Part 1. Overview Information

Participating Organization(s)

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

Components of Participating Organizations

National Institute of Mental Health (NIMH (http://www.nimh.nih.gov/))

Funding Opportunity Title

Neuromodulation/Neurostimulation Device Development for Mental Health Applications (R21 Clinical Trial Optional)

Activity Code

R21 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r21&Search.x=0&Search.y=0&Search_Type=Activity) Exploratory/Developmental Research Grant

Announcement Type

New

Related Notices

- **November 26, 2018** - NIH & AHRQ Announce Upcoming Updates to Application Instructions and Review Criteria for Research Grant Applications. See Notice NOT-OD-18-228 (/grants/guide/notice-files/NOT-OD-18-228.html).
- October 23, 2018 (//grants.nih.gov/grants/guide/notice-files/NOT-MH-18-060.html) -Notice to Extend PAR-18-941. See Notice NOT-MH-18-060 (//grants.nih.gov/grants/guide/notice-files/NOT-MH-18-060.html).

Funding Opportunity Announcement (FOA) Number

PAR-18-941

Companion Funding Opportunity

PAR-18-942 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-942.html) R01, Research Project Grants

Number of Applications

See Section III. 3. Additional Information on Eligibility.

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

93.242

Funding Opportunity Purpose

The purpose of this funding opportunity announcement (FOA) is to encourage applications seeking to develop the next generation of brain stimulation devices for treating mental health disorders. Applications are sought that will either 1) develop novel brain stimulation devices or 2) significantly enhance, by means of hardware/software improvements, the effectiveness of brain stimulation devices that are currently U.S. Food and Drug Administration (FDA)-approved or cleared. Novel devices should move beyond existing electrical/magnetic stimulation and develop new stimulation techniques capable of increased spatiotemporal precision as well as multi-focal, closed-loop approaches. Applications seeking to develop new capabilities should focus on significant enhancement of the spatial resolution, depth of delivery, and/or precision of the device. Incremental changes to existing devices (e.g., software updates) are not within the scope of this announcement. Applications should be submitted by multi-disciplinary teams with diverse expertise including systems neuroscience, engineering, clinical, and regulatory affairs. Applications submitted in response to this FOA should promote the development or significant enhancement of novel tools (hardware/software) for brain stimulation in humans. Although the application should focus on the engineering development and bench top testing of the tool, animals and limited human testing necessary to demonstrate initial proof of concept is allowable. Applications to this FOA are not expected to be hypothesis-driven, but should propose design-directed, developmental, or discovery-driven technology research using integrative approaches. Applications that seek to study scientific or clinical hypotheses that simply utilize devices are outside the scope of this FOA. This FOA uses the R21 grant mechanism, encouraging shorter, higher-risk applications, whereas its companion funding opportunity seeks R01 grant applications.

Key Dates

Posted Date

September 27, 2018

Open Date (Earliest Submission Date)

October 27, 2018

Letter of Intent Due Date(s)

Not Applicable

Application Due Date(s)

New Date November 26, 2018, and then standard dates 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

New Date February 2019 and then standard dates apply

Advisory Council Review

New Date May 2019 and then standard dates apply

Earliest Start Date

July 2019

Expiration Date

New Date September 8, 2021 per issuance of NOT-MH-18-060 (//grants.nih.gov/grants/guide/notice-files/NOT-MH-18-060.html). (Original Expiration Date: November 27, 2018)

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 (http://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.
3. Use Grants.gov (http://www.grants.gov/web/grants/applicants/download-application-package.html#search=true&oppNum=PAR-18-941) 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

The use of brain stimulation devices provides a unique opportunity to develop novel treatments for mental health disorders. Brain stimulation devices provide both the most efficacious (electroconvulsive therapy, ECT) and one of the most recently-cleared (transcranial magnetic stimulation, TMS) treatments for depression. However, while these successes demonstrate the potential to improve clinical care, limitations of the few existing FDA approved/cleared devices (e.g., cognitive side effects of ECT, variability in response to TMS) hamper widespread clinical use. In order to develop efficacious treatments that will be widely utilized across a variety of disorders, the development of innovative brain stimulation devices and novel approaches with existing devices is urgently needed.

