

**Program Announcement**  
for the  
**Department of Defense**  
**Congressionally Directed Medical Research Programs**

**Neurofibromatosis Research Program**

**Clinical Consortium Award**

**Funding Opportunity Number: W81XWH-16-NFRP-CCA**  
**Catalog of Federal Domestic Assistance Number: 12.420 Military Medical**  
**Research and Development**

**SUBMISSION AND REVIEW DATES AND TIMES**

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), June 8, 2016
- **Invitation to Submit an Application:** June 22, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, August 1, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, August 4, 2016
- **Peer Review:** September 2016
- **Programmatic Review:** November/December 2016

*This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.*

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## **I. FUNDING OPPORTUNITY DESCRIPTION**

### **A. Program Description**

Applications to the Fiscal Year 2016 (FY16) Neurofibromatosis Research Program (NFRP) are being solicited by the U.S. Army Medical Research Acquisition Activity (USAMRAA). The managing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). 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 FY15 totaled \$287.85 million (M). The FY16 appropriation is \$15.0M.

**FY16 NFRP Vision:** The vision of the FY16 NFRP is to decrease the clinical impact of neurofibromatosis. To 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.

### **B. Award Information**

The NF Clinical Consortium Award mechanism was first offered in FY06. Two applications were received and one was funded. Thereafter, the mechanism was offered in FY11; one application was received and it was funded.

The FY16 NFRP Clinical Consortium Award is intended to support a major goal/product-driven Consortium of exceptional institutions and investigators that will accelerate the clinical translation of basic NF research and ultimately decrease the impact of the disease. The objectives of the Consortium shall be to conceive, design, develop, and conduct collaborative Phase I and II clinical evaluations of promising therapeutic agents for the management or treatment of NF1, NF2, and schwannomatosis.

### **General Information**

The NF Clinical Consortium needs to be a collaboration of multiple organizations and individuals for the purpose of rapidly executing clinical trials. The Consortium must consist of a single Operations Center and a minimum of five Clinical Trial Sites with a demonstrated history of collaborative research. The participants will be jointly responsible for prioritizing, proposing, conducting, and analyzing Phase I and Phase II clinical trials focused on therapeutic interventions for NF1, NF2, and schwannomatosis.

The Operations Center and associated Clinical Trial Sites must apply to this announcement through a single application submitted by the Operations Center. The Operations Center may also serve as a trial site. A single award will be made to the Operations Center. Award funds are to be used to support the Operations Center's efforts as well as Consortium-associated studies at

each of the Clinical Trial Sites. The Operations Center will provide management and funding through the appropriate subcontract or other instruments for the Clinical Trial Sites.

Award selection will be based on evaluation of the proposed plans for initial clinical trials to be implemented, available capabilities, organization of the Consortium, and feasibility of the collective group to accomplish the overall award objectives (see [Section III.B., Application Review Process](#)). During the performance period of the award, the Operations Center and all Clinical Trial Sites will be responsible for working collaboratively to identify new clinical trials for implementation by the Consortium.

The NFRP is allocating a total of \$9M in support of the Consortium. The Consortium will be funded initially for a total of \$5M with allocations from the FY16 NFRP Congressional appropriation. Two additional option periods, to be included in the application, will be funded for a total of \$2M each (minimum of 1 trial per option must be proposed), subject to receipt of future Congressional appropriations. See [Section I.D., Funding](#), for additional information.

## 1. Consortium Structure

**Operations Center.** The Consortium shall consist of one central Operations Center that will be responsible for facilitating the rapid selection, design, execution and analysis of clinical trials within the Consortium, and will provide the administrative, protocol development and review, regulatory, statistical, resource, and data management and storage functions necessary to facilitate Consortium clinical trials in a timely manner. The Operations Center must contain multidisciplinary expertise and extensive experience in developing and conducting multi-institutional clinical trials of treatment approaches in support of NF research.

The Principal Investigator (PI) of the Consortium must be located at the Operations Center and must provide evidence of prior experience with the design and administration of multi-institutional clinical studies. The PI must also demonstrate a broad understanding of research, including knowledge of the current state of clinical studies and clinical priorities related to Neurofibromatosis. It is expected that there be a succession plan provided to account for any unforeseen change in the Consortium PI.

The application should identify and describe core facilities (i.e., pathology, radiology, etc.) available at the Operations Center and at any member organizations that will serve as official Consortium research core facilities.

**Clinical Trial Sites.** The Consortium shall consist of a minimum number of five Clinical Trial Sites necessary to effectively participate in multiple trials. All sites must be identified and have clinical trials experience and multidisciplinary expertise in supporting NF1 and/or NF2 and/or schwannomatosis clinical research. The exact number of sites is to be proposed by the applicant and inclusion as a Clinical Trial Site must be based on factors including:

- Lead Site PIs' commitment to and experience in NF clinical research. Applications are expected to include a succession plan to account for any unforeseen change in the Lead Site PI;

- Evidence of multidisciplinary clinical and/or laboratory expertise within the institution that could serve as the basis for the development of clinical protocols by the Consortium;
- Demonstration of adequate resources for coordinating with the Operations Center and other sites;
- Demonstration of adequate resources and expertise for data management, and maintenance of data security/confidentiality;
- Evidence of institutional commitment to using facilities and resources in the conduct of Consortium studies as required;
- Documentation of procedures to resolve intellectual and material property issues;
- Demonstration of adequate resources and expertise in NF patient recruitment and processing, including specimen collection; and
- Ability to enroll adequate numbers of evaluable individuals with NF1, NF2, or schwannomatosis per year into Consortium-sponsored studies, **or** to provide such unique expertise or facilities as otherwise justifies inclusion as a site.

