

I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Hearing Restoration Research Program

Focused Research Award

Announcement Type: Initial

Funding Opportunity Number: W81XWH-22-HRRP-FRA

**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), July 22, 2022
- **Invitation to Submit an Application:** September 2022
- **Application Submission Deadline:** 11:59 p.m. ET, November 30, 2022
- **End of Application Verification Period:** 5:00 p.m. ET, December 5, 2022
- **Peer Review:** January 2023
- **Programmatic Review:** March 2023

This program announcement must be read in conjunction with the General Application Instructions, version 702. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the “Package” tab, clicking “Preview,” and then selecting “Download Instructions.”

TABLE OF CONTENTS

I. OVERVIEW OF THE FUNDING OPPORTUNITY.....	1
II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY	3
II.A. Program Description.....	3
II.A.1. FY22 HRRP Focus Areas.....	3
II.A.2. Award History	4
II.B. Award Information	4
II.C. Eligibility Information.....	8
II.C.1. Eligible Applicants	8
II.C.2. Cost Sharing.....	9
II.C.3. Other	9
II.D. Application and Submission Information.....	10
II.D.1. eBRAP and Grants.gov.....	10
II.D.2. Content and Form of the Application Submission	10
II.D.3. Unique Entity Identifier (UEI) and System for Award Management (SAM)	32
II.D.4. Submission Dates and Times.....	32
II.D.5. Funding Restrictions.....	33
II.D.6. Other Submission Requirements	35
II.E. Application Review Information	35
II.E.1. Criteria	35
II.E.2. Application Review and Selection Process.....	38
II.E.3. Integrity and Performance Information.....	39
II.E.4. Anticipated Announcement and Federal Award Dates.....	39
II.F. Federal Award Administration Information	40
II.F.1. Federal Award Notices.....	40
II.F.2. Administrative and National Policy Requirements	41
II.F.3. Reporting.....	41
II.G. Federal Awarding Agency Contacts.....	42
II.G.1. eBRAP Help Desk.....	42
II.G.2. Grants.gov Contact Center	42
II.H. Other Information.....	43
II.H.1. Program Announcement and General Application Instructions Versions.....	43
II.H.2. Administrative Actions.....	43
II.H.3. Application Submission Checklist.....	46
APPENDIX 1: ACRONYM LIST	48

II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

Applications to the Fiscal Year 2022 (FY22) Hearing Restoration Research Program (HRRP) are being solicited by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The execution management agent for this program announcement is the Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC). The HRRP was initiated in 2017 to support innovative and impactful research that pursues the treatment of auditory system injuries and the restoration of hearing. Appropriations for the HRRP from FY17 through FY21 totaled \$50 million (M). The FY22 appropriation is \$10M.

The proposed research must be relevant to active-duty Service Members, Veterans, military beneficiaries, and/or the American public.

It is estimated that more than 30 million Americans over the age of 12 have hearing loss in both ears and an estimated 48 million have hearing loss in at least one ear. The most recent data from the Department of Veterans Affairs (VA) indicates that there are more than 1.3 million Veterans with Service-connected disability due to hearing loss. While hearing loss has profound impact on quality of life, there is no drug approved by the U.S. Food and Drug Administration (FDA) for hearing restoration. Despite significant advances in the understanding of hearing loss in animal models, the development of hearing restoration therapeutics has been hindered by difficulties in validation and translation, and by limitations in precision diagnostic capability. The HRRP aims to advance the science of hearing restoration by funding groundbreaking research that removes barriers in translation and/or diagnosis.

II.A.1. FY22 HRRP Focus Areas

To meet the intent of the award mechanism, all applications to the FY22 HRRP Focused Research Award (FRA) must address research in one or more of the following Focus Areas:

- Accelerate translation of biological regeneration/repair mechanisms into therapies that treat auditory system injury and restore auditory function. For example, but not limited to:
 - Hair cell regeneration/repair/recovery
 - Neural regeneration/repair/recovery
 - Treatment for synaptopathy and hidden hearing loss
- Diagnostic tests that help differentiate sensory, neural, synaptic, and central processing disorders, that may inform applicability and outcomes for current or future hearing restoration therapeutics.

- Develop reliable in-vitro human models to facilitate the understanding, derivation, and characterization of human auditory cells, and/or to facilitate the evaluation of hearing restoration therapies.
- Develop and/or validate techniques/methods beyond the audiogram to diagnose acute auditory system injury in austere or remote environments. For example, but not limited to, simple and rapid assessments that are compatible with portable platforms.

Tinnitus or vestibular-related research is excluded.

II.A.2. Award History

The HRRP FRA mechanism was first offered in FY19. Since then, 119 FRA applications have been received, and 30 have been recommended for funding.

II.B. Award Information

The FY22 HRRP FRA mechanism is intended to support promising research that accelerates drug discovery and therapeutic development for hearing restoration after military-relevant auditory system injury or accelerates advances in diagnosis of auditory dysfunction in austere environments.

Applicants are encouraged to leverage resources and expertise at the National Center for Advancing Translational Sciences (NCATS) to improve efficiency and accelerate the translational process. A list of NCATS programs and resources supporting preclinical innovation can be found at <https://ncats.nih.gov/preclinical>.

Applications involving multidisciplinary collaborations among academia, industry, the military Services, the VA, and other federal government agencies are highly encouraged.

Key Elements

- **Program priorities:** Applicants are strongly encouraged to address the HRRP’s program priorities:
 - **Overcoming major obstacles to hearing restoration.** Currently, no drug has been approved by the FDA to treat hearing loss associated with sensory, neural, synaptic, or central auditory dysfunction. Although significant progress has been made in the molecular and cellular understanding of hearing loss and regeneration mechanisms in the inner ear, the majority of research is preclinical. The unique anatomical features of the inner ear render it difficult to access and not amenable for biopsy. This creates a major obstacle for the clinical validation of preclinical findings and severely hinders the translation of preclinical findings to clinical applications. Furthermore, it has severely hindered the advancement of diagnostic capabilities beyond behavioral functional tests. As potential therapeutics to treat sensory, neural, synaptic, or central auditory dysfunction are discovered in animal studies, it will be crucial for the success of clinical trials to correctly match patient populations to appropriate interventions and accurately measure

outcomes. The HRRP challenges the science community to design innovative studies for precision diagnostics and to validate preclinical results and translate therapies to clinical applications.

