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: HT942524HRRPFRA

Assistance Listing Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application (Letter of Intent) Submission Deadline:** 5:00 p.m. Eastern time (ET), July 22, 2024

- **Application Submission Deadline:** 11:59 p.m. ET, August 9, 2024

- **End of Application Verification Period:** 5:00 p.m. ET, August 15, 2024

- **Peer Review:** October 2024

- **Programmatic Review:** January 2025

This program announcement must be read in conjunction with the General Application Instructions, version 901. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the "Package" tab, clicking "Preview," and then selecting "Download Instructions."

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II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

The U.S. Army Medical Research Acquisition Activity (USAMRAA) is soliciting applications to the fiscal year 2024 (FY24) Hearing Restoration Research Program (HRRP)using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC) is the program management agent for this funding opportunity. Congress initiated the HRRP in 2017 to provide support for research of high potential impact and exceptional scientific merit. Appropriations for the HRRP from FY17 through FY23 totaled $65 million (M). The FY24 appropriation is $5M.

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

A survey conducted by the Centers for Disease Control and Prevention (CDC) found 15% of adults aged 18 and over had some degree of hearing loss, making it the third most common chronic physical condition in the United States, more prevalent than diabetes (9%) or cancer (8%).[1, 2] Study of a random sample of 77,047 U.S. military members from all Service branches and components who were on active rosters as of October 2000 showed that combat experience was associated with a 63% increased risk for hearing loss. The most recent data from the Department of Veterans Affairs (VA) indicates that there are more than 1.4 million Veterans with Service-connected disability due to hearing loss.[3] 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 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. FY24 HRRP Focus Areas

To meet the intent of the funding opportunity all applications to the FY24 HRRP Focused Research Award (FRA) must address research in one or more of the following Focus Areas:

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[1] Blackwell DL, Lucas JW, and Clarke TC. 2014. Summary health statistics for US adults: National Health Interview Survey, 2012. Vital Health Statistics, Series 10, No. 260. National Center for Health Statistics, CDC. Atlanta, Georgia. https://www.cdc.gov/nchs/data/series/sr_10/sr10_260.pdf

[2] Wells TS, Seelig AD, Ryan MA, et al. 2015. Hearing loss associated with US military combat deployment. *Noise Health* 17(74):34-42.

[3] Veterans Benefits Administration Annual Benefits Report, Fiscal Year 2022. Veterans Benefits Administration. U.S. Department of Veterans Affairs. (February 2023) https://www.benefits.va.gov/REPORTS/abr/docs/2022-abr.pdf

- Improve and accelerate the translation of biological regeneration/repair mechanisms into clinical applications. Research addressing the damage, repair, and regeneration of the auditory system after military-relevant injuries is strongly encouraged.

- Develop diagnostic tests that 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.

Tinnitus or vestibular-related research is excluded.

II.A.2. Award History

The HRRP Focused Research Award mechanism was first offered in FY19. Since then, 195 FRA applications have been received, and 46 have been recommended for funding.

II.B. Award Information

The FY24 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.

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 from investigators within the military Services and applications involving multidisciplinary collaborations among academia, industry, the military Services, the VA, and other federal government agencies are highly encouraged. These relationships can leverage knowledge, infrastructure, and access to unique clinical populations that the collaborators bring to the research effort, ultimately advancing research that is of significance to Service Members, Veterans, and/or their Families. If the proposed research relies on access to unique 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.

Key Elements

- **Program priorities:** To maximize impact and return, the HRRP will prioritize investments in research that overcome major scientific 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 hurdle 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 to ***advance diagnostics of auditory system pathobiology, validate preclinical results, and translate potential therapies to clinical applications***. The HRRP FY24 Focus Areas are designed to support these priorities.

- *(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 specific pathology (e.g., sensory, neural, synaptic, or central auditory)* 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 FY24 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 with 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 a non-PCT translational component and a 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 in the Code of Federal Regulations, Title 45, Part 46.102 (45 CFR 46.102) as a research study in which one or more human subjects are *prospectively* assigned to one or more interventions (which may include a placebo or another control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

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

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

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

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

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

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

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 studies are required to register the study in the National Institutes of Health 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 grants (31 USC 6304).

