

Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)

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

Components of Participating Organizations

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

National Eye Institute ([NEI \(http://www.nei.nih.gov\)](http://www.nei.nih.gov))

National Institute on Aging ([NIA \(http://www.nia.nih.gov\)](http://www.nia.nih.gov))

National Institute on Alcohol Abuse and Alcoholism ([NIAAA \(http://www.niaaa.nih.gov\)](http://www.niaaa.nih.gov))

National Institute on Deafness and Other Communication Disorders ([NIDCD \(http://www.nidcd.nih.gov\)](http://www.nidcd.nih.gov))

National Institute on Drug Abuse ([NIDA \(http://www.nida.nih.gov\)](http://www.nida.nih.gov))

Funding Opportunity Title

Discovery of in vivo Chemical Probes for Novel Brain Targets (R01)

Activity Code

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

Announcement Type

Reissue of [PAR-14-279 \(https://grants.nih.gov/grants/guide/pa-files/PAR-14-279.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-14-279.html)

Related Notices

None

Funding Opportunity Announcement (FOA) Number

PAR-17-335

Companion Funding Opportunity

[PAR-17-335 \(https://grants.nih.gov/grants/guide/pa-files/PAR-17-335.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-17-335.html), [R21 \(//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r21&Search.x=0&Search.y=0&Search_Type=Activity\)](http://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r21&Search.x=0&Search.y=0&Search_Type=Activity) Exploratory/Developmental Grant

Number of Applications

See [Section III. 3. Additional Information on Eligibility](#).

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

93.242, 93.173, 93.279, 93.867,93.273

Funding Opportunity Purpose

This Funding Opportunity Announcement (FOA) intends to support investigators who have interest and capability to join efforts for the discovery of *in vivo* chemical probes for novel brain targets. It is expected that applicants will have in hand the starting compounds ("validated hits") for chemical optimization and bioassays for testing new analog compounds.

Through this FOA, NIH wishes to stimulate research in 1) discovery and development of novel, small molecules for their potential use in understanding biological processes relevant to the missions of NIMH, NEI, NIAAA, NIDA, NIA and/or NIDCD and 2) discovery and/or validation of novel, biological targets that will inform studies of brain disease mechanisms. Emphasis will be placed on projects that provide new insight into important disease-related biological targets and biological processes.

Key Dates

Posted Date

July 24, 2017

Open Date (Earliest Submission Date)

September 5, 2017

Letter of Intent Due Date(s)

Not Applicable

Application Due Date(s)

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

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

AIDS Application Due Date(s)

[Standard AIDS dates \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11112\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11112) apply, Year(s), 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

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

Advisory Council Review

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

Earliest Start Date

[Standard dates \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11113\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11113) apply

Expiration Date

September 8, 2020

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the Research (R) Instructions in the [SF424 \(R&R\) Application Guide \(//grants.nih.gov/grants/guide/url_redirect.htm?id=12000\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=12000), except where instructed to do otherwise (in this FOA or in a Notice from the [NIH Guide for Grants and Contracts \(//grants.nih.gov/grants/guide/\)](https://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 to track your application. Check with your institutional officials regarding availability.
3. [Go to Grants.gov](#) to download an application package to complete the application forms offline or create a Workspace to complete the forms online; submit your application to Grants.gov; and track your application in eRA Commons.

Learn more about the various [submission options](#) (<http://grants.nih.gov/grants/ElectronicReceipt/preparing.htm#2>).

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Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Research Scope

Technological innovations in chemical synthesis, cheminformatics, structural biology, and high throughput bioactivity and drug property assays have allowed rapid discovery of novel, small-molecule probes for the study of disease-related biological processes and mechanisms in academic environments.

Through this funding opportunity NIMH, NEI, NIA, NIAAA, NIDA, and/or NIDCD encourage applications to advance the discovery of small molecule chemical probes that would enable, by modulating the function of a protein, mechanistic questions to be addressed in animal studies. This FOA aims to stimulate research in 1) discovery and development of novel in vivo chemical probes for their potential use in understanding biological processes relevant to the missions of the participating NIH Institutes, and 2) use of chemical probes to discover and/or validate novel biological targets that will inform studies of brain disease mechanisms. Emphasis will be placed on research that provides new insight into important disease-related biological targets and biological processes. For example, applications may involve emerging therapeutic targets and mechanisms for the discovery of chemical probes that may lead to further development of therapeutics or provide insight into the biology of relevant diseases.