New devices, developed with a focus on aspects unique to mental health indications, are needed to fully explore the potential of brain stimulation treatments. The majority of clinical studies using brain stimulation therapies for mental health disorders utilize existing devices developed for other neurological conditions. Deep brain stimulation (DBS) and vagal nerve stimulation (VNS) electrodes were developed for the treatment of Parkinson's Disease and epilepsy. They have subsequently been studied, with minimal to no modification, for use in mental health disorders with mixed results. New devices, whose development is informed by basic and clinical science findings in mental health research, may provide improved treatments for patients. For example, while current DBS electrodes are limited to one or two stimulation sites, neuroimaging studies have demonstrated the distributed, network-based nature of mental health disorders. Therefore, distributed, multi-focal electrode arrays may be necessary to modulate networks back into a desired state. New forms of energy (e.g., ultrasound) also have the potential to be incorporated into the next generation of brain stimulation devices.

In addition to the development of new devices, significantly enhancing the capabilities of existing devices presents an opportunity to improve clinical care. While drug treatments become static (in terms of chemical composition) once developed, brain stimulation devices are amenable to hardware/software changes that can readily translate to improved patient care. Examples of these approaches include development of real time electric field (e-field) modeling software and augmented reality delivery systems to enable practitioners to interactively target regions of interest with TMS. The ability to close the loop with a brain stimulation device and neuroimaging/recordings could also result in improved clinical outcomes.

Improved devices that focus on developing novel approaches to delivery of previously demonstrated effective treatments are also of interest. Although ECT provides the best remission rates for

depression, the widespread generalized seizure induced by the device produces cognitive side effects that limit its use. The development of novel devices that deliver more focused stimulation resulting in a smaller, controllable seizure, may produce high levels of response while minimizing side effects. Additionally, approaches that improve the focality, depth, or closed-loop delivery of TMS could improve response rates.

Research Objectives

This funding opportunity announcement (FOA) encourages the development of novel brain stimulation devices and accompanying software/hardware additions that enable improved delivery of brain stimulation treatments for mental health indications. Applications should be submitted by multi-disciplinary teams with expertise in systems neuroscience, engineering, clinical, and regulatory affairs and promote either the development of novel tools (hardware/software) or significant enhancement of existing tools (hardware/software). Applications should be engineering/pre-clinical based and focus on hardware and software development and validation. Although the application should focus on the engineering development of the tool, animal and limited human testing to demonstrate initial proof of concept is allowable. ?Applications that seek to study specific scientific or clinical hypotheses that utilize devices are outside the scope of this FOA. The R21 grant mechanism of this FOA it to encourage high risk, proof of concept, applicationssthat may lack preliminary data, or smaller projects that are closer to final form and do not require longer timefor development and innovation.

Applications may propose to develop novel invasive or non-invasive brain stimulation devices. New devices should be designed to significantly advance the field and go beyond current stimulation and low-channel count recording/stimulating capabilities. Existing magnetic and electrical stimulation methods have limited spatial and temporal precision. To overcome these obstacles and move beyond incremental advances, collaborations between physicists, engineers, neuroscientists, and clinicians are encouraged. The perspective and expertise of such integrative teams could enable the development and testing of novel approaches that leverage other types of energy or stimulation methods in a way that can lead to novel tools for scientific discovery and for therapeutic brain stimulation. Applications that propose to improve spatiotemporal precision, stimulate at depth, enable multi-focal recording/stimulation, and utilize novel stimulation paradigms are encouraged. Appropriate modeling and preliminary data should be presented to demonstrate the feasibility of the stated approach. While the application may be in the initial stages of device development and may therefore still be in the animal testing phase, the proposed tools and methods must be designed for use in humans. Animal testing should focus on questions of safety. Industry partnership is encouraged and should be detailed in the application. The regulatory process for the new technology should be described in the application, when applicable.

Applications may also propose to develop additional capabilities for existing FDA-approved or cleared brain stimulation devices and related technologies. However, proposed improvements to existing devices and related technology should be significant and innovative, rather than incremental. Appropriate improvements may include: 1) incorporating advanced approaches to stimulation delivery, such as real-time realistic head/electric field modeling that incorporates patient-specific tractography or cellular-level resolution; 2) synchronizing behavioral recordings with brain recordings in novel ways; or 3) developing novel delivery methods, such as augmented and virtual-reality approaches. For existing devices, approaches that seek to improve the focality and depth of stimulation, controllability of the delivered dose, sham control delivery, or recording capabilities are encouraged. Software approaches that seek to develop novel approaches (e.g., machine learning) to biomarker-driven targeted delivery of stimulation are also encouraged.

