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

Funding Opportunity Title

Discovery of Biomarkers and Biomarker Signatures for Neurological and Neuromuscular Disorders (R61/R33 Clinical Trial Optional)

Activity Code

R61 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r61&Search.x=0&Search.y=0&Search_Type=Activity)/R33 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r33&Search.x=0&Search.y=0&Search_Type=Activity),Exploratory/Developmental Phased Award

Announcement Type

New

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).
- **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 (/grants/guide/notice-files/NOT-OD-19-137.html).
- **July 26, 2019** - Changes to NIH Requirements Regarding Proposed Human Fetal Tissue Research. See Notice NOT-OD-19-128 (/grants/guide/notice-files/NOT-OD-19-128.html).

Funding Opportunity Announcement (FOA) Number

PAR-19-315

Companion Funding Opportunity

PAR-18-664 (https://grants.nih.gov/grants/guide/pa-files/par-18-664.html), U01 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U01&Search.x=16&Search.y=10&Search_Type=Activity) Research Project – Cooperative Agreements
PAR-18-550 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-550.html), U01 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U01&Search.x=16&Search.y=10&Search_Type=Activity) Research Project – Cooperative Agreements
PAR-18-548 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-548.html), U44 (https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=u44&Search.x=0&Search.y=0&Search_Type=Activity) Small Business Innovation Research (SBIR) Cooperative Agreement – Fast Track
PAR-18-549 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-549.html), U44 (https://grants.nih.gov/grants/funding

/ac_search_results.htm?text_curr=u44&Search.x=0&Search.y=0&Search_Type=Activity) Small Business Innovation Research (SBIR) Cooperative Agreement – Fast Track

Number of Applications

See Section III. 3. Additional Information on Eligibility.

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

93.853

Funding Opportunity Purpose

The overarching purpose of this Funding Opportunity Announcement (FOA) is to promote the discovery and/or early evaluation of strong candidate biomarkers and biomarker signatures that can be used as tools to facilitate the clinical development of neurotherapeutics and their use in clinical practice. Specifically, the focus of this FOA is on the identification and initial biological, analytical and clinical evaluation of biomarkers and biomarker signatures for neurological and neuromuscular disorders/diseases. Although research supported by this FOA can include animal studies, it must also include preliminary human evaluation using carefully standardized human samples or datasets. The goal of this initiative is to deliver candidate biomarkers or biomarker signatures that are ready for definitive analytical and clinical validation studies.

Key Dates

Posted Date

July 10, 2019

Open Date (Earliest Submission Date)

August 04, 2019

Letter of Intent Due Date(s)

30 days prior to the application due date

Application Due Date(s)

September 4, 2019; February 14, 2020; July 20, 2020; February 17, 2021; July 19, 2021; and February 14, 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.

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)

September 7, 2019; May 7, 2020; September 7, 2020; May 7, 2021; September 7, 2021; and May 7, 2022 by 5:00 PM local time of applicant organization. All types of AIDS and AIDS-related 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.

Scientific Merit Review

November 2019; June 2020; November 2020; June 2021; November 2021 and June 2022

Advisory Council Review

January 2020; October 2020; January 2021; October 2021; January 2022; and October 2022

Earliest Start Date

April 2020

Expiration Date

March 08, 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=PAR-19-315) 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.

Table of Contents

Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Purpose

The overarching purpose of this Funding Opportunity Announcement (FOA) is to promote the discovery of strong candidate biomarkers and biomarker signatures for neurological and neuromuscular disorders/diseases that can be used as tools to facilitate the clinical development of neurotherapeutics and their use in clinical practice. Specifically, the focus of this FOA is on the identification and initial biological, analytical and clinical evaluation of biomarkers and biomarker signatures for neurological or neuromuscular disorders/diseases. Although research supported by this FOA can include animal studies, it must also include preliminary evaluation of the biomarker or biomarker signature in carefully standardized human samples or datasets. The goal of this initiative is to deliver candidate biomarkers and biomarker signatures that are ready for definitive analytical and clinical validation studies *(see PAR-18-548 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-548.html), PAR-18-549* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-549.html)*, PAR-18-550* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-550.html) *, PAR-19-220 (https://grants.nih.gov/grants/guide/pa-files/PAR-19-220.html) and PAR-18-664* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-664.html)*).*

Background

A biomarker is a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes or responses to an exposure or intervention, including therapeutic interventions (BEST Resource (https://www.ncbi.nlm.nih.gov/books/NBK326791/pdf/Bookshelf_NBK326791.pdf)). A biomarker signature is a combination of multiple variables to yield a patient-specific indicator of normal biological processes or responses to an exposure or intervention including therapeutic interventions. Biomarker modalities are diverse, and can include genetic, protein, cellular, metabolomic, imaging, behavioral, and physiologic measures.