This program creates an opportunity for integrated research in biology and chemistry on structure-activity relationships (SAR) of novel compounds through an iterative and parallel optimization process, to advance successful development of in vivo chemical probes. Applicants to this FOA should have in hand the

starting compounds (“validated hits”) for chemical optimization and bioassays for testing new analog compounds. The iterative bioassay and chemical optimization cycles may encompass:

- *In vitro* cellular and tissue activities (potency, selectivity, specificity, etc.);
- *In vitro* structural, physicochemical, and biochemical properties (solubility, stability, membrane permeability, protein binding, microsome stability, metabolite identification, CYP inhibition, etc.);
- *In vivo* pharmacokinetics (PK) with absorption, distribution, metabolism, excretion (ADME) and toxicity;
- *In vivo* efficacy

The above-mentioned areas of investigation are representative and not meant to be all-inclusive.

The main emphasis of projects submitted under this FOA should be on chemical probes development rather than drugs or therapeutic discovery. Projects seeking resources for later stage drug development are not suitable for this FOA. Extensive studies required for the preclinical or clinical development of candidate therapeutics, such as IND-directed toxicological testing and Good Manufacturing Practices (GMP) synthesis, are beyond the scope of this FOA.

Data Sharing

A goal of the program is to further research advancements across the scientific community as rapidly as possible. This will require synergies that can be achieved through broad sharing of research efforts in a collaborative and cooperative research environment. The open sharing of data, research tools, and resources will not only encourage scientific rigor in the probe discovery process, but also lead more rapidly to the identification and validation of novel targets for drug discovery, and will facilitate the use of chemical probes by the research community to study brain processes. In order to reap the maximum benefit from this program, assay data, assay protocols, and chemical structures of compounds tested are expected to be made publicly available, consistent with achieving the goals of the program.

For the purpose of this FOA, the following data generated or developed under this FOA are expected to be released to [PubChem \(https://pubchem.ncbi.nlm.nih.gov/\)](https://pubchem.ncbi.nlm.nih.gov/), consistent with achieving the goals of this program: (1) all assay data, (2) protocols for assays implemented, (3) the chemical structure of compounds tested in assays, and (4) synthetic protocols of chemicals.

Institute Interests

NIMH

NIMH is interested in applications proposing the optimization of chemical probes aimed at novel molecular, cellular, or circuit targets relevant to mental disorders, especially treatment-resistant depression, bipolar disorder, schizophrenia, Post-Traumatic Stress Disorder (PTSD), HIV-induced Central Nervous System (CNS) dysfunction and autism spectrum disorder (see From Discovery to Cure: [Accelerating the Development of New and Personalized Interventions for Mental Illnesses \(https://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/fromdiscoverytocure_103739.pdf\)](https://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/fromdiscoverytocure_103739.pdf)). Studies aimed at the development of new ligands for targets where a high quality probe or therapeutic already exists are generally of lower priority.

Projects aimed at the discovery of cell-based chemical probes should consider applying to the companion R01 initiative [PAR-17-335 \(https://grants.nih.gov/grants/guide/pa-files/PAR-17-335.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-17-335.html). Projects aimed at early stages of drug discovery and development should consider the Drug Discovery for Nervous System Disorders [PAR-16-041 \(https://grants.nih.gov/grants/guide/pa-files/PAR-16-041.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-16-041.html) (R01) and [PAR-16-042 \(https://grants.nih.gov/grants/guide/pa-files/PAR-16-042.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-16-042.html) (R21), National Cooperative Drug

