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 (https://www.ninds.nih.gov/))
National Eye Institute (NEI (https://www.nei.nih.gov/))

National Institute on Aging (NIA (https://www.nia.nih.gov/))

National Institute on Alcohol Abuse and Alcoholism (NIAAA (https://www.niaaa.nih.gov/))

National Institute of Biomedical Imaging and Bioengineering (NIBIB (https://www.nibib.nih.gov/))

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD (https://www.nichd.nih.gov/))

National Institute on Deafness and Other Communication Disorders (NIDCD (https://www.nidcd.nih.gov/))

National Institute on Drug Abuse (NIDA (https://www.drugabuse.gov/))

National Institute of Mental Health (NIMH (https://www.nimh.nih.gov/index.shtml))

National Center for Complementary and Integrative Health (NCCIH (https://nccih.nih.gov/))

Funding Opportunity Title

BRAIN Initiative: Biology and Biophysics of Neural Stimulation and Recording Technologies (R01 Clinical Trials Optional)

Activity Code

R01 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r01&Search.x=0&Search.y=0&Search_Type=Activity) Research Project Grant

Announcement Type

Reissue of RFA-NS-18-018 (https://grants.nih.gov/grants/guide/rfa-files/rfa-ns-18-018.html)

Related Notices

March 10, 2020 - Reminder: FORMS-F Grant Application Forms & Instructions Must be Used for Due Dates On or After May 25, 2020- New Grant Application Instructions Now Available. See Notice NOT-OD-20-077 (/grants/guide/notice-files/NOT-OD-20-077.html).

July 26, 2019- Changes to NIH Requirements Regarding Proposed Human Fetal Tissue Research. See Notice NOT-OD-19-128 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-128.html)

August 23, 2019- Clarifying Competing Application Instructions and Notice of Publication of Frequently Asked Questions (FAQs) Regarding Proposed Human Fetal Tissue Research. See Notice NOT-OD-19-137 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-137.html)

Funding Opportunity Announcement (FOA) Number

RFA-NS-20-006

Companion Funding Opportunity

None

Number of Applications

See Section III. 3. Additional Information on Eligibility.

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

93.853; 93.865; 93.866; 93.286; 93.867; 93.173; 93.273; 93.279; 93.242; 93.213

Funding Opportunity Purpose

A central goal of the BRAIN Initiative is to develop new and improved technologies suitable for recording from as well as controlling specified cell types and circuits to modulate and understand function in the central nervous system. In order to accomplish these goals, further information is needed to understand the function of current technologies used for recording or stimulating the nervous system.

This RFA accepts grant applications in two related but distinct areas. The first is to systematically characterize, model, and validate the membrane, cellular, circuit, and adaptive-biological responses of neuronal and non-neuronal cells to various types of stimulation technologies. The second is to understand the biological and bioinformatic content of signals recorded from neuronal and non-neuronal cells and circuits. Development of new technologies, therapies and disease models is outside the scope of this FOA. Activities related to enabling the simultaneous use of multiple recording or stimulation technologies are allowed.

Key Dates

Posted Date

January 2, 2020

Open Date (Earliest Submission Date)

February 24, 2020

Letter of Intent Due Date(s)

30 days prior to the application due date.

Application Due Date(s)

March 24, 2020, June 2, 2020, October 1, 2020, February 2, 2021, June 1, 2021, October 1, 2021, February 1, 2022, June 1, 2022, and October 3, 2022
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.

All applications are due by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on the listed date(s).

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

June 2020, October 2020, February 2021, June 2021, October 2021, February 2022, June 2022, October 2022, February 2023

Advisory Council Review

October 2020, January 2021, May 2021, October 2021, January 2022, May 2022, October 2022, January 2023, May 2023

Earliest Start Date

November 2020, February 2021, June 2021, November 2021, February 2022, June 2022, November 2022, February 2023, June 2023

Expiration Date

October 04, 2022

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the instructions in 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 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 (/grants/guide/ApplyButtonSplash.cfm?dest=https://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.