Biomarkers have become recognized as critical to the discovery and development of therapeutics. For example, they can serve as indicators of therapeutic target engagement and pharmacodynamic (PD) response and provide an early signal of treatment response in a clinical trial. Biomarkers can also improve the accuracy of clinical trial outcomes by stratifying patients to reduce the impact of the variability associated with phenotypic heterogeneity on efficacy. In addition, biomarkers allow the evaluation of therapeutic intervention on disease progression or recurrence, as well as on the clinical manifestation of disease phenotype or severity. Finally, biomarkers are important tools in the evaluation of susceptibility and risk for developing a disease or disorder, thereby improving early diagnosis and therapeutic outcomes in cases where disease or disorder manifestation could be significantly attenuated or prevented with treatment.

Despite the active pace of discovery of novel biomarker candidates, few biomarkers progress beyond discovery to clinical practice, and robust, well-validated biomarkers for use in Phase II clinical trials remain scant. Thus, there is a critical need to advance biomarkers to improve public health, particularly for diseases and disorders of the nervous system where failures to advance drugs from discovery to the market are notorious. The goal of this FOA, therefore, is to promote a rigorous process to facilitate the discovery and/or early evaluation of promising candidate biomarkers and biomarker signatures that will withstand rigorous validation and ultimately provide the tools necessary to enable the clinical development of neurotherapeutics.

Overview of the Biomarker Development Process

The biomarker development process is a systematic and directed endeavor where the degree of validation evidence supporting the use of the biomarker increases as the intended purpose of the biomarker moves from research to clinical trials and clinical practice. The biomarker development process can be conceptualized as a continuum that begins with the ***Discovery Phase*****,** where initial identification and preliminary proof of concept studies of the potential biomarker are conducted. The samples used must be from sources that are carefully standardized across sites, instruments and operators and are thoroughly annotated. Biomarker detection technology is also developed and internally validated during the Discovery Phase, and a hypothesis regarding the Context of Use for the biomarker or biomarker signature is formulated for testing in later validation studies. Finally, initial proof of concept that the biomarker or biomarker signature reflects the intended clinical outcome or concept of interest is evaluated. The biomarker discovery phase, then, includes studies aimed at verifying the accuracy and reliability of the detection method, formulating a hypothesis for the Context of Use, and testing the association between the biomarker or biomarker signature and the clinical outcomes that reflect presence of the disease, disease prognosis, therapeutic target engagement, response to an intervention or potential to respond to an intervention. The next phase of biomarker development is the ***Validation Phase***, which includes two major types of validation: 1) analytical validation, where the performance characteristics of the assay or detection technology are rigorously tested in a manner that is appropriate for the purpose of the biomarker or biomarker signature, and 2) clinical validation, where the biomarker or biomarker signature is rigorously tested for its ability to identify, measure or predict the concept of interest by assessing the sensitivity and specificity of the biomarker for the clinical outcome it is intended to reflect. The degree of evidence required to provide the necessary confidence in biomarker or biomarker signature validation depends upon the Context of Use for the biomarker or biomarker signature. As the Context of Use moves from research to accepted utility in clinical practice (i.e., as a

diagnostic or predictor of therapeutic response), the required degree of validation evidence is increased and should include prospective, multi-site validation data, depending upon the Context of Use.

Note that this FOA is intended to support the Discovery Phase only. For other funding opportunities supporting the Validation Phase, please see *PAR-18-548* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-548.html), *PAR-18-549* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-549.html), *PAR-18-550* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-550.html), *PAR-19-220 (https://grants.nih.gov/grants/guide/pa-files/PAR-19-220.html)* and *PAR-18-664* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-664.html).

Phased Award Mechanism and Transition to R33

This funding opportunity uses a R61/R33 Phased Innovation Award mechanism. The R61 phase will support biomarker and biomarker signature discovery and proof of concept studies including activities such as sample collection, biomarker identification, biomarker detection method development, assessment of the accuracy and reliability of the detection method and correlational studies to define the association between the biomarker with disease prognosis, disease pathology, target engagement of a therapeutic, response to an intervention, potential to respond or susceptibility/risk to develop a disease or disorder. Examples of activities supported in the R33 phase can include more extensive proof of concept and performance of the detection method and must include at least initial research using human samples or measures from human subjects. Transition from the R61 to the R33 phase is contingent upon the successful completion of proposed milestones. The milestones should be clearly defined, quantifiable, and scientifically justified to allow the investigator and program staff to assess progress in the R61 phase (Please refer to Project Milestones, end of Section I).

