I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Joint Warfighter Medical Research Program

Military Medical Research and Development Award

Intramural Funding Opportunity

Announcement Type: Initial

Funding Opportunity Number: HT942524JWMRPMMRDA

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), June 3, 2024
- **Invitation to Submit an Application:** July 3, 2024
- **Application Submission Deadline:** 11:59 p.m. ET, August 29, 2024
- **End of Application Verification Period:** 5:00 p.m. ET, September 3, 2024
- **Peer Review:** November 2024
- **Programmatic Review:** January 2025

This program announcement must be read in conjunction with the General Application Instructions, version 901. The General Application Instructions document is available for downloading via eBRAP.

TABLE OF CONTENTS

II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

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. An intramural submission is 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 academia, biotechnology companies, foundations, government, and research institutes (e.g., intramural investigators submitting through a research foundation). Submissions from extramural investigators to this program announcement will be withdrawn. Extramural applicants applying through extramural organizations should use the separate funding opportunity that is available through the electronic Biomedical Research Application Portal (eBRAP) at https://eBRAP.org/ under funding opportunity number HT942524SJWMRPMMRDA.

II.A. Program Description

The U.S. Army Medical Research Acquisition Activity (USAMRAA) is soliciting applications to the fiscal year 2024 (FY24) Joint Warfighter Medical Research Program (JWMRP) using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC) is the program management agent for this funding opportunity. Congress initiated the JWMRP in 2012 to augment and accelerate high-priority DOD and Service medical requirements and to continue prior year initiatives that are close to achieving their objectives and yielding a benefit to military medicine. The ultimate goal of the program is to expedite the delivery of highly impactful medical solutions to Service Members and Military Health System (MHS) beneficiaries; thus the Service advanced product development communities are critical partners in executing the JWMRP. Appropriations for the JWMRP from FY12 through FY23 totaled $595 million (M). The FY24 appropriation is $20M.

Congressional direction stipulates that the funds from the JWMRP shall not be used for new projects or for basic research. To be eligible for JWMRP funding, applicants must have already received DOD core or DOD Congressional Special Interest funding (including DOD Small Business Innovation Research [SBIR]/Small Business Technology Transfer [STTR] awards) for the same project that is being proposed for continuation under this Military Medical Research and Development Award (MMRDA). The funding shall be awarded at DOD discretion following a review of medical research and development gaps as well as unfinanced medical requirements of the Services.

II.A.1. FY24 JWMRP Focus Areas

The JWMRP Programmatic Panel identified the following Focus Areas as the highest priorities for FY24 JWMRP funding to meet critical research and development gaps and

Service medical requirements. To meet the intent of the funding opportunity, applications to the FY24 JWMRP must address at least one of the Focus Areas listed below.

- Broad spectrum and/or pathogen agnostic approaches to prevent and/or treat endemic or emerging infectious diseases of high operational impact.
- Preventative capabilities to promote the Warfighter's physiological and cognitive (1) performance and readiness and (2) injury prevention.
- Solutions for semi-autonomous or autonomous medical care from point of injury across the continuum of care, including support of triage, prolonged patient care and transport in contested environments.
- Virtual/telehealth and decision support with artificial intelligence solutions to provide combat casualty care/prolonged care.
- Hemorrhage control and resuscitation solutions, including blood and blood products, and anti-shock therapeutics, to enable delivery of life-saving care across the continuum of care.

II.A.2. Award History

JWMRP awards were first offered in FY12. To date, a total of 187 individual projects have received funding.

II.B. Award Information

The MMRDA mechanism is **intended to fund the logical continuation of previously DOD-funded research or development efforts relevant to the above FY24 JWMRP Focus Areas** with the highest potential to augment and accelerate medical product development and health care solutions for active-duty Service Members, their Families, Veterans, and/or the American public. The MMRDA supports a wide range of research projects, spanning late-stage preclinical studies, late-state technology development efforts, technology demonstration, and translational research.

A Clinical Research or Clinical Trial Option is available to specifically support clinical research/observational studies, all phases of clinical trials/interventional studies, and/or correlative studies in support of the development of promising pharmaceutical or biologic candidates, medical devices, and technologies. Note: Applications submitted under this option will be required to submit additional relevant application materials.

Clinical research encompasses research with human data, human specimens, and/or interaction with human subjects. Clinical research is observational in nature and includes:

(1) Research conducted with human subjects and/or material of human origin such as data, specimens, and cognitive phenomena for which an investigator (or co-investigator) does ***not*** seek to assess the safety, effectiveness, and/or efficacy outcomes of an intervention. Research meeting this definition may include but is not limited to: (a) mechanisms of human disease, (b)

diagnostic or detection studies (e.g., biomarker or imaging), (c) health disparity studies, and (d) development of new technologies.

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

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

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

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

Applications received in response to both the FY24 JWMRP BAA and intramural program announcement will be evaluated together and equally considered for funding. No advantage is conferred by submitting an application via one funding opportunity versus the other. The government reserves the right to fund any combination of extramural and/or intramural applications.

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

Submission Options: Applications must be submitted under one of the two following options. It is important to choose the option that is most appropriate for the proposed research and to submit all of the documents required for the option selected. Please contact the Electronic Biomedical Research Application Portal (eBRAP) Help Desk (at help@eBRAP.org or 301-682-5507) if there is any question as to which option should be selected.

- **Military Medical Research and Development Award (MMRDA)**, for applications proposing research that does *not* include human subjects, human biological samples (prospective or retrospective), or human data sets.

- **Military Medical Research and Development Award – Clinical Research or Clinical Trial Option (MMRDA–CRTO)**, for applications proposing research that includes any human subjects, human biological samples (prospective or retrospective), or human data sets.

The anticipated total costs budgeted for the entire period of performance for an FY24 MMRDA Award should not exceed **$2,000,000,** or **$3,400,000** for the MMRDA-CRTO. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

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

The CDMRP expects to allot approximately $7.4M to fund approximately two MMRDA applications and one MMRDA-CRTO application. Funding of applications received is

contingent upon the availability of federal funds for this program, the number of applications received, the quality and merit of the applications as evaluated by peer and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY24 funding opportunity will be funded with FY24 funds, which will expire for use on September 30, 2030.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: ***Applications for this program announcement may only be submitted by intramural DOD organizations. Submissions from extramural applicants to this program announcement will be withdrawn.***

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

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

Awards are made to eligible ***organizations***, not to individuals. Refer to the General Application Instructions, Appendix 1, for additional recipient qualification requirements.

II.C.1.b. Principal Investigator

Independent 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 Principal Investigator (PI), regardless of ethnicity, nationality, or citizenship status, must be employed by or affiliated with an eligible organization.