- **Diagnosis of acute auditory system injury in austere or remote environments.**
Service Members often operate in austere/remote environments without access to a fixed or mobile medical facility and where diagnostic and treatment resources and medical personnel are unavailable or limited for extended periods of time. There is a great need for validated and reliable techniques or methods beyond the audiogram to quickly screen and diagnose acute auditory system injury, including noise-induced hearing loss and hidden hearing loss (e.g., cochlear synaptopathy), in operational and austere/remote environments. The techniques or methods should be eventually compatible with portable platforms and applicable by a non-specialist (e.g., physician assistant, medic, or corpsman).
- **(New for FY22; if the goal of the proposed study is to develop an intervention)**
Experimental design requirements: To maximize the feasibility of eventual clinical application, applications that aim to develop therapeutic interventions must address the following in experimental design:
 - **If proposing research on interventions that aim to restore hearing after established hearing loss,** the experimental design must enable or facilitate *eventual connection of the intervention to precision diagnosis* and application of the intervention to real-world injuries.
 - **If proposing research on interventions that aim to preserve cells/synapses after acute auditory injury, to be administered soon after or before the injury,** the experimental design must enable or facilitate the eventual demonstration that *the benefits of the therapeutic outweigh the potential risks*.

Refer to [Attachment 1](#), Project Narrative, for additional details on these requirements.

- **Funding Levels:** The FY22 HRRP FRA may be used to support preclinical studies in animals and/or clinical research involving human subjects and human anatomical substances. To support research projects at different stages and the exploration/development of ideas of different maturity levels, three funding levels are available under this program announcement. ***When submitting the pre-application, it is the responsibility of the applicant to select the funding level that is most appropriate for the research proposed. The funding level should be selected based on the stage and maturity level of the research project, rather than the amount of the budget.***
 - **Funding Level 1** supports exploratory, high-risk/high-reward research that is in the earliest stages of idea development. Research must have the potential to yield new avenues of investigation, such as new approaches, new research tools, or new paradigms.
 - Preliminary data are allowed but ***not required***. However, applicants must provide solid rationale of the research idea, supported by literature, and the investigating team must have sufficient expertise to test the research idea.

- **Funding Level 2** supports the advancement of more mature research toward clinical translation.
 - Funding Level 2 applications may focus on any phase of research from basic through translational.
 - *Preliminary data supporting the readiness and feasibility of the proposed research are required.*
- **Funding Level 3** supports translational research that includes a Pilot Clinical Trial (PCT).
 - In contrast to regular clinical trials that are designed to determine safety or efficacy, the purpose of the PCT is **to inform the feasibility, rationale, and design of subsequent clinical trials** through limited clinical testing of a novel intervention.
 - Application must have both non-PCT translational component and PCT component to be eligible for Funding Level 3. The PCT must be clearly linked to the non-PCT translational studies that will be performed under the same application.
 - *Preliminary data supporting the readiness and feasibility of the proposed research are required.*

A clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. For more information on how to distinguish clinical trials from observational studies, see the [Human Subject Resource Document](#).

Funded PCTs 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 PCTs are required to register the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 1, Section B, for further details.

Applicants may consult the following resource documents as applicable:

- [Blast Term Dictionary and Guidance Documents for Blast Injury Research](#)
- [A Primer for Conducting Department of Defense \(DOD\) Funded Human Research with Military Populations](#)
- [A Beginner’s Guide to Army Healthcare System](#)

A description of health services across the range of military operations can be found in the [Joint Health Services Joint Publication 4-02](#).

The types of awards made under the program announcement will be assistance agreements. An assistance agreement is appropriate when the federal government transfers a “thing of value” to a “state, local government,” or “other recipient” to carry out a public purpose of support or stimulation authorized by a law of the United States instead of acquiring property or service for the direct benefit and use of the U.S. government. An assistance agreement can take the form of a grant or cooperative agreement. The level of involvement on the part of the DOD during project performance is the key factor in determining whether to award a grant or cooperative agreement. If “no substantial involvement” on the part of the funding agency is anticipated, a grant award will be made (31 USC 6304). Conversely, if substantial involvement on the part of the funding agency is anticipated, a cooperative agreement will be made (31 USC 6305), and the award will identify the specific substantial involvement. Substantial involvement may include, but is not limited to, collaboration, participation, or intervention in the research to be performed under the award. The award type, along with the start date, will be determined during the negotiation process.

The anticipated direct costs budgeted for the entire period of performance for an **FY22 HRRP FRA – Funding Level 1** will not exceed \$250,000. The anticipated direct costs budgeted for the entire period of performance for an **FY22 HRRP FRA – Funding Level 2** will not exceed \$1,000,000. The anticipated direct costs budgeted for the entire period of performance for an **FY22 HRRP FRA - Funding Level 3** will not exceed \$1,250,000. Refer to [Section II.D.5, Funding Restrictions](#), for detailed funding information.

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

The CDMRP expects to allot approximately \$2.0M to fund approximately five HRRP FRA – Funding Level 1 applications, approximately \$4.8M to fund approximately three FRA – Funding Level 2 applications, and approximately \$2.0M to fund approximately one FRA – Funding Level 3 application. Funding of applications received is contingent upon the availability of federal funds for this program as well as the number of applications received, the quality and merit of the applications as evaluated by scientific and programmatic review, and the requirements of the government. 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 FY22 funding opportunity will be funded with FY22 funds, which will expire for use on September 30, 2028.

Rigor of Experimental Design: All projects should adhere to accepted standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. Core standards are described in Landis, S.C., et al., “A call for transparent reporting to optimize the predictive value of preclinical research,” *Nature* 2012, 490:187-191 (<http://www.nature.com/nature/journal/v490/n7419/full/nature11556.html>). While these standards were written for preclinical studies, the basic principles of randomization, blinding/masking, sample-size estimation, and data handling derive from well-established best practices in research and should be applied consistently across basic and translational studies.

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

If the proposed research involves more than one institution, a written plan for single IRB review arrangements must be provided at the time of application submission or award negotiation. The lead institution responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements.

Use of DOD or VA Resources: If the proposed research involves access to active-duty military or VA patient populations and/or DOD or VA resources or databases, the application must describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research. Refer to [Section II.D.2.b.ii, Full Application Submission Components](#), for detailed information. Refer to the General Application Instructions, Appendix 1, for additional information.

Research Involving Animals: All research funded by the FY22 HRRP award mechanism involving new and ongoing research with animals must be reviewed and approved by the USAMRDC ORP Animal Care and Use Review Office (ACURO), in addition to the local Institutional Animal Care and Use Committee (IACUC) of record. IACUC approval at the time of submission is *not* required. *Allow at least 3 to 4 months for ACURO regulatory review and approval processes for animal studies.* Refer to the General Application Instructions, Appendix 1, for additional information.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: All organizations, including foreign organizations, foreign public entities, and international organizations, are eligible to apply.

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

As applications for this program announcement may be submitted by extramural and intramural organizations, these terms are defined below.

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

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

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

II.C.1.b. Principal Investigator

Independent investigators at all academic levels (or equivalent) are eligible to be named by the recipient organization as Principal Investigator (PI) on the applications.

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

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

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

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

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

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

II.D. Application and Submission Information

II.D.1. eBRAP and Grants.gov

The **Electronic Biomedical Research Application Portal (eBRAP)** (<https://ebrap.org>) is a secure web-based system that allows PIs to submit their pre-applications, view and verify extramural full applications submitted to Grants.gov (<https://grants.gov>), receive communications from the CDMRP, and submit documentation during award negotiations and throughout the period of performance. eBRAP also allows intramural organizations to submit full applications following pre-application submission.