The anticipated direct costs budgeted for the entire period of performance for an FY24 HRRP FRA – Funding Level 1 should not exceed **$250,000**. The anticipated direct costs budgeted for the entire period of performance for an FY24 HRRP FRA – Funding Level 2 will not exceed **$750,000**. The anticipated direct costs budgeted for the entire period of performance for an FY24 HRRP FRA – Funding Level 3 will not exceed **$1,000,000**. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

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

The CDMRP expects to allot approximately $400,000 to fund approximately one FRA – Funding Level 1 application, approximately $2.4M to fund approximately two FRA – Funding Level 2 applications, and approximately $1.6M to fund approximately one FRA – Funding Level 3 application. Funding of applications received is contingent upon the availability of federal funds for this program, the number of applications received, the quality and merit of the applications as evaluated by peer and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY24 funding opportunity will be funded with FY24 funds, which will expire for use on September 30, 2030.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: Extramural and Intramural organizations are eligible to apply, including foreign or domestic organizations, for-profit and non-profit organizations, and public entities.

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

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

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

II.C.1.b. Principal Investigator

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

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

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

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

II.D. Application and Submission Information

II.D.1. Location of Application Package

Submission is a two-step process requiring both a *pre-application* submitted via the Electronic Biomedical Research Application Portal (eBRAP.org) and a *full application* (eBRAP.org or

Grants.gov). Depending on the type of submission (i.e., extramural vs. intramural), certain aspects of the submission process will differ.

The CDMRP uses two portal systems to accept pre- and full application submissions.

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

Grants.gov (https://grants.gov) is a federal system that must be used by funding agencies to announce extramural grant applications. Full applications for CDMRP funding opportunities can only be submitted to Grants.gov after submission of a pre-application through eBRAP.

Application Submission Workflow
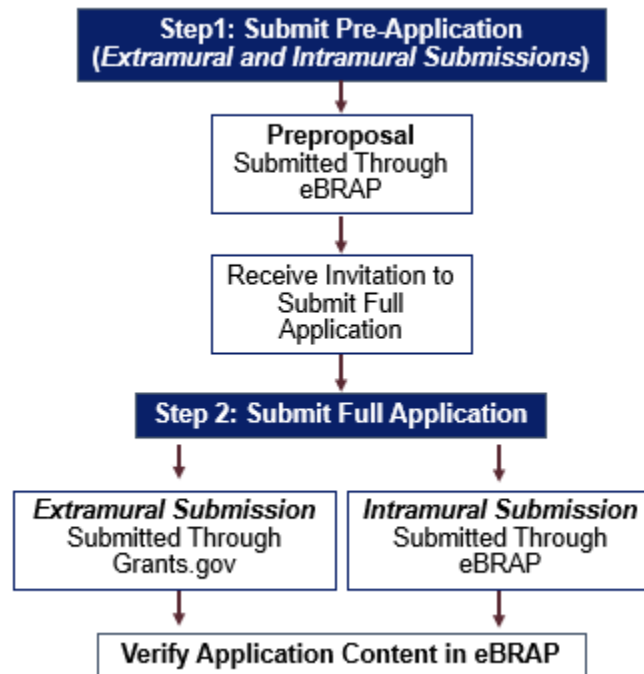
Extramural Submission: An application submitted by an extramural organization for an extramural or intramural PI working within an extramural or intramural organization. For example, a research foundation submitting an application for a DOD employee working within a DOD organization would be considered an extramural submission and should follow instructions specific to extramural submissions. Download application package components for HT942524HRRPFRA from Grants.gov (https://grants.gov). Full applications from extramural organizations **must** be submitted through Grants.gov.

Intramural Submission: An application submitted by an intramural DOD organization for an investigator employed by that organization. Intramural DOD organizations may submit full applications to either eBRAP or Grants.gov. Download application package components for HT942524HRRPFRA from the anticipated submission portal eBRAP (https://ebrap.org) or Grants.gov.

The submission process should be started early to avoid missing deadlines. Regardless of submission type or portal used, all pre- and full application components must be submitted by the deadlines stipulated on the first page of this program announcement. There are no grace periods for deadlines; failure to meet submission deadlines will result in application rejection. ***The USAMRAA cannot make allowances/exceptions for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.***

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

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

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

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

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

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

Regardless of submission type (i.e., extramural or intramural), all pre-application components must be submitted by the PI through eBRAP.

