Department of Health and Human Services
Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH (http://www.nih.gov))

Components of Participating Organizations

National Institute of Neurological Disorders and Stroke (NINDS (http://www.ninds.nih.gov))

Funding Opportunity Title

NeuroNEXT Clinical Trials (U01 Clinical Trial Optional)

Activity Code

U01 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=u01&Search.x=0&Search.y=0&Search_Type=Activity) Research Project – Cooperative Agreements

Announcement Type

Reissue of PAR-16-155 (https://grants.nih.gov/grants/guide/pa-files/PAR-16-155.html)

Related Notices

None

Funding Opportunity Announcement (FOA) Number

PAR-18-528

Companion Funding Opportunity

PAR-18-628 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-628.html), U 44, Small Business Innovation Research (SBIR) Cooperative Agreement –Fast track, Phase II

Number of Applications

See Section III. 3. Additional Information on Eligibility.

Catalog of Federal Domestic Assistance (CFDA) Number(s)

93.853

Funding Opportunity Purpose

This FOA encourages applications for exploratory clinical trials of investigational agents (drugs, biologics, surgical therapies or devices) that may contribute to the justification for and provide the data required for designing a future trial,

for biomarker validation studies, or for proof of mechanism clinical studies. Diseases chosen for study should be based on the NINDS' strategic plan and clinical research interests (www.ninds.nih.gov/funding/areas/index.htm (http://www.ninds.nih.gov/funding/areas/index.htm)). Successful applicants will be given access to the NeuroNEXT infrastructure. Following peer review, NINDS will prioritize and order trials that are given access to the NeuroNEXT infrastructure. The NeuroNEXT Clinical Coordinating Center (CCC) will work with the successful applicant to efficiently implement the proposed study. The NeuroNEXT Data Coordinating Center (DCC) will provide statistical and data management support. The NeuroNEXT clinical sites will provide recruitment/retention support as well as on-site implementation of the clinical protocol.

Applicants do not need to be part of the existing NeuroNEXT infrastructure.

Key Dates

Posted Date

December 21, 2017

Open Date (Earliest Submission Date)

January 5, 2018

Letter of Intent Due Date(s)

30 days prior to the application due date

Application Due Date(s)

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11111) apply , by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on these dates.

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

AIDS Application Due Date(s)

Not Applicable

Scientific Merit Review

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) (http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward) apply

Advisory Council Review

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) (http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward) apply

Earliest Start Date

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) (http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward) apply

Expiration Date

January 8, 2021

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000), except where instructed to do otherwise (in this FOA or in a Notice from the *NIH Guide for Grants and Contracts* (//grants.nih.gov/grants/guide/)). Conformance to all requirements (both in the Application Guide and the FOA) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions. **Applications that do not comply with these instructions may be delayed or not accepted for review.**

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the NIH ASSIST system to prepare, submit and track your application online.

   Apply Online Using ASSIST

2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and eRA Commons (http://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.

3. Use Grants.gov (../ApplyButtonSplash.cfm?oppNum=PAR-18-528) Workspace to prepare and submit your application and eRA Commons (http://public.era.nih.gov/commons/) to track your application.

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Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Background:

To facilitate the cooperation and partnering of public and private funding organizations, universities, academic medical centers, research institutes, contract research organizations, biotechnology companies, and

pharmaceutical companies, NINDS has formed the Neurology Network of Excellence in Clinical Trials (NeuroNEXT, www.NeuroNEXT.org). NeuroNEXT has a Clinical Coordinating Center (CCC), a Data Coordinating Center (DCC) and a group of 25 geographically distributed clinical sites in the United States.

This FOA provides one of a set of three different means by which teams of investigators can gain access to the NeuroNEXT infrastructure. This FOA uses the U01 cooperative agreement mechanism and is open to all eligible applicants, as defined in Section III. Small businesses may wish to consider applying through PAR-17-300 "NeuroNEXT Small Business Innovation in Clinical Trials (U44)" or its reissues. For-profit organizations and Non-profits other than Institutions of Higher Education may wish to consider applying through PAR-15-195 "NeuroNEXT Infrastructure Resource Access (X01)".

Purpose/Research Objectives:

This clinical research network develops and conducts multiple, scientifically sound, possibly biomarker-informed exploratory clinical trials evaluating the most promising therapies, whether from academic, foundation or industry discoveries. Examples include Phase 2 clinical trials and clinical research studies aimed at validating biomarkers and clinical outcomes in preparation for clinical trials. NeuroNEXT provides a robust, standardized, and accessible infrastructure to facilitate rapid development and implementation of protocols in neurological disorders affecting adult and/or pediatric populations. While the network is not specific to one disease, it has the capacity to coordinate a cadre of specialist investigators to implement studies efficiently in response to disease-specific opportunities.

The network is designed to increase the efficiency of clinical trials, to facilitate patient recruitment and retention, to increase the quality of neuroscience clinical trials, and to enable public-private partnerships.

To foster the development of clinical trialists, the NeuroNEXT investigators who have been selected for their experience and training in neurological clinical research will provide a source of strong mentorship and support to investigators who are early in their careers as approved studies are implemented within the infrastructure.

Specific Areas of Research Interest:

This FOA encourages applications for exploratory clinical trials of investigational agents (drugs, biologics, surgical therapies or devices) that may contribute to the justification for and provide the data required for designing a future trial, for biomarker validation studies, or for proof of mechanism clinical studies. Applications for drugs or biologics should provide compelling scientific evidence that the investigational agent proposed for study will reach/act upon the designated target or that its mechanism of action is such that it is expected to be of benefit in ameliorating a specific aspect of the disease. Neurologic diseases chosen for study must fall within the primary responsibility of NINDS (www.ninds.nih.gov/funding/areas/index.htm (http://www.ninds.nih.gov/funding/areas/index.htm)).

Examples of appropriate studies under this FOA include, but are not limited to, those designed to:

- Evaluate and optimize the dose, formulation, safety, tolerability or pharmacokinetics of an intervention in the target population.
- Select or rank the best of two or more potential interventions or dosing regimens to be evaluated in a subsequent trial, based on tolerability, safety data, biological activity, or preliminary clinical efficacy (e.g., futility trials).
- Evaluate biological activity relative to clinical endpoints.
- For medical devices, in addition to providing initial clinical safety data, appropriate studies are those that inform the next phase of development, usually by finalizing the device design, establishing operator technique, and/or finalizing the choice of study endpoints for the design of a pivotal clinical trial.