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

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

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

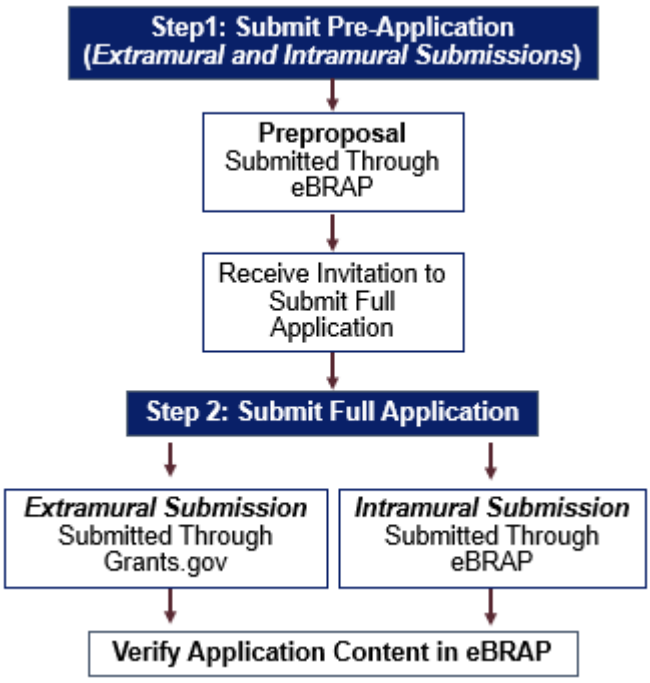
II.D. Application and Submission Information

II.D.1. Location of Application Package

Submission is a two-step process requiring both a ***pre-application*** and a ***full application*** submitted via the eBRAP portal.

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

Application Submission Workflow



Extramural Submission (*Disallowed for this funding opportunity*): An application submitted by an extramural organization for an extramural or intramural PI working within an extramural or intramural organization. For example, a research foundation submitting an application for a DOD employee working within a DOD organization would be considered an extramural submission. Extramural organizations should submit applications under funding opportunity HT942524SJWMRPMMRDA, available from Grants.gov (https://grants.gov).

Intramural Submission: An application submitted by an intramural DOD organization for an investigator employed by that organization. Download and submit application package components for HT942524JWMRPMMRDA from eBRAP (https://ebrap.org).

The submission process should be started early to avoid missing deadlines. Regardless of submission type or portal used, all pre- and full application components must be submitted by the deadlines stipulated on the first page of this program announcement. There are no grace periods for deadlines; failure to meet submission deadlines will result in application rejection.

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

Submitting applications that propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application(s).

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

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

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

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

All pre-application components must be submitted by the PI through eBRAP.

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

To begin the pre-application process, first select whether the submitting organization is extramural or intramural, then confirm your selection or cancel. ***Note: Applications for this program announcement may only be submitted by intramural 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.

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

Application Includes:	Select Option:
NO human subjects, human biological samples (prospective or retrospective), or human data sets	Military Medical Research and Development Award (MMRDA)
Any human subjects, human biological samples (prospective or retrospective), or human data sets	Military Medical Research and Development Award – Clinical Research or Clinical Trial Option (MMRDA–CRTO)

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

Pre-application submissions must include the following components posted in eBRAP:

- **Pre-Application Template (six-page limit)**: Download and provide responses to the questions in the **FY24 JWMRP Pre-Application Template**. Refer to the ***Clinical Trial and Technology/Knowledge Readiness Level Definitions*** (see Appendix 2). No figures, charts, graphs, or other additional material will be accepted during the pre-application process.

  Note: Upload the completed Pre-Application Template as a single PDF file.

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

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

- Whether the pre-application describes the continuation of a prior year effort that is ongoing/active at the time of pre-application submission or that was completed no more than 2 years prior to the pre-application submission deadline.

- Whether the pre-application describes the continuation of a prior year effort that has already achieved a Technology Readiness Level (TRL)/Knowledge Readiness Level (KRL) of 5 or greater (see Appendix 2 for ***Clinical Trial and Technology/Knowledge Readiness Level Definitions***).

- Whether the PI for the proposed follow-on effort is the same as the PI of the prior year effort described in the pre-application.

- How well the pre-application describes a follow-on effort that is a logical continuation of a previously funded, prior year research or materiel/knowledge product development effort, while avoiding interdependency of aims.

- How well the proposed research or development effort addresses one or more of the FY24 JWMRP Focus Areas.
- Relative potential of the proposed effort to augment and/or accelerate clinical, technical, or materiel/knowledge product development with a clear benefit to military medicine.
- How well the pre-application adequately describes the products or deliverables expected from the proposed follow-on effort and any associated challenges.
- How well the regulatory strategy, commercialization strategy, and the estimated TRL/KRL demonstrates the transition potential of the anticipated product/outcome.

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

Following the pre-application screening, PIs will be notified as to whether they are invited to submit full applications. The estimated date when PIs can expect to receive notification of an invitation to submit a full application is indicated in Section I, Overview of the Funding Opportunity. No feedback (e.g., a critique of the pre-application's strengths and weaknesses) is provided at this stage. Because the invitation to submit a full application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

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

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

Full applications ***must*** be submitted through eBRAP. Refer to the General Application Instructions, Section IV, for considerations and detailed instructions regarding full application submission.

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

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

(a) Attachments:

Each attachment to the full application components must be uploaded as an individual file in the format specified and in accordance with the formatting guidelines listed in the General Application Instructions, Appendix 2.

- **Attachment 1: Project Narrative (20-page limit): Upload as "ProjectNarrative.pdf".** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs (uniform resource locators) that provide additional information that expands the Project Narrative and could confer

an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

Describe the proposed project in detail using the outline below.

- Describe the previously funded research or materiel/knowledge product development effort identified in the notification of invitation, including a description of the accomplishments and outcomes from that award. Explain how this proposed effort is a logical continuation of the previous research or materiel/knowledge product development effort.

- Explain how the research has the potential to augment and/or accelerate medical product development in at least one of the FY24 JWMRP Focus Areas.

- Present the scientific rationale behind the proposed research or materiel/knowledge product development effort, including relevant literature citations, preliminary data, and/or preclinical data that led to the development of the proposed research, to support feasibility. Preliminary data may be published or unpublished. Any unpublished preliminary data provided should originate from the laboratory of the PI or member(s) of the collaborating team.

- Describe previous experience among members of the project team most pertinent to the proposed research.

- Clearly demonstrate that there is sufficient scientific evidence to support moving into the proposed stage of research.

- As applicable to the proposed research, provide a summary of relevant studies, clinical studies or clinical trials, and distinguish how the proposed study differs from other relevant or recently completed research or clinical trials. If applicable, 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.

- **Hypotheses/Objectives:** State the hypotheses to be tested and/or the objective(s) 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 this application is part of a larger study, present only tasks that this award would fund. Avoid interdependency of specific aims when possible (i.e., dependency on successful outcomes of other ongoing related research efforts).

