

# **I. OVERVIEW OF THE FUNDING OPPORTUNITY**

**Program Announcement for the Department of Defense**

**Defense Health Program**

**Congressionally Directed Medical Research Programs**

**Neurofibromatosis Research Program**

**Clinical Trial Award**

**Announcement Type: Initial**

**Funding Opportunity Number: HT9425-23-NFRP-CTA**

**Assistance Listing Number: 12.420 Military Medical  
Research and Development**

## **SUBMISSION AND REVIEW DATES AND TIMES**

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), August 11, 2023
- **Application Submission Deadline:** 11:59 p.m. ET, August 25, 2023
- **End of Application Verification Period:** 5:00 p.m. ET, September 1, 2023
- **Peer Review:** October 2023
- **Programmatic Review:** January/February 2024

*This program announcement must be read in conjunction with the General Application Instructions, version 803. 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

Applications to the Fiscal Year 2023 (FY23) Neurofibromatosis Research Award (NFRP) are being solicited by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The execution management agent for this program announcement is the Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC). The NFRP was initiated in 1996 to provide support for research of exceptional scientific merit that promotes the understanding, diagnosis, and treatment of Neurofibromatosis (NF) including NF type 1 (NF1) and type 2 (NF2) and Schwannomatosis. Appropriations for the NFRP from FY96 through FY22 totaled \$402.85 million (M). The FY23 appropriation is \$25M.

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

#### II.A.1. FY23 NFRP Areas of Emphasis

The vision of the FY23 NFRP is to decrease the clinical impact of NF. Toward this end, the NFRP seeks to support innovative, high-impact research that will foster new directions for and address neglected issues in NF research; sponsor multidisciplinary and multi-institutional collaborations that will bring new perspectives to the field; promote translational and clinical studies to move promising ideas from bench to bedside; and develop a balanced portfolio of meritorious research related to all aspects of NF1, NF2, and Schwannomatosis.

**Areas of Emphasis:** The FY23 NFRP strongly encourages research applications that specifically address the critical needs of the NF community in one or more of the Areas of Emphasis listed below. All applications are also encouraged to include materials and data from diverse populations in their research.

- NF2 and Schwannomatosis-related areas (e.g., hearing, balance, schwannoma, ependymoma, meningioma, LZTR1, SMARCB1)
- Endpoint validation, biomarker discovery, and technological innovation for assessments
- Application of data science
- Non-tumor manifestations not limited to:
  - Pain
  - Cognitive manifestations
  - Sleep

- Heterogeneity of NF-related phenotypes
- Genetics, genomics, epigenetics, systems biology, metabolomics, or similar approaches
- Preclinical efficacy studies
- Target identification and drug discovery
- Nutritional, environmental, and other modifiers of NF
- Health services research

*Note: Not all Areas of Emphasis are applicable to every award mechanism. If the proposed research project does not address at least one of the FY23 NFRP Areas of Emphasis, justification should be provided that it addresses an important problem related to NF research and/or patient care.*

**Definition of Health Services Research:** Health services research studies the access, costs, and quality of health care for individuals, families, organizations, institutions, communities, and populations. It is a multidisciplinary field of scientific investigation, including basic and applied research, that examines how social factors, financing systems, organizational structures and functions, health technologies, and personal behaviors affect access to health care, the quality and cost of health care, and ultimately health, well-being, and quantity and quality of life.

The goals are to identify the most effective ways to organize, manage, finance, and deliver high-quality care, reduce medical errors, and improve patient safety. For more information, multiple resources are available, including “Health Services Research: Scope and Significance,” from the National Institutes of Health (NIH) publication *Patient Safety and Quality: An Evidence-Based Handbook for Nurses*, found online at <https://www.ncbi.nlm.nih.gov/books/NBK2660/>.

**NFRP Research Resources Initiative:** Resources developed through NFRP funding that are available to the scientific community can be found at <https://cdmrp.health.mil/nfrp/resources/nfrpresources>. Investigators are urged to leverage and contribute to these resources and include a sharing and distribution plan in the application within the Data and Research Resources Sharing Plan ([Attachment 2](#)). For more guidance on data sharing, refer to the General Application Instructions, Appendix 2, Section K.

## **II.A.2. Award History**

The NFRP Clinical Trial Award mechanism was first offered in FY99. Since then, 87 Clinical Trial Award applications have been received, and 23 have been recommended for funding.

## **II.B. Award Information**

The NFRP Clinical Trial Award supports the rapid implementation of clinical trials with the potential to have a significant impact on the treatment or management of NF. Clinical trials may be designed to evaluate promising new products, pharmacologic agents (drugs or biologics), devices, clinical guidance, and/or emerging approaches and technologies. Proposed projects may

range from small proof-of-concept trials (e.g., pilot, first in human, phase 0) to demonstrate the feasibility or inform the design of more advanced trials through large-scale trials to determine efficacy in relevant patient populations.

***Funding from this award mechanism must support a clinical trial.*** A clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include a placebo or another control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. For more information, a Human Subject Resource Document is provided at

<https://cdmrp.health.mil/pubs/pdf/Human%20Subjects%20Resource%20Document.pdf>.

Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other FY23 NFRP program announcements being offered. ***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, Regulatory Agency refers to the U.S. Food and Drug Administration (FDA) or any relevant international regulatory agency unless otherwise noted.***

***Key aspects of the NFRP Clinical Trial Award mechanism:***

- **Clinical Trial Start Date:** The proposed clinical trial is expected to begin no later than 12 months after the award date or 18 months after the award date for studies regulated by the Regulatory Agency.
- **Preliminary data are required:** Inclusion of preliminary data relevant to the proposed clinical trial is required.
- **Impact:** The proposed intervention(s) to be tested should offer significant potential impact for individuals affected by NF.
- **Scientific Rationale:** The proposed clinical trial must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the relevant literature.
- **Planned Indication:** If appropriate, describe the planned indication for the product label, and include an outline of the product development plan required to support that indication.
- **Endpoints/Outcome Measures:** The proposed clinical trial design should include clearly defined objectives and appropriate endpoints/outcome measures and comply with current Good Clinical Practice (GCP) guidelines.
- **FDA:** The application should reflect the study team's experience interacting with the FDA, including previous FDA submissions, if applicable.
- **Study Population:** The application should demonstrate the availability of and access to a suitable patient population that will support a meaningful outcome for the study. The application should include a discussion of how accrual goals will be achieved, as well as the

strategy for inclusion of women and minorities in the clinical trial appropriate to the objectives of the study.

- **Intervention Availability:** The application should demonstrate the documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate, for the proposed duration of the study.
- **Personnel and Environment:** The application should demonstrate the study team's expertise and experience in all aspects of conducting clinical trials, including appropriate statistical analysis, knowledge of FDA processes (if applicable), and data management. The application should include a study coordinator(s) who will guide the clinical protocol through the local IRB of record and other federal agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual. The application should show strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312), Subpart D, are fulfilled.
- **Statistical Analysis and Data Management Plans:** The application should include a clearly articulated statistical analysis plan, a power analysis reflecting sample size projections that will answer the objectives of the study, and a data management plan and use of an appropriate database to safeguard and maintain the integrity of the data. If required by a Regulatory Agency, the trial must use a 21 CFR 11-compliant database and appropriate data standards.
- **Transition Plan:** The application should include a **transition plan** (including potential funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the FY22 NFRP Clinical Trial Award (see [Attachment 12](#)).
- **Support Structures:** Applicants are encouraged to use biorepositories and establish collaborations with the NF Clinical Trials Consortium and other federal agencies to leverage existing support structures to avoid unnecessary duplication and enhance study design.

If the proposed clinical trial involves the use of a drug that has not been approved by the FDA for the proposed investigational use, then an Investigational New Drug (IND) application to the FDA that meets all requirements under 21 CFR 312 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the FDA if an IND is not required. If an IND is required, the IND application ***must be submitted to the FDA by the Clinical Trial Award [application submission deadline](#)***. The IND should be specific for the product (i.e., the product should not represent a derivative or alternate version of the investigational agent described in the IND application) and indication to be tested in the proposed clinical trial. For more information on IND applications, the FDA has provided guidance at <https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application>.

If the investigational product is a device, then an Investigational Device Exemption (IDE) application to the FDA that meets all requirements under 21 CFR 812 may be required. It is the responsibility of the applicant to provide evidence if an IDE is not required or the device

qualifies for an abbreviated IDE. If an IDE is required, the IDE application ***must be submitted to the FDA by the Clinical Trial Award [application submission deadline](#)***. The IDE should be specific for the device (i.e., should not represent a derivative or modified version of the device described in the IDE application) and indication to be tested in the proposed clinical trial.

If the clinical trial of an investigational product will be conducted at international sites, evidence that an application to the relevant national regulatory agency of the host country(ies) ***has been submitted by the Clinical Trial Award [application submission deadline](#)*** is required.

***Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to register the study in the NIH clinical trials registry, [www.clinicaltrials.gov](http://www.clinicaltrials.gov), prior to initiation of the study. Refer to the General Application Instructions, Appendix 1, Section B, for further details.***

***Optional Qualified Collaboration:*** The NFRP will offer an Optional Qualified Collaboration to encourage leveraging of **existing infrastructure previously funded**. Qualifying organizations ***must*** be a federally funded partnership/consortium, such as the NF Clinical Trials Consortium, with established infrastructure to support multi-institutional studies to leverage shared resources and core capabilities such as data management, clinical trial database administration, statistical analysis, tissue repositories, etc., that will improve study efficiency and reduce redundancies and duplication. ***A letter of collaboration from the collaborating organization demonstrating their commitment*** is required, outlining the services that will be shared to bring value to the government. An additional **\$200,000 in direct costs** will be available for applications with the Optional Qualified Collaboration. The anticipated direct costs budgeted for the entire period of performance for an FY23 NFRP Clinical Trial Award with an Optional Qualified Collaboration should not exceed **\$1.0M**. Refer to [Section II.D.5, Funding Restrictions](#), for detailed funding information.

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

The anticipated direct costs budgeted for the entire period of performance for an FY23 NFRP CTA should not exceed **\$800,000** without an Optional Qualified Collaboration or **\$1.0M** with an

Optional Qualified Collaboration. Refer to [Section II.D.5, Funding Restrictions](#), for detailed funding information.

Awards will be made no later than September 30, 2024. For additional information, refer to [Section II.F.1, Federal Award Notices](#).