Additional competencies of proposed sites may be identified and justified as being essential to the success of the Consortium.

**Steering Committee.** Collectively, each Clinical Trial Site PI and Operations Center PI will constitute the Consortium Steering Committee, which will be responsible for proposing and conducting Phase I and II clinical evaluations of promising therapeutic agents for the management or treatment of NF, and for determining which Consortium Trial Sites will participate in each study. The Operations Center staff will be responsible for facilitating and coordinating this process.

**External Advisory Board.** The United States Army Medical Research and Materiel Command (USAMRMC) will appoint members to an External Advisory Board (EAB) that will be comprised of selected members of the NFRP Programmatic Panel and additional ad hoc representatives (as needed). The role of the EAB will be to advise the NFRP regarding Consortium progress and activities. The Consortium must present written and/or oral annual briefings to the EAB and USAMRMC staff at 1-day meetings, typically held in the Washington, DC metropolitan area.

## 2. Proposed Clinical Trials

Applications must include letters of intent for conducting a **minimum of four clinical trials including at least one NF1- and one NF2-focused study** during the performance period of the award. Two of these studies must be initiated during the first year of the award. Proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium and needs of the NF community. **Clinical trials that include an adult patient population are encouraged.**

The Operations Center will be responsible for coordinating an external scientific peer review of all clinical trial protocols proposed for funding. The results of each review will

be provided to the NFRP for final approval and release of funds to commence the clinical trial(s).

In addition to clinical trials proposed as part of the FY16 NFRP Clinical Consortium application submission, the Consortium is encouraged to submit additional applications to the NFRP when additional funding opportunities are announced. Funding from additional sources including industry, private sector, and other federal organizations is also encouraged.

### 3. Summary of Responsibilities

**Responsibilities of all Consortium Participants.** Procedures for the Consortium, while proposed by the Operations Center staff, should be fully developed and agreed upon by all participants working collaboratively. The process shall be codified in a Manual of Operations or Standard Operating Procedures (SOP) document, which will be provided with the application.

#### **Consortium Operations Center will:**

- Provide the PI for the Consortium who will be the primary liaison with the USAMRMC Grants Officer Representative (GOR) and Science Officer (SO);
- Ensure that the Consortium adheres to the planned timeline and milestones for overall study execution;
- Manage the Consortium organizational structure;
- Manage Consortium-developed procedures for external scientific review, prioritization, and implementation of clinical studies proposed by or through Consortium members;
- Manage procedures to ensure that all sites maintain compliance with local Institutional Review Boards (IRBs) and the USAMRMC Human Research Protection Office (HRPO) for the proper conduct of clinical studies and the protection of human subjects;
- Provide a Consortium Clinical Research Manager who will oversee the efforts of the Research Coordinators at each of the Clinical Trial Sites. The Consortium Clinical Research Manager will be responsible for coordinating and facilitating clinical protocol approval, patient accrual, and study activities across all sites;
- Ensure that all investigators are U.S. Food and Drug Administration (FDA) registered to use Investigational New Drugs (INDs); and manage procedures for ensuring compliance with FDA requirements for investigational agents, devices, and procedures;
- Manage a communications plan and a real-time communications system between the Operations Center and Clinical Trial Sites;
- Manage standardization and, when appropriate, centralized review of imaging, histopathology, neuropsychological, and other data through committees and scientific core facilities. Use of the Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) criteria for response data is encouraged.
- Manage Consortium-developed quality assurance and quality control mechanisms for study monitoring, including but not limited to:

- On-site monitoring program (to include safety)
- Management plan for the handling, distribution, and banking of specimens and imaging products generated from Consortium studies
- Registration, tracking, and reporting of participant accrual
- Timely medical review, rapid reporting, and communication of adverse events as well as establishment of a safety committee to provide timely analysis of adverse events
- Interim evaluation and consideration of measures of outcome
- Manage Consortium-developed comprehensive data collection and data management systems that address the needs of all Clinical Trial Sites in terms of access to data, data security, and data integrity measures;
- Implement statistical execution plans/support for all Consortium clinical studies;
- Manage costs to support the Clinical Trial Sites, including provision of personnel, equipment, and materials required to conduct approved clinical studies;
- Manage Consortium-developed intellectual and material property issues among organizations participating in the Consortium;
- Manage Consortium-developed procedures for the timely publication of major findings and other public dissemination of data;
- Coordinate the preparation of written and/or oral yearly briefings to the EAB and USAMRMC staff at 1-day meetings to be held in the Washington DC metropolitan area; and
- Develop, organize, and submit quarterly written progress reports, annual reports, and a final written comprehensive report to the USAMRMC;
- Oversee site performance monitoring and evaluations.