Discovery/Development Groups (NCDDG) for the Treatment of Mental Disorders, Drug or Alcohol Addiction [PAR-17-186 \(https://grants.nih.gov/grants/guide/pa-files/PAR-17-186.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-17-186.html) (U19) and [PAR-17-185 \(https://grants.nih.gov/grants/guide/pa-files/PAR-17-185.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-17-185.html) (U01). Projects at the development stage should consider applying to the NIMH SBIR/STTR Programs <https://www.nimh.nih.gov/funding/small-business-research-programs.shtml> (<https://www.nimh.nih.gov/funding/small-business-research-programs.shtml>). Projects at the early clinical trials phase should consider the NIMH SBIR Program or the First in Human and Early Stage Clinical Trials of Novel Investigational Drugs or Devices for Psychiatric Disorders (U01) <https://grants.nih.gov/grants/guide/pa-files/PAR-14-107.html> (<https://grants.nih.gov/grants/guide/pa-files/PAR-14-107.html>). Details on these and additional funding opportunity announcements and therapeutic discovery resources are listed on the [NIH/NIMH Therapeutics Discovery Research \(https://www.nimh.nih.gov/research-priorities/therapeutics/index.shtml\)](https://www.nimh.nih.gov/research-priorities/therapeutics/index.shtml) webpage.

The purpose of in vivo measures should be carefully considered. Given the lack of predictive preclinical behavioral measures of clinical efficacy for mental disorders, the NIMH is particularly interested in the development and testing of novel interventions that target operationally defined, biologically linked functional domains whose disruption is hypothesized to drive functional deficits in mental disorders. For example, NIMH [Research Domain Criteria \(RDoC\) \(https://www.nimh.nih.gov/research-priorities/rdoc/index.shtml\)](https://www.nimh.nih.gov/research-priorities/rdoc/index.shtml) constructs may inform mechanism-based hypotheses and the selection of interventions, outcome measures and clinical subjects. Intervention targets related to RDoC constructs and underlying circuits are of interest for this FOA, but other, biologically relevant targets are also of interest.

Scientific rigor and transparency in conducting biomedical research is key to the successful application of knowledge toward improving health outcomes. In support of this important goal, investigators must follow NIH Guidance on addressing rigor and reproducibility in grant applications (<http://grants.nih.gov/reproducibility/index.htm> ([//grants.nih.gov/reproducibility/index.htm](http://grants.nih.gov/reproducibility/index.htm))).

Further information on NIMH research priorities can be found in the [NIMH Strategic Plan \(http://www.nimh.nih.gov/about/strategic-planning-reports/index.shtml\)](http://www.nimh.nih.gov/about/strategic-planning-reports/index.shtml), [Strategic Research Priorities \(http://www.nimh.nih.gov/about/strategic-planning-reports/strategic-research-priorities/index.shtml\)](http://www.nimh.nih.gov/about/strategic-planning-reports/strategic-research-priorities/index.shtml), and [Interventions Workgroup Report \(http://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/fromdiscoverytocure_103739.pdf\)](http://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/fromdiscoverytocure_103739.pdf). Applicants are strongly encouraged to discuss applications with NIMH staff listed in Section VII - Agency Contact(s) Scientific/Research Contacts prior to submission to determine alignment of the planned studies with NIMH priorities and to assess whether this or other NIMH funding opportunities are most appropriate.

NIA:

NIA is interested in HTS assays and chemical probes that are relevant to the process of normal aging (including normal cognitive aging) and age-related diseases and conditions in a variety of tissues. Examples include Mild Cognitive Impairment (MCI), Alzheimer's disease and other dementias of aging, osteoporosis, sarcopenia, and other age-related changes that occur during the human lifespan. NIA is particularly interested in assays and chemical probes that will be useful in identifying new therapeutic targets and, novel therapeutic and imaging agents. NIA is also interested in assays to screen for compounds that affect protective factors or processes that may contribute to slowing or reversing the progression of age-related adverse molecular, biochemical, genetic, cellular, or physiological changes that contribute to multiple age-related diseases, and which hence could contribute to longer health span.