*The CDMRP expects to allot approximately \$1.6M to fund approximately one Clinical Trial Award application. Funding of applications received is contingent upon the availability of federal funds for this program as well as the number of applications received, the quality and merit of the applications as evaluated by scientific and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY23 funding opportunity will be funded with FY23 funds, which will expire for use on September 30, 2029.*

**Research Involving Human Data, Human Anatomical Substances, Human Subjects, or Human Cadavers:** All DOD-funded research involving new and ongoing research with human data, human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRDC Office of Human and Animal Research Oversight (OHARO), Office of Human Research Oversight (OHRO), prior to research implementation. This administrative review requirement is in addition to the local IRB or Ethics Committee (EC) review. Local IRB/EC approval at the time of application submission is *not* required; however local IRB/EC approval is necessary prior to OHRO review. Allow up to 3 months to complete the OHRO regulatory review and approval process following submission of *all required and complete* documents to the OHRO. Refer to the General Application Instructions, Appendix 1, and the OHARO web page ([https://mrhc.health.mil/index.cfm/collaborate/research\\_protections/hrpo](https://mrhc.health.mil/index.cfm/collaborate/research_protections/hrpo)) for additional information.

As of January 20, 2020, U.S. institutions engaged in non-exempt cooperative research *must* rely on a single IRB to review and approve the portion of the research conducted at domestic sites (45 CFR 46.114(b)). If the proposed, non-exempt research involves more than one U.S.-based institution, a written plan for single IRB review arrangements must be provided at the time of application submission or award negotiation. The lead institution responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements.

Communication and data transfer between or among the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the application. A separate intellectual and material property plan agreed on by all participating institutions is also required for multi-institutional clinical trials.



## **II.C. Eligibility Information**

### **II.C.1. Eligible Applicants**

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

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

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

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

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

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

### **II.C.1.b. Principal Investigator**

PIs must be *at or above* the level of Assistant Professor (or equivalent).

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

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

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

### **II.C.2. Cost Sharing**

Cost sharing/matching is not an eligibility requirement.

### II.C.3. Other

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

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

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

## II.D. Application and Submission Information

*Submission of applications that are essentially identical or 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).*

Inclusion of classified research data within the application and/or proposing research of which the anticipated outcomes may be classified or deemed sensitive to national security concerns may result in application withdrawal. Refer to the General Application Instructions Appendix 2, Section E.

### II.D.1. eBRAP and Grants.gov

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

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

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

#### ***Extramural Submission:***

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

### ***Intramural DOD Submission:***

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

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

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

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

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

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

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

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

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

All pre-application components must be submitted by the PI through eBRAP (<https://eBRAP.org>).

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

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

**When starting the pre-application, PIs should ensure that they have selected the appropriate application category in eBRAP:**

- Clinical Trial Award - CTA
- Clinical Trial Award with Optional Qualified Collaboration - CTA-OQC

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

- **Tab 1 – Application Information**

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

- **Tab 2 – Application Contacts**

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

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

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

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

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

[FY23 NFRP Programmatic Panel members](#) should not be involved in any pre-application or application. For questions related to panel members and pre-applications or applications, refer to [Section II.H.2.c, Withdrawal](#), or contact the eBRAP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507.

- **Tab 4 – Conflicts of Interest**

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

- **Tab 5 – Pre-Application Files**

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

- **Tab 6 – Submit Pre-Application**

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

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

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

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

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

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

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

**Table 1. Full Application Submission Guidelines**

Extramural Submissions	Intramural DOD Submissions
<b>Application Package Location</b>	
<p>Download application package components for HT9425-23-NFRP-CTA from Grants.gov (<a href="https://grants.gov/">https://grants.gov/</a>) and create a Grants.gov Workspace. Workspace allows online completion of the application components and routing of the application package through the applicant organization for review prior to submission.</p>	<p>Download application package components for HT9425-23-NFRP-CTA from eBRAP (<a href="https://ebrap.org">https://ebrap.org</a>).</p>
<b>Full Application Package Components</b>	
<p><b>SF424 Research &amp; Related Application for Federal Assistance Form:</b> Refer to the General Application Instructions, Section III.A.1, for detailed information.</p>	<p><b>Tab 1 – Summary:</b> Provide a summary of the application information.</p> <p><b>Tab 2 – Application Contacts:</b> This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.</p>
<p>Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> <li>• <a href="#">Attachments</a></li> <li>• <a href="#">Research &amp; Related Personal Data</a></li> <li>• <a href="#">Research &amp; Related Senior/Key Person Profile (Expanded)</a></li> <li>• <a href="#">Research &amp; Related Budget</a></li> <li>• <a href="#">Project/Performance Site Location(s) Form</a></li> <li>• <a href="#">Research &amp; Related Subaward Budget Attachment(s) Form</a></li> </ul>	<p><b>Tab 3 – Full Application Files:</b> Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> <li>• <a href="#">Attachments</a></li> <li>• <a href="#">Key Personnel</a></li> <li>• <a href="#">Budget</a></li> <li>• <a href="#">Performance Sites</a></li> </ul> <p><b>Tab 4 – Application and Budget Data:</b> Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.</p>
<b>Application Package Submission</b>	
<p><b>Create a Grants.gov Workspace.</b> Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission.</p> <p><b>Submit a Grants.gov Workspace Package.</b> An application may be submitted through Workspace by clicking the “Sign and Submit” button on the “Manage Workspace” page, under the “Forms” tab. Grants.gov recommends</p>	<p><b>Submit package components to eBRAP (<a href="https://ebrap.org">https://ebrap.org</a>).</b></p> <p><b>Tab 5 – Submit/Request Approval Full Application:</b> After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided next to “Enter Your Password Here” and press the “Submit Full Application” button. eBRAP will notify your</p>

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

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

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

- **Extramural Applications Only**

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

- **Extramural and Intramural Applications**

**Attachments:**

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

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

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

*The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6–9 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.*

Describe the proposed project in detail using the outline below.