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

When starting the pre-application, applicants will be asked to select a "Mechanism Option". Based on the intended funding level of your application, please be sure to select the correct option when submitting your pre-application:

Intended Funding Level of Application:	Select Option:
FRA – Funding Level 1	FRA-FL1
FRA – Funding Level 2	FRA-FL2
FRA – Funding Level 3	FRA-FL3

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

Pre-application submissions must include the following components (refer to the General Application Instructions, Section III.B, for detailed instructions regarding pre-application submission):

- **Letter of Intent (LOI) (one-page limit):** Provide a brief description of the research to be conducted, including the following information:

    ○   Funding Level

    ○   Focus Area(s) that the research aligns to

    ○   The research question(s) to be answered

    ○   Whether the research will involve human subjects or samples

    LOIs are used for program planning purposes only (e.g., reviewer recruitment) and will not be reviewed during either the peer or programmatic review. An invitation to submit a full application is *NOT* provided after LOI submission and applicants are *NOT* required to have such an invitation in order to proceed to submitting a full application. *Applicants are encouraged to develop pre-application and full application components concurrently and can proceed to submit a full application any time AFTER successful submission of the pre-application and before the full application deadline.*

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

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

Extramural Submissions: Full applications from extramural organizations *must* be submitted through Grants.gov Workspace. Full applications from extramural organizations, including non-DOD federal organizations, received through eBRAP will be withdrawn. Refer to the General Application Instructions, Section IV, for considerations and detailed instructions regarding extramural full application submission.

Intramural Submissions: Intramural DOD organizations may submit full applications through either eBRAP or Grants.gov. There is no preference from the CDMRP for which submission portal is utilized; submission through one portal or the other does not provide the application any

advantage during the review process. Intramural DOD organizations that choose to submit through Grants.gov should follow Extramural Submission instructions. Intramural DOD organizations that are unable to submit through Grants.gov should submit through eBRAP. For the remainder of this program announcement, it will be assumed intramural DOD submissions will proceed through eBRAP. Refer to the General Application Instructions, Section V, for considerations and detailed instructions regarding intramural DOD full application submission.

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

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

(a) SF424 Research & Related Application for Federal Assistance Form *(Extramural Submissions Only)***:** Refer to the General Application Instructions, Section IV.B, for detailed information.

(b) Attachments:

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

○ **Attachment 1: Project Narrative (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 that expands 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:** 6-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 with specific pathology (e.g., sensory, neural, synaptic, or central auditory) 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 the Regulatory Agency and potential users.

- ❖ For the purposes of this funding opportunity, Regulatory Agency refers to the FDA or any relevant international regulatory agency unless otherwise noted.

- ❖ If the applicant has engaged the Regulatory Agency and received guidance on the acceptability of the proposed criteria, please include that information in the application.

- ❖ If the applicant has engaged potential users to estimate/predict the level of user acceptance, please include that 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, and Attachment 11, Regulatory Strategy.**

- ▪ 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 filing with the Regulatory Agency.

- ▪ Address potential problems that may arise and present alternative methods and approaches to mitigate or resolve the problems.

- ▪ Explain how the research can be completed within the proposed period of performance.

- ❖ If proposing animal or human research, provide a timeline for protocol approvals and, if applicable, the current status of approvals.

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

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

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

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

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

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

– **Letters of Organizational Support (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 and/or organization demonstrating that the PI has the support and resources necessary for the proposed work. If an investigator at an intramural DOD organization is named as a collaborator on a full application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural DOD organization authorizing the collaborator's involvement.

– **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 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.

– **DOD Data Management Plan (two-page limit is recommended):** Describe the data management plan in accordance with Section 3.c, Enclosure 3, [DoD Instructions 3200.12](#). *Do not duplicate the Data and Research Resources Sharing Plan.* Refer to General Application Instructions, Section IV.B, Attachments Form, Attachment: Supporting Documentation, for detailed information regarding Data Management Plan content.

– **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.

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

  ▪ Data reporting to Federal Interagency Traumatic Brain Injury Research (FITBIR) is an opportunity for investigators to facilitate their own research and to collaborate with others engaged in similar research. While 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. FITBIR guidance and policies, as well as the considerable advantages of FITBIR participation to the researcher, are detailed at http://fitbir.nih.gov/.

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

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

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

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 FY24 HRRP Focus Areas.

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

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

▪   *Funding Level 3 only:* Clearly identify which aims involve non-PCT translational studies and which aim involves a PCT.