Research Objectives

The research objectives for this FOA are: 1) identification of a biomarker or biomarker signature, 2) development of a working hypothesis regarding Context of Use, 3) development and initial internal validation of the biomarker detection method and 4) initial proof of concept for the biomarker or biomarker signature within the stated Context of Use. In summary, completion of a research project resulting from successful application to this FOA should result in a candidate biomarker or biomarker signature that meets the entry criteria for the companion FOAs related to analytical validation of a candidate biomarker (*PAR-18-549* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-549.html) *and* *PAR-18-550* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-550.html)).

Applications to this FOA must propose a research plan designed to discover a biomarker or biomarker signature that will inform either clinical trial design for potential neurotherapeutics or treatment decisions in clinical practice. The biomarker or biomarker signature should reflect neurological- or neuromuscular-pathophysiology, target engagement or the pharmacodynamic response of a therapeutic intervention. In addition, the biomarker or biomarker signature can act as an early indicator of a clinical response to a therapeutic intervention, a means to stratify subjects into more homogeneous subgroups or a method to detect susceptibility/risk of developing a disease or disorder. Biomarker discovery includes activities such as biomarker identification, detection method development, initial proof of concept, evaluation of the detection method and correlations between the biomarker and disease pathophysiology or therapeutic intervention using standardized samples or measures from human subjects. Separate FOAs are available for later stage, multi-center validation studies; please see *PAR-18-548* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-548.html), *PAR-18-549* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-549.html), *PAR-18-550* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-550.html), *PAR-19-220 (https://grants.nih.gov/grants/guide/pa-files/PAR-19-220.html)* and *PAR-18-664* (https://grants.nih.gov/grants/guide/pa-files/PAR-18-664.html).

The definitions of the terms internal validation and Context of Use are provided below for the purposes of this FOA:

- **Internal Validation of the detection method:** Establishing that the performance characteristics of a measurement are acceptable in terms of its sensitivity, specificity, accuracy, precision, and other relevant performance characteristics using a specified technical protocol (which may include sample collection and standardization procedures).
- **Proof of Concept:** Establishing that the biomarker acceptably identifies, measures or predicts the concept of interest.
- **Context of Use (COU):** A statement that fully and clearly describes the way the biomarker is to be used and the biomarker-related purpose of the use. Considerations involved in defining the COU can include biomarker modality and method of detection, clinical population characteristics, unmet need for the new biomarker and type of biomarker (response prediction, stratification, prognostic, diagnostic, target engagement, susceptibility/risk, etc.). Context of Use statements are discussed extensively in the following link: https://www.fda.gov/media/119271/download (https://www.fda.gov/media/119271/download)
- **Use of the BEST (Biomarkers, EndpointS, and Other Tools Resource) standardized biomarker definitions (https://www.ncbi.nlm.nih.gov/books/NBK338448/ (https://www.ncbi.nlm.nih.gov/books/NBK338448/)) is required for all studies.**

Entry Criteria

- **Biological rationale:** Projects should be supported by a cogent biological rationale supporting the concept of the candidate biomarker or biomarker signature, as well as a discussion regarding its unmet need. The biological rationale should include rigorously obtained evidence that the proposed biomarker or biomarker signature *concept* may be an indicator of normal biological processes, potential susceptibility or risk, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions.
- **Relevance for neurotherapeutic development:** Projects should address the relevance of the candidate biomarker or biomarker signature for neurotherapeutic development or clinical practice.
- **Demonstration of proficiency in the biomarker modality proposed:** Projects should be supported by data or publications showing that the investigative team is capable of carrying out the proposed biomarker studies

Project Characteristics

The biomarker or biomarker signature must be focused on a neurological or neuromuscular disease or disorder.