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

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

Extramural Submission:

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

Intramural DOD Submission:

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

Note: Applications from an intramural DOD organization or from an extramural federal government organization may be submitted to Grants.gov through a research foundation.

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

Submission is a two-step process requiring both ***pre-application*** (eBRAP.org) and ***full application*** (eBRAP.org or Grants.gov) as indicated below. The submission process should be started early to avoid missing deadlines. There are no grace periods. Full application submission guidelines differ for extramural (Grants.gov) and intramural (eBRAP.org) organizations (refer to [Table 1, Full Application Guidelines](#)).

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

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

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

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

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

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

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

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

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

- **Tab 1 – Application Information**

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

- **Tab 2 – Application Contacts**

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

Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 Research & Related Form), and click on “Add

Organizations to this Pre-application.” The organization(s) must be either selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.

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

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

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

[FY22 HRRP Programmatic Panel members](#) should not be involved in any pre-application or application. For questions related to panel members and pre-applications or applications, refer to [Section II.H.2.c. Withdrawal](#), or contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

- **Tab 4 – Conflicts of Interest**

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

- **Tab 5 – Pre-Application Files**

Note: Upload documents as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

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

The Preproposal Narrative should include the following:

- **Research Idea/Rationale**

- **Funding Level 1:** Describe the research idea to be explored and the rationale. Concisely explain how the idea may yield new avenues of investigation, such as new approaches, new research tools, or new paradigms.
- **Funding Level 2:** Describe the proposed research and the rationale and preliminary data supporting its readiness and feasibility. Explain how it is designed to advance a line of research toward clinical translation.

- **Funding Level 3:** Describe the proposed research and the rationale and preliminary data supporting its readiness and feasibility. Explain how the non-PCT translational research component and the PCT component are connected and form a cohesive plan to advance the research toward clinical translation.
- **All Funding Levels:** Explain how the research idea meets the intent of the FY22 HRRP FRA and addresses an important problem within one or more of the [FY22 HRRP Focus Areas](#).
- **Objective(s)/Hypothesis(es), Specific Aims, and Approaches:** Concisely state the project’s objective(s)/hypothesis(es), specific aims, and describe the scientific approaches. Explain how the aims and approaches form a coherent research plan to address the objective(s)/hypothesis(es). Include a description of controls, as appropriate. As applicable, identify the animal model(s) to be studied, the data to be analyzed, and/or the human subject population(s) to be engaged during the study.
 - If proposing research on interventions that aim to restore hearing after established hearing loss, briefly describe how the experimental design will enable or facilitate eventual connection of the intervention to precision diagnosis and application of the intervention to real-world injuries.
 - If proposing research on interventions that aim to preserve cells/synapses after acute auditory injury, to be administered soon after or before the injury, briefly please describe how the experimental design will enable or facilitate the eventual demonstration that the benefits of the therapeutic outweigh the potential risks.
 - (**Funding Level 3 only**) Clearly identify which aims involve non-PCT translational studies and which aim involves a PCT. Describe how the PCT is designed to inform the feasibility, rationale, and design of subsequent clinical trials.
- **Impact:** Describe how the short- and long-term outcome(s) of the proposed research, if successful, will advance diagnosis/treatment of auditory system injury and/or restoration of auditory function.
- **Personnel:** Briefly state the qualifications of the PI and key personnel. Clearly demonstrate that the investigating team has sufficient expertise that is appropriate for the research idea and the proposed phase/type of study.
- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application *must be uploaded as individual files* and are limited to the following:
 - **References Cited (one-page limit):** List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, reference title, and reference source, including volume, chapter, page numbers, and publisher, as appropriate

- **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
 - **Key Personnel Biographical Sketches (six-page limit per individual):** *All biographical sketches should be uploaded as a single combined file.* Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.
- **Tab 6 – Submit Pre-Application**

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

Pre-Application Screening

- **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 HRRP, pre-applications will be screened based on the following criteria:

- **Research Idea/Rationale**
 - **Funding Level 1:** How well the research idea is supported by rationale. To what extent it is designed to yield new avenues of investigation.
 - **Funding Level 2:** How well the readiness and feasibility of the proposed research is supported by rationale and preliminary data. To what extent it is designed to advance a line of research toward clinical translation.
 - **Funding Level 3:** How well the readiness and feasibility of the proposed research is supported by rationale and preliminary data. To what extent the non-PCT translational research component and the PCT component are connected and form a cohesive plan to advance the research toward clinical translation.
 - **All Funding Levels:** How well the research idea meets the intent of the FY21 HRRP FRA and addresses an important problem within one or more of the [FY22 HRRP Focus Areas](#).
- **Objective(s)/Hypothesis(es), Specific Aims, and Approaches:** Whether the proposed research has clear objective(s)/hypothesis(es). To what extent the specific aims and approaches, including controls if applicable, form a coherent research plan to address the objective(s)/hypothesis(es).
 - As applicable, whether the experimental design will enable/facilitate eventual connection of the intervention to precision diagnosis and application of the intervention to real-world injuries, or the eventual demonstration that the benefits of the therapeutic outweigh the potential risks.

- (Funding Level 3 only) To what extent the PCT will inform the feasibility, rationale, and design of subsequent clinical trials.
 - **Impact:** To what extent the short- and long-term outcome(s) of the proposed study, if successful, will advance diagnosis/treatment of auditory system injury and/or restoration of auditory function.
 - **Personnel:** To what extent the investigating team has sufficient qualification and expertise to perform the proposed research.
- **Notification of Pre-Application Screening Results**

Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated in [Section I, Overview of the Funding Opportunity](#). Invitations to submit a full application are based on the Pre-Application Screening Criteria listed above.

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

Applications will not be accepted unless notification of invitation has been received.

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

Each application submission must include the completed full application package for this program announcement. The full application package is submitted by the Authorized Organizational Representative through Grants.gov (<https://grants.gov/>) for extramural organizations or through eBRAP (<https://ebrap.org/>) for intramural organizations. See Table 1 below for more specific guidelines.