3. Use Grants.gov (/grants/guide/ApplyButtonSplash.cfm?dest=GrantsGov&oppNum=RFA-NS-20-006) Workspace to prepare and submit your application and eRA Commons (/grants/guide/ApplyButtonSplash.cfm?dest=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

The BRAIN Initiative

The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative® is aimed at revolutionizing our understanding of the human brain. By accelerating the development and application of innovative technologies, researchers will be able to produce a new dynamic picture of the brain that, for the first time, will show how individual cells and complex neural circuits interact in both time and space. It is expected that the application of these new tools and technologies will ultimately lead to new ways to treat and prevent brain disorders.

NIH is one of several federal agencies involved in the BRAIN Initiative. Planning for the NIH component of the BRAIN initiative is guided by the long-term scientific plan, "BRAIN 2025: A Scientific Vision (http://braininitiative.nih.gov/pdf/BRAIN2025_508C.pdf)," which details seven high-priority research areas and calls for a sustained federal commitment of $4.5 billion over 12 years. This Funding Opportunity Announcement (FOA) and other FOAs issued in Fiscal Year 2020 are based on careful consideration by the NIH of the recommendations of the BRAIN 2025 Report, and input from the NIH BRAIN Multi-Council Working Group. Videocasts of the NIH BRAIN Multi-council Working Group are available at http://www.braininitiative.nih.gov/about/mcwg.htm (http://www.braininitiative.nih.gov/about/mcwg.htm).

To enable rapid progress in development of new technologies as well as in theory and data analysis, the BRAIN Initiative encourages collaborations between neurobiologists and scientists from statistics, physics, mathematics, engineering, and computer and information sciences; and NIH welcomes applications from investigators in these disciplines.

As noted in NOT-OD-20-031 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-031.html), NIH encourages BRAIN Initiative applications from investigators that are underrepresented in the biomedical, behavioral, or clinical research workforce (see data at http://www.nsf.gov/statistics/showpub.cfm?TopID=2&SubID=27 (http://www.nsf.gov/statistics/showpub.cfm?TopID=2&SubID=27) and the most recent report on Women, Minorities, and Persons with Disabilities in Science and Engineering (http://www.nsf.gov/statistics/women/)). Such individuals include those from underrepresented racial and ethnic groups, those with disabilities, and those from disadvantaged backgrounds.

NIH also encourages businesses to participate in the BRAIN Initiative. It is possible for companies to submit applications directly to BRAIN Initiative program announcements or to collaborate with academic researchers in joint submissions. Small businesses should consider applying to one of the BRAIN Initiative small business FOAs (http://braininitiative.nih.gov/funding/index.htm (http://braininitiative.nih.gov/funding/index.htm)).

In addition to the BRAIN Initiative, the NIH continues to have a substantial annual investment in neuroscience research. The Institutes and Centers contributing to the NIH BRAIN Initiative (http://braininitiative.nih.gov/ (http://braininitiative.nih.gov/%20)) support those research efforts through investigator-initiated applications as well as through specific FOAs. Potential applicants to this FOA are strongly encouraged to contact Scientific/Program staff if they have any questions about the best FOA for their research.

The BRAIN Initiative will require a high level of coordination and sharing between investigators. While this FOA does not use a cooperative agreement mechanism, it is expected that BRAIN Initiative awardees will cooperate and coordinate their activities after awards are made by participating in Program Director/Principal Investigator (PD/PI) meetings and in other activities.

Objectives

This FOA is related to the recommendations in sections III.4. of the BRAIN 2025 report on demonstrating causality through the use of precise interventional tools that change the neural circuit dynamics and/or generating circuit diagrams that span resolutions from synapses to the whole brain as outlined in section III.2. The report also acknowledges that in order to "probe the mechanics of the brain more deeply, we must develop a better understanding of the biophysical properties of modulating neurons. In the same way that the basic electrophysiological properties of single neurons are common across brain areas and species, it is likely that many fundamental forms of neural dynamics will generalize as well." Implicit in this is the need to understand the cellular and local circuit responses to neural technologies that are used to record, stimulate, and modulate neural dynamics.