- **Research Strategy and Feasibility:**

  - Describe the experimental design, methods, and analyses, including appropriate controls, choice of animal model (if applicable), and the endpoints/outcome measures to be used, in sufficient detail for evaluation of feasibility and effectiveness in supporting completion of the project aims.

- Applications that include research on animal models are also required to submit Attachment 8, Animal Research Plan.

- Applications that include any human subjects, human biological samples (prospective or retrospective), or human data sets are also required to submit Attachment 10, Human Subjects/Sample Acquisition and Safety Procedures.

- If the proposed research involves access to active-duty military and/or VA patient populations and/or DOD or VA resources or databases, describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research.

- Describe potential problem areas and discuss alternative methods/approaches that may be employed to overcome them, including interdependency of aims (i.e., dependency on successful outcomes of other ongoing related research efforts).

For applications submitted under the 'Clinical Research or Clinical Trial Option':

- Provide detailed plans for initiating and conducting the clinical study or trial during the course of this award. Describe the type of clinical study or trial to be performed (e.g., observational, treatment, prevention, diagnostic), the phase of trial and/or class of device (as appropriate), and the study model (e.g., single group, parallel, crossover).

- Identify and describe the hypothesis/intervention to be studied and the projected outcomes.

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

- Provide a brief description of the study population, criteria for inclusion/exclusion, and the methods that will be used for recruitment/accrual of human subjects, samples, and/or human data sets.

- Describe measures that will be taken to reduce bias, such as blinding of subjects, clinicians, data analysts, and/or others during the study.

- Discuss risk/benefit considerations, including a clear and detailed description of potential ethical issues raised by the proposed study, and a detailed plan for how the ethical issues will be addressed.

- Document the availability and accessibility of the drug/compound, device, or other materials needed for the duration of the proposed study and describe how quality control will be addressed.

- Describe the potential for subject loss to follow-up, and how such loss will be handled/mitigated.

- **Data and Statistical Analysis Plan:**

  - Describe how data will be collected and analyzed in a manner that is consistent with the study objectives. If applicable, include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Specify the approximate number of human subjects/samples that will be accrued, if applicable. If multiple study sites are involved for human subject recruitment, state the approximate number to be enrolled at each site.

  - Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the U.S. Food and Drug Administration (FDA), if applicable.

- **Study Personnel:** Identify the key members of the study team and describe their roles on the project, including sufficient clinical and/or statistical expertise. For studies involving human subjects, an independent research monitor (external to the study), study coordinator(s), and statistician should be included as applicable.

- **Attachment 2: Supporting Documentation: Combine and upload as a single file named "Support.pdf".** Start each document on a new page. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

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

  - **References Cited:** List the references cited (including URLs, if available) in the Project Narrative using a standard reference format.

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

  - **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present government award under which the facilities or equipment items are now accountable. There is no form for this information.

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

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

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

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

  - **Background and Proprietary Information**: Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used.

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

- **Data and Research Resources Sharing Plan:** Describe the type of data or research resources to be made publicly available as a result of the proposed work. Describe how data and resources generated during the performance of the project will be shared with the research community. Include the name of the repository(ies) where scientific data and resources arising from the project will be archived, if applicable. If a public repository will not be used for data or resource sharing, provide justification. Provide a milestone plan for data/results dissemination including when data and resources will be made available to other users, including dissemination activities with a particular focus on feeding back the data to affected communities. Refer to CDMRP's Policy on Data & Resources Sharing located on the eBRAP "Funding Opportunities & Forms" web page https://ebrap.org/eBRAP/public/Program.htm for more information about CDMRP's expectations for making data and research resources publicly available.

- **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 U.S. Department of Veterans Affairs (VA) Resources *(if applicable)*:** Provide a letter of support signed by the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the Associate Chief of Staff for Research and Development (ACOS/R&D) or the Clinical Service Chief, confirming access to VA patients, resources, and/or VA research space. If the VA-affiliated non-profit corporation is not identified as the applicant organization for administering the funds, include a letter from the VA ACOS/R&D confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.

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

  - Technical abstracts should be written using the outline below. Clarity and completeness within the space limits are highly important. **Background:** State how the proposed research addresses at least one of the FY24 JWMRP Focus Areas. Present the scientific rationale behind the proposed work. Include the current TRL/KRL of the product or knowledge outcome (must be 5 or greater), and the estimated target TRL/KRL upon completion of the proposed research (see Appendix 2 for ***Clinical Trial and Technology/Knowledge Readiness Level Definitions***).

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

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

  - **Study Design:** Briefly describe the study design including appropriate controls.

  - **Impact:** Highlight the likely contributions of the initiative to augment and/or accelerate a materiel/knowledge product development effort. Briefly explain how the proposed project will have an immediate or potential long-term benefit that may lead to a major impact on the health and well-being of Service Members, their Families, Veterans, and/or the American public.

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

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

- Summarize the objectives and rationale for the proposed research.
- What population will the research help, and how will it help them?
- What are the potential applications, benefits, and risks of the anticipated outcomes?
- What are the likely contributions of the proposed research project to advancing research, patient care, and/or quality of life?

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

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

- **Attachment 6: Impact Statement (two-page limit): Upload as "Impact.pdf".** Explain why the proposed research or materiel/knowledge product development effort is important and relevant to the role of the JWMRP in addressing high-priority DOD medical requirements and capability gaps and accelerating the development of products that will impact the Warfighter within the context of the FY24 JWMRP Focus Area(s) being addressed.

  - ***Describe the potential impact on civilian and military populations:*** Provide information about the incidence and/or prevalence of the disease or condition in the civilian population, as well as in Service Members, their Families, and/or Veterans. Explain how the knowledge, technologies, or products gained from the research could be implemented in a dual-use capacity to benefit the civilian population and address the health care needs of Service Members, their Families, and/or Veterans, as appropriate. Describe how the research will result in faster and/or better delivery of health care solutions for the Warfighter.

  - ***Describe the short-term impact:*** Detail the anticipated short-term outcome(s)/product(s) (knowledge and/or materiel) that will be directly attributed to the results of the proposed research or materiel/knowledge product development effort and describe how they will impact the relevant populations. Describe how the study will augment and/or accelerate product development, as applicable.

  - ***Describe the long-term impact:*** Explain the anticipated long-term gains from this research and describe how they may impact the health and readiness of Warfighters. Compare to the information known/products currently available, as applicable.

- **Attachment 7: Transition Plan (three-page limit): Upload as "Transition.pdf".** Describe/discuss the methods and strategies proposed to move the product/knowledge/

intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Demonstrate how the proposed product or knowledge outcome is currently at a minimum TRL or KRL of 5 and estimate the target TRL/KRL upon completion of the proposed research (see Appendix 2 for ***Clinical Trial and Technology/Knowledge Readiness Level Definitions***). Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The plan for post-award transition of the anticipated research outcomes should include the components listed below, as appropriate and applicable to the research proposed.