A separate clinical trials network has been established and funded by NINDS to conduct clinical trials and biomarker studies for stroke treatment, prevention and recovery; thus NeuroNEXT has been established for the conduct of studies in neurological disorders other than stroke.

Implementation

Applicants should make note of the following:

(1) Applicants to this FOA will be required to incorporate the NeuroNEXT infrastructure (www.neuronext.org (http://www.neuronext.org/)) into their proposed study. Additional (ad-hoc) sites may be proposed to fulfill specific study requirements. All applicants will be required to use the master clinical trial agreements and central IRB that have been established for NeuroNEXT.

(2) Efficacy: This FOA is not intended to support the conduct of a clinical trial where the primary aim is to confirm efficacy of a drug or biologic.

(3) Secondary Aims:

For drugs and biologics, issues of study feasibility and refinement of study procedures may be addressed as secondary aims in an exploratory clinical trial, but not as the primary aim. Examples of such secondary aims include, but are not limited to, the following:

- Determining the optimal measure (endpoint), its variability, and/or the optimal timing of outcome evaluations in the context of the intervention
- Collecting information on the utility of questionnaires, rating scales, or biomarkers

For medical device, Early Feasibility or Traditional Feasibility studies, issues of study feasibility and refinement of study procedures are expected to be addressed as primary aims in addition to providing initial clinical safety data at this stage. These may include:

- Identifying appropriate modifications to the procedure or device to enable a subsequent Pivotal study on a finalized system;
- Refining the intended use population;
- Developing and refining data collection procedures;
- Refining the non-clinical test plans or methodologies; and
- Developing subsequent clinical study protocols.

(4) The NIH recognizes that devices can vary greatly in terms of basic form and function, physiological bases for therapy, degree of invasiveness, etc. Consequently, the appropriate pathway to market may require a traditional Feasibility and Pivotal study in support of an eventual Pre-Market Approval submission, or may require a more limited study to address specific issues in support of an FDA 510(k) or 510(k) De Novo submission. Clinical studies involving devices may utilize the entire NeuroNEXT Network, or a more limited subset of centers selected based on appropriate expertise for the given device. Investigators are encouraged to contact NINDS Program Staff as early as possible to discuss how the NeuroNEXT network may best be utilized in support of their specific device project. NINDS anticipates that the majority of device projects utilizing NeuroNEXT will be traditional Feasibility Studies in order to best leverage the advantages of the network. An Early Feasibility Study should be designed [in accordance with FDA's draft guidance, "Investigational Device Exemptions (IDE) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies", see http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm277670.htm (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm277670.htm) to allow for early clinical evaluation of devices to provide proof of principle and initial clinical safety data while device design and operations are still in development. A Traditional Feasibility Study is a clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan a Pivotal Study.

Early Feasibility and Traditional Feasibility study designs may include single-arm case series, on-off interventions (patients as own controls), device-device comparisons, comparisons to historic controls, comparisons to performance controls, or adaptive/Bayesian designs.

(5) Rare Diseases: Applications in rare diseases are encouraged while recognizing that available patient pools may not be adequate to meet the sample size requirements normally required to establish the efficacy of an intervention. NINDS acknowledges that innovative, non-traditional trial designs including adaptive designs may be appropriate in rare disease studies. While NeuroNEXT is primarily intended for exploratory trials, the network will consider Phase2/3 trials in diseases with a US prevalence of under 5,000 persons.

(6) Rationale: Exploratory trials primarily test hypotheses in relatively small programs so that the acceptable risk and uncertainty are higher than in later stage programs. Exploratory clinical trials must anchor their rationale in (1) an unmet medical need; (2) a plausible biological mechanism; (3) non-clinical (in vitro and/or in vivo) data; and/or (4) early clinical data. Their individual weight should be carefully assessed in the specific context of the application at hand; there is no requirement to provide support from all four areas. Applicants should consider the limitations of those studies with regards to the scientific rigor guidelines published by NINDS (see https://grants.nih.gov/grants/guide/notice-files/NOT-NS-11-023.html (https://grants.nih.gov/grants/guide/notice-files/NOT-NS-11-023.html)). Preclinical data (such as from animal studies) that do not sufficiently meet the rigor guidelines or are not sufficiently associated with the human condition may be inadequate to support the rationale for the study.

(7) Pharmacometrics: Applications seeking to obtain data needed for pharmacometric modeling are encouraged, with the ultimate aim of enabling the optimal design of a future efficacy trial of an intervention.

(8) The award and continuation of funding are subject to milestones to be specified in the notice of grant award according to NINDS policies.

(9) NIH Resources: As appropriate, applicants are encouraged to make use of the following resources for clinical research including:

(a) Clinical and Translational Science Award (CTSA) program (https://www.ctsacentral.org (https://www.ctsacentral.org/));

(b) NeuroQOL (http://www.neuroqol.org (http://www.neuroqol.org/));

(c) NIH Toolbox (http://www.nihtoolbox.org (http://www.nihtoolbox.org/));

(d) PROMIS (http://www.nihpromis.org (http://www.nihpromis.org/)); and

(e) NINDS Common Data Elements (http://www.commondataelements.ninds.nih.gov (http://www.commondataelements.ninds.nih.gov/)).

(10) Mobile Technologies: Applicants are encouraged to consider utilizing (at least experimentally) mobile technologies to facilitate data collection and protocol adherence on the part of research participants and study site staff.

Working with NeuroNEXT is a cooperative venture between NINDS, the NeuroNEXT network and the applicant. NINDS will provide guidance to potential applicants with input from NINDS Program Staff and the NeuroNEXT Executive Committee. Potential applicants are strongly encouraged to contact NINDS Scientific/Research Contacts (see Agency Contacts, Section VII) in order to discuss the feasibility of conducting the proposed trial through the NeuroNEXT infrastructure before submitting an application. Pre-application consultation may include an introductory teleconference (at least 3 months prior to submission), followed by a conference call or in-person meeting with NINDS staff, if needed.

Funding decisions will also be based on a study's fit for the network relative to other proposed and ongoing trials.