The current suite of BRAIN Initiative FOAs ranges from testing new concepts for large scale recording and modulation, developing and optimizing tools for invasive and non-invasive neuromodulation, to pre-clinical and

clinical studies of next generation recording and modulation technologies. This FOA fills the gap in understanding how fields produced by stimulating technologies affect the brain at a basic cellular or circuit level and understanding the origin of biological signals recorded from the brain. The new stimulation, recording, and mapping tools developed within the BRAIN initiative provide an ample toolset that can now be employed to address this gap.

The goal of this FOA is two-fold: (1) To systematically characterize, model, and validate the neurobiological, cellular, and circuit responses of neuronal and non-neuronal cells in the central nervous system (CNS) to fields produced by neural stimulation, and (2) To understand the biological and bioinformatic content of signals recorded from neuronal and non-neuronal cells and circuits in terms of the shape, size, orientation, propagation, and location of signal generators at varying temporal/spatial scales. Proposed studies should lead to deeper understanding of how electrical and chemical activities in different populations of neurons and glia are represented in macroscopic-level measurements of brain structure and function. In this context, “validation” is defined as models at the cellular and local circuit level, however, models may span multiple scales from non-invasively applied fields down to electrical stimulation from micro and nanoscale devices. Proposed outcomes from these efforts may include: cell activation thresholds, sub-threshold changes to membrane voltage, cellular morphological changes, metabolic changes, changes in cell-cell interactions, the many possible aspects of local circuit plasticity in response to varied stimulation protocols, defining principles by which signals decay or amplify across scales, and/or understanding of the structure/function relationship of defined units in the brain using recording techniques.

Examples of In Scope Activities:

- Experiments to characterize cellular responses to stimulation in appropriate model systems (e.g., in cells or tissues, animals, humans), including effects on metabolic processes, cell morphology, and cell-cell interactions
- Use of model systems ranging in scales from in vitro testing to understanding stimulation fields in humans
- Characterizing safety limits for various neural stimulation technology paradigms on tissues
- Field modeling of non-homogenous neural tissues to understand field dynamics to inform stimulating/recording strategies
- Spatio-temporal models across scales defining the location and degree of activation of different cell types
- Exploration of differences in expression (genes and proteins) of neurons and non-neuronal cells exposed to acute and chronic stimulation fields of different pulse shapes and waveforms using state of the art stimulating technologies
- Bioinformatic studies aimed at understanding the epigenetic implications of chronic stimulation
- Experiments using multiple modalities to evaluate biological and biophysical characteristics of stimulating and recording technologies as long as at least one modality has sufficient resolution to evaluate the neurobiology at a cellular or local circuit level. One example isneural stimulation via an electrocorticography (ECoG) grid, with a high-resolution tool used concurrently to record. Another example is exploring the biophysical sources of the major brain rhythms that are present in electroencephalography (EEG) or magnetoencephalography (MEG) recordings.
- Studies to understand the origin (biology, biophysics, and spatial/temporal dynamics, etc.) of biological and bioinformatic content of data collected from cellular or local circuit level central nervous system recording techniques
- Experiments to determine the structural and functional underpinning, such as synaptic activity and the organization of neuronal and non-neuronal cells, of recorded biological signals
- Use of drugs and other chemical perturbations are responsive if used towards understanding the mechanism of the neural simulation or recording modality
- Experiments focused on understanding the effects of material properties or coatings on the short and / or long-term recording/stimulation performance of implanted devices

Examples of Out of Scope / Non-responsive Activities:

- Development of novel tools for recording or modulation, as these are covered under other BRAIN Initiative opportunities (RFA-NS-18-019 (https://grants.nih.gov/grants/guide/rfa-files/RFA-NS-18-019.html), RFA-NS-18-020 (https://grants.nih.gov/grants/guide/rfa-files/RFA-NS-18-020.html), RFA-MH-20-310 (https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-20-310.html))
- Studies focusing on functional magnetic resonance imaging (fMRI), as these have been extensively covered under other BRAIN Initiative opportunities (RFA-MH-17-235 (https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-17-235.html))
- Investigating the effect of a stimulation technology or recording technique in a disease model system
- Evaluation of therapies to alleviate a disease / disorder in humans
- Validating models using non-neurophysiological measures or behavioral measures in the absence of cellular and circuit recordings

- Development of theoretical models without experimental validation
- Studies aimed at understanding or using magnetic resonance imaging, electroencephalography (EEG), electrocorticography (ECoG), or similar superficial or global recording techniques *in isolation* are not responsive to this FOA as they do not provide sufficient resolution to evaluate the neurobiology at a cellular or local circuit level.

If proposing a clinical trial, this FOA will only accept applications that propose mechanistic trials/studies. NIH defines a mechanistic clinical trial as follows: "A mechanistic study is designed to understand a biological or behavioral process, the pathophysiology of a disease, or the mechanism of action of an intervention."

The goal is to address basic questions and to interrogate concepts in biology, biophysics, and physiology that will provide insight into understanding neural stimulation and recording techniques. Such studies may seek to understand a biological process or the mechanism of action of an intervention or provide information about physiological function. The submitted studies may be defined as clinical trials (as noted above) but do not seek to answer specific questions about safety, tolerability, clinical efficacy, effectiveness, clinical management, and/or implementation of pharmacologic, behavioral, biologic, surgical, or device (invasive or non-invasive) interventions.

Consortium Details: Investigators will be required to participate in a consortium to develop standards and model systems for the evaluation of current and next generation neuromodulation technologies. All investigators should plan to share data and models with the consortium within the early stages of the award, as well as public sharing to the greater community at predefined stages throughout the project. Plans for data sharing and consortium participation should be included as project milestones. See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Grant: A support mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity.

Application Types Allowed

New
Renewal
Resubmission
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. Only those application types listed here are allowed for this FOA.

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

NIH anticipates providing $10M per year to fund an estimated 10 to 15 awards

Award Budget

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

Award Project Period

The scope of the proposed project should determine the project period. The maximum project period is 5 years.

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 - Including the NIH Intramural Program
- 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/) – 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 to register in eRA Commons.Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration, but all registrations must be in place by time of submission. 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 – 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

The application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional system-to-system solution. Links to apply using ASSIST or Grants.gov Workspace 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 instructions in 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.

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:

Sahana N. Kukke, PhD
National Institute of Neurological Disorders and Stroke (NINDS)
Email: BRAIN-FOAs@nih.gov (mailto:BRAIN-FOAs@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.

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 include funds necessary for travel for key personnel to participate in a NIH-organized BRAIN investigator meeting, lasting not more than four days and including up to four overnight stays, for each year of the project. Funds should also be requested for an additional one-day data sharing consortium meeting per year, as well as funds necessary to facilitate sharing of data, models, and other work products developed as part of the application.

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: Research Strategy: The purpose of this FOA is to understand the mechanism of action of how applied neural stimulation affects the CNS, to understand the biological and bioinformatic content of data collected from the CNS, as well as develop protocols for testing the next generation of tools and techniques that are developed within the BRAIN Initiative. To this end, experiments should be designed toward modeling or advancing the state of biological knowledge of applied stimulation on complex neural tissue or understanding the biological origins of recorded signals from the brain, rather than technology development. Applicants are expected to explain the model system to be used. As opposed to more traditional hypothesis-driven scientific exploration, it is expected that the proposed studies to this FOA systematically evaluate parameters relevant to the stimulating or recording technique being studied.