NIAAA:

NIAAA is interested in applications for novel clinically-relevant targets with the goal of transforming target discovery into treatment of alcohol dependence. NIAAA is also interested in the development of novel ligands to be used as tools for investigating biological processes contributing to alcohol dependence. Alcohol dependence is a complex disorder involving many neurotransmitter receptors and transporters, ion channels, neuromodulators, hormones, and intracellular signaling networks. This provides a number of potential target sites for which new pharmaceutical agents may be developed. Examples of interest include: modulators of dynorphin, glutamate, GABA, endocannabinoid, glucocorticoid and neuropeptide systems (e.g., NPY, CRF, substance P, orexin, oxytocin), agents that alter signal transduction pathways (such as protein kinase effectors, protein phosphatase inhibitors, G-protein regulators and calcium signaling disruptors), and modulators of neuroimmune and neuroinflammatory pathways.

NIDA:

NIDA is interested in funding projects that will lead to the discovery and early development of chemical probes for substance use disorders to substance use disorders (SUDs). Proposal topics might include, for example, target identification/validation, assay development, lead discovery and/or preliminary, iterative chemical probe development (SAR). Chemical probes could be used as: (i) tools for elucidating SUD-related mechanistic processes, or (ii) future lead pharmacotherapeutic candidates for the treatment of SUDs. Projects that are further along in the medications development pipeline (e.g., lead optimization or preclinical IND-preparatory studies) should consider applying to alternative FOAs, such as [PAR-16-431 \(https://grants.nih.gov/grants/guide/pa-files/PAR-16-431.html\)](https://grants.nih.gov/grants/guide/pa-files/PAR-16-431.html). Investigators are strongly encouraged to discuss potential research plans with the scientific contact below prior to submission.

NIDCD:

The NIDCD is interested in the development of chemical probes that might have potential therapeutic value in the treatment, protection or prevention of communication disorders, including hearing, balance, smell/taste, voice, speech and language. Applications could include, but are not limited to, identification of clinically-relevant targets that might lead to translatable therapeutics in hearing/balance areas of otoprotection, regeneration, otitis media, tinnitus, and normal/abnormal development; chemosensory abnormalities such as they relate to serious diseases of obesity, diabetes, Parkinson's disease, Alzheimer's disease, and multiple sclerosis; disorders involving voice speech, language, including swallowing, aphasia or dysarthria, and laryngeal replacement. Potential applicants are encouraged to review the NIDCD mission at <http://www.nidcd.nih.gov> (<http://www.nidcd.nih.gov/>) prior to submitting an application.

NEI:

The NEI is especially interested in applications to develop novel, clinically-relevant targets, which can be transformed into therapeutics for treatment of visual diseases and disorders. Appropriate research areas include, but are not limited to, inflammatory, vascular, and degenerative diseases of the eye, such as diabetic retinopathy, age-related macular degeneration, retinitis pigmentosa, glaucoma, ocular infections, corneal wound healing, and dry eye syndrome. Proposed projects should be relevant to NEI's mission of supporting basic science discoveries and translating these discoveries into new therapeutic interventions that will lead to sight-saving treatments, reduce visual impairment and blindness, and improve the quality of life for people of all ages.

See [Section VIII. Other Information](#) for award authorities and regulations.

Section II. Award Information

Funding Instrument

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

Application Types Allowed

New
Resubmission
Revision

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

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 total project period may not exceed 3 years.

NIH grants policies as described in the [NIH Grants Policy Statement \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made in response to 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](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11118) ([//grants.nih.gov/grants/guide/url_redirect.htm?id=11118](http://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](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-039.html) ([//grants.nih.gov/grants/guide/notice-files/NOT-OD-15-039.html](http://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) (<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 \(SAM\) \(https://www.sam.gov/portal/public/SAM/\)](https://www.sam.gov/portal/public/SAM/) (formerly CCR) – Applicants must complete and maintain an active registration, **which requires renewal at least annually**. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
 - [NATO Commercial and Government Entity \(NCAGE\) Code \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11176\)](https://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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11123\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Applicants must have an active DUNS number and SAM registration in order to complete the eRA Commons registration. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- [Grants.gov \(//grants.nih.gov/grants/guide/url_redirect.htm?id=82300\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82300) – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

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

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

Eligible Individuals (Program Director/Principal Investigator)

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

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

2. Cost Sharing

This FOA does not require cost sharing as defined in the [NIH Grants Policy Statement \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11126\)](https://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 \(//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-101.html\)](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-11-101.html)).