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

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

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

Table 1. Full Application Submission Guidelines

Extramural Submissions	Intramural DOD Submissions
Application Package Location	
Download application package components for W81XWH-22-HRRP-FRA from Grants.gov (https://grants.gov) and create a Grants.gov Workspace. Workspace allows online completion of the application components and routing of the application package through the applicant organization for review prior to submission.	Download application package components for W81XWH-22-HRRP-FRA from eBRAP (https://ebrap.org).
Full Application Package Components	
SF424 Research & Related Application for Federal Assistance Form: Refer to the General Application Instructions, Section III.A.1, for detailed information.	Tab 1 – Summary: Provide a summary of the application information. Tab 2 – Application Contacts: This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.
<p>Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> • Attachments • Research & Related Personal Data • Research & Related Senior/Key Person Profile (Expanded) • Research & Related Budget • Project/Performance Site Location(s) Form • Research & Related Subaward Budget Attachment(s) Form 	<p>Tab 3 – Full Application Files: Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> • Attachments • Key Personnel • Budget • Performance Sites <p>Tab 4 – Application and Budget Data: Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.</p>
Application Package Submission	
<p>Create a Grants.gov Workspace. Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission.</p> <p>Submit a Grants.gov Workspace Package. An application may be submitted through Workspace by clicking the “Sign and Submit” button on the “Manage Workspace” page, under the “Forms” tab. Grants.gov recommends submission of the application package at least</p>	<p>Submit package components to eBRAP (https://ebrap.org).</p> <p>Tab 5 – Submit/Request Approval Full Application: After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided next to “Enter Your Password Here” and press the “Submit Full Application” button. eBRAP will notify your Resource Manager/ Comptroller/Task Area Manager or equivalent</p>

Extramural Submissions	Intramural DOD Submissions
<p>24-48 hours prior to the close date to allow time to correct any potential technical issues that may disrupt the application submission.</p> <p><i>Note:</i> If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a “Changed/Corrected Application” with the previous Grants.gov Tracking ID <i>prior to</i> the application submission deadline. <i>Do not password protect any files of the application package, including the Project Narrative.</i></p>	<p>Business Official by email. <i>Do not password protect any files of the application package, including the Project Narrative.</i></p>
<u>Application Verification Period</u>	
<p>The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package may be modified <i>with the exception of the Project Narrative and Research & Related Budget Form.</i></p>	<p>After eBRAP has processed the full application, the organizational Resource Manager/Comptroller/ Task Area Manager or equivalent Business Official and PI will receive email notification of this status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package may be modified <i>with the exception of the Project Narrative and Research & Related Budget Form.</i> Your Resource Manager/ Comptroller/Task Area Manager or equivalent Business Official should log into eBRAP to review and to approve prior to the application verification deadline.</p>
Further Information	
<p>Tracking a Grants.gov Workspace Package. After successfully submitting a Workspace package, a Grants.gov Tracking Number is automatically assigned to the package. The number will be listed on the “Confirmation” page that is generated after submission.</p> <p>Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.</p>	<p>Refer to the General Application Instructions, Section IV, for further information regarding eBRAP requirements.</p>

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

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

- **Extramural Applications Only**

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

- **Extramural and Intramural Applications**

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 4.

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

- **Attachment 1: Project Narrative (page limit varies by funding level; see below for 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 to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

Page Limit:

- **Funding Level 1:** Six-page limit
- **Funding Level 2 or Funding Level 3:** 12-page limit

Describe the proposed project in detail using the outline below.

- **Background/Rationale:** Explain the rationale for the proposed research.
 - **Funding Level 1:** Describe the idea that the proposed research will explore and develop, clearly stating the objective(s) to be reached and/or the hypothesis(es) to be tested. Present sufficient literature to support the rationale for testing the idea. *Preliminary data are allowed but not required.*
 - **Funding Level 2:** Describe the proof-of-concept finding(s) that the proposed research aims to move forward to the next phase of development, clearly stating the objective(s) to be reached and/or the hypothesis(es) to be tested. Present

sufficient preliminary data to support the readiness of the objective(s), the soundness of the hypothesis(es), and the feasibility of the approach(es).

- **Funding Level 3:** Describe the promising discovery that the proposed research aims to move forward to clinical trials, clearly stating the objective(s) to be reached and/or the hypothesis(es) to be tested. Present sufficient preliminary data to support the readiness of the objective(s), the soundness of the hypothesis(es), and the feasibility of the approach(es).
- **All Funding Levels:** If proposing to develop an intervention, clearly state whether the intervention is for restoring hearing after established hearing loss or for preserving cells/synapses after acute auditory injury, to be administered soon after the injury.
- **Specific Aims:** Concisely describe the project’s specific aims. Explain how the aims address the objective(s) and/or hypothesis(es) of the proposed research.
 - (*Funding Level 3 only*) Clearly identify which aims involve preclinical or clinical studies and which aim involves a PCT.
- **Research Strategy:** Describe the experimental design, methods, and analyses, including controls, in sufficient detail so that the appropriateness and feasibility of the research strategy, including whether the proposed work can be completed within the proposed period of performance, can be fully evaluated.
 - If proposing research on interventions that aim to restore hearing after established hearing loss, describe how the experimental design will enable or facilitate eventual connection of the intervention to precision diagnosis and application of the intervention to real-world injuries.
 - ❖ Describe plans to examine, document, and interpret the damage to hair cells and/or synapses after injury. Such plans should include histopathological examinations of cellular/synaptic damage or the examination of biomarkers, or strong justification for not including them must be provided. Explain why the level of cellular/synaptic damage is appropriate for assessing the effect of potential therapeutics and is clinically relevant.
 - ❖ Describe plans to examine, document, and interpret the effect of treatment(s) on hair cells and/or synapses.
 - If proposing research on interventions that aim to preserve cells/synapses after acute auditory injury, to be administered soon after or before the injury, describe the rationale used to develop the criteria for safety and describe *any known side effects*. Explain the criteria by which the research team will determine that the benefits of the therapeutic outweigh the potential risks, and explain why the criteria will likely be accepted by regulatory authorities (e.g., the FDA) and potential users.

- ❖ If the applicant has engaged the FDA or equivalent regulatory authorities and received guidance on the acceptability of the proposed criteria, please include the information in the application.
- ❖ If the applicant has engaged potential users to estimate/predict the level of user acceptance, please include the information in the application.
- If cell lines or animals are to be used, justify the selection of the proposed cell line(s) or animal model(s). Be specific as to why the cell line or animal model was chosen over other cell lines or models, how it is appropriate for addressing the study aims, and how it is relevant to human auditory biology and/or injury. Further details of research involving animals will be required in [Attachment 8, Animal Research Plan](#), as applicable.
- If human subjects or human biological samples will be used, describe the study population and include a detailed plan for the recruitment of subjects or the acquisition of samples. Further details of research involving human subjects or human biological substances will be required in [Attachment 9, Human Subjects/Samples Acquisition and Safety Procedures](#), as applicable. Additionally, **Funding Level 3 should include [Attachment 10, Pilot Clinical Trial Plan](#), [Attachment 11, Regulatory Strategy](#), and [Attachment 12, Post-Award Transition Plan](#).**
- Describe the statistical plan and the rationale for the statistical methodology. Provide a sample size estimate and the method by which it was derived, including power analysis calculation, if applicable. ***Note for Funding Level 3 applications:*** The statistical plan under Research Strategy is for the preclinical and/or non-PCT clinical studies that will also be performed through this award. The statistical plan for the PCT should be included in the [Attachment 10, Pilot Clinical Trial Plan](#).
- Describe measures to be taken to reduce bias and achieve reproducible and rigorous results, including controls, blinding, randomization, and data handling, as applicable.
- Describe how data will be reported and, if applicable, how it will be assured that the documentation will support potential regulatory filing with the FDA.
- Address potential problems that may arise and present alternative methods and approaches to mitigate or resolve the problems.
- **Attachment 2: Supporting Documentation: Combine and upload as a single file named “Support.pdf”.** Start each document on a new page. If documents are scanned to PDF, the lowest resolution (100 to 150 dpi) should be used. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

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

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

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

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

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

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

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

Intellectual Property: Information can be found in the Code of Federal Regulations, Title 2, Part 200.315 (2 CFR 200.315), “Intangible Property.”