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



of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

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

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses.
- **Study Design:** Describe the type of study to be performed (e.g., treatment, prevention, diagnostic), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to show a clear course of action.
  - Identify the intervention to be tested and describe the projected results. Additional details should be provided in [Attachment 6: Intervention](#).
  - Define the primary and any secondary or interim endpoints/outcome measures, outline why they were chosen, and describe how and when they will be measured. Include a description of appropriate controls. Outline the timing and procedures planned during the follow-up period.
  - Describe and justify the study population and the inclusion and exclusion criteria that will be used to meet the needs of the proposed clinical trial.
  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random). Additional details should be provided in [Attachment 7: Human Subject Recruitment and Safety Procedures](#).
  - Define each arm/study group of the proposed trial, if applicable. Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures). Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
  - Outline whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.
  - If using psychometric measures, describe their reliability and validity.
  - Describe potential problem areas and discuss alternative methods/approaches that may be employed to overcome them. Estimate the potential for subject loss to follow-up, and how such loss will be handled/mitigated.

- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study and all proposed correlative studies. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study. For phase 3 clinical trials, describe plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity as appropriate for the scientific goals of the study. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.
- **Attachment 2: Supporting Documentation: Combine and upload as a single file named “Support.pdf”.** Start each document on a new page. If documents are scanned to PDF, the lowest resolution (100 to 150 dpi) should be used. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

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

- **References Cited:** List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
- **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols.
- **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether 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 (one-page limit per letter):** 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, one-page limit per letter; *required if submitting under the Qualified Collaborator Option*):** Provide a signed letter from each collaborating individual or organization demonstrating that the PI has the support or resources necessary for the proposed work. If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator’s Commander or Commanding Officer at the intramural organization that authorizes the collaborator’s involvement.
- **Letters of Commitment (if applicable, two-page limit per letter):** 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 the availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
- **Intellectual Property:** Information can be found in 2 CFR 200.315, “Intangible Property.”
  - **Intellectual and Material Property Plan (if applicable):** Provide a plan for resolving intellectual and material property issues among participating organizations.
- **Data and Research Resources Sharing Plan:** Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 2, Section K, for more information about the CDMRP expectations for making data and research resources publicly available.
- **Attachment 3: Technical Abstract (one-page limit): Upload as “TechAbs.pdf”.** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

Technical abstracts should be written using the outline below. Programmatic reviewers typically do not have access to the full application and 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.

- **Background:** Present the ideas and rationale behind the proposed clinical trial.
- **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.
- **Study Design:** Briefly describe the study design, including appropriate controls.
- **Clinical Impact:** Briefly describe how the proposed project will have an impact on research and patient care in the specified disease(s)/condition(s).
- **Attachment 4: Lay Abstract (one-page limit): Upload as “LayAbs.pdf”.** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information. Do not duplicate the technical abstract.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

Lay abstracts should be written using the outline below.

- Clearly describe the objectives and rationale for the proposed study and intervention in a manner readily understood by readers without a background in science or medicine.
- Describe the ultimate applicability and impact of the research.
  - What types of patients will it help, and how will it help them?
  - What are the potential clinical applications and benefits?
  - What are the likely contributions of the proposed clinical trial to advancing patient care, treatment, quality of life, and/or management of NF?
  - How will the data and resources generated during the performance of the proposed research project be shared with the research community (scientific and advocacy organizations) and the public?
- **Attachment 5: Statement of Work (SOW) (six-page limit): Upload as “SOW.pdf”.** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>). Recommended strategies for assembling the SOW can be found at <https://ebrap.org/eBRAP/public/Program.htm>. For the NFRP Clinical Trial Award mechanism, refer to the “Suggested SOW Strategy for Clinical Research and/or Clinical Trials” document for guidance on preparing the SOW and use the blank SOW format titled “Suggested SOW Format”. The SOW must be in PDF format prior to attaching.

- **Attachment 6: Intervention (no page limit): Upload as “Intervention.pdf”.** The Intervention attachment should include the components listed below.

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

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

- **Study Procedures:** Describe the interaction with the human subject, including the study intervention that they will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Clearly delineate research procedures from routine clinical procedures. Discuss how compliance with current Good Laboratory Practice (GLP) guidelines, Good Manufacturing Practices (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.
- **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 7: Human Subject Recruitment and Safety Procedures (no page limit): Upload as “HumSubProc.pdf”.** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

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

at each study site. Demonstrate that the research team has access to the proposed study population at each site, and describe the efforts that will be made to achieve accrual goals. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention. Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress. Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender. ***For clinical trials proposing to include military personnel, refer to the General Application Instructions, Appendix 1, for more information.***

- **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.
- **Women and Minorities in the Study:** Consistent with the Belmont Report, “Ethical Principles and Guidelines for the Protection of Human Subjects,” and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRDC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Describe the strategy for the inclusion of women and minorities in the clinical trial 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 IRB review) are exempt from this requirement. Provide an anticipated enrollment table(s) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The Public Health Service (PHS) Inclusion Enrollment Report is a three-page fillable PDF form, which can be downloaded from eBRAP at <https://ebrap.org/eBRAP/public/Program.htm>.
- **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification).
  - Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
  - If human subjects will be compensated for participation in the study, include a detailed description of and justification for the compensation plan.

- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.
- **Description of the Informed Consent Process:** Specifically describe the plan for obtaining informed consent from human subjects.
  - *For the proposed study, provide a draft, in English, of the Informed Consent Form.*
  - Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects’ questions will be addressed during the consent process and throughout the trial.
  - Include information regarding the timing and location of the consent process.
  - Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
  - Address how privacy and time for decision-making will be provided and whether the potential human subject will be allowed to discuss the study with anyone before making a decision.
  - Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
  - Describe the plan for the consent of the individual’s Legally Authorized Representative (LAR) to be obtained prior to the human subject’s participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. **Note:** In compliance with 10 USC 980 (<https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf>), the application must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial. If applicable, refer to the General Application Instructions, Appendix 1, for more information.
  - **Assent:** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.
- **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine

eligibility/suitability for study participation and the diagnostic criteria for entry.  
*Note:* Some screening procedures may require a separate consent or a two-stage consent process.

– **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is exposed to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. Consider how the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
  - **Risk management and emergency response:**
    - ❖ Appropriate to the study’s level of risk, describe how safety monitoring and reporting to the IRB and Regulatory Agency (if applicable) will be managed and conducted.
    - ❖ Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
    - ❖ Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, including who will be responsible for the cost of such care.
    - ❖ Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
    - ❖ Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
  - **Potential benefits:** Describe known and potential benefits of the study to the human subjects who will participate in the study. Articulate the importance of the knowledge to be gained as a result of the proposed research. Discuss why the potential risks to human subjects are reasonable in relation to the anticipated benefits to the human subjects and others that may be expected to result.
- **Attachment 8: Data Management (no page limit): Upload as “Data\_Manage.pdf”.**  
The Data Management attachment should include the components listed below.



- **Data Management:** Describe the data to be gathered and all methods used for collection, including the following:
  - **Data:** The types of data, software, or other materials to be produced.
  - **Acquisition and processing:** How the data will be acquired, including the time and location of data acquisition, if scientifically pertinent. If use of existing data resources is proposed, describe the origin of the dataset. Provide an account of the standards to be used for data and metadata format and content. Explain how the data will be processed.
  - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
  - **Confidentiality**
    - ❖ Explain measures taken to protect the privacy of human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
    - ❖ Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DOD are eligible to review study records.
    - ❖ Address requirements for reporting sensitive information to state or local authorities.
  - **Data capture, verification, and disposition:** Describe how data will be captured and verified, including the quality assurance and quality control measures taken during collection, analysis, and processing. Describe where data (both electronic and hard copy) will be stored; who will keep the data; how the data will be stored, if applicable; the file formats and the naming conventions that will be used; the process for locking the database at study completion; and the length of time that data will be stored, along with a justification for the time frame of preservation, which may include considerations related to the balance between the relative value of data preservation and other factors such as the associated cost and administrative burden of data storage. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process. For studies requiring Regulatory Agency oversight, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.
  - **Data reporting:** Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with a Regulatory Agency, if applicable.

- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether the results of screening and/or study participation will be shared with human subjects or their primary care provider, including results from any screening or diagnostic tests performed as part of the study. In cases of national security or controlled unclassified information concerns, include a statement that the data cannot be made available to the public (e.g., “This data cannot be cleared for public release in accordance with the requirements in DoD Directive 5230.09.”).
- **Laboratory Evaluations**
  - **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
  - **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).
  - **Storage:** Describe specimen storage, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the plan to store specimens for future use, including considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
  - **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, the applicable quality standard, and any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.
- **Attachment 9: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “Regulatory.pdf”.** 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., IND, 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.
- For the FY23 NFRP Clinical Trial Award, ***if an IND or IDE is required, the application must be submitted to the FDA prior to the FY23 NFRP Clinical Trial Award application submission deadline.*** The IND or IDE should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical trial. Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold). If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of this product. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.
- If available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed.
- If an active IND or IDE for the investigational product is in effect, but an amendment is needed to include the proposed trial, describe the type and nature of the amendment(s) and the timeline for submission. Indicate whether the amendment increases the risk of the intervention.
- If the clinical trial will be conducted at international sites, provide equivalent information and supporting documentation relevant to the product indication/label and regulatory approval and/or filings in the host country(ies).

- Provide the current status for manufacturing development (e.g., manufacturer’s name, GMP-compliant lots available, status of stability testing), non-clinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support phase I testing), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).
- Describe the overall regulatory strategy and product development plan that will support the planned product indication/label. Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of Regulatory Agency meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.
- **Attachment 10: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as “Personnel.pdf”.** The Study Personnel and Organization attachment should include the components listed below.
  - **Organizational Chart:** Provide an organizational chart that identifies key members of the study team and provides an outline of the governing structure for multi-institutional studies. Identify collaborating organizations, centers, and/or departments and name each person’s position on the project. Include any separate laboratory or testing centers. Identify the data and clinical coordinating center(s) and note any involvement from Contract Research Organizations, as appropriate. Identify and provide justification for the inclusion of international sites, as appropriate. If applicable, identify the Regulatory Agency sponsor and any external consultants or other experts who will assist with Regulatory Agency sponsor applications. While there is no specified format for this information, a table(s) or diagram is recommended. *Note:* This item may be made available for programmatic review.
  - **Study Personnel Description:** Briefly describe the composition of the study team, including roles of the individuals listed in the organizational chart on the project. Study coordinator(s) should be included. Describe how the levels of effort for each individual are appropriate to successfully support the proposed research. Describe relevant background and qualifications that demonstrate appropriate expertise to accomplish the proposed work, including previous interactions with the relevant Regulatory Agency, if applicable.
  - **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial involves more than one institution, clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions. Provide a regulatory submission plan for the master protocol and master consent form by the lead institution. If the research involves more than one institution, a single IRB is required for all institutions located in the United States. If applicable, describe how communication and data transfer between/among the collaborating institutions will

occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.