**Clinical Trial Sites will:**

- Designate a lead site PI, and develop a succession plan in case of departure of the site PI; the site PI must participate fully in the Consortium Steering Committee;
- Identify potential studies and develop proposals in accordance with the Consortium Standard Operating Procedure (SOP) for consideration for funding by the NFRP during the performance period of the award;
- Collaborate with other Consortium Clinical Trial Sites;
- In accordance with Consortium-developed guidelines, maintain a minimum combined accrual across all Consortium-associated studies, as well as a maximum contributed percentage for each individual study in accordance with Consortium-developed guidelines;
- Provide a Clinical Research Coordinator who will interact with the Clinical Research Coordinators of other Clinical Trial Sites and the Consortium Clinical Research Manager at the Operations Center to expedite and guide clinical protocols through

regulatory approval processes, and to coordinate patient accrual and study activities across sites;

- Implement the Consortium's core data collection methodology and strategies;
- Comply with Consortium-developed quality assurance and quality control procedures, as appropriate, including:
  - Participation in an on-site monitoring program to be managed by the Operations Center
  - Implementation of the Consortium-developed management plan for acquisition and aggregation of protocol-specified specimens, biological fluids, and relevant clinical data to the appropriate laboratories for testing or storage necessary for the conduct and analyses
  - Submission of appropriate data and materials to allow for verification and review of protocol-related procedures (e.g., pathology, imaging techniques, surgical methods, and therapeutic use)
- Implement procedures established by the Operations Center for ensuring compliance with FDA requirements for investigational agents, as appropriate;
- Implement procedures established by the Operations Center to meet local IRB and USAMRMC HRPO requirements for the conduct of clinical trials and the protection of human subjects;
- Serve as a resource or core for the conduct of protocol-specified laboratory projects (including correlative studies), as appropriate;
- Participate in Consortium-developed procedures for the timely publication of major findings;
- Participate in Consortium-developed procedures for resolving intellectual and material property issues among organizations participating in the Consortium;
- Participate in the preparation of written and oral yearly briefings to the EAB and USAMRMC staff at 1-day meetings to be held in the Washington DC metropolitan area;
- Assist with the preparation of quarterly written progress reports, annual reports, and a final comprehensive report; and
- Prepare for a site visit audit, if requested by the NFRP.

#### 4. Performance Metrics

Applicants must provide a plan for the number and types of clinical studies the Consortium expects to execute. As a preliminary guideline, the Consortium should be prepared to execute a minimum of four clinical trials during the performance period of the award, depending upon the size and complexity of each study. Within the first year of the performance period, at least one NF1- and one NF2-focused study must have been initiated. A timeline outlining the overall plan for study initiation, performance, and analyses shall be developed, with clear milestones **to which the Consortium will be held accountable**. The Government reserves the right to suspend and/or terminate the award if

the recipient fails to meet this requirement. The Consortium Steering Committee will determine appropriate overall minimum and maximum accrual metrics for the Clinical Trial Sites per trial as part of the Consortium SOP. It is anticipated that each Clinical Trial Site will have the ability to enroll adequate numbers of evaluable individuals with NF1, NF2, or schwannomatosis per year into Consortium-sponsored studies, OR to provide such unique expertise or facilities as otherwise justifies inclusion as a site. For individual clinical studies, the Operations Center should ensure the maintenance of overall patient accrual per year, appropriate for the target population. The Consortium SOP should also contain a plan to address underperforming sites, and a succession plan for any unforeseen change in the lead PI. The Operations Center will be required to submit quarterly and annual written reports that outline accrual and retention statistics, any problems with study execution, and actions to disseminate study results.

## 5. Oversight of the Consortium

An EAB comprised of government and non-government personnel will be appointed by the USAMRMC. The EAB will make recommendations to the NFRP regarding progress and proposed Consortium studies prior to implementation and it may recommend future studies to the Consortium. The Consortium must present written and oral briefings to the EAB and USAMRMC. Based on these reports and presentations, the EAB will advise the GOR. USAMRMC staff will evaluate progress, provide feedback, and recommend modifications as needed to facilitate the success of the Consortium. The Consortium Steering Committee, through the Operations Center PI, will be expected to maintain monthly, or more frequent, contact with a government appointed GOR/SO. The USAMRAA Grants Officer will issue final approvals to release funds for initiation of any proposed clinical trial.

**Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers:** All Department of Defense (DoD)-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), HRPO prior to research implementation. This administrative review requirement is in addition to the local IRB or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is *not* required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB/EC. *Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes.* The HRPO reviews and approves the participation of each site in the clinical trial. Refer to the General Application Instructions, Appendix 6, and the Human Subject Resource Document available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information.

*The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section K.*

### C. Eligibility Information

- The Operations Center PI must be an independent investigator at or above the level of Associate Professor (or equivalent) with experience in developing and running large scale initiatives such as clinical trials or consortia.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include Federal agencies, national, international, for-profit, nonprofit, public, and private organizations.
- An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Submissions from intramural (DoD) organizations are allowed and encouraged for this Program Announcement/Funding Opportunity. Applicants submitting through their intramural organizations are reminded to coordinate receipt and commitment of funds through their respective resource managers. *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.*
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

### D. Funding

A single award to the Operations Center applicant will be made to support the FY16 NFRP Clinical Consortium. The Operations Center will provide funding support for the selected Clinical Trial Sites as sub awards or other appropriate contracting instrument.