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

Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 2, Section K, for more information about the CDMRP expectations for making data and research resources publicly available.

- All TBI clinical research projects are required to report data to the Federal Interagency TBI Research (FITBIR) informatics system (<https://fitbir.nih.gov/>) on a quarterly basis. There is no direct charge to users of the FITBIR Informatics System. A project estimation tool (<https://fitbir.nih.gov/jsp/contribute/fitbir-costs.jsp>) is available to help estimate costs and manpower needs that may be associated with data submission

Quad Chart: Provide a Quad Chart for the proposed project. The format for the quad chart is available on the eBRAP “Funding Opportunities & Forms” web page at <https://ebrap.org/eBRAP/public/Program.htm>.

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

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

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

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

Technical abstracts should include the following elements:

- **Research Idea/Rationale:** Present the ideas and scientific rationale behind the proposed research project. Clearly indicate whether the proposed project is exploring early ideas with the potential to yield new avenues of investigation or is advancing more mature research toward clinical translation. Describe how the proposed research aligns with one or more of the [FY22 HRRP Focus Areas](#).
- **Objective(s) and/or Hypothesis(es):** Clearly state the objective(s) to be reached and/or the hypothesis(es) to be tested.
- **Specific Aims:** State the specific aims.
 - **(Funding Level 3 only)** Clearly identify which aims involve non-PCT translational studies and which aim involves a PCT.
- **Study Design:** Briefly describe the study design, including appropriate controls.
- **Impact:** Briefly describe how the proposed project, if successful, will impact the field of hearing restoration research and the auditory health of Service Members, Veterans, and the American public.
- **Attachment 4: Lay Abstract (one-page limit): Upload as “LayAbs.pdf”.** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. **Do not include proprietary or confidential information. Do not duplicate the technical abstract.** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

The lay abstract is an important component of the application review process, because it addresses issues of particular interest to the consumer advocate community. Lay abstracts should be written using the outline below in a manner **readily understood by readers without a background in science or medicine**. Minimize use of acronyms and abbreviations, where appropriate.

- Clearly describe the rationale, objective, and aims of the application.
- Describe the anticipated short-term and long-term outcomes of the proposed research. Explain how the outcomes will impact the field of hearing restoration research and the auditory health of Service Members, Veterans, and the American public.
 - If applicable, how will the proposed research open new avenues of investigation? Why is that important?
 - If applicable, how will the proposed research make significant advancements toward clinical translation?

- **Attachment 5: Statement of Work (three-page limit): Upload as “SOW.pdf”.** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>). Recommended strategies for assembling the SOW can be found at <https://ebrap.org/eBRAP/public/Program.htm>.

For the FRA mechanism, refer to the “*Suggested SOW Strategy Generic Research*” document for guidance on preparing the SOW and use the blank SOW format titled “Suggested SOW Format”. The SOW must be in PDF format prior to attaching.

- **Attachment 6: Impact Statement (one-page limit): Upload as “Impact.pdf”.** Describe the anticipated short- and long-term impact of the proposed work on hearing restoration research and/or patient care. This should be written with a broad audience in mind, including readers without a background in science or medicine.
 - **Funding Level 1:** Explain how the proposed work, if successful, will open new avenues of investigation such as new approaches, new research tools, or new paradigms.
 - **Funding Level 2:** Explain how the proposed research, if successful, will lead to significant advancement toward clinical translation.
 - **Funding Level 3:** Explain how the proposed research, if successful, will propel a promising discovery toward a clinical trial.
- **Attachment 7: Relevance to Military Health Statement (one-page limit): Upload as “Military.pdf”.** Explain how the proposed research is applicable to the operational performance, medical readiness, and quality of life of Service Members and Veterans with auditory system injuries and/or to their family members and caregivers.

As applicable, include the element(s) below:

- Identify any element(s) or special consideration(s) related to the applicability of the ultimate outcome of the research in the military operational environment (e.g., battlefield, Battalion Aid Stations, Forward Support Medical Battalions). Applicants may consult [A Beginner’s Guide to Military Healthcare System \(Audiology & Otolaryngology\)](#) and the [Joint Health Services Joint Publication 4-02](#) for descriptions of health services across the range of military operations.
- If active-duty military, Veteran, or military family member population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed research, and the feasibility of using the population. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population.
- If applicable, provide a description of how the knowledge, information, products, or technologies gained from the research could be implemented in a dual-use capacity to both benefit the civilian population and address a military need.

- **Attachment 8: Animal Research Plan, if applicable (required if the proposed research involves the use of animals; no page limit): Upload as “AnimalResPlan.pdf”.** Describe the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be submitted to the IACUC as the Animal Research Plan. Consult the Animal Research: Reporting *In Vivo* Experiments (ARRIVE) guidelines 2.0 (ARRIVE) (<https://arriveguidelines.org/arrive-guidelines>) to ensure that animal research is adequately planned for and will be adequately reported. The Animal Research Plan should address the following points for each proposed animal study:
 - Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study’s relevance to human biology.
 - Summarize the procedures to be conducted and the endpoints/outcome measures.
 - Describe how the study will be controlled. Identify the ages, sex, and total number of animals by species to be used.
 - Describe the randomization and blinding procedures for the study, and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.
 - Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.
 - Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, statistical methods for data analysis, and identification of the primary endpoint(s).
 - Describe how data will be reported and how it will be assured that the documentation will support potential regulatory filing with the FDA, if applicable.
- **Attachment 9: Human Subjects/Samples Acquisition and Safety Procedures (required if the proposed research involves human subjects or human biological samples; no page limit): Upload as “HumProc.pdf”.** Include the components listed below as applicable.
 - **Study Population and Recruitment Process:** Describe the study population (i.e., Service Members/Veterans/civilians, approximate number, age ranges, sex/gender, racial and ethnic groups, and other pertinent demographic characteristics), criteria for inclusion/exclusion, and the methods that will be used for recruitment/accrual/retention of human subjects.