–   **Study Design:** 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, and addresses issues of particular interest to the affected community. *Abstracts of all funded research projects will be posted publicly.* Use only

characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed. ***Do not duplicate the technical abstract.***

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

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

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

FITBIR-eligible research should also include the following subtasks:

- FITBIR investigator and study registration within the first 30 days of the award

- Sharing of draft data collection forms with FITBIR

- Annual FITBIR data submission

○ **Attachment 6: Impact Statement (one-page limit): Upload as "Impact.pdf".** Describe the anticipated short-term 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 elements below:

- 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.

- If the ultimate outcome of the research is intended to be applicable in the military operational environment (e.g., battlefield, Battalion Aid Stations, Forward Support Medical Battalions), identify any element(s) or special consideration(s) related to the intended applicability. 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.

○ **Attachment 8: Animal Research Plan (no page limit): Upload as "AnimalResPlan.pdf".** *(Attachment 8 is only applicable and required for applications proposing animal studies.)*

- 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 filing with the Regulatory Agency, 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.

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

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

    ❖ Provide an anticipated enrollment table(s) for the inclusion of women and minorities using the Public Health Service (PHS) Inclusion Enrollment

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

- 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 "PCT.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 a Regulatory Agency:

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

  For products that require regulation by a Regulatory Agency:

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

  – If the product is marketed in the United States, state the product label indication. State whether the proposed research involves a change to the approved label

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

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

- If an IND or 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, Good Manufacturing Practice [GMP]-compliant lots available, status of stability testing), non-clinical development (e.g., test facility name, status of pivotal Good Laboratory Practice [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 Good Clinical Practice (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".** Describe/discuss the methods and strategies proposed to move the anticipated research outcome (e.g., intervention, product, methodology, finding) to the next phase of development (e.g., clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. Applicants are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. *The post-award transition plan should include the components listed below:*

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

– A description of the next phase of development to advance the research outcome.

○ If applicable, describe the planned indication for the product label 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 Regulatory Agency meetings to be held, the submission filing strategy, and considerations for compliance with GMP, GLP, and GCP guidelines, if appropriate.

– 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.

– Collaborations and other resources that are in place or will be established to advance the research outcome to the next phase of development.

– Details of the funding strategy to transition to the next level of investigation, development, and/or commercialization. This may include commercial sponsorship, venture capital, federal or non-federal funding opportunities, etc.

– Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award, including a plan for resolving intellectual and material property issues among participating organizations, if applicable.

- An assessment of the opportunities available and potential barriers that would impact the next phase of development and/or the eventual clinical translation of the research outcome.

- ○ **Attachment 13: Representations** *(Extramural Submissions Only)***: Upload as "RequiredReps.pdf".** All extramural applicants must complete and submit the Required Representations template available on eBRAP (https://ebrap.org/eBRAP/public/Program.htm). For more information, see the General Application Instructions, Appendix 8, Section B, Representations.

- ○ **Attachment 14: Suggested Intragovernmental/Intramural Budget Form** *(if applicable)***: Upload as "IGBudget.pdf".** If an [intramural DOD organization](https://ebrap.org/eBRAP/public/Program.htm) will be a collaborator in performance of the project, complete a separate budget using the "Suggested Intragovernmental/Intramural Budget Form", available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). The budget should cover the entire period of performance for each intramural DOD site and include a budget justification as instructed. The *total* costs per year for each subaward (direct and indirect costs) should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section V.A.(e), for additional information and considerations.

(c) Research & Related Personal Data: For extramural submissions, refer to the General Application Instructions, Section IV.B.(c), and for intramural submissions, refer to the General Application Instructions, Section V.A.(c), for detailed instructions.

(d) Research & Related Senior/Key Person Profile (Expanded): For extramural submissions, refer to the General Application Instructions, Section IV.B.(d), and for intramural submissions, refer to the General Application Instructions, Section V.A.(d), for detailed instructions.

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

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

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

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

(e) Research & Related Budget: For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), for detailed instructions.

- ○ **Budget Justification (no page limit):** For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Section L, for instructions. For intramural

submissions, refer to General Application Instructions, Section V.A.(e), Budget Justification Instructions.

(f) Project/Performance Site Location(s) Form: For extramural submissions, refer to the General Application Instructions, Section IV.B.(f), and for intramural submissions, refer to the General Application Instructions, Section V.A.(f), for detailed instructions.

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Extramural Submissions Only)***:** Refer to the General Application Instructions, Section IV.B.(g), for detailed instructions.

- ○ **Extramural Subaward:** Complete the Research & Related Subaward Budget Form and upload through Grants.gov.