Applications that do not include the appropriate documentation listed in section 4.6 of the Human Subjects-Clinical Trials Form will be withdrawn and not reviewed. Prior to grant award, awardees who do not have an exemption from the FDA must provide any additional FDA correspondence regarding the status of the protocol to the NINDS, especially if the trial has been placed under full or partial hold.

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Cooperative Agreement: A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will

assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this FOA.

Application Types Allowed

New
Renewal
Resubmission
Revision

The OER Glossary (//grants.nih.gov/grants/guide/url_redirect.htm?id=11116) and the SF424 (R&R) Application Guide provide details on these application types.

Clinical Trial?

Optional: Accepting applications that either propose or do not propose clinical trial(s)

Need help determining whether you are doing a clinical trial? (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

Award Budget

Application budgets are not limited but need to reflect the actual needs of the proposed project.

Award Project Period

The maximum request cannot exceed 5 years but the actual funded project period is dependent on reaching specific milestones as described in this FOA.

NIH grants policies as described in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this FOA.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

The following types of Higher Education Institutions are always encouraged to apply for NIH support as Public or Private Institutions of Higher Education:

- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions

- Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)
- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Institutions)

Foreign Institutions

Non-domestic (non-U.S.) Entities (Foreign Institutions) **are** eligible to apply.
Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.
Foreign components, as defined in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are** allowed.

Required Registrations

Applicant Organizations

Applicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications (//grants.nih.gov/grants/guide/notice-files/NOT-OD-15-039.html) states that failure to complete registrations in advance of a due date is not a valid reason for a late submission.

- Dun and Bradstreet Universal Numbering System (DUNS) (http://fedgov.dnb.com/webform) - All registrations require that applicants be issued a DUNS number. After obtaining a DUNS number, applicants can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- System for Award Management (SAM) (https://www.sam.gov/portal/public/SAM/) (formerly CCR) – Applicants must complete and maintain an active registration, **which requires renewal at least annually**. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
    - NATO Commercial and Government Entity (NCAGE) Code (//grants.nih.gov/grants/guide/url_redirect.htm?id=11176) – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in order to register in SAM.

- eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Applicants must have an active DUNS number and SAM registration in order to complete the eRA Commons registration. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- Grants.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=82300) – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF424 (R&R) Application Guide.

2. Cost Sharing

This FOA does not require cost sharing as defined in the *NIH Grants Policy Statement*. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11126)

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see NOT-OD-11-101 (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-101.html)).

Section IV. Application and Submission Information

1. Requesting an Application Package

Buttons to access the online ASSIST system or to download application forms are available in Part 1 of this FOA. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000), except where instructed in this funding opportunity announcement to do otherwise. Conformance to the requirements in the Application Guide is required and strictly

enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

For information on Application Submission and Receipt, visit Frequently Asked Questions – Application Guide, Electronic Submission of Grant Applications (//grants.nih.gov/grants/guide/url_redirect.htm?id=41137).

Letter of Intent

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

By the date listed in Part 1. Overview Information, prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

The letter of intent should be sent to:

Janice Cordell, RN, MPH
Telephone: 301-451-4299
Fax: 301-480-1080
Email: JC53A@NIH.GOV (mailto:JC53A@NIH.GOV)

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits (//grants.nih.gov/grants/guide/url_redirect.htm?id=11133) must be followed.

Instructions for Application Submission

The following section supplements the instructions found in the SF424 (R&R) Application Guide and should be used for preparing an application to this FOA.

SF424(R&R) Cover

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Project/Performance Site Locations

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Other Project Information

All instructions in the SF424 (R&R) Application Guide must be followed.

Facilities and Other Resources: A specific statement should be included regarding how Clinical and Translational Science Award (CSTA) program (https://ctsacentral.org (https://ctsacentral.org)) resources will be leveraged, if applicable. Describe what CTSA services will be used at each participating CTSA site and how the use of the CTSA impacts the trial budget.

SF424(R&R) Senior/Key Person Profile

All instructions in the SF424 (R&R) Application Guide must be followed.

R&R or Modular Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

The budget should be largely planned on a fee-for-service basis with detailed per-patient costs. That budget may include clinical trial costs such as:

Up to 2.4 person months for the protocol PD(s)/PI(s) (even if that person is also a NeuroNEXT site PD(s)/PI(s))

- Up to 3 person months of support for a study-specific clinical coordinator at the applicant's site if the NIH-funded site coordinator is at capacity with NeuroNEXT trials or does not have necessary expertise to assist with the proposed study. If the applicant is not at a NeuroNEXT clinical site, up to 12 person months support for a study-specific clinical coordinator may be included.
- Study-related procedures/materials
- Clinical site operations for any ad hoc sites which are proposed

The budget will not include costs which are already covered by the NINDS infrastructure:

- NeuroNEXT site PD(s)/PI(s) time other than the protocol PD(s)/PI(s)
- NeuroNEXT site coordinator time.

NINDS expects that the total cost for the proposed project (direct cost plus F&A) will not exceed $25,000 per subject randomized into the trial. Budgets exceeding this guideline should be adequately justified in the application. The NINDS strongly encourages applicants to consider simple and/or pragmatic trial designs that minimize per-subject data collection and cost.

R&R Subaward Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Cover Page Supplement

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Research Plan

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Specific Aims: Applicants should describe the potential impact of the proposed research. The hypotheses and specific aims of the trial must be clearly and concisely stated. The primary and secondary outcomes to be measured must be defined. The inclusion of secondary aims should be justified by describing the importance of the supportive or explanatory data.

Research Strategy:

Significance and Biological Relevance

Applicants must state concisely the need, rationale, timeliness, and scientific relevance of the proposed study. It is particularly important that there be a discussion of how the study will test the hypothesis proposed and how results of the study (positive or negative) may be explained based on the biological action of the proposed intervention. The application must present an overview of the state of the science, current status of therapeutics for the disease, and relevance of the trial. The applicant should also discuss the place of the proposed trial in the development pipeline of therapeutic interventions for the targeted disease. The timeliness of the proposed study should be discussed in the application.

Potential Impact of the trial: Applicants should also include a description of the potential impact of the proposed research on clinical care - regardless of the results - and estimate the public health impact relative to the number of afflicted individuals in the U.S. and/or global population annually.