Section IV. Application and Submission Information

1. Requesting an Application Package

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

2. Content and Form of Application Submission

It is critical that applicants follow the Research (R) Instructions in the [SF424 \(R&R\) Application Guide \(//grants.nih.gov/grants/guide/url_redirect.htm?id=12000\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=12000), including [Supplemental Grant Application Instructions \(https://grants.nih.gov/grants/funding/424/SupplementalInstructions.pdf\)](https://grants.nih.gov/grants/funding/424/SupplementalInstructions.pdf) except where instructed in this funding opportunity announcement to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

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

Page Limitations

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

Instructions for Application Submission

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

SF424(R&R) Cover

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

SF424(R&R) Project/Performance Site Locations

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

SF424(R&R) Other Project Information

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

SF424(R&R) Senior/Key Person Profile

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

Is expected that the PD/PI(s) are reasonably knowledgeable and experience:

- about the biological target area of science

- to carry out the assays and capable of advancing active compounds
- to conduct chemical optimization of starting validated hit compounds

R&R or Modular Budget

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

R&R Subaward Budget

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

PHS 398 Cover Page Supplement

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

PHS 398 Research Plan

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

Research Strategy: In the Research Strategy applicants must address the following topics as they pertain to the research project proposed:

1. *Biological Target.* The applicants should address the novelty and significance of the biological target or biological process. The applicant should clearly describe any known small molecule modulators and the need for better small molecule modulators against for the intended biological target or biological process.

2. *Validated Hits.* Various approaches may be adopted toward pursuing a validated hit, including high throughput screening (HTS) of a large collection of structurally diversified or privileged compounds, virtual screening, fragment-based screening, affinity-based compound library screening, and structure-based *de novo* design. For a hit compound to be accepted as the starting point of this program, it should have the following well-characterized properties:

- elicit a reproducible response in at least two orthogonal assay types and also elicit a dose-response over a hundred-fold concentration range;
- be analytically validated in terms of integrity and purity (e.g., use of resynthesized powder sample of high purity in the preliminary assays);
- demonstrate adequate potency;
- demonstrate adequate potential for selectivity;
- possess a tractable starting point of chemical optimization with no obvious major chemical liabilities.

When possible, multiple series of scaffolds may be submitted for parallel optimization to enhance the likelihood of success of the project.

3. *Assays.* A cascade of *in vitro* and *in vivo* assays needs to be in place to efficiently test analog compounds derived from the submitted hits. The applicants are expected to perform *in vitro* and *in vivo* SAR assays related to their research fields. The *in vitro* SAR assays may include target-, pathway-, and phenotype-based assays. Some examples are: a) target-based biochemical or cellular assays that measure activities of enzymes, receptor-ligand bindings, protein-protein interactions, ion channels, transporters, nuclear receptors, and other new targets emerging from genetic and other omics research in model systems and in human diseases; b) cell- or organism-based assays that detect phenotypic changes that may involve unidentified molecular targets; and c) non-traditional targets of interest such as nucleic acids, protein folding, polymorphic gene products, post-transcriptional editing or splicing of gene products, and protein or RNA stabilization. The assay detection methods may include fluorescence, luminescence,

absorbance, fluorescence resonance energy transfer (FRET), time-resolved fluorescence resonance energy transfer (TR-FRET), fluorescence polarization, flow cytometric measurements, fluorescence imaging, bioluminescence resonance energy transfer (BRET), AlphaScreen, scintillation proximity assay (SPA), electrophysiology, and varieties of biophysical readouts. Assays adaptable to microtiter plates (96-, 384-well plates) are advantageous in rapid generation of assay data to enhance SAR iteration efficiency.

Applicants should clearly demonstrate that the proposed assays are adequate for the iterative study of structure-activity relationships and that the proposed assay reagents and protocols are in place and will be readily implemented.

The *in vivo* activity assays may be proof-of-concept assays using one, well-characterized animal species model. Recognizing that very few disease models are clinically validated, applicants are expected to present a convincing argument that the models selected, endpoints measured, and levels of activity observed are likely to be clinically relevant. These preclinical "proof-of-concept" studies must be sufficiently powered, controlled, and replicated to lend a high degree of confidence to the results.