Experimental designs should be largely driven by parameters that have shown pre-clinical or clinical efficacy in prior studies. However, exploration of novel waveforms that may enable fine-tuned control of neural tissue is also encouraged.

Current State of the Art: Applicants should describe the type of applied stimulation or recording signal/technique proposed in their study and compare it to the current state-of-the-art in device/modalities and its significance in current experimental/clinical use. Applicants should propose advanced techniques for evaluating cellular and circuit level activity. Since many of these techniques are actively being developed, it is expected that investigators will have little to no preliminary data applying these techniques towards understanding the measured activity and responses to stimulation. However, it is expected that investigators assemble a multidisciplinary team that is sufficiently experienced in these varied techniques to apply them to this problem area.

Milestones and Timeline: A timeline and milestones must be included that propose indicators of progress at critical junctures. These should be tailored to the unique scope of each project and written concretely enough to evaluate what exactly will have been achieved at timepoints along the course of the project.

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.
The following modifications also apply:

A central goal of this FOA is to further advance research by generating computational models and new methods that will be widely used throughout the research community. Applications are expected to include a detailed plan for dissemination and sustainability of proposed resources, consistent with achieving the goals of this program.

- Investigators will be required to participate in a consortium to develop standards and model systems for the evaluation of current and next generation neuromodulation technologies. All investigators should plan to share data and models with the consortium within the early stages of the award, as well as public sharing to the greater community at predefined stages throughout the project.
- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan. The BRAIN Initiative has published a guide notice in reference to data sharing (NOT-MH-19-010 (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-19-010.html)). Data sharing plans should reflect the guidance in this notice.

Appendix:

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

PHS Human Subjects and Clinical Trials Information

When involving human subjects research, clinical research, and/or NIH-definedclinical 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.

Delayed Onset Study
Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).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 described throughout the SF424 (R&R) Application Guide.

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.html?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 How to Apply – Application Guide (https://grants.nih.gov/grants/how-to-apply-application-guide.html). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Dealing with System Issues (https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm) guidance. 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 and responsiveness by components of participating organizations, NIH. Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed. **Applications Involving the NIH Intramural Research Program**

The requests by NIH Intramural Scientists will be limited to the incremental costs required for participation. As such, these requests will not include any salary and related fringe benefits for career, career conditional or other Federal employees (civilian or uniformed service) with permanent appointments under existing position ceilings or any costs related to administrative or facilities support (equivalent to Facilities and Administrative or F&A costs). These costs may include salary for staff to be specifically hired under a temporary appointment for the project, consultant costs, equipment, supplies, travel, and other items typically listed under Other Expenses. Applicants should indicate the number of person-months devoted to the project, even if no funds are requested for salary and fringe benefits.

If selected, appropriate funding will be provided by the NIH Intramural Program. NIH intramural scientists will participate in this program as PDs/PIs in accord with the Terms and Conditions provided in this FOA. Intellectual property will be managed in accord with established policy of the NIH in compliance with Executive Order 10096, as amended, 45 CFR Part 7; patent rights for inventions developed in NIH facilities are NIH property unless NIH waives its rights.

Should an extramural application include the collaboration with an intramural scientist, no funds for the support of the intramural scientist may be requested in the application. The intramural scientist may submit a separate request for intramural funding as described above.

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. Applications submitted to the NIH in support of the NIH mission (//grants.nih.gov/grants/guide/url_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

For this particular announcement, note the following:

The nature of the proposed work in this FOA likely results in the proposed studies being more exploratory and design-driven as opposed to hypothesis-driven. Experimental designs evaluating stimulating technologies should be largely driven by parameters that have shown pre-clinical or clinical efficacy in prior studies, but may also include exploration of novel waveforms. The applications should be evaluated in that context with an emphasis on the systematic approach for evaluation and use of advanced techniques for evaluating cellular and circuit level activity. Since many of these techniques are actively being developed, it is expected that investigators will have little to no preliminary data applying these techniques towards understanding these measurements. However, it is expected that investigators assemble a multidisciplinary team that is sufficiently experienced in these varied techniques to apply them to this problem area.