All applicants are to propose a minimum of four clinical trials in letters of intent to address at least 1 NF1- and 1 NF2-focused trial that must be initiated in the first year of the award. Proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium. Budget out-years should be projected based on the proposed costs of the initial studies, with appropriate escalation factors included. Provide an estimated budget for each trial using the R&R Sub award Budget Attachment Form. Following award, a budget for each study will be negotiated individually once study selections are made.

- The maximum period of performance is 4 years.
- The maximum allowable total costs for the entire period of performance are **\$9M**, of which only **\$5M** is currently available. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **\$9M** direct costs or using an indirect rate exceeding the organization's negotiated rate
- The PI may request up to \$5M in total costs (direct + indirect costs) for the full proposed period of performance (up to 4 years) to cover Operations Center costs,

Consortium activities, and clinical trials. This will be funded using allocations from the FY16 NFRP Congressional appropriation. A budget for the Operations Center should be submitted using the SF424 Research & Related Budget Form. Separate budgets for each clinical trial should be submitted using R&R Sub award Budget Attachment Forms. The total for this segment must not exceed \$5M in total costs.

- In addition, the PI may request two option periods of up to \$2M in total costs each, to fund additional clinical trials and associated Operations Center costs and Consortium activities. Funding for these option periods is contingent upon receipt of future Congressional appropriations. A budget for the Operations Center and budgets for each clinical trial should be shown on separate R&R Sub award Budget Attachment Forms. The total for these two option periods must not exceed \$4M in total costs. Also, these option periods, if funded, are to be conducted within the maximum period of performance (up to 4 years).
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.

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

- Travel costs for the Operations Center PI(s) and site PIs to disseminate project results at one yearly 1-day briefing with the EAB and USAMRMC staff. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary support;
- Implementation of Consortium-developed standardization plan, data management program, real-time communications system, and administration plans for the Consortium;
- Support of Consortium-related meetings, teleconferences, and travel among participating investigators;
- Costs associated with the external scientific peer review of clinical studies/research;
- Purchase of computers, specialized software, and specialized software licenses for Clinical Study Sites when required to fulfill Operations Center-specific tasks;
- Purchase of minor equipment necessary for specimen collection and data storage and transfer;
- Costs associated with using Consortium Core facilities;
- Costs associated with conducting the IRB review of the clinical protocols and informed consent/assent forms;
- Research-related subject costs;
- Clinical research costs;
- Costs associated with the supply or availability of intervention(s);
- Other costs directly associated with planning and developing the Consortium.

May not be requested for:

- Travel costs for investigator(s) to travel to scientific/technical meeting(s) in addition to the required meeting described above.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural (DoD) agencies and other Federal agencies may be managed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR]; Funding Authorization Document [FAD] process; or DD Form 1144 Support Agreement). Direct transfer of funds from the recipient to a DoD agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4., 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 Section II.C.4. of the General Application Instructions.***

***The CDMRP expects to allot approximately \$5M of the \$9M from the FY16 budget and the remaining \$4M from future years' appropriations to fund approximately 1 Clinical Consortium Award application, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.***

## **II. SUBMISSION INFORMATION**

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (<https://eBRAP.org/>) and (2) application submission through Grants.gov (<http://www.grants.gov/>). Refer to the General Application Instructions, Section II.A., for registration and submission requirements for eBRAP and Grants.gov.

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

***The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent for the entire pre-***

***application and application submission process. Inconsistencies may delay application processing and limit the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507 prior to the application deadline.***

Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. ***The Project Narrative and Budget cannot be changed after the application submission deadline.*** Prior to the full application deadline, a corrected or modified full application package may be submitted. Other application components may be changed until the end of the [application verification period](#). After the end of the application verification period, the full application cannot be modified.

#### **A. Where to Obtain the Grants.gov Application Package**

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-16-NFRP-CCA in Grants.gov (<http://www.grants.gov/>).

#### **B. Pre-Application Submission Content**

***The pre-application process should be started early to avoid missing deadlines. There are no grace periods. During the pre-application process, each submission is assigned a unique log number by eBRAP. This unique eBRAP log number will be needed during the application process on Grants.gov.***

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

PIs and organizations 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 PI must contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507.

A change in PI or organization after submission of the pre-application may be allowed after review of a submitted written appeal (contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507) and at the discretion of the USAMRAA Grants Officer.