Examples of Biomarker or Biomarker Signature Discovery Studies and Activities Include But Are Not Limited to:

- Identification and procurement of sample sources necessary for biomarker discovery and assurance of source standardization across sites along with adequate annotation
- Identification and initial evaluation of a potential biomarker or biomarker signature for a neurological or neuromuscular disorder
- Mechanistic and/or theoretical and computational modeling to tie biomarkers to their mechanistic underpinnings, specifically studies aimed at understanding whether the biomarker is relevant to the disease pathophysiology, PD response, treatment pathway, etc.
- Longitudinal studies to understand developmental trajectories of biomarkers (e.g., in pediatric populations) or the effects of disease progression on the biomarker
- Multidimensional analyses (e.g., studies involving combinations of molecular signals, electrophysiology and/or neuroimaging) with the goal of gaining a deeper understanding of the biomarker signal
- Unbiased discovery approaches and continuous monitoring of signals in naturalistic settings to identify novel biomarkers
- Development of biomarkers in animal models of neurological or neuromuscular disorders that could be measured in humans including parallel/iterative studies in animal models and humans using equivalent platforms
- Development of a set of biological and/or clinical markers associated with neurological or neuromuscular disorders, including algorithms for combined biomarkers that form a “signature” for the selected neurological disorder
- Development of bioinformatics and/or statistical approaches to support biomarker identification
- Development and evaluation of biomarker detection or measurement technology, including internal validation of the detection technology within the scope of the intended Context of Use
- Proof of concept studies using human tissue, biofluids or imaging samples to confirm biomarker identification obtained using animal tissue sources

Internal Validation can include the following metrics

- Precision
- Accuracy
- Analytical sensitivity
- Analytical specificity including interfering substances
- Reportable range of test results for the test system
- Reference intervals (range of normal values) with controls and calibrators
- Harmonization of analytical performance if the assay or method of detection is to be performed in multiple laboratories
- Establishment of appropriate quality control and improvement procedures
- Any other performance characteristic required for test performance with determination of calibration and control procedures

Clinical Evaluation can include the following metrics

- Demonstration that the result of the biomarker assay is associated with a clinical endpoint (e.g., response to a therapeutic, target engagement, neuro-pathophysiology or clinical manifestation) in samples or data from patients that have been exposed to a uniform intervention or that have or will develop a disease or disorder
- Demonstration of sensitivity and specificity for the intended use of the biomarker or biomarker signature

Examples of Studies That Are Not Appropriate For This FOA

- Biomarker or biomarker signature studies for diseases or disorders outside the mission of NINDS
- Natural history studies aimed at understanding disease pathophysiology, genetic, or epigenetic mechanisms *in the absence* of biomarker identification, development of detection technology and early validation
- Use of non-standardized sample sources
- Prospective design clinical validation studies
- Prospective design clinical utility studies
- Therapeutic target validation in order to identify a neurotherapeutic entity
- Preclinical animal studies without a transition to studies involving human samples or data
- Development of candidate therapeutics
- Efficacy testing as the primary intent of the proposal

Considerations for clinical trials

This FOA supports the discovery of biomarkers that indicate pharmacodynamic responses to neurotherapeutics, that predict an efficacy or safety response to a neurotherapeutic or that can be used to monitor a therapeutic response to a neurotherapeutic. Thus, while the studies outlined in an application may meet the definition of a clinical trial, and may make measurements in subjects on specific therapies, the study should not seek to answer specific questions about safety, tolerability, clinical efficacy, effectiveness, and/or clinical intervention and management. For the reasons outlined above, this FOA typically supports only mechanistic types of clinical trials.

Investigators are encouraged to form collaborations with individuals knowledgeable in biomarker development, bioinformatics, statistical analysis, detection technology development and validation, tissue source standardization, neurological and neuromuscular disorder/disease pathophysiology, clinical experience appropriate for the type of biomarker, as well as those familiar with the ultimate goal of a successful project for this FOA, which is to have a robust candidate biomarker or biomarker signature that is ready for a rigorous prospective clinical validation process that is appropriate for the Context of Use of that biomarker or biomarker signature.

Leveraging Existing Research Resources

Applicants are strongly encouraged to leverage existing NINDS research resources for their studies whenever possible. Such resources may include tissue, cellular, or DNA samples from NINDS BioSEND (https://www.biosend.org/ (https://www.biosend.org/)) or other existing biospecimen, imaging and data repositories, such as the NINDS Human Cell and Data Repository or The Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system. The NINDS BioSEND repository receives, processes, stores, and distributes biospecimen resources from NINDS funded studies that can be shared by the neuroscience research community, and currently banks a variety of biospecimens including DNA, plasma, serum, RNA, CSF, and saliva. The NINDS Human Cell and Data Repository (https://nindsgenetics.org/) provides 1) disease-relevant stem cell lines for biomarker discovery, and/or 2) the capacity to bank blood for the creation of new cell lines relevant to their disease of interest. The FITBIR system provides access to a data sharing platform for the Traumatic Brain Injury (TBI) community. Leveraging the resources and support from neurological disorder advocacy groups, private research foundations, academic institutions, other government agencies and the NIH Intramural program are also encouraged. Finally, applicants are encouraged to leverage the resources of ongoing clinical trials supported through other Federal or private funds.