Topics of interest for this FOA include, but are not limited to:

- Multi-focal electrode interfaces. These devices should demonstrate the capability to record and stimulate distributed brain regions implicated in mental health disorders.
- Devices capable of both recording and stimulating neural activity, with the ability for closed-loop

control. These devices should be able to demonstrate clear capability to record oscillations of interest to mental health applications.
- Improved capabilities to synchronize behavioral data with neural data. Dense behavioral phenotyping is now possible, both in the lab and in naturalistic environments. The ability to temporally synchronize large behavioral data sets with large neural data sets is of high priority.
- Devices that enable targeted stimulation via optogenetic (or other circuit therapeutic) techniques in humans.
- Next-generation ECT devices that more focally deliver energy for controllable seizure generation.
- Validation of novel approaches, such as transcranial ultrasound for neuromodulation to stimulate the brain focally.
- A wireless, miniaturized, portable, and closed-loop EEG-stimulation system. Ideally, this should be of a size to be easily worn (i.e., fits comfortably inside a baseball cap).
- Improved portability of brain stimulation devices, without reduction in targeting capabilities.
- Pre-clinical studies necessary to obtain regulatory approval for human testing.
- Development of higher spatial resolution realistic head modeling approaches that improve the delivery of FDA-cleared treatments, such as TMS.
- Improved focality and depth of stimulation, along with controllability for FDA- approved or cleared devices for a particular indication.
- Development of closed-loop recording and stimulating for non-invasive devices, such that imaging/recording informs active stimulation.
- Software approaches, such as machine learning, that incorporate patient-specific biomarkers into brain stimulation treatment algorithms.
- New approaches to sham conditions that enable more reliable controlled trials.

Topics of low program priority include:

- Devices with low spatial resolution.
- Models that focus on standard brains and are not specific to individual patient anatomy.
- Incremental improvements to existing devices, such as operating software system updates.
- Devices with no clear potential for human application.

Innovation in this biomedical engineering FOA has a broad definition that includes development of new methods, ideas, or tools, integration of existing components into new combinations that deliver greater capabilities, new efficiencies, and/or greater effects. Applications to this FOA are not expected to be hypothesis-driven, but should propose design-directed, developmental, or discovery-driven technology research using integrative approaches. Overall impact of these advances may include reducing disparities in care, promoting wellness and independent living, increasing access to and utility of technologies to improve quality of life, reducing cost and complexity of procedures, and increasing throughput, sensitivity and specificity of diagnostic tests.

Applications seeking to explore scientific questions (in humans or animals) using novel brain stimulation devices should apply to the

NIH Parent R01 or NIH Parent Clinical Trial Required R21 (PA-18-344 (https://grants.nih.gov/grants/guide/pa-files/PA-18-344.html)) or NIMH R21 (PA-18-350 (https://grants.nih.gov/grants/guide/pa-files/PA-18-350.html)) funding opportunities.

Those seeking to assess devices as treatments in a clinical population should refer to the NIMH Policy for Submission of Applications Containing Clinical Trials NOT-MH-14-007 (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-14-007.html) and NIMH Only Accepts Clinical Trial Applications Proposing Mechanistic Studies for Clinical Trial Parent R01 and R21 Announcements NOT-MH-18-004 (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-18-004.html) for information on NIMH requirements.
This FOA will support mechanistic clinical trials, as defined by the NIH to include studies designed to

understand a biological or behavioral process, the pathophysiology of a disease, or the mechanism of action of an intervention. The proposed human clinical studies will meet the NIH definition of a clinical trial (see NOT-OD-15-015 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html)), but will not include studies whose primary purpose is to evaluate safety; clinical efficacy, effectiveness, and management; and/or implementation. Such trials will not be supported by this FOA. NIH Guide Notice NOT-MH-18-004 (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-18-004.html) describes the types of clinical trials that NIMH supports under the NIH Parent R01 (https://grants.nih.gov/grants/guide/pa-files/PA-18-345.html) and R21 Clinical Trial (https://grants.nih.gov/grants/guide/pa-files/PA-18-344.html) FOAs.

All applicants are strongly encouraged to contact the designated Scientific/Research Contacts at NIMH prior to submission. Applicants who seek to propose a larger project should respond to the companion R01 PAR-18-942 (//grants.nih.gov/grants/guide/pa-files/PAR-18-942.html)FOA. Small businesses should consider applying to the SBIR/STTR programs to support the technology development.