For other studies, such as biomarker studies or other non-clinical trials, the above instructions still apply, and the description should emphasize the specific need and potential impact for diagnosis, therapy development, etc. as appropriate.

Prior Studies and Rationale for Development

Exploratory clinical trials must anchor their rationale in (1) an unmet medical need; (2) a plausible biological mechanism; (3) non-clinical (in vitro and/or in vivo) data; and/or (4) early clinical data. Their individual weight should be carefully assessed in the specific context of the application at hand; the applicant is not required to provide support from all four areas. The major findings of the studies, whether pre-clinical or clinical, that led to the proposed clinical trial should provide a compelling rationale for the belief that the proposed intervention may be effective. Data from pre-clinical and pilot studies demonstrating the need for and the feasibility of the trial should be presented when available. While the NINDS recognizes that informative animal models are not available

for many neurological disorders, the applicant should specifically address the rigor of any animal studies being used as support (https://grants.nih.gov/grants/guide/notice-files/NOT-NS-11-023.html (https://grants.nih.gov/grants/guide/notice-files/NOT-NS-11-023.html)). Applicants should describe the full body of evidence being used to support the proposed study and comment on the justification for moving forward with the proposed clinical study. Applications for drugs or biologics should provide compelling scientific evidence that the investigational agent proposed for study will reach/act upon the designated target or that its mechanism of action is such that it is expected to be of benefit in ameliorating a specific aspect of the disease.

Approach

Applicants should provide a brief description of their proposed study, including a discussion of the potential biases in the study and how they will be addressed. A detailed protocol is not required for submission, but a synopsis should be included. Following peer review, applicants who are granted network access will work with the NeuroNEXT team and the NINDS to develop a detailed protocol. The NeuroNEXT team was established by NINDS based on peer- and Council review to form a group of outstanding clinical trial experts from the field of neurology and statistics with a proven record of developing high quality protocols.

Letter of Support: If there will be subcontracts or service agreements for personnel or facilities, include documentation of such commitments, co-signed by a business official and the investigator at the participating center.

If there are agreements with collaborating industry partners, include documentation of the agreements, co-signed by a business official and an appropriate official at the company.

If CTSA resources will be utilized, include a letter of support from each site CTSA program officer concurring with the specific plan for using these resources.

If some trial costs are to be borne by sources other than NIH, include documentation of this support, signed by individuals who have the authority to make a commitment on behalf of the organization they represent.

Applicants are encouraged to include letters from patient organizations or other supporting documentation to show that patients were included as partners in the concept development and design of the trial.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide, with the following modification:

Resource Sharing Plans (Data Sharing Plan, Sharing Model Organisms, and Genomic Data Sharing Policy) are expected when applicable. Consistent with achieving the goals of the program, final de-identified public use datasets are expected to be submitted to NINDS for archiving and dissemination within 12 months of end of study (or timeline specified in the Notice of Grant Award if different).

- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

Appendix:

Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

Clinical Protocol. A full clinical protocol of the proposed study is required. Applicants may wish to use the Clinical Trial Protocol Template for Phase 2 and 3 IND/IDE Studies developed by NIH and FDA, which should be modifiable to any type of clinical trial, available at http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials (http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials). See https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-064.html (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-064.html) for additional information about the protocol template.

Where applicable, the following optional elements may also be provided in the appendix:

Non-referenced or non-published, non-standardized clinical assessments and data collection tools.

Investigator Brochures, see 21 CFR 312.23 (a)(5) for format

Clinical pharmacology justifying the proposed dosing regimen.

PHS Human Subjects and Clinical Trials Information

Use only for applications with due dates on or after January 25, 2018. When involving NIH-defined human subjects research, clinical research, and/or clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the SF424 (R&R) Application Guide must be followed with the following additional instructions:

Section 2.5, Recruitment and Retention Plan*:*

Documentation of availability of eligible subjects at clinical sites, presented in tabular format and a supporting letter from the NeuroNEXT Executive Committee indicating their ability and capacity to collaborate and conduct the proposed study.

Section 2.7: Milestone Plan. Applications must include proposed yearly go/no-go milestones. While final milestones will be determined at the time of grant award, the applicant should propose clear milestones that provide objective, quantitative outcomes that will justify continuing the project. Milestones are not equivalent to aims but rather are determinants of whether a study continues or stops. The proposed milestones must include achievable goals for the start-up stage, feasibility stage, and completion stage of the project as follows:

Completion of start-up activities (finalization of protocol, contracting of sites, registration in ClinicalTrials.gov, completion of any final regulatory approvals, etc.)

Enrollment of the first subject

Enrollment of 25%, 50%, 75% and 100% of the projected recruitment for all study subjects, including women, minorities and children (as appropriate)

Expected timing of proposed interim analyses and, for adaptive designs, implementation of pre-specified adaptation plan

Completion of data collection time period

Completion of primary endpoint and secondary endpoint data analyses

Completion of final study report

Publication of primary study results

Reporting of results in ClinicalTrials.gov

Submission of final public use dataset to NINDS

Proposed milestones should be included for the entire trial, including any anticipated time beyond the five-year award. This information will be used for planning purposes and to support the rationale for the full trial but does not guarantee continued funding beyond the initial funding cycle.

3.1 Protection of Human Subjects

Assurance of the protection of human participants and the biohazard safety of employees (if applicable) must be provided for the overall study and for each clinical site. The applicant must discuss any issues which might lead

to concern for the welfare of participants. Additionally, the human subjects section of the application must address data security measures and confidentiality.

Section 4 - Protocol Synopsis

Protocol synopsis. A draft clinical protocol of the proposed study should be included. At the time of this writing, the FDA and NIH had developed a draft Clinical Trial Protocol Template for Phase 2 and 3 IND/IDE Studies (http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials (http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials)), which should be modifiable to any type of clinical trial.