- **Attachment 11: Questionnaires and Other Research Data Collection Instruments, if applicable (no page limit): Upload as “Data\_Collection.pdf”.** The Questionnaires and Other Research Data Collection Instruments attachment should include a copy of the most recent version of questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.
- **Attachment 12: Transition Plan (three-page limit): Upload as “Transition.pdf”.** Describe/discuss the methods and strategies proposed to move the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization’s Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The post-award transition plan should include the components listed below.
  - Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., specific industry partners, specific funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.
  - For knowledge products, a description of collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. (A “knowledge product” is a non-materiel product that addresses an identified need, topic area, or capability gap; is based on current evidence and research; aims to transition into medical practice, training, or tools or to support materiel solutions [systems to develop, acquire, provide, and sustain medical solutions and capabilities]; and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.)
  - A brief schedule and milestones for transitioning the intervention (e.g., next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by a Regulatory Agency).
  - Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the government’s ability to access such products or technologies in the future.

- A risk analysis for cost, schedule, manufacturability, and sustainability.
- A plan to distribute the findings or intervention to the neurofibromatosis community.
- **Attachment 13: Impact Statement (two-page limit): Upload as “Impact.pdf”.** The Impact Statement should be written with a broad audience in mind, including readers without a background in science or medicine.
  - Identify the volunteer population(s) that will participate in the proposed intervention, inclusive of sex, gender, and/or minorities if applicable; describe how they represent the target population that would benefit from the intervention, and describe the potential impact and anticipated outcomes of the proposed clinical trial on the lives and health of the target population with regard to the [FY23 NFRP Areas of Emphasis](#).
  - ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial and describe anticipated short-term benefits for individuals.
  - ***Describe the long-term impact:*** Explain the long-range vision for implementation of the intervention in the clinic or field, and describe the anticipated long-term benefits on patient care and/or quality of life for the targeted population.
  - Describe any relevant controversies or treatment issues that will be addressed by the proposed clinical trial.
  - Describe any potential issues that might limit the impact of the proposed clinical trial.
  - Describe how well the potential outcome of the study will advance the development of a potential therapeutic for NF.
  - Describe how the intervention represents an improvement over currently available interventions and/or standards of care.
  - Describe how the data and resources generated during the performance of the proposed research project will be shared with the research community (scientific and advocacy organizations) and the public.
- **Attachment 14: Representations, if applicable (extramural submissions only): Upload as “RequiredReps.pdf”.** All extramural applicants must complete and submit the Required Representations template available on eBRAP (<https://ebrap.org/eBRAP/public/Program.htm>). For more information, see the General Application Instructions, Appendix 5, Section B, Representations.
- **Attachment 15: Suggested Collaborating DOD Military Facility Budget Format, if applicable: Upload as “MFBudget.pdf”.** If a military facility (Military Health System facility, research laboratory, medical treatment facility, dental treatment facility, or a DOD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete a separate budget using “Suggested Collaborating

DOD Military Facility Budget Format,” available for download on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>), including a budget justification, for each military facility as instructed. The costs per year should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section III.A.8, for detailed information.

- **Extramural and Intramural Applications**

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

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

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

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

- Key Personnel Previous/Current/Pending Support (no page limit): Upload as “Support\_LastName.pdf”.
  - For extramural submissions, refer to the General Application Instructions, Section III.A.4, for detailed information.
  - For intramural submissions, refer to the General Application Instructions, Section IV.A.3, for detailed information.

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

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

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

- **Extramural Applications Only**

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

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov. (Refer to the General Application Instructions, Section III.A.7, for detailed information.) Verify subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period.
- **Intramural DOD Collaborator(s):** Complete the Suggested Collaborating DOD Military Facility Budget Format and upload to Grants.gov attachment form as [Attachment 15](#). (Refer to the General Application Instructions, Section IV.A.4, for detailed information.) Each Intramural DOD Collaborator should include costs per year on the Grants.gov Research & Related Budget Form under subaward costs.

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

The applicant organization must be registered as an entity in SAM (<https://www.sam.gov/SAM/>) and receive confirmation of an “Active” status before submitting an application through Grants.gov. *As of April 2022, all federal awards including, but not limited to, contracts, grants, and cooperative agreements will use the UEI generated through SAM.gov.* Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.



#### II.D.4. Submission Dates and Times

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

#### Applicant Verification of Full Application Submission in eBRAP

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

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

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

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

## II.D.5. Funding Restrictions

The maximum period of performance is 4 years.

The application's direct costs budgeted for the entire period of performance should not exceed **\$800,000** without an Optional Qualified Collaborator. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate.

If requesting an Optional Qualified Collaborator, the application's direct costs budgeted for the entire period of performance should not exceed **\$1.0M**. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

*A Clinical Trial Award – Optional Qualified Collaboration application that does not meet the criteria specified for that option may be funded at the lower maximum direct costs of \$800,000, i.e., at the base level (without an Optional Qualified Collaboration), as described above.*

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

The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum 4 years.