- A description of the funding strategy to transition to the next level of development and/or commercialization. Include details of partnerships with DOD organizations, small business, and/or industry, as well as other resources, including specific funding opportunities or other financial support, that will be used to provide continuity of development. Include a description of whether there is a commercial market for the product/knowledge/ intervention or if the anticipated medical solutions are specific for a military market.

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

- A brief schedule and milestones for transitioning the anticipated research outcomes to the next phase of development (i.e., next-phase clinical trials, commercialization/ transition to industry, delivery to market, incorporation into clinical practice, and/or approval by a Regulatory Agency). Describe the steps necessary to adapt and transition the civilian product/knowledge/intervention for military fielding/adoption/use.

- 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 SBIR/STTR data supports the proposed follow-on development effort, describe the connection between the prior SBIR/STTR and the current project and explain all active SBIR/STTR data rights.

- If applicable, state and identify the proprietary information that will be provided to the government and indicate whether the applicant will require a waiver of the federal purpose license.

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

- **Attachment 8: Animal Research Plan (*only applicable and required for applications proposing animal studies*; three-page limit): Upload as "AnimalResPlan.pdf".** If the proposed study involves animals, a summary describing the animal research that will be conducted must be included in the application. ***Proposed studies should not rely on samples, reagents, or tools that are contingent upon completion of other ongoing efforts outside the scope of this proposal.*** Consult the ARRIVE guidelines 2.0 (Animal Research: Reporting of *In Vivo* Experiments) to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines 2.0 can be found at https://arriveguidelines.org/arrive-guidelines. The Animal Research Plan may not be an exact replica of the protocol(s) submitted to the Institutional Animal Care and Use Committee (IACUC). The Animal Research Plan should address the following points to achieve reproducible and rigorous results for each proposed animal study:

  - Briefly describe the research objective(s) of the animal study. 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.

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

  - Describe the randomization and blinding procedures for the study and 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 endpoints(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: Intervention (*only applicable and required for clinical trial applications submitted under the 'Clinical Research or Clinical Trial Option';* no page limit): Upload as "Intervention.pdf".** The Intervention attachment should include the components listed below.

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

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

- **Study Procedures:** Describe the interaction with the human subject, including the study intervention that they will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention). Describe measures to ensure consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions). Clearly delineate research procedures from routine clinical procedures. 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. Discuss how compliance with current Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) guidelines and other regulatory considerations will be established, monitored, and maintained, as applicable.

- **Laboratory Evaluations:** State the biospecimen that will be collected along with the collection schedule and amount. Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects). Describe the specimen storage plan, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the actions to be taken to allow the use of stored specimens in future research studies, if applicable. Identify the laboratory performing each evaluation, the applicable quality standard, and any special precautions that should be taken in handling the samples. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Questionnaires and Other Research Data Collection Instruments:** Include a copy of the most recent version of questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.

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

- **Attachment 10: Human Subjects/Sample Acquisition and Safety Procedures (*applicable and required for all applications submitted under the 'Clinical Research or Clinical Trial Option'*; no page limit): Upload as "HumSubProc.pdf".** If the proposed study involves human subjects, human biological samples (prospective or retrospective), or human data sets the applicant is required to submit a summary describing the human research that will be conducted. ***Proposed studies should not rely on samples, reagents, or tools that are contingent upon completion of other ongoing efforts outside the scope of this proposal.***

  - **Study/Sample 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/sample population at each site and describe the efforts that will be made to achieve accrual goals. For clinical studies/trials proposing to include military personnel, refer to the General Application Instructions, Appendix 4, for more information.***

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

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

research. Describe the strategy for the inclusion of women and minorities appropriate to the objectives of the study, including a description of the composition of the proposed study population in terms of sex/gender, racial, and ethnic group, and an accompanying rationale for the selection of subjects. ***Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement.***

- **Inclusion Enrollment Plan:** Provide an anticipated enrollment table(s) for the inclusion of women and minorities using the Public Health Service (PHS) Inclusion Enrollment Report, a three-page fillable PDF form that can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm. The enrollment table(s) should be appropriate to the objectives of the study with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. ***Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement.***

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

  - Describe the recruitment process in detail. Address the availability of human subjects for each enrollment site. 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.

  - Discuss past efforts in recruiting human subjects from the target population for previous related clinical studies/trials performed by the research team (if applicable).

  - Address any potential barriers to human sample or subject accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention for example. Identify ongoing clinical studies/trials that may compete for the same patient population and how they may impact enrollment progress.

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

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

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

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

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

- Address how privacy and time for decision-making will be provided and whether the potential human subject will be allowed to discuss the study with anyone before making a decision.

- 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/trial.

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

– **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry.

– **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:**

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

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

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

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

- **Attachment 11: Regulatory Strategy (*applicable and required for all product development efforts and all applications submitted under the 'Clinical Research or Clinical Trial Option'*; no page limit). If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** Answer the following questions and provide supporting documentation as applicable.

  - State the product/intervention name.

  For products/interventions that do not require regulation by a Regulatory Agency:

  - Provide evidence that the clinical study/trial does not require regulation by a Regulatory Agency. No further information for this attachment is required.

  For products/interventions that require regulation by a Regulatory Agency:

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

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

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

- If the proposed research or trial requires an Investigational New Drug (IND) application or an Investigational Device Exemption (IDE) application, the application must be submitted to the FDA by/before September 30, 2025. The IND or IDE should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical study/trial. Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold). If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of this product. A copy of the Regulatory Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application. The government reserve the right to withdraw funding if an IND or IDE is necessary but has not been submitted to the FDA by/before ***September 30, 2025***.

- If available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed. The government reserves the right to withdraw funding if this documentation has not been obtained by ***March 31, 2026***.

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

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

- Provide the current status for manufacturing development (e.g., manufacturer's name, GMP-compliant lots available, status of stability testing), 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) to demonstrate readiness for the next level of development and/or commercialization.

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

- **Attachment 12: Data Management (*applicable and required for all applications submitted under the 'Clinical Research or Clinical Trial Option'*; no page limit): Upload as "Data_Manage.pdf".** The Data Management attachment should include the components listed below.

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

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

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

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

    - **Confidentiality:**

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

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

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

    - **Data capture, verification, and disposition:** Describe how data will be captured and verified, including the quality assurance and quality control measures taken during collection, analysis, and processing. Describe where data (both electronic and hard copy) will be stored; who will keep the data; how the data will be stored, if applicable; the file formats and the naming conventions that will be used; the process for locking the database at study completion; and the length of time that data will be stored, along with a justification for the time frame of preservation, which may include considerations related to the balance between the relative

value of data preservation and other factors such as the associated cost and administrative burden of data storage. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process. For studies requiring Regulatory Agency oversite, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.

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

- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether the results of screening and/or study participation will be shared with human subjects or their primary care provider, including results from any screening or diagnostic tests performed as part of the study. In cases of national security or controlled unclassified information concerns, include a statement that the data cannot be made available to the public (e.g., "This data cannot be cleared for public release in accordance with the requirements in DoD Directive 5230.09.").