- Applicants should ensure that this section includes the following:
- A description and rationale for the selected trial design.
- A description of the study population and why it is an appropriate group to answer the question under study.
- A description and rationale for selection of the study outcomes and endpoints.
- A list of subject inclusion/exclusion criteria, or of group eligibility criteria for group-randomized trials.
- Subject recruitment and retention plans, including a discussion of the ability of sites to recruit and retain the proposed number of subjects, including women and minorities.
- Applicants must include a plan to enroll women and minorities. Considerations that may contribute to successful inclusion are appropriate site selection, patient- or community-engagement for the major elements of the project, use of focus groups to address barriers to inclusion, etc. Applicants should also include a discussion of how the gender and minority findings will be reported to the NINDS. For exploratory trial applications, investigators should consider including a section that addresses how the results in women and minorities will inform the design of the next steps.
- A description of the intervention to be tested and how it will be administered.
- A description of all assessments including clinical, laboratory, physiological, behavioral, patient-centered, or other outcomes addressing the primary and secondary research questions. Use of patient reported outcomes, including those available through PROMIS and NeuroQoL, as well as non-traditional data collection approaches (e.g., telephone, mobile devices or web-based systems) should be considered.
- A discussion regarding how the following resources for clinical research will be utilized, as applicable:
    - · NeuroQOL (http://neuroqol.org);
    - · NIH Toolbox (http://www.nihtoolbox.org);
    - · PROMIS (http://nihpromis.org); and
    - · NINDS Common Data Elements (http://www.commondataelements.ninds.nih.gov (http://www.commondataelements.ninds.nih.gov/))
- A discussion of potential biases and/or challenges in the protocol and how they will be addressed.

For an exploratory trial of a drug, device or biologic, plans for the next steps of the therapy's development (such as a future efficacy trial) and proposed go/no-go criteria must be succinctly stated. A brief description of the potential future phase 3 study should be included, along with a description of how this phase 3 study would be different from the proposed phase 2 study.

4.4 Statistical Design and Power

Statistical Analysis Plan (SAP). This document should provide a proposed draft of the planned analyses, including a description of how the statistical analysis of the primary, secondary and other endpoints will be performed, how the sample size was determined, how missing data will be handled, plans for interim analyses for safety, efficacy and futility, plans for recalculation of the sample size midway through the trial (if applicable), etc. If computer simulations were used to investigate the operating characteristics of complex clinical trial designs (such as adaptive designs), to choose between alternative outcome measures, or to determine sample size, by taking into account the impact of noncompliance, missing data, subject eligibility criteria, etc., sufficient details about the simulations should be provided in the SAP.

Section 4.6:

Documentation of availability of interventional agent(s) or device(s) as well as plans and support for acquisition and distribution of interventional agent(s) or device(s).

Regulatory Approvals. If the intervention is a drug, biologic, or device, applicants must provide documentation from the FDA providing information on one of the following scenarios:

(a) The protocol has been submitted under an open IND and the IND is not under full or partial hold. Under this scenario, applicants must provide documentation such as a "may proceed" email or letter from the FDA.

(b) The protocol has been submitted as an original IDE or as a new study under an open IDE, and FDA has fully approved the IDE or IDE supplement. Under this scenario, applicants must provide documentation of an IDE or IDE supplement full approval letter from the FDA.

(c) The protocol has been submitted under an IND and is on full or partial hold. Under this scenario applicants must provide full documentation from the FDA on the reasons for hold and the FDA recommendations. Applicants should discuss how they intend to address the hold issues and when they believe they will have FDA approval to proceed with trial implementation.

(d) The protocol has been submitted as an original IDE or as a new study under an open IDE, and FDA has conditionally approved the IDE or IDE supplement. Under this scenario applicants must provide full documentation from the FDA on the conditions of approval. Applicants should discuss how they intend to address these conditions and when they believe they will have FDA approval to proceed with trial implementation.

(e) The protocol is exempt from an IND. Under this scenario applicants must provide a copy of the exemption email or letter from the FDA.

(f) The protocol is either exempt from the IDE regulations or does not require IDE approval because it is determined to be nonsignificant risk. Under this scenario applicants must provide either an IDE exemption letter or a copy of the risk determination letter from the FDA.

4.7 Dissemination Plan

The National Institutes of Health (NIH) Policy on Dissemination of NIH-funded Clinical Trial Information establishes the expectation that all NIH-funded awardees and investigators conducting clinical trials, funded in whole or in part by the NIH, will ensure that their NIH-funded clinical trials are registered at, and that summary results information is submitted to, ClinicalTrials.gov for public posting (see NOT-OD-16-149 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html)). The purpose of the policy is to promote broad and responsible dissemination of information from NIH-funded clinical trials through ClinicalTrials.gov. Applicants must submit a plan for the dissemination of NIH-funded clinical trial information that will address how the expectations of this policy will be met.

Delayed Onset Study

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS Assignment Request Form

All instructions in the SF424 (R&R) Application Guide must be followed.

Foreign Institutions

Foreign (non-U.S.) institutions must follow policies described in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11137), and procedures for foreign institutions.

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

See Part 1. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and

Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov

4. Submission Dates and Times

Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or Federal holiday (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to Grants.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the NIH Policy on Late Application Submission.

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the SF424 (R&R) Application Guide.

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11142)

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11143).

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the SF424 (R&R) Application Guide. Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically (//grants.nih.gov/grants/guide/url_redirect.htm?id=11144). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Guidelines for Applicants Experiencing System Issues (//grants.nih.gov/grants/ElectronicReceipt/support.htm#guidelines). For assistance with application submission, contact the Application Submission Contacts in Section VII.

Important reminders:

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF424(R&R) Application Package**.** Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this FOA for information on registration requirements.

The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the SF424 (R&R) Application Guide.

See more tips (//grants.nih.gov/grants/guide/url_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review, NIH. Applications that are incomplete or non-compliant will not be reviewed.

Requests of $500,000 or more for direct costs in any year

Applicants requesting $500,000 or more in direct costs in any year (excluding consortium F&A) must contact a Scientific/ Research Contact at least 6 weeks before submitting the application and follow the Policy on the Acceptance for Review of Unsolicited Applications that Request $500,000 or More in Direct Costs as described in the SF424 (R&R) Application Guide.

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in the policy (//grants.nih.gov/grants/guide/url_redirect.htm?id=82299). Any instructions provided here are in addition to the instructions in the policy.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. As part of the NIH mission (//grants.nih.gov/grants/guide/url_redirect.htm?id=11149), all applications submitted to the NIH in support of biomedical and behavioral research are evaluated for scientific and technical merit through the NIH peer review system.

In addition, for applications proposing clinical trials:

A proposed Clinical Trial application may include study design, methods, and intervention that are not by themselves innovative but address important questions or unmet needs. Additionally, the results of the clinical trial may indicate that further clinical development of the intervention is unwarranted or lead to new avenues of scientific investigation.