In addition, for applications involving 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 leads to new avenues of scientific investigation.

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 the prior research that serves as the key support for the proposed project rigorous? 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 involving 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?

Specific to this announcement:

- If successful, will the results be generalizable to other uses of the stimulation modality and lay the foundation for understanding how neural stimulation affects the CNS?
    - Will information from this study be useful for the development of protocols for testing the next generation of tools and techniques that are developed within the BRAIN Initiative?
- Will achieving the research goals likely improve our understanding of cellular mechanisms underlying commonly measured brain signals observed through recording techniques? Has the state-of-the-art been accurately described?

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 involving 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?

Specific to this announcement:

Does this application include a multidisciplinary team with expertise spanning the required neuroscience, cellular / molecular biology, and neural stimulation or recording necessary to accomplish the proposed work? Is sufficient expertise present on the team to extrapolate the acquired data into useful models and work products that can be shared with the broader consortium and the BRAIN community?

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 involving 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 included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed 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 involving 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?

Specific to this announcement:

- Are the experiments formulated to understand how the applied neural stimulation field interacts with cells and circuits or to understand biological and bioinformatic signals recorded from cells and circuits?
- Are the experiments formulated to understand how neural stimulation technologies affect surrounding neuronal and / or non-neuronal cells and/or understanding relevant signals from these cell populations?
- Are the experiments designed in a sufficiently systematic way to explore the vast parameter space to reveal mechanisms of action for the proposed neural stimulation modality or recording technique?
- Is the proposed suite of tools utilized to evaluate the neural stimulation modality/recording technique of sufficient temporal and spatial specificity to appropriately probe the underlying functional mechanisms?
- Have appropriate milestones been identified to measure progress? Is the proposed timeline reasonable to accomplish the planned experiments?

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 individuals of all ages (including children and older adults), 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 involving 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.

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 for applications involving 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)?

Protections for Human Subjects

For research that involves human subjects but does not involve one of thecategories 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 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 Individuals Across the Lifespan

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 individuals of all ages (including children and older adults) 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

Not Applicable

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), 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.

Appeals (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-064.html) of initial peer review will not be accepted for applications submitted in response to this FOA. Applications will be assigned to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications submitted in response

to this FOA. Following initial peer review, recommended applications will receive a second level of review by the National Advisory Neurological Disorders and Stroke 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.

Additionally, ICs may specify any special reporting requirements for the proposed clinical trial to be included under IC-specific terms and conditions in the NoA. For example: If the proposed clinical trial has elevated risks, ICs may require closer programmatic monitoring and it may be necessary to require the awardee to provide more frequent information and data as a term of the award (e.g., to clarify issues, address and evaluate concerns, provide documentation). 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.

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.

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 https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/index.html (https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/index.html). The HHS Office for Civil Rights also provides guidance on complying with civil rights laws enforced by HHS. Please see https://www.hhs.gov/civil-rights/for-individuals/section-1557/index.html (https://www.hhs.gov/civil-rights/for-individuals/section-1557/index.html)https://www.hhs.gov/civil-rights/for-providers/laws-regulations-guidance/index.html (https://www.hhs.gov/civil-rights/for-providers/laws-regulations-guidance/index.html). Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see https://www.hhs.gov/civil-rights/for-individuals/disability/index.html (https://www.hhs.gov/civil-rights/for-individuals/disability/index.html). Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at https://www.hhs.gov/ocr/about-us/contact-us/index.html (https://www.hhs.gov/ocr/about-us/contact-us/index.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).

Cooperative Agreement Terms and Conditions of Award

Not Applicable

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 agreementsare 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, application errors and warnings, documenting system problems that threatensubmission by the due date, and 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)

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

Grants.gov Customer Support(Questions regarding Grants.gov registration and Workspace)
Contact Center Telephone: 800-518-4726
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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?01-03-20)
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