- Describe the rationale for the selection of subjects. Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender.
 - Provide an anticipated enrollment table(s) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The Public Health Service (PHS) Inclusion Enrollment Report is a three-page fillable PDF form, which can be downloaded from eBRAP at <https://ebrap.org/eBRAP/public/Program.htm>.
 - ***Women and Minorities in the Study: Describe the strategy for the inclusion of women and minorities appropriate to the objectives of 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.
 - Demonstrate that the research team has access to the proposed study population. If applicable, discuss past efforts in recruiting human subjects from the target population for previous clinical studies. Address any potential barriers to accrual and plans for addressing unanticipated delays.
 - Describe how the subject-to-group assignments process will be conducted (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable.
 - Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.
 - ***For clinical studies proposing to recruit military personnel, refer to the General Application Instructions, Appendix 1, for more information on recruitment process and considerations, payment, and confidentiality. If a non-military population will be used for the proposed clinical study, explain how results obtained will be applicable to military personnel.***
- **Informed Consent Process:** Describe the plan for obtaining informed consent from human subjects. Include relevant draft process documents. **Provide a draft, in English, of the Informed Consent Form.**
 - **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:** Identify all foreseeable study risks (physical, psychological, social, legal, and other). Discuss the importance of the knowledge to be gained in relation to the risks to subjects. Clearly describe measures of risk

management and plans for emergency response. Describe known and potential benefits, which may or may not be direct to subjects, in relation to risks.

Note: Payment and/or other compensation for participation are not considered benefits and must be addressed in Study Population and Recruitment Process.

- **Human Samples:** Describe the types and source(s) of specimens, records, or data to be collected and evaluated. Include information about specimen storage (i.e., location, duration, special handling conditions). Describe the identifiers that will be associated with the human specimens and data and provide a list of who has access to subjects' identities. Describe how individually identifiable private information will be protected.
- **Attachment 10: Pilot Clinical Trial Plan (required only for Funding Level 3, no page limit): Submit this attachment only if required. Upload as "PilotClinicalTrial.pdf".**

Describe the plans for initiating and conducting the PCT during the course of this award.

- Describe how the PCT is linked to the translational studies that will also be performed through this award.
- Describe the objective(s) of the PCT; explain how it will inform the feasibility, rationale, and design of subsequent clinical trials.
- Describe the design of the PCT and outline the proposed methodology in sufficient detail to show a clear course of action. Identify the intervention to be tested, projected outcomes, study variables, controls, and endpoints. Demonstrate the availability of, and access to, the intervention to be tested.
- As appropriate for the proposed PCT, describe the statistical model and data analysis plan. If applicable, include power analysis calculations.
- Describe potential challenges and alternative strategies, where appropriate.
- **Attachment 11: Regulatory Strategy (required only for Funding Level 3; no page limit): Submit this attachment only if required. 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 the FDA or an international regulatory agency:

Explain why the product/intervention is exempt from FDA oversight. Provide confirmation that the PCT does not require regulation by the FDA. If the PCT will be

conducted at international sites, provide equivalent information relevant to the host country(ies) regulatory requirements. No further information for this attachment is required.

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

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

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

If the product is not currently FDA-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification. **Identify the regulatory sponsor. Include a signed sponsor commitment letter** acknowledging the regulatory sponsor's understanding of all sponsor responsibilities described in 21 CFR 312, Subpart D, and commitment to oversee execution of the study.

If an Investigational New Drug (IND) or Investigational Device Exemption (IDE) is required, provide documentation of submission (e.g., a copy of the FDA acknowledgment letter to include submission date and receipt date, status of the application) or a timeline for planned submission. ***Submission must be made prior to the award date. The government reserves the right to withdraw funding if an IND or IDE is necessary but has not been submitted to the FDA prior to the award date, or if documented status of the IND or IDE has not been obtained within 6 months of the award date.***

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 PCT.

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

If a technical or a protocol amendment to an IND/IDE is necessary to conduct the PCT, provide a copy of the FDA acknowledgment letter and meeting minutes (pre-IND/pre-IDE and/or Type C) that confirm the FDA's concurrence to the proposed regulatory approach. Documents must demonstrate clear evidence that the proposed investigational drug or device will not require new IND/IDE submission pertaining to the indication and formulation to be used in the PCT.

- If the PCT 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, etc.), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).
- Describe the overall regulatory strategy and product development plan that will support the planned product indication/label. Include considerations for compliance with current GMP, GLP, and GCP guidelines.
- **Attachment 12: Post-Award Transition Plan (required only for Funding Level 2 and Funding Level 3; three-page limit): Submit this attachment only if required. Upload as “Transition.pdf”.** Assuming the project will be successful, investigators should plan in advance the methods and strategies to transition the anticipated outcomes of the proposed research to the next phases of development and to eventual clinical use. Applicants are strongly encouraged to work with their organization’s Technology Transfer Office (or equivalent) to develop the Post-Award Transition Plan. However, *regardless of the availability of support from a Technology Transfer Office, the Post-Award Transition Plan must provide sufficient details for each required component to allow appropriate peer review.* PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the anticipated research outcomes into the next phase of development.

The Post-Award Transition Plan should include the components listed below:

- The next phase of development (e.g., clinical trials, transition to industry, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA) after the successful completion of the proposed study.
- The methods and strategies to move the anticipated research outcomes to the next phase of development.
- A brief schedule and feasible milestones for transitioning the anticipated research outcomes to the next phase of development.
- The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication (e.g., Target Product Profile). Describe in detail the regulatory strategy, including the number and types of studies proposed to reach approval, licensure, or clearance, the types of FDA (or international regulatory agency, if applicable) meetings to be held, the submission filing strategy, and considerations for compliance with GMP, GLP, and GCP guidelines, if appropriate.

- Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., specific potential industry partners, internal/external funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.
 - If applicable, a description of collaborations and other resources that will be used to provide continuity of development for knowledge products, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications.
 - 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 applicable, a risk analysis for cost, schedule, manufacturability, and sustainability.
- **Attachment 13: Representations, if applicable (extramural submissions only): Upload as “RequiredReps.pdf”.** All extramural applicants must complete and submit the Required Representations template available on eBRAP (<https://ebrap.org/eBRAP/public/Program.htm>). For more information, see the General Application Instructions, Appendix 5, Section B, Representations.
 - **Attachment 14: Suggested Collaborating DOD Military Facility Budget Format, if applicable: Upload as “MFBudget.pdf”.** If a military facility will be a collaborator in performance of the project, complete a separate budget using “Suggested Collaborating DOD Military Facility Budget Format”, available for download on the eBRAP “Funding Opportunities & Forms” page (<https://ebrap.org/eBRAP/public/Program.htm>). A military facility may be a Military Health System facility, research laboratory, medical treatment facility, dental treatment facility, or DOD activity embedded with a civilian medical center. Include a budget justification for each military facility as instructed. The costs per year should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section III.A.8, for detailed information.

- **Extramural and Intramural Applications**

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

Research & Related Personal Data: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.3, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.2, for detailed information.

Research & Related Senior/Key Person Profile (Expanded): For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.4, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.3, for detailed information.