Applications proposing to collect biospecimens are strongly recommended to use the NINDS Biomarkers Repository BioSpecimen Exchange for Neurological Disorders (BioSEND) (https://www.biosend.org/) *protocols and procedures, and all specimens collected and banked with BioSEND must come from individuals who have consented to banking and sharing broadly with academia and industry.*

Note that costs for collection are NOT included as a component of the NINDS Biomarkers Repository award. Therefore, most costs for the biospecimen banking are borne by the grantees utilizing this resource (see NOT-NS-15-046 (https://grants.nih.gov/grants/guide/notice-files/NOT-NS-15-046.html)*). Applicants planning projects in which biospecimens will be collected are strongly advised to consult the NINDS Biomarkers Repository website for more information about samples banked at the repository (https://www.biosend.org* (https://www.biosend.org/)*). In addition, applicants are advised to consult with NINDS Biomarkers Repository staff to obtain a quote for biospecimen banking costs (email:biosend@iu.edu* (mailto:biosend@iu.edu)*).*

Another data sharing resource that is available through NIH is The Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system, which was developed to share data across the entire Traumatic Brain Injury (TBI) research field and to facilitate collaboration between laboratories, as well as interconnectivity with other informatics platforms. Sharing data, methodologies, and associated tools, rather than summaries or interpretations of this information, can accelerate research progress by allowing re-analysis of data, as well as re-aggregation, integration, and rigorous comparison with other data,

tools, and methods. This community-wide sharing requires common data definitions and standards, as well as comprehensive and coherent informatics approaches. It is expected that NINDS Common Data Elements (CDE) will be used when appropriate. Finally, TBI-relevant grants are expected to comply with data sharing requirements as outlined in NOT-NS-17-029. For more information about this resource, please see: https://fitbir.nih.gov/ (https://fitbir.nih.gov/)

Project Milestones

A project timeline including milestones is a required component of the application (see Section IV.2). Milestones are quantitative goals that can be used for go/no-go decision making as the project advances from the R61 to the R33 phase, and therefore should have quantitative criteria associated with them. All milestones should be useful as a measure of progress toward the overall goal of the project. A list of activities planned for each phase are not considered milestones because they do not provide decision-making goals. Milestones will provide clear indicators of a project's continued success or emergent difficulties. Milestones could address, for example, 1) The desired magnitude and reliability of the association between the biomarker and disease pathophysiology, target engagement of a therapeutic or responses to an intervention in preliminary animal studies or studies with human samples, 2) Desired precision, accuracy and dynamic range of the biomarker/endpoint detection method, and/or 3) Feasibility of biomarker/endpoint measurement. Progress toward achievement of milestones will be evaluated by NIH Program Staff, and funding for the project may be discontinued if milestones are not met.

The NIH Program Official will contact the applicant to discuss the proposed milestones prior to the award. The Program Official will discuss with the Program Director(s)/Principal Investigator(s) any recommended changes to the research plan or suggestions from peer reviewers, and the plan will be revised as appropriate prior to the award.

Pre-Application Consultation

Applicants are strongly encouraged to consult with NIH Scientific/Research Staff early on during the planning for an application. This early contact will provide an opportunity to discuss and clarify NINDS policies and guidelines, including the scope of the project relative to the NINDS mission and intent of this FOA. *These discussions also provide important information on how to develop an appropriate timeline and milestone plan, which are subject to peer review under this program.*

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

Clinical Trial?

Optional: Accepting applications that either propose or do not propose clinical trial(s)
Need help determining whether you are doing a clinical trial? (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

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

Award Budget

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

Award Project Period

The R61 phase can be from 1-3 years and the R33 phase can be 1-2 years, with a total project duration of no more than 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
- 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:

Mary Ann Pelleymounter, Ph.D

National Institute of Neurological Disorders and Stroke (NINDS)
Telephone: 301-451-4551
Fax: 301-219-9346
Email: mary.pelleymounter@nih.gov (mailto:mary.pelleymounter@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 with the following additional instructions..
Applications should include an Intellectual property (IP) strategy. Applicants are encouraged to prepare this section of the application in consultation with their institution's technology transfer officials.