- **Attachment 13: Study Personnel and Organization (*applicable and required for all applications submitted under the 'Clinical Research or Clinical Trial Option'*; no page limit): Start each document on a new page. Combine into one document and upload as "Personnel.pdf".** The Study Personnel and Organization attachment should include the components listed below.

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

  - **Study Personnel Description:** Briefly describe the composition of the study team, including roles of the individuals listed in the organizational chart on the project along with any external consultants or advisors who will provide critical guidance and input to the study team (e.g., statistician, regulatory expert, commercialization consultant, clinical ethicist, patient advocate). Study coordinator(s) should be included. Describe how the levels of effort for each individual are appropriate to successfully support the proposed research. Describe relevant background and qualifications that demonstrate appropriate expertise to accomplish the proposed

work, including previous interactions with the relevant Regulatory Agency, if applicable.

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

- **Research & Related Personal Data:** Refer to the General Application Instructions, Section V.A.(c), for detailed instructions.

- **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section V.A.(d), for detailed instructions.

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

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

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

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

- **Intragovernmental/Intramural Budget:** Use the "Suggested Intragovernmental/Intramural Budget Form", available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). The budget should cover the entire period of performance and include a budget justification. For each subaward (intramural or extramural), complete a separate form and justification. Upload as a single document titled **IGBudget.pdf** to eBRAP. Refer to the General Application Instructions, Section V.A.(e), for additional information and considerations.

  - **Budget Justification (no page limit):** Refer to General Application Instructions, Section V.A.(e), Budget Justification Instructions.

- **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section V.A.(f), for detailed instructions.

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

Once the full application is submitted it is transmitted to and processed in eBRAP. At this stage, the PI and organizational representatives will receive an email from eBRAP instructing them to log into eBRAP to review, modify, and verify the full application submission. Verification is strongly recommended but not required. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in the "Full Application Files" tab in eBRAP. However, eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the program announcement. ***The Project Narrative and Intragovernmental/Intramural Budget Form cannot be changed after the application submission deadline. If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the full application submission deadline.*** Other application components, including subaward budget(s) and subaward budget justification(s), may be changed until the end of the application verification period. The full application cannot be modified once the application verification period ends.

II.D.3. Submission Dates and Times

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Failure to meet either of these deadlines will result in submission rejection.

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

II.D.4. Funding Restrictions

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

The application's total costs budgeted for the entire period of performance should not exceed **$2,000,000 for the MMRDA or $3,400,000 for the MMRDA-CRTO**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

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

The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **3** years.

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

- Travel between/among collaborating organizations (as applicable)
- Travel costs for one investigator to disseminate project results at two separate DOD-sponsored meetings (e.g., the MHS Research Symposium)

- Travel costs for one investigator to travel to one scientific/technical meeting per year, after the first year of the period of performance, to present project information or disseminate project results from the FY24 JWMRP MMRDA

II.D.5. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

To determine technical merit, all applications will be individually evaluated according to the following **scored criteria**, of which **Research Strategy and Feasibility** and **Impact** are equally of most importance, with the remaining criteria listed in decreasing order of importance:

- **Research Strategy and Feasibility**
    - How well the application presents the scientific rationale behind the proposed research or materiel/knowledge product development effort, including relevant literature citations, preliminary data, and/or preclinical data, to support feasibility.
    - How well the application states the hypotheses to be tested and/or the objective(s) to be reached.
    - How well the application describes the experimental design, methods, and analyses, including appropriate controls, choice of animal model (if applicable), and the endpoints/ outcome measures to be used, in sufficient detail for evaluation of feasibility and effectiveness in supporting completion of the project aims.
    - How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.
    - Whether the SOW indicates a feasible plan and timeline to conduct the research and how well it provides clearly defined milestones to be accomplished.
    - How well the application describes potential problem areas and discusses alternative methods/approaches that may be employed to overcome them, including interdependency of aims (i.e., dependency on successful outcomes of other ongoing related research efforts).
- **Impact**
    - The degree to which the proposed effort is relevant to the role of the JWMRP in addressing high-priority DOD medical requirements and capability gaps and accelerating

the development of products that will impact the Warfighter within the context of the FY24 JWMRP Focus Area(s) being addressed.

- To what degree the knowledge, technologies, or products gained from the research could benefit the civilian population and also address the health care needs of Service Members, their Families, and/or Veterans.
- To what degree the research will result in faster and/or better delivery of high-priority health care solutions for the Warfighter.
- To what degree the anticipated short-term outcomes(s)/products(s) (knowledge and/or materiel) of the proposed effort will impact the relevant populations, and augment and/or accelerate product development as applicable.
- How significantly the long-term gains from this research may impact the health and readiness of Warfighters.

- **Transition Plan and Regulatory Strategy**
  - Whether the transition plan and regulatory strategy are appropriate and well described.
  - Whether the proposed research meets a current TRL or KRL of 5 or higher, and whether the proposed target TRL or KRL is realistic and appropriate.
  - Whether the funding strategy to transition to the next level of development and/or commercialization (e.g., specific partnerships, specific funding resources, commercial and/or military market) is reasonable and achievable.
  - For knowledge products, whether the proposed collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of CPGs and recommendations, provider training materials, patient brochures, clinical support tools, scientific journal publications, models, simulations, and applications are established and/or achievable.
  - Whether the schedule and milestones for transitioning the anticipated research outcomes to the next phase of development (i.e., next-phase clinical trials, commercialization/ transition to industry, delivery to market, incorporation into clinical practice, and/or approval by the FDA) are achievable.
  - Whether the steps for adapting and transitioning the civilian product/knowledge/ intervention for military fielding/adoption/use are reasonable and achievable.
  - How well the application identifies intellectual property ownership rights and/or demonstrates the appropriate access to the intellectual property necessary for the development and/or commercialization of products or technologies supported by this funding opportunity announcement and identifies the government's ability to access such products or technologies in the future.

- How well the application describes any active SBIR/STTR data rights (if applicable).
- How well the application describes an appropriate Intellectual and Material Property Plan for resolving intellectual and material property issues among participating organizations (if applicable).
- If applicable, whether the risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
- The extent to which the regulatory strategy to support the product label indication or product label change, if applicable, is appropriate and well described.
- Whether the application explains why the product/intervention is exempt from FDA oversight, or, for products that require FDA regulation, whether the plans/timeline for IND or IDE application submission to the FDA are appropriate, or the IND or IDE submission has already taken place.
- To what degree the application describes how the data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA, if applicable.
- If clinical studies will be conducted outside of the United States, whether there is documentation of pre-IND communication between the applicant and the FDA regarding phase 1 studies.
- Whether the identified status for manufacturing development, non-clinical development, and clinical development demonstrates readiness for the next level of development and/or commercialization.
- Whether 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 are appropriate.
- Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.