- PI Biographical Sketch (six-page limit): Upload as “Biosketch_LastName.pdf”. The suggested biographical sketch format is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP. The National Institutes of Health (NIH) Biographical Sketch may also be used. All biographical sketches should be submitted in uneditable PDF format.
- PI Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf”.
 - For extramural submissions, refer to the General Application Instructions, Section III.A.4, for detailed information.
 - For intramural submissions, refer to the General Application Instructions, Section IV.A.3, for detailed information.
- 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”.

Research & Related Budget: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.5, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.4, for detailed information.

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

Project/Performance Site Location(s) Form: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.6, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.5, for detailed information.

- **Extramural Applications Only**

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

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov. (Refer to the General Application Instructions, Section III.A.7, for detailed information.) Verify subaward budget(s) and budget justification forms are

present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period.

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

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

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

II.D.4. Submission Dates and Times

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

Applicant Verification of Full Application Submission in eBRAP

For Both Extramural and Intramural Applicants: eBRAP allows an organization’s representatives and PIs to view and modify the full application submissions associated with them. Following retrieval and processing of the full application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the full application submission. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in an email to the PI and in the “Full Application Files” tab in eBRAP. eBRAP does not confirm the accuracy of file

content. Application viewing, modification, and verification in eBRAP are strongly recommended, but not required. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the program announcement. ***If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the application submission deadline. The Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline.*** Other application components may be changed until the end of the application verification period. Verify that subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

Extramural Submission: The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package, ***with the exception of the Project Narrative and Budget Form,*** may be modified.

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

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

II.D.5. Funding Restrictions

The requested funding level should be based on the stage and maturity level of the research project, rather than the amount of the budget.

Funding Level 1:

The maximum period of performance is **2** years.

The anticipated direct costs budgeted for the entire period of performance will not exceed **\$250,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **\$250,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

Funding Level 2:

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

The anticipated direct costs budgeted for the entire period of performance will not exceed **\$1,000,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **\$1,000,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

Funding Level 3:

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

The anticipated direct costs budgeted for the entire period of performance will not exceed **\$1,250,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **\$1,250,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate.

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

The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **2** years for **Funding Level 1** or **3** years for a **Funding Level 2** or **Funding Level 3**.

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

- Travel in support of multidisciplinary collaborations.
- Travel for one investigator to travel to one scientific/technical meeting per year to present project information or disseminate project results from the FY22 HRRP FRA.

For Funding Level 2 or Funding Level 3, direct costs must be requested for:

- Travel costs for the PI to present project information or disseminate results at one DOD-sponsored meeting to be specified by the program office during award negotiations (e.g., the Military Health System Research Symposium). For planning purposes, it should be assumed that the meeting will be held in the Central Florida Area. Costs associated with travel to this meeting should be included in year 2 or 3 of the budget. This is in addition to the annual scientific/technical meeting described above.

For extramural awards with an intragovernmental component, direct transfer of funds from an extramural award recipient to a DOD or other federal agency is not allowed except under very limited circumstances. Funding to intramural DOD and other federal agencies will be managed through a direct funds transfer. Intramural applicants are responsible for coordinating through their agency's procedures the use of contractual or assistance funding awards or other appropriate agreements to support extramural collaborators.

Refer to the General Application Instructions, Section III.A.5, for budget regulations and instructions for the Research & Related Budget. *For federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in the General Application Instructions, Section III.A.5.*

II.D.6. Other Submission Requirements

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

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

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

- **Impact**
 - To what extent the proposed research will impact hearing restoration research and/or patient care.
 - **Funding Level 1:** If successful, to what extent the proposed work will open new avenues of investigation.
 - **Funding Level 2:** If successful, to what extent the proposed research will lead to significant advancement toward clinical translation.
 - **Funding Level 3:** If successful, to what extent the proposed research will propel a promising discovery toward a clinical trial.
- **Research Rationale and Strategy**
 - To what extent the idea of the proposed research, including the objective(s) and/or hypothesis(es), is supported by rationale, critical analysis of literature, and, if applicable, preliminary data.
 - To what extent the specific aims are appropriate to address the objective(s) and/or hypothesis(es) of the proposed research.
 - To what extent the experimental design, methods, and analyses are appropriate and feasible.
 - If proposing research on interventions, is it clear whether the intervention is for restoring hearing after established hearing loss or for preserving cells/synapses after acute auditory injury, to be administered soon after the injury.

- As applicable, to what extent the experimental design will enable/facilitate eventual connection of the intervention to precision diagnosis and application of the intervention to real-world injuries, or the eventual demonstration that the benefits of the therapeutic outweigh the potential risks.
- If applicable, how well the animal study is designed to achieve the study objectives, including choice of animal model(s), the endpoints/outcome measures, and how well the animal model chosen is relevant to human auditory biology or injury.
- If applicable, how well the human study is designed to achieve the study objectives, including description of and access to the study population(s) or sample(s), plans for subject recruitment, consent, screening and retention, and plans for addressing ethical and regulatory considerations.
- If applicable, whether the strategy for the inclusion of women and minorities and distribution of proposed enrollment is appropriate for the proposed study.
- To what extent the statistical plan, including sample size estimate, is appropriate.
- How well the proposed research is designed to reduce bias and achieve reproducible and rigorous results.
- To what extent the measures to reduce bias and achieve reproducible and rigorous results are appropriate.
- How well the application acknowledges potential problems and addresses alternative approaches.
- Whether the research can be completed within the proposed period of performance.
- For Funding Level 3 applications, the following *additional* criteria apply:
 - How well the PCT is linked to the translational studies to be performed through this award.
 - To what extent the objective(s) of the PCT are clear and appropriate.
 - To what extent the design of the PCT supports its objective and demonstrates a clear course of action, including intervention to be tested, projected outcomes, study variables, controls, and endpoints.
 - To what extent the statistical plan of the PCT, including sample size estimate, is appropriate.
 - To what extent the application demonstrates availability of, and access to, the intervention to be tested.

- To what extent the Regulatory Strategy provides sufficient evidence for IND/IDE exemption or, if IND/IDE is required, an appropriate plan/timeline for applying for and obtaining IND/IDE status (or other approvals by the FDA or international regulatory agency).
- **Post-Award Transition Plan (for Funding Level 2 and Funding Level 3 applications only)**
 - Whether the identified next phase of development and/or commercialization is realistic.
 - Whether the methods and strategies to move the anticipated research outcomes to the next phase of development and/or commercialization are feasible.
 - Whether the schedule and milestones for bringing the anticipated research outcomes to the next level of development are achievable.
 - If the ultimate goal is to produce a regulated product (e.g., drug, biologics, or device), to what extent the regulatory strategy and product development plan are appropriate to support a regulatory filing with the FDA or international regulatory agency.
 - Whether the funding strategy to bring the anticipated research outcomes to the next level of development is reasonable and realistic.
 - As applicable, whether the proposed collaborations and other resources for providing continuity of development are established and/or achievable.
 - As applicable, whether the applicant has identified intellectual property ownership, demonstrated appropriate access to all intellectual property rights necessary for development and/or commercialization, and described an appropriate intellectual and material property plan among participating organizations for products or technologies supported by this award.
 - As applicable, whether the risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
- **Personnel**
 - To what extent the backgrounds, expertise, experience, and past accomplishments of the PI and key personnel are appropriate to accomplish the proposed research project.
 - Whether the levels of effort by the PI and key personnel are appropriate for the successful conduct of the proposed work.