- Applicants should describe the IP landscape surrounding their biomarker or biomarker signature and its measurement. Applicants should describe any known constraints that could impede biomarker or biomarker signature development (e.g., certain restrictions under transfer or sharing agreements, applicants' previous or present IP filings and publications, similar biomarkers that are under patent protection and/or on the market, etc.) and how these issues could be addressed with achieving the goals of this program. If the applicant proposes using an agent(s) whose IP is not owned by the applicant's institution, either an investigational therapeutic, FDA-approved therapeutic, or other licensed

product, the applicant should include a letter (see letter of support) from any entities owning the IP indicating there will not be any limitations imposed on the studies or the project which would impede achieving the goals of the funding program.
- If patents pertinent to the biomarker being developed under this application have been filed, the applicant should indicate the details of filing dates, what type of patents are filed, and application status, and associated USPTO links, if applicable. Applicants should also provide information regarding foreign interests and patents.
- Applicants should discuss future IP filing plans. For a multiple-PD/PI, multiple-institution application, applicants should describe 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. Applicants should clarify how IP will be shared or otherwise managed if multiple PD/PIs and institutions are involved.

SF424(R&R) Senior/Key Person Profile

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

R&R 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:

Specific Aims:

Within the Specific Aims section, include headers titled R61 Phase Specific Aims and R33 Phase Specific Aims. Under each header, state the specific objectives of the efforts. Briefly provide the context for the proposed set of studies, with an emphasis on the biological research rationale for the biomarker or biomarker signature concept, along with a cogent argument outlining its importance and unmet need. In addition, the major objectives of the proposed study should be stated, including the technical questions to be answered to further develop and evaluate the biomarker or biomarker signature.

Research Strategy:

The Research Strategy Section should include the following sections:

1. Rationale and Unmet Need

- Define the neurological or neuromuscular disease or disorder to be addressed and the unmet need for neurotherapeutics in the specific area.
- Provide a strong biological rationale that supports the scheme for discovery and feasibility of the putative biomarker or biomarker signature.
- Describe the possible methods of detection for the biomarker or biomarker signature and address the feasibility of this method of detection for use in Phase II clinical trials or clinical practice.
- Propose the intended clinical Context of Use for the biomarker or biomarker signature and its detection method. Include information on characteristics of the sample (i.e., specimen, image, EEG, behavioral or physiological readout) to be used for the measurement and how the measurement result will be used.
- If applicable, provide a comparison to other biomarker approaches for the specified neurological or neuromuscular disorder, discussing the advantages of the proposed biomarker approach and addressing the unmet need for a biomarker.
- Describe the potential for the proposed studies to significantly advance translational medicine for the neurological or neuromuscular disorder described.
- Address the probability for the biomarker or biomarker signature and its detection method to be broadly adopted by the health care community for use in treatment or prevention. Address exactly how clinical trialists and health care professionals would use the proposed biomarker or biomarker signature to make decisions.

2. Preliminary Data

- Provide a clear outline of the preliminary data supporting the biological rationale for the discovery scheme of the new biomarker or biomarker signature. Describe the overall strengths, weaknesses, and rigor of the preliminary data.
- Provide any existing natural history data that is relevant to the biomarker or biomarker signature discovery scheme.
- Provide data addressing the feasibility and utility of any existing detection method or biomarker that is related to the proposed discovery scheme.
- Provide the preliminary rationale for the proposed Context of Use.

3. Approach - address each of the items below.

- Plan for identification and early verification of the biomarker relative to its underlying biology and/or Context of Use.
- Plan to ensure appropriate standardization of samples and data (across sites, instruments and technicians) that are used in the biomarker identification and early evaluation process.
- Biomarker detection methodology development and validation approach.
- Bioinformatics and statistical designs for analysis or deconvolution of sample data and refinement of biomarker identity and power analysis.
- If biomarker identification and initial proof of concept are based on animal data, outline the approach for translation to human pathophysiology, target engagement or prediction of response to an intervention.
- Plans to obtain proof of concept for the biomarker or biomarker signature using human samples or data.
- Plan for developing the Context of Use for the biomarker or biomarker signature.
- Plan for refinement and development of the biomarker or biomarker signature.