Institute Staff Involvement
A grant awarded under this FOA may be converted to a cooperative agreement (UH2) if substantial NIH scientific programmatic staff involvement is needed. NIH ICs routinely consider the desirability of substantial continued staff involvement in a supportive mode during the period of grant performance. Additional staff involvement may include review of the study protocol, participation on the steering committee and related meetings, and oversight of a data and safety monitoring board. If it is determined that the cooperative agreement mechanism is appropriate for an ongoing grant award, NIH program staff will consult with the grantee institution to mutually effect the conversion.

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
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

The combined budget for direct costs for the two-year project period may not exceed $275,000. No more than $200,000 may be requested in any single year.

Award Project Period

The total project period may not exceed 2 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
- 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 – 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.

Due to the transdisciplinary nature of the projects and the focus on collaboration and expertise sharing, this FOA requires the applicants to comprise a transdisciplinary team of investigators with expertise from fields such as engineering, device development, regulatory, physical, mathematical, computational sciences, as well as neuroscience, neuropsychiatry, and other areas of the biological sciences.

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 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.
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).

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.

Other Attachment:

Intellectual Property (IP) Strategy:

Applications are expected to include an IP strategy, and the page limit must be no more than three pages. Applications that exceed this limit will not be reviewed. This attachment should be entitled "IP Strategy.pdf". Applicants are encouraged to prepare this section of the application in consultation with their institution's technology transfer officials, if applicable.

A goal of this program initiative is to advance research towards the development of products that will benefit the public. Accordingly, applicants should describe the IP landscape surrounding their therapeutic device. This should include any known constraints that could impede the development of their therapeutic device or diagnostic (e.g., certain restrictions under transfer or sharing agreements, applicants' previous or present IP filings and publications, similar technologies that are under patent and/or on the market, etc.) and how these issues could be addressed as appropriate and consistent with achieving the goals of the program. If the applicant proposes using a device or technology whose IP is not owned by the applicant's institution, either an investigational therapeutic, FDA-approved therapeutic, or other licensed product, the applicant should address any questions that may constrain or impede its ability to operate and move the technology forward consistent with achieving the goals of the program. If patents pertinent to the therapeutic device being developed under this application have been filed, the applicants should indicate the details of filing dates, what types of patents are filed, application status, and associated United States Patent Office (USPTO) links, if applicable.

Applicants should also discuss future IP filing plans. For a multiple-PD/PI, multiple-institution application, applicants should describe how IP will be shared or otherwise managed, and the infrastructure of each institution for bringing the technologies to practical application and for coordinating these efforts (e.g., licensing, managing IP) among the institutions.

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.

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:

The Research Strategy should clearly address the purpose of this FOA and indicate:

- How the proposed approach will use the concepts from engineering, physical science, computational or other multidisciplinary methods to address the biomedical problem identified in the application.
- How the investigative team demonstrates sufficient depth and breadth of the multiple disciplines necessary to complete the project.
- Anticipated risks and limitations.

Any animal or human testing should be justified in the context of necessity for device development. Any proposed work in animals must include a description of how the methods would be scaled up for use in humans. In recognition of the fact that these methods might be in early stages of development, work with human volunteers can, but does not need to, be included.

Applications should also include the following sections in the Research Strategy:

Current State-of-the-Art:

Investigators should define the current state of technology as a benchmark against which their proposed new technology or improvements will be measured. Given that projects are likely to be early-stage and high-risk in nature, this should include the specific proof-of-concept test(s) that will indicate whether/how a proposed tool actually "works", along with alternative strategies should that effort fail to perform as expected. Tests should include a comparison against existing benchmark technologies; if a tool is truly first-in-class, comparisons may be done against a nearest neighbor technology. Investigators should briefly note how results will be used to inform future phases of tool development, such as testing in other model systems or in human brain.

Industry Partners:

Investigators should describe any relationship with industry/commercial partners. This should include details on what, if any material, partners are providing. If a memorandum of understanding (MOU), confidential disclosure agreement (CDA), or collaborative research agreement (CRA) has been signed by both parties, this should be described by the applicant.

Translational Plan:

Investigators should describe the potential translational pathway for their devices. This should include a description of the regulatory and reimbursement pathway for their device or specific type of technology. Future commercialization, implementation, and dissemination plans should be discussed.

Milestones and Timeline:

A timeline and milestones should 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 (e.g., crucial steps in tool making) during the course of the project. Quantitative benchmarks for success should be included.