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

- **Environment**
 - To what extent the scientific environment is appropriate for the proposed research project.
 - How well the research requirements are supported by the availability of, and accessibility to, facilities and resources (including collaborative arrangements).
 - To what extent the quality and level of institutional support are appropriate for the proposed research project.
- **Budget**
 - Whether the **direct** costs exceed the allowable direct costs as published in the program announcement.
 - Whether the budget is appropriate for the proposed research.
- **Environment**
 - If applicable, to what degree the intellectual and material property plan is appropriate
- **Application Presentation**
 - To what extent the writing, clarity, and presentation of the application components influence the review.

II.E.1.b. Programmatic Review

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

- Ratings and evaluations of the peer reviewers
- Relevance to the mission of the DHP and FY22 HRRP, as evidenced by the following:
 - Adherence to the intent of the award mechanism
 - Relative Impact
 - Relevance to military health
 - Program portfolio composition

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.army.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 panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review and approval process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review and approval process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with 18 USC 1905.

II.E.3. Integrity and Performance Information

Prior to making an assistance agreement award where the federal share is expected to exceed the simplified acquisition threshold, as defined in 2 CFR 200.1, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in the Federal Awardee Performance and Integrity Information System (FAPIIS).

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

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

II.E.4. Anticipated Announcement and Federal Award Dates

All application review dates and times are indicated in [Section I, Overview of the Funding Opportunity](#).

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

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Awards supported with FY22 funds are anticipated to be made no later than September 30, 2023. Refer to the General Application Instructions, Appendix 2, for additional award administration information.

After email notification of application review results through eBRAP, and if selected for funding, a representative from the USAMRAA will contact the Business Official authorized to negotiate on behalf of the PI's organization.

Pre-Award Costs: An institution of higher education, hospital, or non-profit 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 III.A.5.

Only an appointed USAMRAA Grants Officer may obligate the government to the expenditure of funds. No commitment on the part of the government should be inferred from discussions with any other individual. **The award document signed by the Grants Officer is the official authorizing document.**

Federal Government Organizations: Funding made to federal government organizations (to include intramural DOD organizations) will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

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

Unless otherwise restricted, changes in PI or organization will be allowed at the discretion of the USAMRAA Grants Officer, provided the intent of the award mechanism is met.

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

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

Refer to the General Application Instructions, Appendix 2, Section B, for general information on organization or PI changes.

II.F.2. Administrative and National Policy Requirements

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

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

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

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

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

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

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

II.F.3. Reporting

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

Annual progress reports as well as a final progress report, including quad charts, will be required. Quarterly progress reports are required for Funding Level 3 awards.

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

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the 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 (*only required for clinical research studies*): Enrollment reporting on the basis of sex/gender, race, and/or ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP.

Awards resulting from this program announcement may entail additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have federal contract, grant, and cooperative agreement awards with a cumulative total value greater than \$10M are required to provide information to FAPIIS about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a federal award. These recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 5, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

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

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

Email: support@grants.gov

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

II.H. Other Information

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

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 702b. The program announcement numeric version code will match the General Application Instructions version code 702.

II.H.2. Administrative Actions

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

II.H.2.a. Rejection

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

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

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Pre-application was not submitted.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- ***For Funding Level 3 applications:*** Human Subjects/Samples Acquisition and Safety Procedures (Attachment 9) is missing.
- ***For Funding Level 3 applications:*** Pilot Clinical Trial Plan (Attachment 10) is missing.
- ***For Funding Level 3 applications:*** Regulatory Strategy (Attachment 11) is missing.

II.H.2.b. Modification

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

II.H.2.c. Withdrawal

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

- An FY22 HRRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. *A list of the FY22 HRRP Programmatic Panel members can be found at <https://cdmrp.army.mil/hrrp/panels/panels22>.*
- The application fails to conform to this program announcement description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY22, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<https://cdmrp.army.mil/about/2tierRevProcess>). Applications that include names of personnel from either of these companies may be administratively withdrawn.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP may be withdrawn.
- Applications submitted by an intramural DOD organization may be withdrawn if the intramural organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to extramural collaborators.
- The invited application proposes a different research project than that described in the pre-application.
- An application that proposes tinnitus or vestibular-related research.
- The PI does not meet the eligibility criteria.

- The application does not address at least one of the FY22 HRRP Focus Areas.

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. Application Submission Checklist

Application Components	Action	Completed
SF424 Research & Related Application for Federal Assistance (extramural submissions only)	Complete form as instructed	
Summary (Tab 1) and Application Contacts (Tab 2) (intramural submissions only)	Complete tabs as instructed	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf"	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf"	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf"	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf"	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf"	
	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf"	
	Relevance to Military Health Statement: Upload as Attachment 7 with file name "Military.pdf"	
	Animal Research Plan: Upload as Attachment 8 with file name "AnimalResPlan.pdf" if applicable	
	Human Subjects/Samples Acquisition and Safety Procedures: Upload as Attachment 9 with file name "HumProc.pdf" if applicable	
	Pilot Clinical Trial Plan: Upload as Attachment 10 with file name "PilotClinicalTrial.pdf" if applicable	
	Regulatory Strategy: Upload as Attachment 11 with file name "Regulatory.pdf" if applicable	
	Post-Award Transition Plan: Upload as Attachment 12 with file name "Transition.pdf" if applicable	
	Representations (extramural submissions only): Upload as Attachment 13 with file name "RequiredReps.pdf"	
	Suggested Collaborating DOD Military Facility Budget Format: Upload as Attachment 14 with file name "MFBudget.pdf" if applicable	

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

APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
ACURO	Animal Care and Use Review Office
ARRIVE	Animal Research: Reporting <i>In Vivo</i> Experiments
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
DHP	Defense Health Program
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Numbering System
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FAPIIS	Federal Awardee Performance and Integrity Information System
FDA	U.S. Food and Drug Administration
FRA	Focused Research Award
FY	Fiscal Year
HRPO	Human Research Protection Office
HRRP	Hearing Restoration Research Program
K	Thousand
IACUC	Institutional Animal Care and Use Committee
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
M	Million
MB	Megabytes
MIPR	Military Interdepartmental Purchase Request
NCATS	National Center for Advancing Translational Sciences
NIH	National Institutes of Health
ORCID	Open Researcher and Contributor ID, Inc.
ORP	Office of Research Protections
PCT	Pilot Clinical Trial
PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
SAM	System for Award Management

SOW	Statement of Work
URL	Uniform Resource Locator
UEI	Unique Entity Identifier
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	Department of Veterans Affairs