4. Timeline and Proposed Milestones (required)

- Transition from the R61 to the R33 phase is contingent upon the successful completion of one set of proposed milestones. The specific milestone(s) proposed in the application will depend on the goals of the application and the accomplishments necessary in the R61 phase for advancement into the R33 phase. Milestones must be provided *under a separate, specific* heading at the end of the Research Strategy Section and will be evaluated as part of the scientific and technical merit of the R61/R33 application.
- Milestones should be proposed for completion at the end of the R61 phase. Quantitative milestones are required to provide clear indicators of a project's feasibility, continued progress or emergent difficulties and will be used to evaluate the application not only in peer review but also in consideration of the awarded project for funding of the R33 phase.
- Please see “Project Milestones” (End of Section I) for guidance in writing Go-No Go, quantitative milestones.
- Provide a detailed timeline for the anticipated attainment of milestones and the overall goal. Indicate when it is anticipated that essential components of the project will be completed.
- Identify any impediments that could require an addendum to the research plan, milestones, or timeline with a discussion of alternative approaches.

Team Management Plan:

- Applicants are strongly encouraged to form multidisciplinary teams that consist of biomarker development, bioinformatics and statistical experts, technical experts with experience relevant for the detection method, clinical scientists, clinicians with drug development experience, regulatory experts, and other academic/industry experts relevant to the therapeutic modality. Describe the team's ability to design the details of the plans and experiments, and to execute the research strategy.
- Describe how the team will work together (e.g., data generation, reporting of data and integrated review across teams with various disciplines, decision-making, etc.) over the course of the project (and include letters of support below). This description should include an outline of roles and responsibilities for each team member.

Letters of Support:

- Applicants should include letters of support from consultants, contractors, and collaborators.
- If applying from an academic institution, include a letter of support from the technology transfer official who will be managing intellectual property associated with this project.
- If research will be performed at more than one institution, include a letter of support from each institution clarifying how intellectual property will be shared or otherwise managed across the institutions.
- If collaborating with a private entity, include a letter of support that addresses any agreement to provide agent(s), any limits on the studies that can be performed with said agent(s), any limitations on sharing of data (including negative results), and whether a licensing agreement(s) will be needed and in place once the project is funded. This letter should come from a high official within the private entity who has authority to speak on these issues.
- If an application plans to utilize the infrastructure or resources of existing projects, whether funded by the NINDS, other governmental or non-governmental entities, letters of support detailing the terms of collaboration and data sharing must be included.
- If utilization of extant samples is proposed as a component of the study, letters of support or approval for use of those samples 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.

- If patent protection is being sought, investigators should explain how data will be shared after filing for patent protection to allow for both further research and the development of commercial products to advance forward, consistent with achieving the goals of the program.
- Applicants utilizing NINDS data and resource sharing repositories should address fulfillment of compliance requirements for the resource they have chosen to utilize in the Resource/Data Sharing Plan.

Appendix:

Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.
Applicants proposing to collect samples from subjects are encouraged to provide the following information in the Appendix:

Study Protocol, Consent Forms

For Ancillary studies:

- The protocol for the parent study
- Investigator's Brochure, if applicable, for the parent clinical study
- Consent forms (for both the parent clinical study and the ancillary studies, if different)
- Written agreement to conduct the ancillary study from parent clinical study sponsors.

IRB approval of the informed consent forms is not required at the time of submission of the application. However, drafts of informed consent forms must be included.

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
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 Applications that are incomplete and/or non-compliant will not be reviewed.

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

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

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in the policy (//grants.nih.gov/grants/guide/url_redirect.htm?id=82299). Any instructions provided here are in addition to the instructions in the policy. In addition, the Scientific Review Officer (SRO) will accept regulatory meeting minutes and transcripts, patents, and late-breaking data not to exceed 2 pages and not later than 30 calendar days prior to the peer review meeting.

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.

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

This FOA supports studies focused on the discovery of promising candidate biomarkers or biomarker signatures for neurological and neuromuscular disorders/diseases that will withstand rigorous validation and ultimately provide the tools necessary for the development of neurotherapeutics.

Priority will be given to technologies that: 1) address an unmet medical need for the neurological or neuromuscular disorder/disease specified, 2) are supported by a strong biological rationale for the technology concept, 3) include a carefully designed plan for sample collection that is supported by a strong biological and statistical rationale, 4) include a well thought-out plan for development and evaluation of detection technology that carefully considers the feasibility of the detection method for use in a clinical trial setting, 5) include a rigorous plan for biological proof of concept and 6) have the potential to produce a candidate biomarker that can withstand rigorous prospective clinical and analytical validation studies.

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?