- **Clinical Strategy** ***(for applications submitted under the 'Clinical Research or Clinical Trial Option')***
  - As applicable, how well the application describes the type of clinical study/trial to be performed, the phase of trial and/or class of device, and the study model.
  - How well the application identifies and describes the hypothesis/intervention to be studied and the projected outcomes.
  - To what degree the observational study or intervention addresses high-priority clinical needs and represents an advancement over currently available standards of care and/or interventions.

- How well the application provides a brief description of the study/sample population, criteria for inclusion/exclusion, and the methods that will be used for recruitment/accrual of human subjects, samples, and/or data sets.

- Whether the application demonstrates that the research team has access to the proposed study/sample population at each site and describes the efforts that will be made to achieve accrual goals.

- How well the application addresses any potential barriers to human sample or subject accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment and/or poor retention for example.

- Whether the strategy for the inclusion of women and minorities and distribution of proposed enrollment are appropriate for the proposed research and whether justification is provided if any groups will be excluded.

- As applicable, how well the application describes the plan for obtaining informed consent from human subjects.

- How well the application describes measures that will be taken to reduce bias, such as blinding of subjects, clinicians, data analysts, and/or others during the study.

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

- How well the application discusses risk/benefit considerations, including a clear and detailed description of potential ethical issues raised by the proposed study, and a detailed plan for how the ethical issues will be addressed.

- How well the application explains measures taken to protect the privacy of human subjects and/or maintains confidentiality of study data.

- To what degree the application includes preclinical and/or clinical evidence to support the safety and stability (as appropriate) of the intervention.

- How well the application documents access to the intellectual property rights to the intervention for the duration of the proposed clinical study/trial (if applicable).

- **Data and Statistical Analysis Plan**

  - To what degree the data analysis plan is consistent with study objectives.

  - To what degree the statistical plan, including power analysis for sample size projections, is appropriate to meet the objectives of the study.

- **Personnel**
    - To what degree the background and expertise of the PI and other key personnel demonstrate their ability to accomplish the proposed work, including whether there is evidence of sufficient clinical and/or statistical expertise (as applicable).
    - To what degree the levels of effort by the PI and other key personnel are appropriate for successful conduct of the proposed work.

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

- **Environment**
    - How the scientific environment is appropriate for the proposed research and/or materiel/knowledge product development effort.
    - How the research and/or product development requirements are supported by the availability of, and accessibility to, facilities and resources (including collaborative arrangements).
    - How the quality and extent of institutional support are appropriate for the proposed effort.
- **Budget**
    - Whether the budget is appropriate for the proposed research.
- **Application Presentation**
    - To what extent the writing, clarity, and presentation of the application components influence the review.

II.E.1.b. Programmatic Review

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

- Ratings and evaluations of the peer reviewers
- Relevance to the priorities of the DHP and FY24 JWMRP, as evidenced by the following:
    - Military relevance, including alignment with and balance within and across the identified DOD and Services medical research priorities and portfolios
    - Relative potential of the research to augment and/or accelerate clinical, technical, or materiel/knowledge product development efforts that directly benefit military medicine

- Relative transition potential of the anticipated product/outcome
- Relative impact of the research on Service Members, their Families, and Veterans

II.E.2. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding General, USAMRDC. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in Section II.E.1.b, Programmatic Review.*** Additional information about the two-tier process used by the CDMRP can be found at https://cdmrp.health.mil/about/2tierRevProcess.

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

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

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

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

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

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

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

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

II.F.2. PI Changes and Award Transfers

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

The organizational transfer of an award supporting a clinical trial is strongly discouraged and, in most cases, will not be allowed. Approval of a transfer request will be on a case-by-case basis.

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

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

II.F.3. Administrative and National Policy Requirements

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

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

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

Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR

219. Funded studies are required to register the study in the National Institutes of Health (NIH) clinical trials registry, https://www.clinicaltrials.gov/, prior to initiation of the study. Refer to the General Application Instructions, Appendix 6, Section F, for further details.

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

II.F.4. Reporting

Refer to General Application Instructions, Appendix 9, for general information on reporting requirements.

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

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the final progress report. Use the one-page template "Award Expiration Transition Plan," available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) under the "Progress Report Formats" section. The Award Expiration Transition Plan must outline 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: Enrollment reporting on the basis of sex/gender, race, and ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP.

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

II.H. Other Information

II.H.1. Program Announcement and General Application Instructions Versions

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 901a. The program announcement numeric version code will match the General Application Instructions version code 901.

II.H.2. Administrative Actions

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

II.H.2.a. Rejection

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

- FY24 JWMRP Pre-Application is missing or incomplete.
- FY24 JWMRP Pre-Application Template exceeds page limit.

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

- Submission of an application for which a letter of invitation was not issued.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.

For applications involving animal research:

- Attachment 8, Animal Research Plan is missing.

For applications submitted under the 'Clinical Research or Clinical Trial Option' and/or involving human subjects/samples/data:

- Attachment 10, Human Subjects/Sample Acquisition and Safety Procedures, is missing.
- Attachment 11, Regulatory Strategy, is missing.
- Attachment 12, Data Management, is missing.

II.H.2.b. Modification

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

II.H.2.c. Withdrawal

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

- An FY24 JWMRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation, including letters of support/recommendation. ***A list of the FY24 JWMRP Programmatic Panel members can be found at https://cdmrp.health.mil/jwmrp/panels/panels24.***
- The application fails to conform to this program announcement description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Applications that include names of personnel from either of the CDMRP peer or programmatic review companies for which conflicts cannot be adequately mitigated. For FY24, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.health.mil/about/2tierRevProcess).
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP.
- Applications submitted by a federal government organization (including an intramural DOD organization) may be withdrawn if (a) the organization cannot accept and execute the entirety of the requested budget in current fiscal year (FY24) funds and/or (b) the federal government organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to collaborators.
- Application includes research data that are classified and/or proposes research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns.
- The PI does not meet the eligibility criteria.
- The application does not address at least one of the FY24 JWMRP Focus Areas.

- The invited application proposes a different research project than that described in the pre-application.
- The invited application proposes research that is not a logical continuation of the previously DOD-funded research or development effort identified in the notification of invitation.