4. *Probe criteria.* The application should (1) define the specific criteria that a compound must meet to be considered a probe for the project, (2) provide a thorough literature and informatics analysis about any known small molecule probe for the intended biological target or biological process, and (3) provide evidence that the validated hit to be optimized is engaging its target *in vivo*.

5. *Critical path.* The application should include a flow diagram to outline all critical steps in sequential and/or parallel manners with appropriate benchmarks and timelines, including but not limited to iterative chemical optimization and bioassays to be implemented, alternative approach (e.g., computational docking) to ensure success of the probe discovery, *in vivo* pharmacokinetic/pharmacodynamic assays to characterize chemical probes, study of structure-activity relationships, assay and chemistry responsibilities of each party involved.

6. *Future plan.* The application should also include a plan to briefly describe existing and potential follow-up assays to advance chemical probes in the future.

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

For the purpose of this FOA, the following data generated or developed under this FOA are expected to be released to PubChem, consistent with achieving the goals of this program:

- (1) all assay data,
- (2) protocols for assays implemented,
- (3) the chemical structure of compounds tested in assays, and
- (4) synthetic protocols of chemicals.

Applications should include a statement of willingness to deposit the aforementioned data to PubChem within the Data Sharing section of the application.

Appendix:

Do not use the Appendix to circumvent page limits. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

PHS Inclusion Enrollment Report

When conducting clinical research, follow all instructions for completing PHS Inclusion Enrollment Report as described in the SF424 (R&R) Application Guide.

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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11137\)](https://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](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82380) contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or [Federal holiday \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82380\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to [Grants.gov \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11128\)](https://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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11123\)](https://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. \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11142\)](https://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 \(//grants.nih.gov/grants/guide/uri_redirect.htm?id=11120\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the [NIH Grants Policy Statement \(//grants.nih.gov/grants/guide/uri_redirect.htm?id=11143\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=11143).

7. Other Submission Requirements and Information

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

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

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

Important reminders:

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

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

See [more tips \(//grants.nih.gov/grants/guide/uri_redirect.htm?id=11146\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=11146) for avoiding common errors.

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

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

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

Use of Common Data Elements in NIH-funded Research

NIH encourages the use of common data elements (CDEs) in basic, clinical, and applied research, patient registries, and other human subject research to facilitate broader and more effective use of data and advance research across studies. CDEs are data elements that have been identified and defined for use in multiple data sets across different studies. Use of CDEs can facilitate data sharing and standardization to improve data quality and enable data integration from multiple studies and sources, including electronic health records. NIH ICs have identified CDEs for many clinical domains (e.g., neurological disease), types

of studies (e.g., genome-wide association studies (GWAS)), types of outcomes (e.g., patient-reported outcomes), and patient registries (e.g., the Global Rare Diseases Patient Registry and Data Repository). NIH has established a "Common Data Element (CDE) Resource Portal" (<http://cde.nih.gov/> (<http://cde.nih.gov/>)) to assist investigators in identifying NIH-supported CDEs when developing protocols, case report forms, and other instruments for data collection. The Portal provides guidance about and access to NIH-supported CDE initiatives and other tools and resources for the appropriate use of CDEs and data standards in NIH-funded research. Investigators are encouraged to consult the Portal and describe in their applications any use they will make of NIH-supported CDEs in their projects.

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in [the policy](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82299) (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82299).

Section V. Application Review Information

1. Criteria

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

Overall Impact

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

Scored Review Criteria

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

Significance

Does the project address an important problem or a critical barrier to progress in the field? Is there a strong scientific premise for the project? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? Are well-defined goals clearly described for the use of identified chemical probes as research tools?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, or 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? Are the investigators knowledgeable and experienced to carry out the assays and capable of advancing active compounds?

Are the investigators knowledgeable and experienced to conduct chemical optimization of starting hit compounds?

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? Is this project for a novel biological target or process? Does the application address whether or not known small molecule modulators are available for this biological target or process? Is there a need for better small molecule modulators against the target or process?