For this award mechanism, direct costs may be requested for (not all-inclusive):

- Travel in support of multidisciplinary collaborations required for the performance of this award.
- Travel costs for one investigator to travel to one scientific/technical meeting per year in addition to the required meeting described above. The intent of travel costs to scientific/technical meetings is to present project information or disseminate project results and/or attend workshops from/of the NFRP Clinical Trial Award.

Must not be requested for:

- Preclinical research costs

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

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

## **II.D.6. Other Submission Requirements**

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

## **II.E. Application Review Information**

### **II.E.1. Criteria**

#### **II.E.1.a. Peer Review**

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

- **Clinical Impact**
  - How impactful the anticipated outcomes of the proposed clinical trial would be to the target population with regard to the [FY23 NFRP Areas of Emphasis](#) and/or a critical problem in NF patient care.
  - To what extent the anticipated outcomes of the proposed clinical trial are relevant to individuals with NF.
  - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
  - How the anticipated outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals.
  - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
  - How well the potential outcome of the study will advance development of a potential therapeutic for NF.
- **Research Strategy and Feasibility**
  - How well the scientific rationale for the proposed clinical trial is supported by the preliminary data, critical review and analysis of the literature, relevant ongoing, planned, or complete clinical trials, and/or laboratory/preclinical evidence.
  - How well the study questions, specific aims, hypotheses and/or objective(s), experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective and purpose.
  - How well the inclusion/exclusion criteria and group assignment process meet the needs of the proposed clinical trial.

- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
- To what degree the data collection instruments, if applicable, are appropriate to the proposed study.
- How well research procedures are clearly delineated from routine clinical procedures.
- **Intervention**
  - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
  - To what degree the intervention addresses the clinical need(s) described.
  - How the intervention compares with currently available interventions and/or standards of care.
  - To what degree the application includes preclinical and/or clinical evidence to support the safety and stability (as appropriate) of the intervention.
  - How well research procedures are clearly delineated from routine clinical procedures.
  - Whether measures are described to ensure the consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions).
  - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
- **Regulatory Strategy and Transition Plan**
  - How the regulatory strategy and development plan to support the product indication or product label change, if applicable, are appropriate and well described.
  - Whether the application includes documentation that the study is exempt from the FDA or other international regulatory agency, or that the IND or IDE application (and/or international equivalent) has been submitted to the Regulatory Agency, as appropriate.
  - How well the documentation provided supports the feasibility of acquiring an active IND or IDE (and/or international equivalent) covering the proposed trial, if applicable.
  - For investigator-sponsored regulatory exemptions (e.g., IND, IDE, or other international equivalent), whether there is evidence of appropriate institutional support.
  - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
  - Whether the identified next level of development and/or commercialization is realistic.

- Whether the funding strategy described to bring the intervention to the next level of development (e.g., specific industry partners, specific funding opportunities to be applied for) is reasonable and achievable.
- For knowledge products, whether the proposed collaborations and other resources are achievable to provide continuity of development.
- Whether the schedule and milestones for bringing the intervention to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into clinical practice, and/or approval by the Regulatory Agency) are achievable.
- Whether the potential risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
- How well the application identifies intellectual property ownership, demonstrates the appropriate access to all intellectual property rights necessary for development and commercialization, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this program announcement.
- **Recruitment, Accrual, and Feasibility**
  - How well the application addresses the availability of human subjects for the clinical trial and the prospect of their participation.
  - Whether the application demonstrates access to the proposed human subject population.
  - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
  - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate mitigation plans to resolve them.
  - To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study.
  - Whether the strategy for the inclusion of women and minorities is appropriate to the objectives of the study.
  - Whether the distribution of the proposed enrollment on the basis of sex/gender, race, and/or ethnicity is appropriate for the proposed research.
- **Statistical Plan and Data Analysis**
  - To what degree the statistical model and data analysis plan are suitable for the planned study.

- How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.
  - Whether the plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity for phase 3 clinical trials are appropriate for the proposed research.
- **Personnel and Communication**
    - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
    - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
    - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
    - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.
    - For clinical trials that involve more than one institution, to what degree the multi-institutional structure governing the research protocol(s) across all participating institutions and regulatory submission plan are described and appropriate.
    - For multi-site clinical trials, how well the lead site responsibilities and human research protections regulatory coordination are defined and planned for.
    - ***For the Qualified Collaboration Option:*** Whether the proposed collaboration with an existing federally funded organization is described and supported with an appropriate letter of collaboration describing their commitment.
- **Environment**
    - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
    - Whether there is evidence of appropriate institutional commitment from each participating institution.
    - If applicable, to what degree the intellectual and material property plan is appropriate.

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

- **Ethical Considerations**

- Whether the population selected to participate in the trial stands to benefit from the knowledge gained.
- If applicable, how well the inclusion of international sites is justified.
- How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
- To what degree privacy and confidentiality issues are appropriately considered.
- To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **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.

- **Application Presentation**

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

### **II.E.1.b. Programmatic Review**

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

- Ratings and evaluations of the peer reviewers
- Relevance to the mission of the Defense Health Program and FY23 NFRP, as evidenced by the following:
  - Adherence to the intent of the award mechanism
  - Program portfolio composition
  - Programmatic relevance to [FY23 NFRP Areas of Emphasis](#)
  - Relative clinical impact

## **II.E.2. Application Review and Selection Process**

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

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

## **II.E.3. Integrity and Performance Information**

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

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

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



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

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

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

## **II.F. Federal Award Administration Information**

### **II.F.1. Federal Award Notices**

Awards supported with FY23 funds are anticipated to be made no later than September 30, 2024. Refer to the General Application Instructions, Appendix 2, for additional award administration information.