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**
- **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 (R&R Form). The Business Official must either be 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 (R&R) Form), and click on “*Add Organizations to this Pre-application.*” The organization(s) must either be selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.
- It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

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

- Enter the name, organization, and role of all collaborators and key personnel associated with the application.
- FY16 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 IV.C., Withdrawal](#), or contact the CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507.
- 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 application preparation, research, or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<http://cdmrp.army.mil/about/2tierRevProcess>). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- **Tab 4 – Conflicts of Interest (COIs)**

- List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship). Refer to Appendix 1, Section C, of the General Application Instructions for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

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

**Preproposal Narrative (5-page limit):** The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs

that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

The Preproposal Narrative should include the following:

- **Overall Goals:** Provide a brief description of the overall goals of the Consortium in the clinical evaluations of promising therapeutic agents for the management or treatment of NF1, NF2, and schwannomatosis.
- **Consortium Structure:** Outline the organizations that will participate in the Consortium. Briefly discuss the qualifications of key personnel in the administration and conduct of multi-institutional clinical studies. Discuss potential core facilities, shared resources, and other elements of the Consortium that will promote synergy.
- **Research Plan:** Provide a brief description of the initial clinical studies to be proposed. Describe the reasoning on which the studies are based, the target patient population(s), and the outcomes to be measured. Include a table and description of potential pharmaceuticals to be used in the proposed clinical trials which should include:
  - Stage of development, indication in NF1 and/or NF2, the sites involved in conducting the clinical trial, and the state of each intervention’s IND status, if applicable.

**Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application *must be uploaded as individual files* and are limited to:

- References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, 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 used in the Preproposal Narrative.
- Biographical Sketches of Coordinating Center and Clinical Site PIs (five-page limit per individual). *All biographical sketches should be uploaded as a single combined file.* Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

- **Tab 6 – Submit Pre-Application**

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

## Pre-Application Screening

- **Pre-Application Screening Criteria**

To determine the technical merits of the pre-application and the relevance to the mission of the NFRP, pre-applications will be screened based on the following criteria:

- Overall Goals: How the overall goals of the Consortium will have an impact on the clinical evaluation of promising therapeutic agents for the management or treatment of NF1, NF2, and schwannomatosis.
- Consortium Structure: How well the outlined Consortium structure will support timely and efficient multi-institutional clinical trials of varying scope and size. The appropriateness of the administrative and research teams' background and expertise with respect to clinical evaluations of promising therapeutic agents for the management or treatment of NF.
- Research Plan: How well the proposed initial studies align with the NFRP Clinical Consortium Award's goals. The degree to which the proposed studies address important questions that will further the clinical approaches for the management or treatment of NF.

- **Notification of Pre-Application Screening Results**

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

## C. Full Application Submission Content

The application process should be started early on Grants.gov to avoid missing deadlines. There are no grace periods. Verify the status of the applicant's organization's Entity registration in the SAM well in advance of the application submission deadline. Allow 3 to 4 weeks to complete the entire SAM registration process. Refer to the General Application Instructions, Section II, for additional information.

***Applications will not be accepted unless the PI has received notification of invitation.***

***All contributors and administrators to the application must use matching compatible versions of Adobe software when editing and preparing application components. The use of different software versions will result in corruption of the submitted file. See Section II.C. of the General Application Instructions for details on compatible Adobe software.***

***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 Grants.gov application package for this Program Announcement/Funding Opportunity. The Grants.gov application package is submitted

by the Authorized Organizational Representative through the Grants.gov portal (<http://www.grants.gov/>).

**Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline.**

If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form 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 *prior to the application submission deadline*.

**Grants.gov application package components:** For the Clinical Consortium Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

**1. SF424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

**2. Attachments Form**

Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

- **Attachment 1: Project Narrative (70-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, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

Describe the key features of the Consortium in detail using the outline below.

- **Overall Structure and Goals:**

- Identify major gaps in the field that the Consortium seeks to address.
- Describe the broad research goals of the Consortium and how the Consortium structure is suited to meet its goals.
- Identify all proposed sites, ad hoc sites, and future potential sites. Include descriptions of any committees and/or working groups. Reference and include Consortium SOPs/Manual of Operations and By-laws in Attachment 8.

○ **Operations Center Expertise and Resources:**

Describe the following:

- Previous experience of the Operations Center, the PI, and key personnel with the design, administration, and day-to-day management of multi-institutional clinical studies.
- A succession plan for the Operations Center PI and lead PIs for the Clinical Trial Sites.
- Information technology infrastructure and resources necessary to coordinate and implement proposed trials, and a plan for making those resources available.
- Key core facilities and resources available to support Consortium-initiated clinical trials.
- Plans for addressing human subject protection requirements as described by HRPO, and coordinating IRB submissions and approvals at participating sites.
- Plans for oversight and coordination of Clinical Trial Sites. Include relevant personnel and organizational experience with implementing multi-institutional real-time communications.
- Plans for monitoring site performance, including strategies to deal with sites with low performance and missed patient recruitment goals.

○ **Clinical Trial Site(s) Expertise and Resources**

Describe the following:

- Current, ad hoc, and potential future Clinical Trial Site(s).
- Previous experience of key personnel at each site with the development and conduct of clinical studies, specifically any multi-institutional clinical trials that demonstrate past experience and willingness to participate in the Consortium.
- Any site-specific areas of clinical research interest or expertise, such as novel drugs, surgical interventions, and imaging techniques. Include a description of the multi-disciplinary capabilities of each site.
- Patient populations at each current and potential future Clinical Trial Site, and elaborate on the ability to enroll adequate patient numbers into Consortium-sponsored studies. Provide an estimate of case enrollment/patient load and the track record of research in this area for each Clinical Trial Site and each Site PI.
- Resources and expertise available within each Clinical Trial Site for the care of NF1 and/or NF2 patients.