For this particular announcement, note the following:

1. Approved projects will be implemented through the NeuroNEXT infrastructure and will make use of previously approved sites, resources, and investigators at the NeuroNEXT Clinical Coordinating Center, Data Coordinating Center, and clinical sites. The applicant will work closely with the NeuroNEXT investigators who have been selected for their experience and training in neurological clinical research. While some applicants will be relatively junior in their careers, NeuroNEXT provides a cadre of experienced clinical trial experts who can ensure high quality implementation and oversight of studies. The PD(s)/PI(s) therefore do not need to bring as much clinical research experience as they would have to bring to a non-NeuroNEXT project.

The NeuroNEXT infrastructure (CCC, DCC and clinical hubs) was selected following peer review to provide an optimal environment and mechanism for conducting relevant projects, including centralized clinical trial management, data management, and oversight of activities at clinical centers.

2. Exploratory clinical trials must anchor their rationale in (1) an unmet medical need; (2) a plausible biological mechanism; (3) non-clinical (in vitro and/or in vivo) data; and/or (4) early clinical data. Their individual weight should be carefully assessed in the specific context of the application at hand; the applicant is not required to provide support from all four areas. Reviewers will focus on the overall impact of the study which will also include the evaluation of the experimental design and all of the review criteria described below.

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the project proposed).

Scored Review Criteria

Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance

Does the project address an important problem or a critical barrier to progress in the field? Is there a strong scientific premise for the project? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

In addition, for applications proposing clinical trials

Are the scientific rationale and need for a clinical trial to test the proposed hypothesis or intervention well supported by preliminary data, clinical and/or preclinical studies, or information in the literature or knowledge of biological mechanisms? For trials focusing on clinical or public health endpoints, is this clinical trial necessary for testing the safety, efficacy or effectiveness of an intervention that could lead to a change in clinical practice, community behaviors or health care policy? For trials focusing on mechanistic, behavioral, physiological, biochemical, or other biomedical endpoints, is this trial needed to advance scientific understanding?

Is there adequate and scientifically rigorous preclinical or clinical research to support the trial rationale? How compelling is the justification for the development of the proposed intervention in

terms of potential advances in clinical practice, public health, and/or patient quality of life? How convincing is the evidence that equipoise exists in the medical and patient communities and the intervention is ready for clinical development?

Is the proposed project likely to yield the answers needed to proceed to the next step in developing the intervention? For exploratory trials, biomarker studies, or clinical endpoint studies, evaluate whether the proposed project is likely to yield the answers needed to proceed to the next step in developing the intervention. Is it clear why the proposed exploratory trial is essential to inform the design and implementation of a subsequent efficacy trial, or enable a “go/no-go” decision regarding further clinical development of the intervention? Is there compelling justification for the development of the proposed intervention in terms of potential advances in clinical practice, public health, unmet medical need, and/or patient quality of life? How would the intervention, if it were ultimately successful, affect patients with the disease? How would the project advance the field regardless of its outcome?

Does the proposed trial have the potential to advance the field (e.g., by evaluating a new target mechanism, or by advancing the validation of a biological or clinical outcome) even if (a) the proposed study design, methods, and intervention are not innovative, and/or (b) the results of the trial indicate that further clinical development of the intervention is unwarranted?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

In addition, for applications proposing clinical trials

With regard to the proposed leadership for the project, do the PD/PI(s) and key personnel have the expertise, experience, and ability to organize, manage and implement the proposed clinical trial and meet milestones and timelines? Do they have appropriate expertise in study coordination, data management and statistics? For a multicenter trial, is the organizational structure appropriate and does the application identify a core of potential center investigators and staffing for a coordinating center?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

In addition, for applications proposing clinical trials

Does the design/research plan include innovative elements, as appropriate, that enhance its sensitivity, potential for information or potential to advance scientific knowledge or clinical practice?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

In addition, for applications proposing clinical trials

Does the application adequately address the following, if applicable

Study Design

Is the study design justified and appropriate to address primary and secondary outcome variable(s)/endpoints that will be clear, informative and relevant to the hypothesis being tested? Is the scientific rationale/premise of the study based on previously well-designed preclinical and/or clinical research? Given the methods used to assign participants and deliver interventions, is the study design adequately powered to answer the research question(s), test the proposed hypothesis/hypotheses, and provide interpretable results? Is the trial appropriately designed to conduct the research efficiently? Are the study populations (size, gender, age, demographic group), proposed intervention arms/dose, and duration of the trial, appropriate and well justified?

Are potential ethical issues adequately addressed? Is the process for obtaining informed consent or assent appropriate? Is the eligible population available? Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate? Has the need for randomization (or not), masking (if appropriate), controls, and inclusion/exclusion criteria been addressed? Are differences addressed, if applicable, in the intervention effect due to sex/gender and race/ethnicity?

Are the plans to standardize, assure quality of, and monitor adherence to, the trial protocol and data collection or distribution guidelines appropriate? Is there a plan to obtain required study agent(s)? Does the application propose to use existing available resources, as applicable?

Data Management and Statistical Analysis

Are planned analyses and statistical approach appropriate for the proposed study design and methods used to assign participants and deliver interventions? Are the procedures for data management and quality control of data adequate at clinical site(s) or at center laboratories, as applicable? Have the methods for

standardization of procedures for data management to assess the effect of the intervention and quality control been addressed? Is there a plan to complete data analysis within the proposed period of the award?

How appropriate are the primary and secondary outcome measures? How appropriate are the eligibility criteria, randomization plan (if applicable), methods of blinding, sample size, trial power, data management plans, and plans for training of site personnel?

How appropriate are the plans for subject outreach, recruitment, retention and follow-up?

How well does the project leverage the use of existing NIH tools, CTSA resources, and/or other resources?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of children, justified in terms of the scientific goals and research strategy proposed?

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

In addition, for applications proposing clinical trials

If proposed, are the administrative, data coordinating, enrollment and laboratory/testing centers, appropriate for the trial proposed?

Does the application adequately address the capability and ability to conduct the trial at the proposed site(s) or centers? Are the plans to add or drop enrollment centers, as needed, appropriate?

If international site(s) is/are proposed, does the application adequately address the complexity of executing the clinical trial?