Letters of Support:

A letter of support from any industry partners should be included.?

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:

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

There is no prescribed single license for the distribution of standards produced through grants responding to this announcement. However, the data sharing plan is expected to discuss: (1) how the

standard will be made widely available; (2) transferability, i.e., ability of another individual or team to continue development as appropriate; (3) terms of availability that will enable researchers to enhance the standard and share those enhancements with colleagues

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 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.

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 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 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.

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

NEW **Important Update:** See NOT-OD-18-228 (/grants/guide/notice-files/NOT-OD-18-228.html) for updated review language for due dates on or after January 25, 2019.

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.

For this particular announcement, note the following:

The R21 exploratory/developmental grant supports investigation of novel scientific ideas or new model systems, tools, or technologies that have the potential for significant impact on biomedical or biobehavioral research. An R21 grant application need not have extensive background material or preliminary information. Accordingly, reviewers will emphasize the conceptual framework, the level of innovation, and the potential to significantly advance our knowledge or understanding. Appropriate justification for the proposed work can be provided through literature citations, data from other sources, or, when available, from investigator-generated data. Preliminary data are not required for R21 applications; however, they may be included if available.

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?

Will the advance proposed improve human health, decrease disparities or increase access? Will this work use concepts from the computational and physical sciences to advance biomedical research and generate resources that would be widely used? Does this work address an important unmet need or solve an unaddressed problem? Are there plans for active dissemination of tools and technologies to promote widespread adoption and use by potential end users?

Current State-of-the-Art:

- Does the investigator detail the current state-of-the-art and explain how their technology will be benchmarked, when possible, against existing technology?

Translational Plan:

- Is the translational plan adequate?

- Does it detail the potential future regulatory and reimbursement pathway for the proposed technology?

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?

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?

Do the investigators have the experience and range of engineering and technical skills necessary to complete the proposed work? Does the team have experience developing and validating quantitative tools and technologies using bioengineering approaches?

Industry Partners:

- ?If included, is the description of industry partners adequate and complete?

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?

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?

Does the proposed project address a significant biomedical research problem by the development, optimization, and validation of new quantitative methods, technologies, or tools? Will the proposed integration of existing components into a new combination lead to a new capability?

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 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?

Are the experiments formulated to validate the technology and demonstrate its capabilities, rather than advancing the state of biological knowledge? Are there proposed development milestones that are adequate, measurable and feasible?

Are the engineering, computational and physical science approaches proposed appropriate and integrated into the research strategy? Has feasibility already been established for the technologies involved?

Has any animal or human testing been thoroughly justified in the context of necessity for device development?

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?

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?

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?

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?

Does the application describe resources and arrangements that will promote a multidisciplinary approach?

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.

Project Milestones and Timeline:

- *Are the milestones and timeline appropriate for the proposed project ?*
- *Do they provide quantitative metrics for evaluating device development?*

Intellectual Property (IP) strategy:

- *If applicable, are potential issues regarding the IP landscape for the device being developed and means for addressing any IP hurdles/barriers addressed? Do the IP Strategy attachment and related letters of support address potential concerns?*
- *Are there any known constraints that could impede the development of the device?*
- *If applicable, are IP filing plans described and appropriate??*

Study Timeline

Specific to 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 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

Not Applicable

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 Center for Scientific Review, 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 on the basis of established PHS referral guidelines . 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 National Advisory Mental Health 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.

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 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).

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 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, application errors and warnings, documenting system problems that threaten on-time submission, 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 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
Email: support@grants.gov (mailto:support@grants.gov)

Scientific/Research Contact(s)

David McMullen, M.D.
National Institute of Mental Health (NIMH (https://www.nimh.nih.gov/index.shtml))
Telephone: 301-451-0180
Email: david.mcmullen@nih.gov (mailto:david.mcmullen@nih.gov)

Peer Review Contact(s)

Joseph Rudolph, Ph.D.
Center for Scientific Review (CSR)
Telephone: 301-408-9098
Email: ? (mailto:josephru@mail.nih.gov)josephru@mail.nih.gov (mailto:josephru@mail.nih.gov)

Financial/Grants Management Contact(s)

Rebecca Claycamp
National Institute of Mental Health (NIMH (https://www.nimh.nih.gov/index.shtml))
Telephone: 301-443-2811
Email: rclaycam@mail.nih.gov (mailto:rclaycam@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?09-28-18)
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