- Resources and expertise of each participating Clinical Trial Site for data management and maintenance of data security/confidentiality.
- Previous experience of conducting multi-institutional trials.
- **Clinical Trial Development and Implementation:**
  - Include a projection of the types of clinical trials to be conducted by the Consortium over the entire award period.
  - Outline a plan for the conceptualization, design, development, and prioritization of potential future Consortium trials for implementation. Include a mechanism for determining Clinical Trial Site participation.
  - Describe plans for coordinating the submission, review, and implementation of clinical trials within the Consortium. Include plans for appropriate approvals/clearances from the FDA, when applicable.
- **Study Management and Monitoring:**
  - Describe plans for real-time communication among all organizations participating in the Consortium (including the rapid dissemination of adverse events). Include a named Consortium Clinical Research Manager who will interact with other individual Clinical Trial Site research coordinators to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.
  - Outline procedures for quality assurance, quality control, safety, and study monitoring, including an independent safety oversight group to invoke stopping rules as necessary after defined adverse events.
- **Specimen Handling and Distribution:** Describe plans and methods for the handling, distribution, analysis, banking, and security of any specimens and/or imaging products generated from Consortium-sponsored studies.
- **Fiscal Administration:** Describe previous experience with the financial management of multi-institutional clinical research studies. Outline a strategy for achieving financial self-sufficiency of the Consortium after the end of the performance period for the Clinical Consortium Award. Describe any plans to leverage existing clinical or translational funding programs and infrastructure for the proposed Consortium.
- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named “Support.pdf.” If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.***
  - References Cited: List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation

(i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
- Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
- Publications and/or Patents: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.
- Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.
- Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
- Intellectual Property
  - Intangible property acquired, created or developed under this award will be subject to all rights and responsibilities established at 2 CFR 200.315. Should the applicant intend to use, in the performance of this program, pre-existing, legally protected and perfected intangible property and for which no Federal funds had been used in the development of said property, the applicant must:
    - Clearly identify all such property;
    - Identify the cost to the Federal government for use or license of such property, if applicable; or
    - Provide a statement that no property meeting this definition will be used on this project.
  - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- **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 are used by all reviewers. Of particular importance, programmatic reviewers may not have access to the full application and therefore rely on the technical abstract for appropriate description of the proposed research project’s key aspects. Clarity and completeness within the space limits of the technical abstract are highly important.

The technical abstract should be structured as follows:

- ***Background:*** Describe the general management and organizational structure of the Consortium. Outline the management and clinical expertise of Consortium personnel at the Operations Center and Clinical Trial Sites.
  - ***Objectives:*** Describe the Consortium’s overall clinical research goals and agenda.
  - ***Research Plan:*** Briefly describe the clinical studies the Consortium plans to pursue during the performance period.
- **Attachment 4: Lay Abstract (one-page limit): Upload as “LayAbs.pdf.”** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

Consumer reviewers refer to the lay abstract and other components of the application package.

The lay abstract should be composed using the outline below:

- Clearly describe, in a manner readily understood by lay persons, the clinical objectives and rationale for the application.
  - Do not duplicate the technical abstract.
- Describe the ultimate applicability of the Consortium’s clinical research.
  - What types of patients will it help, and how will it help them?
  - What are the potential clinical applications, benefits, and risks?
  - What is the projected time it may take to achieve a clinically relevant outcome?
- What are the likely contributions of this study to advancing the field of NF research or the impacts on NF patient treatment, quality of life, or patient care?

- **Attachment 5: Statement of Work (SOW) (ten-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>). The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.
- **Attachment 6: Clinical Trial Letters of Intent: Upload as “Trials.pdf.”** Include Letters of Intent for a minimum of four clinical trials addressing at least one NF1- and one NF2-focused study for implementation by the Consortium within the first year of the performance period. Each trial plan must include the following:
  - **Research Idea:** For each proposed clinical trial, describe the ideas and reasoning on which it is based, and how the study addresses a central problem in NF1 or NF2.
  - **Research Strategy:** Concisely state each clinical trial’s objectives and specific aims. Describe the patient populations and study sites that will be utilized for each study. Include recruitment goals and timelines for study implementation. Define study endpoints and outcomes, and the probability that each described trial will have sufficient power with the suggested patient accrual to answer the study questions within the defined time period of trial execution.
  - **Clinical Impact:** Briefly describe how the proposed clinical trial will have an impact on NF patient treatment, quality of life, or patient care.
- **Attachment 7: Data Management Plan: Upload as “DataPlan.pdf.”** Provide a data management plan that includes: (1) Descriptions of the overall approach to data collection and management, (2) a statistical plan that includes methods to monitor quality and consistency of data collection, and methods to measure outcomes, (3) a plan for real-time data transfer, and (4) data security measures.
- **Attachment 8: Manual of Operations and By-Laws: Upload as “Manual.pdf.”** Provide a copy of a Manual of Operations or SOPs by which the Consortium will operate. Also include documents that describe governance and guidelines by which the Consortium membership operates.
- **Attachment 9: Data and Research Resources Sharing Plan: Upload as “DataSharing.pdf.”** Describe how data and resources generated during the performance period of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, for more information about the CDMRP’s expectations for making data and research resources publicly available.
- **Attachment 10: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as “MFBudget.pdf.”** If a Military Facility (military health system facility, research laboratory, 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 the Collaborating DoD Military Facility

Budget Form, 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 and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

**3. Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., 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 five-page National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the portable document format (pdf) that is not editable.