- ○ **Intramural DOD Subaward:** Complete a separate "Suggested Intragovernmental/Intramural Budget Form" for each intramural DOD subaward and upload as a single document titled **IGBudget.pdf** to Grants.gov as Attachment 14.

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

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

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

The applicant organization must be registered as an entity in SAM (https://www.sam.gov/content/home) and receive confirmation of an "Active" status before submitting an application through Grants.gov. Organizations must include the UEI generated by SAM in applications to this funding opportunity.

II.D.4. Submission Dates and Times

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

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

II.D.5. Funding Restrictions

Funding Level 1:

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

The application's direct costs budgeted for the entire period of performance should 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. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

Funding Level 2:

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

The application's direct costs budgeted for the entire period of performance should not exceed **$750,000**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

Funding Level 3:

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

The application's direct costs budgeted for the entire period of performance should 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. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

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

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

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

- **All Funding Levels:** Costs for one investigator to travel to one scientific/technical meeting per year. The intent of travel to scientific/technical meetings should be to present project information or disseminate project results from the FY24 HRRP FRA.

- **Funding Level 2 and Funding Level 3 Only:** Costs for the PI to travel to one DOD-sponsored meeting to be specified by the program office during award negotiations (e.g., the Military Health System Research Symposium). The intent of travel to scientific/technical meetings should be to present project information or disseminate project results from the

FY24 HRRP FRA to DOD stakeholders. 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. These travel costs are in addition to those allowed for annual scientific/technical meetings.

II.D.6. Other Submission Requirements

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

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

To determine technical merit, all applications will be individually evaluated according to the following **scored criteria**, which are 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 specific pathology (e.g., sensory, neural, synaptic, or central auditory) 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(s) 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.

○ How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.

○ 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 a Regulatory Agency).

- **Post-Award Transition Plan (for Funding Level 2 and Funding Level 3 applications only)**

  - Whether the identified next phase of development is realistic.

  - If the ultimate goal is to produce a regulated product, to what extent the development plan and regulatory strategy are appropriate to support a regulatory filing with a Regulatory Agency.

  - Whether the methods and strategies to move the anticipated research outcomes to the next phase of development are feasible.

  - Whether the schedule and milestones for bringing the anticipated research outcomes to the next level of development are achievable.

  - As applicable, whether the proposed collaborations and other resources for providing continuity of development are established and/or achievable.

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

  - 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 plan for resolving intellectual and material property issues among participating organizations.

  - Whether the assessment of the opportunities available and potential barriers 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 criteria will also contribute to the overall evaluation of the application, but will not be individually scored and are therefore termed **unscored criteria:**

- **Budget**

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

  - Whether the budget is appropriate for the proposed research.

- **Environment**

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

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

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

- **Application Presentation**

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

II.E.1.b. Programmatic Review

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

- Ratings and evaluations of the peer reviewers

- Relevance to the priorities of the Defense Health Program and FY24 HRRP, as evidenced by the following:

  ○ Adherence to the intent of the funding opportunity, including alignment with at least one of the FY24 HRRP Focus Areas

  ○ Relative Impact

  ○ Relevance to military health

  ○ Contribution to program portfolio

II.E.2. Application Review and Selection Process

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

the two-tier process used by the CDMRP can be found at
https://cdmrp.health.mil/about/2tierRevProcess.

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

II.E.3. Integrity and Performance Information

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

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

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

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

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

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

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

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

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

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

II.F.2. PI Changes and Award Transfers

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

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 7, Section F, for general information on organization or PI changes.

II.F.3. Administrative and National Policy Requirements

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

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

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

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

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

The HRRP requires that all TBI-related clinical research with at least 50 subjects funded by this program be shared through the jointly supported DOD-NIH FITBIR. Recipients will be required to upload study data annually and in accordance with the FITBIR data submission policies. There is no fee to use FITBIR, and detailed guidance and policies, including a cost estimator tool for budgeting considerations, can be found at https://fitbir.nih.gov.

II.F.4. Reporting

Annual technical progress reports and quad charts as well as a final technical progress report and quad chart will be required. Annual and final technical reports must be prepared in accordance with the Research and Performance Progress Report (RPPR). Quarterly technical progress reports are required for Funding Level 3 awards.

The Award Terms and Conditions will specify whether additional and/or more frequent reporting is required.