Further criteria specific to this opportunity: 1) What is the potential of the biomarker discovery plan to identify a candidate biomarker or biomarker signature to address an unmet medical need in the specified neurological or neuromuscular disorder/disease? 2) What is the strength of the biological rationale for the biomarker or biomarker signature discovery scheme? 3) What is the overall potential for the proposed studies to significantly advance biomarkers and translational medicine for the neurological or neuromuscular disorder/disease described? 4) How likely are the biomarker or biomarker signature and its assay to be broadly adopted by the health care community for use in treatment or prevention?

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 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?

Further criteria specific to this opportunity: 1) Are the investigators knowledgeable and experienced about the biomarker or biomarker signature target(s) and/or disease biology? 2) Do the investigators have sufficient expertise in the biomarker biology, neurological or neuromuscular disorder, clinical phenotype, bioinformatics, detection technology, etc. in order to design and implement a robust identification/evaluation plan for the biomarker or biomarker signature? 3) Will the team be able to manage the discovery process for the biomarker or biomarker signature and/or its assay? 4) Are the roles of each collaborator carefully defined in the research plan?

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?

Further criteria specific to this opportunity: How is the biomarker or biomarker signature and/or its detection method within the clinical context both innovative and feasible?

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?

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?

Further criteria specific to this opportunity: 1) Does the applicant provide carefully considered plans to obtain samples standardized across sites, instruments, operators, etc. and to assure rigorous collection principles guided by a well thought out experimental design? 2) Are the plans for bioinformatic and statistical analysis or deconvolution of data leading to initial biomarker identification sufficiently rigorous and feasible? 3) Are the plans for initial proof of concept and evaluation logical and based on a clear understanding of the neurological disorder or disease phenotype and biological basis? 4) Do the plans for development and evaluation of the detection technology show evidence of adequate knowledge of analytical design and requirements? 5) Will a biomarker or biomarker signature identified and developed using the applicant’s proposal be likely to withstand rigorous prospective clinical validation?

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 and potential context of use 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?

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

Milestones and Timelines
Are the milestones robust and associated with clear, quantitative criteria for success that allow go/no-go decisions at the R61/R33 transition point? Does the set of milestones allow the evaluation of progress in the R61 phase and will successful completion of these milestones provide confidence that the investigator will be able to successfully implement the R33 phase and achieve its end goals within the timeline of this grant mechanism? If a criterion is not to be used for go/no-go decisions, is it justifiable? Are the timelines proposed for achieving the milestones realistic and inclusive of necessary steps, but also efficient without adding unnecessary steps?

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 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 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

Not Applicable

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.

Intellectual Property

1) Does the application outline any known constraints that could impede biomarker or biomarker signature development (e.g., certain restrictions under transfer or sharing agreements, applicants' previous or present IP filings and publications, similar biomarkers or biomarker signatures that are under patent protection and/or on the market, etc.) and how these issues could be addressed while achieving the goals of this program? 2) Does the applicant outline the IP landscape of their biomarker or biomarker signature and/or its method of detection? 3) If applicable, how strong is the applicant's IP portfolio/position (pertinent to the proposed project), and to what extent does the applicant have a reasonable strategy to protect its IP going forward? 4) If the applicant has filed patents pertinent to the biomarker or biomarker signature and/or its method of detection, do they provide details about those patents? 5) If IP will be shared among co-investigators, does the applicant provide details about the plans for IP sharing?

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.

The review will be convened by the National Institute for Neurological Disorders and Stroke (NINDS)

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 on the basis of established PHS referral guidelines 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 appropriate national Advisory Council or Board. 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 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 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 submission 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
Email: support@grants.gov (mailto:support@grants.gov)

Scientific/Research Contact(s)

Mary Ann Pelleymounter, PhD
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National Institute on Aging (NIA)
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Email: petanceskas@nia.nih.gov (mailto:petanceskas@nia.nih.gov)

Peer Review Contact(s)

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

Financial/Grants Management Contact(s)

Chief Grants Management Officer
National Institute of Neurological Disorders and Stroke (NINDS)
Email: ChiefGrantsManagementOfficer@ninds.nih.gov (mailto:ChiefGrantsManagementOfficer@ninds.nih.gov)

Jillian Morris
National Institute on Aging (NIA)
Telephone: 301-496-8986
Email: morrisjil@mail.nih.gov (mailto:morrisjil@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?07-12-19)
NIH Funding Opportunities and Notices (/grants/guide/index.html)

National Institutes of Health (/grants/oer.htm)
Office of Extramural Research

(http://www.hhs.gov/) Department of Health and Human Services (HHS)

(http://www.usa.gov/)

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