Biographical Sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

- PI Previous/Current/Pending Support (no page limit): Upload as “Support\_LastName.pdf.”
- 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.”

**4. Research & Related Budget:** Refer to the General Application Instructions, Section II.C.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.

**5. Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

**6. R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

Collaborating DoD Military Facilities Form: A Military Facility collaborating in the performance of the project should be treated as a subaward for budget purposes. However, do not complete the Grants.gov R & R Subaward Budget Attachment Form; instead, complete the Collaborating DoD Military Facility Budget Form (use Attachment 10, Collaborating DoD Military Facility Budget Form) to show all direct and indirect costs. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

## **D. Applicant Verification of Grants.gov Submission in eBRAP**

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the Grants.gov application submission. eBRAP will validate retrieved files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the Program Announcement/Funding Opportunity. ***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 prior to the application submission deadline.*** The Project Narrative and Budget Form cannot be changed after the application submission deadline.

## **E. Submission Dates and Times**

All submission dates and times are indicated on the [title page](#) of this Program Announcement/Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in submission rejection.

## **F. Other Submission Requirements**

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

All extramural applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Section II.A., for information on Grants.gov registration requirements.

## **III. APPLICATION REVIEW INFORMATION**

### **A. 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 of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, USAMRMC, based on technical merit, the relevance to the mission of the DoD and NFRP, the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement/Funding Opportunity. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. ***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 III.B.2., Programmatic Review](#).* Additional information about the two-tier process used by the CDMRP can be found at <http://cdmrp.army.mil/about/fundingprocess>.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement 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 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 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 Title 18 United States Code 1905.

## **B. Application Review Process**

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

- **Consortium Structure and Goals**
  - The degree of impact the overall goals of the Consortium are likely to have on the clinical evaluation of promising therapeutic agents for the management or treatment of NF1, NF2, and schwannomatosis.
  - How appropriate the proposed overall organizational structure of the Consortium is to rapidly developing and implementing clinical trials for NF1, NF2, and schwannomatosis.
  - How effectively the Operations Center addresses a plan to oversee and coordinate all Consortium Clinical Trial Sites.
  - How effectively the Operations Center and each Clinical Trial Site will function as an integrated unit.
  - To what degree the appropriate resources are provided for full participation at each Consortium Site.
- **Operations Center Expertise and Resources**
  - To what extent the Operations Center's experience, track record, and expertise are appropriate with respect to the ability to manage and oversee multi-institutional NF clinical studies.
  - How effectively the plan for the establishment and maintenance of core facilities and other resources will support Consortium activities.
  - The degree to which the information technology and real-time communications capabilities are appropriate.

- How appropriate the plans are for addressing human subject protection requirements as described by HRPO and coordinating IRB submissions and approvals at participating sites.
- How appropriate are the ability and experience of the organization with the financial management of multi-institutional research studies?
- **Clinical Trial Sites Expertise and Resources**
  - How appropriate the research teams' background, track record, and expertise are at each Clinical Trial Site with respect to the successful conduct of NF studies and participation in multi-center clinical studies.
  - Whether the organizations have demonstrated access to appropriate patient populations for conduct of Consortium clinical studies.
  - How appropriate the facilities and resources are within each Clinical Trial Site for NF patients.
  - How appropriate the resources and expertise at each organization are for data management and coordination of specimen collection and processing.
- **Clinical Trial Development and Implementation**
  - The degree to which plans for conceptualization, design, development, and prioritization of clinical trials within the performance period are appropriate.
  - How appropriate and well-considered the plans are for developing procedures to ensure compliance with FDA regulations for investigational agents.
  - How well the planned trials address critical needs of the NF patients..
- **Study Management and Monitoring**
  - How appropriate the plans are for real-time communication among all organizations participating in the Consortium, including complete and timely reporting, review, and appropriate responses to adverse events (including suspension of a trial, modification of a trial protocol, or cessation of a trial) in facilitating Consortium activities.
  - The extent of the named Consortium Clinical Research Manager's experience with guiding clinical protocols through the regulatory approval processes, coordinating participant accrual, and coordinating study activities across sites.
  - How adequate the outlined procedures are for quality assurance, quality control, safety, and study monitoring with regard to conducting multi-institutional clinical studies.
  - How appropriate the plans are for specimen handling, distribution, analysis, banking, and security with regard to facilitating Consortium activities.
- **Data Management**
  - The degree to which the overall approach to data collection, management, analysis, and security measures is appropriate.