Approach

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

Has the biological activity of the hits been adequately characterized and validated by orthogonal assays? Are the biological and physicochemical qualities of the hits adequate as the starting material for *in vivo* probe development? Are the proposed assays adequate for the iterative study of structure-activity relationships? If so, are the proposed assay reagents and protocols in place and will they be readily implemented? Is the proposed chemical optimization approach adequate and efficient?

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?

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.

Protections for Human Subjects

Not Applicable

Inclusion of Women, Minorities, and Children

Not Applicable

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](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11150) ([//grants.nih.gov/grants/guide/url_redirect.htm?id=11150](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11150)).

Biohazards

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

Resubmissions

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

Renewals

Not Applicable

Revisions

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

Additional Review Considerations

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

Applications from Foreign Organizations

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

Select Agent Research

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

Resource Sharing Plans

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

([//grants.nih.gov/grants/guide/url_redirect.htm?id=11152](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11152)); and (3) [Genomic Data Sharing Plan \(GDS\) \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11153\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11153).

Authentication of Key Biological and/or Chemical Resources:

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

Budget and Period of Support

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

2. Review and Selection Process

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

As part of the scientific peer review, all applications:

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

Applications will be assigned 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. 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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11123\)](https://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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11156\)](https://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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11157\)](https://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.

2. Administrative and National Policy Requirements

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

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

For additional guidance regarding how the provisions apply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA. HHS provides general guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see <http://www.hhs.gov/ocr/civilrights/resources/laws/revisedlep.html>. The HHS Office for Civil Rights also provides guidance on complying with civil rights laws enforced by HHS. Please see <http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html>; and <http://www.hhs.gov/ocr/civilrights/understanding/index.html> (<http://www.hhs.gov/ocr/civilrights/understanding/index.html>). Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see <http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html> (<http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html>). Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at

<http://www.hhs.gov/ocr/office/about/rqn-hqaddresses.html> (<http://www.hhs.gov/ocr/office/about/rqn-hqaddresses.html>) or call 1-800-368-1019 or TDD 1-800-537-7697. Also note it is an HHS Departmental goal to ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations. For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at <http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53> (<http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53>).

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

Cooperative Agreement Terms and Conditions of Award

Not Applicable

3. Reporting

When multiple years are involved, awardees will be required to submit the [Research Performance Progress Report \(RPPR\) \(//grants.nih.gov/grants/rppr/index.htm\)](http://grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the [NIH Grants Policy Statement. \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11161\)](http://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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11161\)](http://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 \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11170\)](http://www.fsrs.gov) on all subawards over \$25,000. See the [NIH Grants Policy Statement \(//grants.nih.gov/grants/guide/url_redirect.htm?id=11171\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11171) for additional information on this reporting requirement.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value greater than \$10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of information reported in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached

final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). As required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 2011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

Section VII. Agency Contacts

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

Application Submission Contacts

eRA Service Desk (Questions regarding ASSIST, eRA Commons registration, submitting and tracking an application, documenting system problems that threaten submission by the due date, post submission issues)

Finding Help Online: <http://grants.nih.gov/support/> ([//grants.nih.gov/support/](http://grants.nih.gov/support/)) (preferred method of contact)

Telephone: 301-402-7469 or 866-504-9552 (Toll Free)

[Grants.gov Customer Support](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82301) ([//grants.nih.gov/grants/guide/url_redirect.htm?id=82301](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82301)) (Questions regarding Grants.gov registration and submission, downloading forms and application packages)

Contact Center Telephone: 800-518-4726

Email: support@grants.gov (<mailto:support@grants.gov>)

GrantsInfo (Questions regarding application instructions and process, finding NIH grant resources)

Email: GrantsInfo@nih.gov (<mailto:GrantsInfo@nih.gov>) (preferred method of contact)

Telephone: 301-945-7573

Scientific/Research Contact(s)

Enrique L. Michelotti, Ph.D.

National Institute of Mental Health ([NIMH](http://www.nimh.nih.gov/index.shtml) (<http://www.nimh.nih.gov/index.shtml>))

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Section VIII. Other Information

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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.

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