II.H.2.d. Withhold

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

II.H.3. Full Application Submission Checklist

Full Application Components	Uploaded
Attachments	
Project Narrative – Attachment 1, upload as "ProjectNarrative.pdf"	☐
Supporting Documentation – Attachment 2, upload as "Support.pdf"	☐
Technical Abstract – Attachment 3, upload as "TechAbs.pdf"	☐
Lay Abstract – Attachment 4, upload as "LayAbs.pdf"	☐
Statement of Work – Attachment 5, upload as "SOW.pdf"	☐
Impact Statement – Attachment 6, upload as "Impact.pdf"	☐
Transition Plan – Attachment 7, upload as "Transition.pdf"	☐
Animal Research Plan – Attachment 8, upload as "AnimalResPlan.pdf" if applicable	☐
Intervention – Attachment 9, upload as "Intervention.pdf" if applicable	☐
Human Subjects/Sample Acquisition and Safety Procedures – Attachment 10, upload as "HumSubProc.pdf" if applicable	☐
Regulatory Strategy – Attachment 11, upload as "Regulatory.pdf" if applicable	☐
Data Management – Attachment 12, upload as "Data_Manage.pdf" if applicable	☐
Study Personnel and Organization – Attachment 13, upload as "Personnel.pdf" if applicable	☐
Research & Related Personal Data	☐
Research & Related Senior/Key Person Profile (Expanded)	☐
Attach PI Biographical Sketch (Biosketch_LastName.pdf)	☐
Attach PI Previous/Current/Pending Support (Support_LastName.pdf)	☐
Attach Key Personnel Biographical Sketches (Biosketch_LastName.pdf) for each senior/key person	☐
Attach Key Personnel Previous/Current/Pending Support (Support_LastName.pdf) for each senior/key person	☐
Intragovernmental/Intramural Budget Include budget justification	☐
Project/Performance Site Location(s) Form	☐

APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
ARRIVE	Animal Research: Reporting of In Vivo Experiments
BAA	Broad Agency Announcement
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
CPG	Clinical Practice Guideline
DHP	Defense Health Program
DOD	Department of Defense
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FDA	U.S. Food and Drug Administration
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
IACUC	Institutional Animal Care and Use Committee
ICH E6	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
JWMRP	Joint Warfighter Medical Research Program
KRL	Knowledge Readiness Level
LAR	Legally Authorized Representative
M	Million
MHS	Military Health System
MIPR	Military Interdepartmental Purchase Request
MMRDA	Military Medical Research and Development Award
MMRDA–CRTO	Military Medical Research and Development Award – Clinical Research or Clinical Trial Option
PHS	Public Health Service
PI	Principal Investigator
SOW	Statement of Work
SBIR	Small Business Innovation Research
STTR	Small Business Technology Transfer

TBI	Traumatic Brain Injury
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	U.S. Department of Veterans Affairs

APPENDIX 2: CLINICAL TRIAL AND TECHNOLOGY/KNOWLEDGE READINESS LEVEL DEFINITIONS

Drug and Biologic Preclinical and Clinical Trial Definitions

Phase	Population	- Number of Subjects Required*	Purpose
Pre-clinical	Highly controlled (GLP) studies in animals	Hundreds to Thousands	Safety, toxicity, effectiveness. Provides evidence to FDA safe enough to try in humans
0	Healthy volunteers Exception: Cancer/AIDS etc.	10 to 15 subjects/trial	Limited exposure, short duration, with no therapeutic or diagnostic Intent. Helps identify promising candidates and assess feasibility for further development. Particularly useful when developing products for serious diseases. Often referred to as Exploratory IND studies.
1	Healthy volunteers Exception: Cancer/AIDS etc.	20 to 80 subjects/trial	Safety
2	Subjects with the Illness (narrow population)	24 to 300 subjects/trial	Safety Effectiveness Dose
3	Subjects with the Illness (broad population)	250 to 3000 subjects/trial	Confirming safety and effectiveness in diverse populations
4	Subjects with the Illness; Special population (very broad population)	FDA and Sponsor negotiate	After FDA approval (Post-licensure), for safety and/or other uses

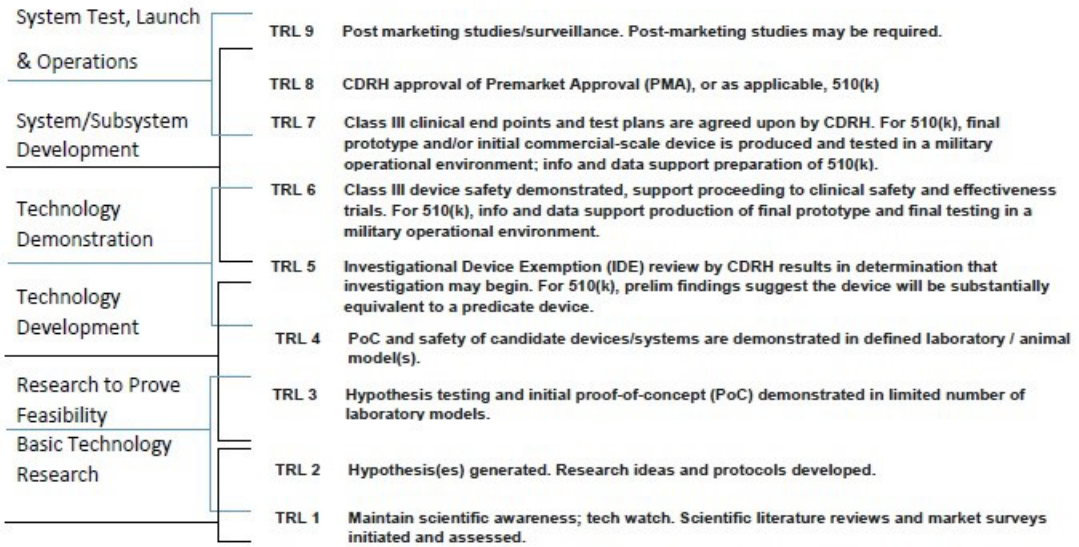
*The number of subjects in a clinical trial varies greatly by the type of product and FDA input/feedback

Biomedical Technology Readiness Levels

D – Pharmaceutical (Drugs); B/V- Pharmaceutical (biologics, Vaccines); Same for All