- How clearly the PI and key personnel have demonstrated effective application of methods to monitor quality and consistency of data collection, and methods to measure outcomes in previously conducted clinical trials.
- How adequate the plan is for real-time data transfer with regard to supporting the Consortium-associated activities.
- **Clinical Trials**
  - The extent to which the plans are appropriate and feasible for the estimated number and types of studies to be conducted during the duration of this award.
  - How well the scientific rationale and preliminary data support each of the proposed initial study's design and objectives.
  - The degree to which the patient populations and sample size are appropriate for each proposed initial study.
  - The degree to which proposed methods and outcome measures are appropriate for the purposes of each proposed initial study.
  - The degree to which each proposed initial study makes an impact on NF patient treatment, quality of life, or patient care.
- **Personnel**
  - The extent to which the PI and other key personnel at the Operations Center have expertise in the design, administration, and financial management of multi-institutional NF clinical studies, including the distribution and management of funds.
  - The extent to which the Clinical Site PIs have expertise in the conduct of clinical trials.
  - The extent to which the levels of effort are appropriate for successful conduct of the proposed work.
  - The qualifications of the Consortium Clinical Research Manager, who will interact with all Clinical Trial Site Research Coordinators to coordinate regulatory approvals and Consortium activities.
  - The extent to which all participating personnel are willing to commit adequate time, resources, and human subjects to the Consortium.

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

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

- **Community Needs**
    - How well the application reflects the knowledge and respect for the needs of the community of individuals affected
  - **Application Presentation**
    - To what extent the writing, clarity, and presentation of the application components influence the review.
  - **Environment**
    - If applicable, to what degree the intellectual and material property plan is appropriate.
- 2. 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:
- a. Ratings and evaluations of the peer reviewers**
  - b. Relevance to the mission of the FY16 NFRP, as evidenced by the following:**
    - Adherence to the intent of the award mechanism
    - Program portfolio composition]
    - Programmatic relevance to NFRP
    - Relative impact and innovation
    - Ratings and evaluations of the peer reviewers

### **C. Recipient Qualification**

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

### **D. Application Review Dates**

All application review dates and times are indicated on the [title page](#) of this Program Announcement/Funding Opportunity.

### **E. Notification of Application Review Results**

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.

## **IV. ADMINISTRATIVE ACTIONS**

After receipt of pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

## A. Rejection

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

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

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Clinical Trial Letters of Intent are missing.
- Pre-application was not submitted.

## B. Modification

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

## C. Withdrawal

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

- An FY16 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 FY16 NFRP Programmatic Panel members can be found at <http://cdmrp.army.mil/nfrp/panels/panels16>.*
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- 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 FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<http://cdmrp.army.mil/about/2tierRevProcess>). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed

appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The invited application does not propose the same research project described in the pre-application.
- Total costs as shown on the Research and Related Budget form exceed the maximum allowed by this Program Announcement/Funding Opportunity.

#### **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.

### **V. AWARD ADMINISTRATION INFORMATION**

#### **A. Award Notice**

Awards will be made no later than September 30, 2017. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards" (2 CFR part 200).

#### **B. Administrative Requirements**

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

#### **C. National Policy Requirements**

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

#### **D. Reporting**

Refer to the General Application Instructions, Appendix 4, Section H, for general information on reporting requirements.

Quarterly technical progress reports will be required in addition to annual and final reports. Reports must be in the form of a single comprehensive report encompassing activities at the Operations Center and all Clinical Trial Sites.

In addition to written progress reports, awardees may expect requests for formal progress presentations in clinical symposia to accelerate transition into clinical practice.

#### **E. Award Transfers**

The Operations Center of the NFRP Clinical Consortium Award cannot be transferred to another organization. Clinical Trial Sites cannot be transferred to another organization.

Refer to the General Application Instructions, Appendix 4, Section L, for general information on organization or PI changes.

#### **F. Pre-Award Meeting**

At the Government's discretion, the consortium PI, Clinical Trial Site lead PIs, and Clinical Research Manager or other personnel may be requested to participate in a pre-award meeting at the Government's expense.

### **VI. VERSION CODES AND AGENCY CONTACTS**

#### **A. Program Announcement/Funding Opportunity and General Application Instructions Version**

Questions related to this Program Announcement/Funding Opportunity should refer to the Program name, the Program Announcement/Funding Opportunity name, and the Program Announcement/Funding Opportunity version code 20160210i. The Program Announcement/Funding Opportunity numeric version code will match the General Applications Instructions version code 20160210.

#### **B. CDMRP Help Desk**

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

Phone: 301-682-5507

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

#### **C. Grants.gov Contact Center**

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S.

Federal holidays). Note that the CDMRP 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/Funding Opportunity 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.***

## VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Clinical Trial Letters of Intent: Upload as Attachment 6 with file name "Trials.pdf."	
	7	Data Management Plan: Upload as Attachment 7 with file name "DataPlan.pdf."	
	8	Manual of Operations and By-Laws: Upload as attachment 8 with file name "Manual.pdf."	
	9	Data and Research Resources Sharing Plan: Upload as Attachment 9 with file name "DataSharing.pdf."	
	10	Collaborating DoD Military Facility Budget Form(s): Upload as Attachment 10 with file name "MFBudget.pdf," if applicable.	
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		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	