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

**Pre-Award Costs:** An institution of higher education, hospital, other non-profit or for-profit organization may, at its own risk and without the government's prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new award. Refer to the General Application Instructions, Section III.A.5.

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

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

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

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

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

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

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

### **II.F.2. Administrative and National Policy Requirements**

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

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

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

Refer to full text of the latest [DoD R&D General Terms and Conditions](#) and the [USAMRAA General Research Terms and Conditions: Addendum to the DoD R&D General Terms and Conditions](#) for further information.

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

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

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

### **II.F.3. Reporting**

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

Quarterly and annual progress reports as well as a final progress report will be required.

The Award Terms and Conditions will specify if 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: Enrollment reporting on the basis of sex/gender, race, and ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP.

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

## **II.G. Federal Awarding Agency Contacts**

### **II.G.1. eBRAP Help Desk**

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

Phone: 301-682-5507

Email: [help@eBRAP.org](mailto:help@eBRAP.org)

### **II.G.2. Grants.gov Contact Center**

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

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

Email: [support@grants.gov](mailto:support@grants.gov)

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

## **II.H. Other Information**

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

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 803Ta. The program announcement numeric version code will match the General Application Instructions version code 803.

### **II.H.2. Administrative Actions**

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

#### **II.H.2.a. Rejection**

The following will result in administrative rejection of the application:

- Pre-application was not submitted.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Letter of Collaboration ([Attachment 2](#)) is missing (if applying for the Optional Qualified Collaboration).
- Intervention ([Attachment 6](#)) is missing.
- Human Subject Recruitment and Safety Procedures ([Attachment 7](#)) is missing.
- Data Management ([Attachment 8](#)) is missing.
- Regulatory Strategy ([Attachment 9](#)) 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 pre-application or application:

- An FY23 NFRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. *A list of the FY23 NFRP Programmatic Panel members can be found at <https://cdmrp.health.mil/nfrp/panels/panels23>.*
- The application fails to conform to this program announcement description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY23, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<https://cdmrp.health.mil/about/2tierRevProcess>). Applications that include names of personnel from either of these companies may be administratively withdrawn.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP may be withdrawn.
- Applications submitted by an intramural DOD organization may be withdrawn if the intramural organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to extramural collaborators.
- Application including classified research data and/or proposing research of which the anticipated outcomes may be classified or deemed sensitive to national security concerns will be considered for application withdrawal.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The proposed research is not a clinical trial.
- The PI does not meet the eligibility criteria.

- An IND or IDE application (and/or international equivalent) has not been submitted prior to the [\*application submission deadline\*](#) for an FDA-regulated (and/or relevant international regulatory agency) study.
- An application to the relevant national regulatory agency of the host country(ies) (if the clinical trial of an investigational product will be conducted at an international site) is not submitted by the submission deadline.
- The proposed project includes preclinical research.
- Preliminary data relevant to the proposed clinical trial is not included.

#### **II.H.2.d. Withhold**

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

### II.H.3. Application Submission Checklist

Application Components	Action	Completed
SF424 Research & Related Application for Federal Assistance ( <b>extramural submissions only</b> )	Complete form as instructed.	
Summary (Tab 1) and Application Contacts (Tab 2) ( <b>intramural submissions only</b> )	Complete these tabs as instructed.	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf"	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf"	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf"	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf"	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf"	
	Intervention: Upload as Attachment 6 with file name "Intervention.pdf"	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 7 with file name "HumSubProc.pdf"	
	Data Management: Upload as Attachment 8 with file name "Data_Manage.pdf"	
	Regulatory Strategy: Upload as Attachment 9 with the file name "Regulatory.pdf"	
	Study Personnel and Organization: Upload as Attachment 10 with file name "Personnel.pdf"	
	Questionnaires and Other Research Data Collection Instruments: Upload as Attachment 11 with file name "Data_Collection.pdf"	
	Transition Plan: Upload as Attachment 12 with file name "Transition.pdf"	
	Impact Statement: Upload as Attachment 13 with file name "Impact.pdf"	
	Representations (extramural submissions only): Upload as Attachment 14 with file name "RequiredReps.pdf"	
	Suggested Collaborating DOD Military Facility Budget Format: Upload as Attachment 15 with file name "MFBudget.pdf" if applicable	

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



## APPENDIX 1: ACRONYM LIST

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
FAPIIS	Federal Awardee Performance and Integrity Information System
FDA	U.S. Department of Food and Drug Administration
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
LAR	Legally Authorized Representative
LOI	Letter of Intent
M	Million
MB	Megabytes
MIPR	Military Interdepartmental Purchase Request
NF1	Neurofibromatosis Type 1
NF2	Neurofibromatosis Type 2
NFRP	Neurofibromatosis Research Program
NIH	National Institutes of Health
OHARO	Office of Human and Animal Research Oversight (previously Office of Research Protections)
OHRO	Office of Human Research Oversight (previously Human Research Protection Office)
ORCID	Open Researcher and Contributor ID, Inc.
PDF	Portable Document Format
PHS	Public Health Service

PI	Principal Investigator
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