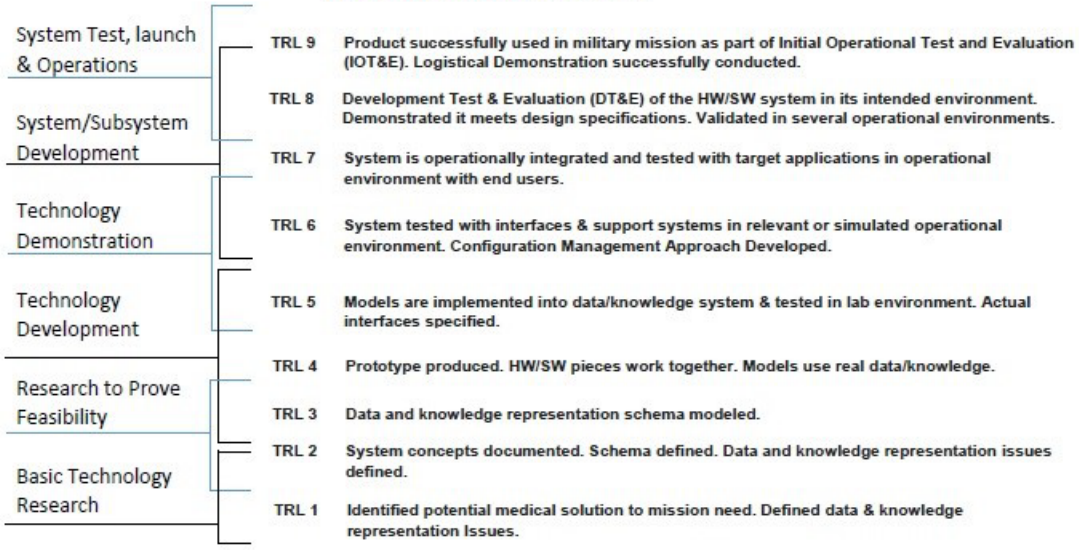
Biomedical Technology Readiness Levels

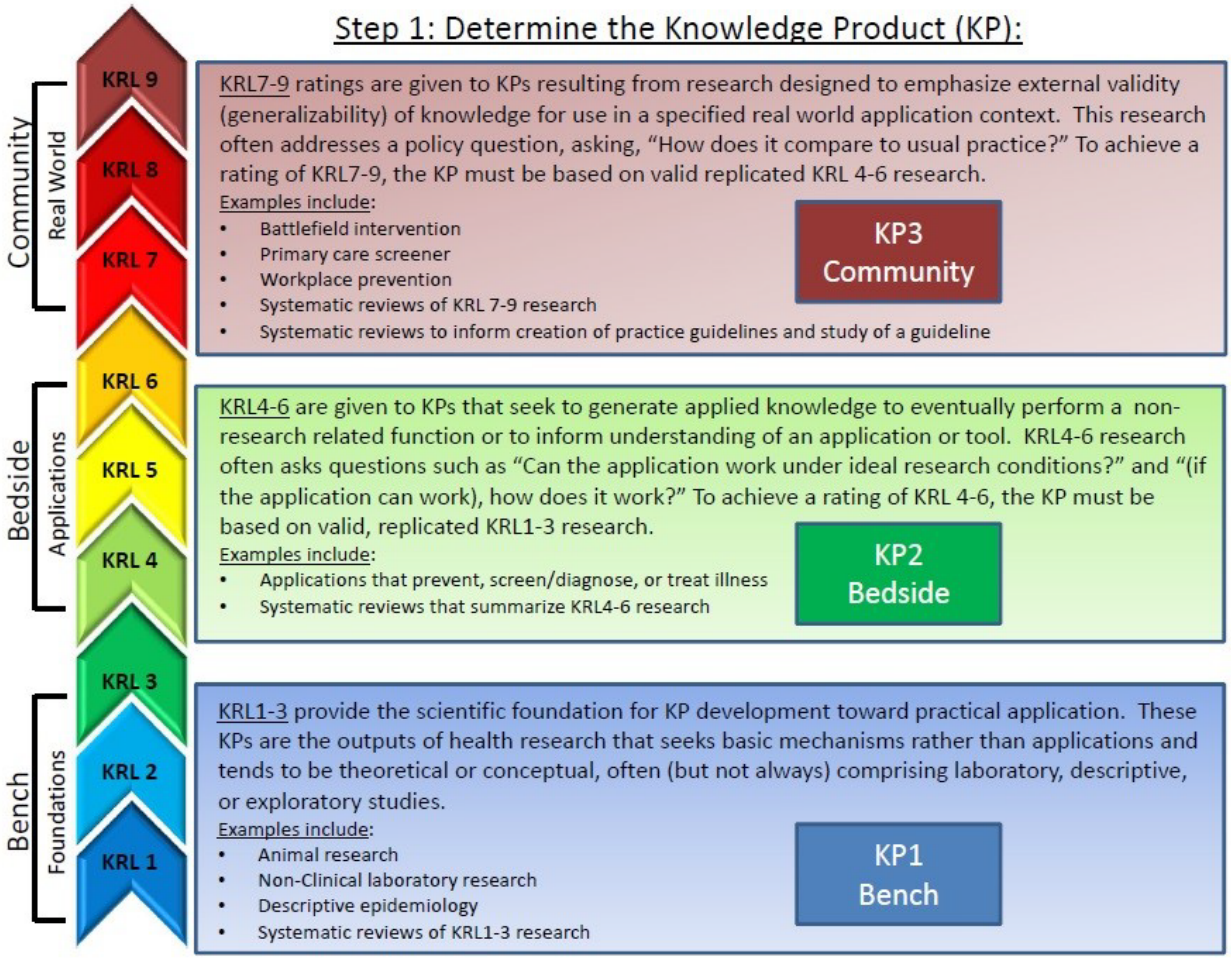
MD – Medical Devices

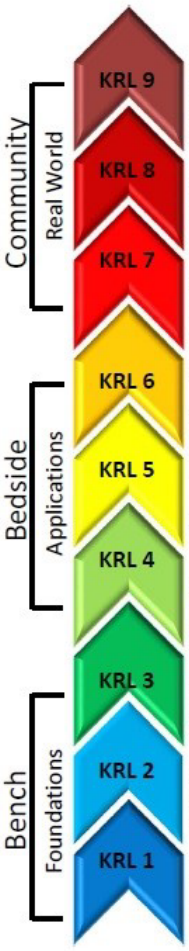


Biomedical Technology Readiness Levels

Medical IM/IT & Medical Informatics




Step 1: Determine the Knowledge Product (KP):
Community
Real World
KRL 9
KRL 8
KRL 7
KRL7-9 ratings are given to KPs resulting from research designed to emphasize external validity (generalizability) of knowledge for use in a specified real world application context. This research often addresses a policy question, asking, "How does it compare to usual practice?" To achieve a rating of KRL7-9, the KP must be based on valid replicated KRL 4-6 research.
Examples include:
Battlefield intervention
Primary care screener
Workplace prevention
Systematic reviews of KRL 7-9 research
Systematic reviews to inform creation of practice guidelines and study of a guideline
KP3 Community
Bedside
Applications
KRL 6
KRL 5
KRL 4
KRL4-6 are given to KPs that seek to generate applied knowledge to eventually perform a non-research related function or to inform understanding of an application or tool. KRL4-6 research often asks questions such as "Can the application work under ideal research conditions?" and "(if the application can work), how does it work?" To achieve a rating of KRL 4-6, the KP must be based on valid, replicated KRL1-3 research.
Examples include:
Applications that prevent, screen/diagnose, or treat illness
Systematic reviews that summarize KRL4-6 research
KP2 Bedside
Bench
Foundations
KRL 3
KRL 2
KRL 1
KRL1-3 provide the scientific foundation for KP development toward practical application. These KPs are the outputs of health research that seeks basic mechanisms rather than applications and tends to be theoretical or conceptual, often (but not always) comprising laboratory, descriptive, or exploratory studies.
Examples include:
Animal research
Non-Clinical laboratory research
Descriptive epidemiology
Systematic reviews of KRL1-3 research
KP1 Bench



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.)