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the final progress report. Use the one-page template "Award Expiration Transition Plan," available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) under the "Progress Report Formats" section. The Award Expiration Transition Plan must outline whether and how the research supported by this award will progress and must include source(s) of funding, either known or pending.

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

Awards resulting from this program announcement may entail additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have federal contract, grant, and cooperative agreement awards with a cumulative total value greater than $10M are required to provide information to SAM about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a federal award. These recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 8, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

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

> Phone: 301-682-5507

> Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

Questions regarding Grants.gov registration and Workspace

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

> Email: support@grants.gov

II.H. Other Information

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

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 900b. The program announcement numeric version code will match the General Application Instructions version code 900.

II.H.2. Administrative Actions

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

II.H.2.a. Rejection

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

- Letter of Intent 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 Project Narrative.

- Documents not requested will be removed.

II.H.2.c. Withdrawal

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

- An FY24 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, including letters of support/recommendation. *A list of the FY24 HRRP Programmatic Panel members can be found at https://cdmrp.health.mil/hrrp/panels/panels24.*

- The application fails to conform to this program announcement description.

- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.

- Applications that include names of personnel from either of the CDMRP peer or programmatic review companies. For FY24, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.health.mil/about/2tierRevProcess).

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

- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP.

- Applications submitted by a federal government organization (including an intramural DOD organization) may be withdrawn if (a) the organization cannot accept and execute the entirety of the requested budget in current fiscal year (FY24) funds and/or (b) the federal government organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to collaborators.

- Application includes research data that are classified and/or proposes research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns.

- The application proposes tinnitus or vestibular-related research.

- The PI does not meet the eligibility criteria.

II.H.2.d. Withhold

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

II.H.3. Full Application Submission Checklist

Full Application Components	Uploaded
SF424 Research & Related Application for Federal Assistance *(Extramural submissions only)*	☐
Summary (Tab 1) and Application Contacts (Tab 2) *(Intramural submissions only)*	☐
Attachments	
Project Narrative – Attachment 1, upload as "ProjectNarrative.pdf"	☐
Supporting Documentation – Attachment 2, upload as "Support.pdf"	☐
Technical Abstract – Attachment 3, upload as "TechAbs.pdf"	☐
Lay Abstract – Attachment 4, upload as "LayAbs.pdf"	☐
Statement of Work – Attachment 5, upload as "SOW.pdf"	☐
Impact Statement – Attachment 6, upload as "Impact.pdf"	☐
Relevance to Military Health Statement – Attachment 7, upload as "Military.pdf"	☐
Animal Research Plan – Attachment 8, upload as "AnimalResPlan.pdf" if applicable	☐
Human Subjects/Samples Acquisition and Safety Procedures – Attachment 9, upload as "HumProc.pdf" if applicable	☐
Pilot Clinical Trial Plan - Attachment 10, upload as "PilotClinicalTrial.pdf" if applicable	☐
Regulatory Strategy – Attachment 11, upload as "Regulatory.pdf" if applicable	☐
Post-Award Transition Plan – Attachment 12, upload as "Transition.pdf" if applicable	☐
Representations *(Extramural submissions only)* – Attachment 13, upload as "RequiredReps.pdf"	☐
Suggested Intragovernmental/Intramural Budget Form *(if applicable)* – Attachment 14, upload as "IGBudget.pdf"	☐
Research & Related Personal Data	☐
Research & Related Senior/Key Person Profile (Expanded)	☐
Attach PI Biographical Sketch (Biosketch_LastName.pdf)	☐
Attach PI Previous/Current/Pending Support (Support_LastName.pdf)	☐
Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person	☐
Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person	☐
Research & Related Budget *(Extramural submissions only)* Include budget justification	☐

Full Application Components	Uploaded
Budget *(Intramural submissions only)* Include budget justification	☐
Project/Performance Site Location(s) Form	☐
Research & Related Subaward Budget Attachment(s) Form *(if applicable)*	☐

APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
CDC	Centers for Disease Control and Prevention
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FDA	U.S. Food and Drug Administration
FRA	Focused Research Award
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HRRP	Hearing Restoration Research Program
IRB	Institutional Review Board
LOI	Letter of Intent
M	Million
MIPR	Military Interdepartmental Purchase Request
NCATS	National Center for Advancing Translational Sciences
NIH	National Institutes of Health
PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
RPPR	Research Performance Progress Report
SAM	System for Award Management
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
UEI	Unique Entity Identifier
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	U.S. Department of Veterans Affairs