If multi-sites/centers, is there evidence of the ability of the individual site or center to: (1) enroll the proposed numbers; (2) adhere to the protocol; (3) collect and transmit data in an accurate and timely fashion; and, (4) operate within the proposed organizational structure?

Are there characteristics of the proposed research that specifically lend themselves to deployment within the NeuroNEXT infrastructure?

While the NIH NeuroNEXT environment has already undergone peer review and is fully established, the following issues should be considered with respect to each application: Have the sites provided adequate or reasonable estimates of the number of patients that they expect to be able to enroll? Does this project include a partnership with the private sector (e.g. patient groups and/or industry), and if so, have agreements with proposed partners been established? Have any foreign organizations involved in the proposed study documented the compatibility of their data collection methods with U.S. data collection methods? Is there evidence that the study drug or device will be available in sufficient quantities to ensure feasibility of the project? Are substantive letters of support or other documentation provided to assure commitment of subcontractors, consultants, and/or service agreements for personnel and facilities?

Additional Review Criteria

As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

Study Timeline

Specific to applications proposing clinical trials

Is the study timeline described in detail, taking into account start-up activities, the anticipated rate of enrollment, and planned follow-up assessment? Is the projected timeline feasible and well justified? Does the project incorporate efficiencies and utilize existing resources (e.g., CTSAs, practice-based research networks, electronic medical records, administrative database, or patient registries) to increase the efficiency of participant enrollment and data collection, as appropriate?

Are potential challenges and corresponding solutions discussed (e.g., strategies that can be implemented in the event of enrollment shortfalls)?

Are the proposed milestones appropriate?

Protections for Human Subjects

For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the Guidelines for the Review of Human Subjects (//grants.nih.gov/grants/guide/url_redirect.htm?id=11175).

Inclusion of Women, Minorities, and Children

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of children to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research (//grants.nih.gov/grants/guide/url_redirect.htm?id=11174).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. Reviewers will assess the use of chimpanzees as they would any other application proposing the use of vertebrate animals. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (//grants.nih.gov/grants/guide/url_redirect.htm?id=11150).

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmissions

For Resubmissions, the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewals

For Renewals, the committee will consider the progress made in the last funding period.

Revisions

For Revisions, the committee will consider the appropriateness of the proposed expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

Additional Review Considerations

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Applications from Foreign Organizations

Reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: (1) Data Sharing Plan (//grants.nih.gov/grants/guide/url_redirect.htm?id=11151); (2) Sharing Model Organisms (//grants.nih.gov/grants/guide/url_redirect.htm?id=11152); and (3) Genomic Data Sharing Plan (GDS) (//grants.nih.gov/grants/guide/url_redirect.htm?id=11153).

Authentication of Key Biological and/or Chemical Resources:

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by NINDS, in accordance with NIH peer review policy and procedures (//grants.nih.gov/grants/guide/url_redirect.htm?id=11154), using the stated review criteria. Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications:

- May undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.
- Will receive a written critique.

Applications will be assigned to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications . Following initial peer review, recommended applications will receive a second level of review by the NINDS Council. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.

- Relevance of the proposed project to program priorities.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.

Information regarding the disposition of applications is available in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11156).

Section VI. Award Administration Information

1. Award Notices

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the grants management officer is the authorizing document and will be sent via email to the grantee's business official.

Awardees must comply with any funding restrictions described in Section IV.5. Funding Restrictions. Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

Any application awarded in response to this FOA will be subject to terms and conditions found on the Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158) website. This includes any recent legislation and policy applicable to awards that is highlighted on this website.

All additional communications and information related to programmatic monitoring must be documented and incorporated into the official project file. Individual awards are based on the application submitted to, and as approved by, the NIH and are subject to the IC-specific terms and conditions identified in the NoA. ClinicalTrials.gov: If an award provides for one or more clinical trials. By law (Title VIII, Section 801 of Public Law 110-85), the "responsible party" must register and submit results information for certain "applicable clinical trials" on the ClinicalTrials.gov Protocol Registration and Results System Information Website (https://register.clinicaltrials.gov). NIH expects registration of all trials whether required under the law or not. For more information, see http://grants.nih.gov/ClinicalTrials_fdaaa/

Institutional Review Board or Independent Ethics Committee Approval: Grantee institutions must ensure that the application as well as all protocols are reviewed by their IRB or IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the awardee must provide NIH copies of documents related to all major changes in the status of ongoing protocols. Data and Safety Monitoring Requirements: The NIH policy for data and safety monitoring requires oversight and monitoring of all NIH-conducted or -supported human biomedical and behavioral intervention studies (clinical trials) to ensure the safety of participants and the validity and integrity of the data. Further information concerning these requirements is found at http://grants.nih.gov/grants/policy/hs/data_safety.htm and in the application instructions (SF424 (R&R) and PHS 398).

Investigational New Drug or Investigational Device Exemption Requirements: Consistent with federal regulations, clinical research projects involving the use of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) in humans under a research protocol must be performed under a Food and Drug Administration (FDA) investigational new drug (IND) or investigational device exemption (IDE).

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) as part of the NoA. For these terms of award, see the *NIH Grants Policy Statement* Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157) and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (//grants.nih.gov/grants/guide/url_redirect.htm?id=11159). More information is provided at Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158).

Recipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights law. This means that recipients of HHS funds must ensure equal access to their programs without regard to a person's race, color, national origin, disability, age and, in some circumstances, sex and religion. This includes ensuring your programs are accessible to persons with limited English proficiency. HHS recognizes that research projects are often limited in scope for many reasons that are nondiscriminatory, such as the principal investigator's scientific interest, funding limitations, recruitment requirements, and other considerations. Thus, criteria in research protocols that target or exclude certain populations are warranted where nondiscriminatory justifications establish that such criteria are appropriate with respect to the health or safety of the subjects, the scientific study design, or the purpose of the research.

For additional guidance regarding how the provisions apply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA. HHS provides general guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see http://www.hhs.gov/ocr/civilrights/resources/laws/revisedlep.html. The HHS Office for Civil Rights also provides guidance on complying with civil rights laws enforced by HHS. Please see http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html (http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html); and http://www.hhs.gov/ocr/civilrights/understanding/index.html (http://www.hhs.gov/ocr/civilrights/understanding/index.html). Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html (http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html). Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at http://www.hhs.gov/ocr/office/about/rgn-hqaddresses.html (http://www.hhs.gov/ocr/office/about/rgn-hqaddresses.html) or call 1-800-368-1019 or TDD 1-800-537-7697. Also note it is an HHS Departmental goal to ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations. For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53 (http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53).

