in the project during the initial budget period, whether or not salaries are requested. Include all collaborating investigators, research associates, individuals in training, mentor (if applicable), and support staff.

- **Role on Project:** Identify the role of each participant listed. Describe their specific functions in the proposed research in the budget justification.

- **Type of Appointment (Months):** List the number of months per year reflected in an individual's contractual appointment with the applicant organization. The government assumes that appointments at the applicant organization are full time for each individual. If an appointment is less than full time (e.g., 50%), note this with an asterisk (*) and provide a full explanation in the budget justification. Individuals may have split appointments (e.g., for an academic period and a summer period). For each type of appointment, identify and enter the number of months on separate lines.

- **Annual Base Salary:** Enter the annual organizational base salary (based on a full-time appointment) for each individual listed for the project.

- **Effort on Project:** List the percentage of each appointment to be spent on this project for all staff members including unpaid personnel.

- **Salary Requested:** Enter the salary for each position for which funds are requested. This is calculated automatically from the data provided. If you do not wish this to be calculated for you, uncheck the small "Calculate Salary" checkbox located in the lower portion of the field. Calculate the salary request by multiplying an individual's organizational base salary by the percentage of effort on the project.

- **Fringe Benefits:** Enter the fringe benefits requested for each individual in accordance with organizational guidelines.

- **Totals:** Calculated automatically from the data provided.

- **Major Equipment:** Provide an itemized list of proposed equipment, showing the cost of each item. Equipment is any article of nonexpendable tangible property having a useful life of more than 1 year and an acquisition cost of $5,000 or more per unit.

- **Materials, Supplies, and Consumables:** The budget justification for supporting material and supply (consumable) costs should include a general description of expendable material and supplies.

- **Travel Costs:** PIs are responsible for budgeting for all costs associated with travel, including airfare, hotel, etc., associated with the trip. Anticipated travel costs should be built into the budget at current or projected DOD per diem rates. Travel for military and DOD civilians will be funded through DTS. Travel costs may include:

    - Travel costs for up to one investigator to travel to one scientific/technical meeting per year.

    - Travel costs between collaborating organizations.

- **Research-Related Subject Costs:** Include itemized costs of subject participation in the proposed research. These costs are strictly limited to expenses specifically associated with the proposed research.

- **Other Direct Costs:** Itemize other anticipated direct costs such as publication and report costs, equipment rental (provide hours and rates), communication costs, and organizationally provided services. Unusual or expensive items should be fully explained and justified. Estimate the costs of publishing and reporting research results, including direct charges for clerical services, illustrations, reprints, and distribution. Organizationally provided services should be supported by the organization's current cost/rate schedule. These items should be described in detail and clearly justified.

- **Contract Costs (Partnership/Collaboration Costs):** Should an intramural organization propose collaboration with an extramural entity for part of the research effort, the intramural organization will receive all funds and is responsible for executing all necessary contractual or assistance funding awards to collaborating partners through the agency's procedures. **All direct and indirect costs of any partnership/collaboration costs must be included in the total direct costs of the primary award**. The nature of the partnership/collaboration should be described in the Budget Justification section.

- **Total Direct Costs:** Calculated automatically from the data provided for the initial budget period and for the entire proposed period of support.

- **Total Indirect Costs:** If funds for indirect costs are requested, sufficient justification must be provided in the Justification section. Travel costs for any resultant award will be

funded directly via DTS and shall not be included in the basis for indirect cost calculations. The government reserves the right to disallow any indirect costs not sufficiently justified. All direct and indirect costs of any proposed collaborator must be included in the total direct costs of the primary award. Refer to Section II.D.4, Funding Restrictions, of the program announcement for detailed information.

- **Total Costs:** This section is calculated automatically from the data provided.

- **Fee:** A profit or fixed fee is not allowable on awards or on subawards.

***Budget Justification Instructions*:** Provide a clear budget justification for each item in the budget over the entire period of performance in the Justification section of the Suggested DOD Military Budget. Itemize direct costs within each budget category for additional years of support requested beyond year one.

- **Federal Agency Financial Plan (required):** Provide a detailed Federal Agency Financial Plan after the budget justification information in the DOD Military Budget. The plan delineates how all FY22 funding will be obligated by **September 30, 2023**. The plan must include the funding mechanism(s) or contractual arrangements that will be used to carry over funds between fiscal years, if applicable. Any FY22 funding not obligated by September 30, 2023 may be withdrawn by the issuing Comptroller.