In accordance with the statutory provisions contained in Section 872 of the Duncan Hunter National Defense Authorization Act of Fiscal Year 2009 (Public Law 110-417), NIH awards will be subject to the Federal Awardee Performance and Integrity Information System (FAPIIS) requirements. FAPIIS requires Federal award making officials to review and consider information about an applicant in the designated integrity and performance system (currently FAPIIS) prior to making an award. An applicant, at its option, may review information in the designated integrity and performance systems accessible through FAPIIS and comment on any information about itself that a Federal agency previously entered and is currently in FAPIIS. The Federal awarding agency will consider any comments by the applicant, in addition to other information in FAPIIS, in making a judgement about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review of risk posed by applicants as described in 45 CFR Part 75.205 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable OMB administrative guidelines, HHS grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for:

defining of research objectives and approaches, planning, conducting, analyzing, and publishing results, interpretations, and conclusion of their studies and for providing overall scientific and administrative leadership for the Research Project.

Supervising of the clinical study with consistent emphasis on collaborative interactions between investigators, advisory and steering committees, and NINDS representatives.

Interacting with the NeuroNEXT Clinical Coordinating Center and the NeuroNEXT Data Coordinating Center as well as any ad hoc sites.

Acquiring an IND from the FDA if an investigational agent is to be used,

Acting as a member of the NeuroNEXT steering committee for the duration of the study with possible participation in steering groups for planning, quality control, capitation, publications etc.

Awardees will retain custody of and have primary rights to data and software developed under this award, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

NINDS staff will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

NINDS staff involvement will include oversight of the IRB approved protocol by the NINDS Program Official, documentation of adequate serious adverse event management and reporting, and regular communications with the principal investigator and staff; additional involvement generally includes participation in meetings of the steering committee and other leadership committees. Specifically:

An NINDS Project Scientist working with the network investigators will develop milestones for the study. Failure to meet the agreed upon milestones may result in reduced funding or early termination of the cooperative agreement. The NINDS retains the option to obtain periodic external peer review of progress.

The NINDS Project Scientist will function as one of several co-investigators, collaborating and interacting as necessary with the Principal Investigators in accomplishing the overall goals of the Research Program.

In addition, an NINDS Program Official will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice.

A separate NINDS Program Official, from the Office of Clinical Research, will serve as the NINDS liaison to the Data and Safety Monitoring Board.

If the proposed trial should require that FDA issue an IND, the NINDS Project Scientist and/or Program Official(s) will be present at any meetings held with the FDA related to this NIH-funded protocol.

As with any award, even during the period recommended for support, continuation is conditional upon satisfactory progress. If, at any time, recruitment falls significantly below the projected milestones for recruitment,

the NINDS will consider ending support and negotiating a phase-out of the award. The NINDS retains the option to obtain periodic external peer review of progress. Milestones will be established by the NINDS prior to the award of the grant based on recommendations from the primary review group. NINDs will make an award for 2 to 3 years in order to start-up the trial and establish performance feasibility. Continuation of the award past this feasibility period will be contingent upon a demonstrated ability to meet milestones indicating that the trial can be implemented as planned. Feasibility milestones will be defined at the start of each trial and will be monitored closely by the Institute-appointed Data and Safety Monitoring Board (DSMB) and NINDS Program Official. Achievement of these milestones will be evaluated by NINDS prior to releasing funding for each year of the award and failure to achieve these milestones may lead to study termination.

Areas of Joint Responsibility include:

None; all responsibilities are divided between awardees and NIH staff as described above.

Dispute Resolution:

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to dispute resolution. A Dispute Resolution Panel composed of three members will be convened. It will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure in no way affects the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulations 45 CFR Part 16.

3. Reporting

When multiple years are involved, awardees will be required to submit the Research Performance Progress Report (RPPR) (//grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161)

A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161).

The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for awardees of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All awardees of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11170) on all subawards over $25,000. See the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11171) for additional information on this reporting requirement.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value greater than $10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of information reported in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). As required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 2011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts

eRA Service Desk (Questions regarding ASSIST, eRA Commons registration, submitting and tracking an application, documenting system problems that threaten submission by the due date, post submission issues)
Finding Help Online: http://grants.nih.gov/support/ (//grants.nih.gov/support/) (preferred method of contact)
Telephone: 301-402-7469 or 866-504-9552 (Toll Free)

Grants.gov Customer Support (//grants.nih.gov/grants/guide/url_redirect.htm?id=82301) (Questions regarding Grants.gov registration and submission, downloading forms and application packages)
Contact Center Telephone: 800-518-4726
Email: support@grants.gov (mailto:support@grants.gov)

GrantsInfo (Questions regarding application instructions and process, finding NIH grant resources)
Email: GrantsInfo@nih.gov (mailto:GrantsInfo@nih.gov) (preferred method of contact)
Telephone: 301-945-7573

Scientific/Research Contact(s)

Codrin Lungu, MD
National Institute of Neurological Disorders and Stroke (NINDS)
Telephone: 301-496-9135
Email: lunguci@ninds.nih.gov (mailto:lunguci@ninds.nih.gov)

Peer Review Contact(s)

Scientific Review Branch
National Institute of Neurological Disorders and Stroke (NINDS)
Telephone: 301-496-9223
Email: nindsreview.nih.gov@mail.nih.gov (mailto:nindsreview.nih.gov@mail.nih.gov).

Financial/Grants Management Contact(s)

Tijuanna DeCoster, MPA, Ph.D.
National Institute of Neurological Disorders & Stroke (NINDS)
Telephone: 301-496-9231
Email: decoster@mail.nih.gov (mailto:decoster@mail.nih.gov)

Section VIII. Other Information

Recently issued trans-NIH policy notices (//grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the *NIH Guide for Grants and Contracts* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 45 CFR Part 75.

Weekly TOC for this Announcement (/grants/guide/WeeklyIndex.cfm?12-22-17)
NIH Funding Opportunities and Notices (/grants/guide/index.html)