

Part I Overview Information

Department of Health and Human Services

Participating Organizations

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

Components of Participating Organizations

National Institute on Aging (NIA), (<http://www.nia.nih.gov>)

Title: The Role of Apolipoprotein E, Lipoprotein Receptors and CNS Lipid Homeostasis in Brain Aging and Alzheimer's Disease (R01)

Announcement Type

New

Program Announcement (PA) Number: PA-09-217

NOTICE: Applications submitted in response to this Funding Opportunity Announcement (FOA) for Federal assistance must be submitted electronically through Grants.gov (<http://www.grants.gov>) using the SF424 Research and Related (R&R) forms and the SF424 (R&R) Application Guide.

APPLICATIONS MAY NOT BE SUBMITTED IN PAPER FORMAT.

This FOA must be read in conjunction with the application guidelines included with this announcement in Grants.gov/Apply for Grants (hereafter called Grants.gov/Apply).

A registration process is necessary before submission and applicants are highly encouraged to start the process at least four (4) weeks prior to the grant submission date. See Section IV.

Apply for Grant Electronically

A compatible version of Adobe Reader is required for download. For Assistance downloading this or any Grants.gov application package, please contact Grants.gov Customer Support at <http://grants.gov/CustomerSupport>.

Catalog of Federal Domestic Assistance Number(s)
93.866

Key Dates

Release/Posted Date: July 6, 2009

Opening Date: September 5, 2009 (Earliest date an application may be submitted to Grants.gov)

NOTE: On-time submission requires that applications be successfully submitted to

Grants.gov no later than 5:00 p.m. local time (of the applicant institution/organization).

Application Due Date(s): Standard dates apply, please see <http://grants1.nih.gov/grants/funding/submissionschedule.htm>

AIDS Application Due Dates: Standard dates apply, please see <http://grants1.nih.gov/grants/funding/submissionschedule.htm#AIDS>

Peer Review Date(s): Standard dates apply, please see <http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward>

Council Review Date(s): Standard dates apply, please see <http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward>

Earliest Anticipated Start Date(s): <http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward>

Additional Information To Be Available Date (URL Activation Date): Not Applicable

Expiration Date: September 8, 2012

Due Dates for E.O. 12372

Not Applicable

Additional Overview Content

Executive Summary

- **Purpose.** This FOA encourages multidisciplinary and interdisciplinary research to elucidate how Apolipoprotein E, lipoprotein receptors and CNS lipid homeostasis influence brain aging and the transition to neurodegeneration in Alzheimer's disease (AD). The ultimate goal is to gain an in depth understanding of the mechanisms by which the Apolipoprotein E e4 allele confers increased AD risk for the purpose of advancing the overall search for efficacious AD treatments and Apolipoprotein E e4-directed therapeutics in particular. To this end we encourage research spanning multiple levels of analysis in multiple species (from mice to man). Studies aimed at identifying new therapeutic targets for the treatment of AD and other age-related neurodegenerative conditions associated with lipid neurobiology are strongly encouraged. Also of great interest are projects that aim to use lipidomics, various types of imaging and other cutting edge technologies to identify and develop early biomarkers of neurodegeneration associated lipid dyshomeostasis.
- **Mechanism of Support.** This FOA will utilize the R01 grant mechanism.
- **Funds Available and Anticipated Number of Awards.** During Fiscal Year 2010, the estimated amount of funds available to support projects under this FOA is \$2,500,000. Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Given the likely range of budgets, it is anticipated that 4 to 7 awards could be made during Fiscal Year 2010. The availability of funds and the number of awards in future years will depend upon annual appropriations.

- **Budget and Project Period.** The total project period for an application submitted in response to this funding opportunity may not exceed 5 years.
- **Application Research Plan Component Length:** The R01 application Research Plan component of the PHS398 may not exceed 25 pages, including tables, graphs, figures, diagrams, and charts.
See http://grants1.nih.gov/grants/funding/funding_program.htm
- **Eligible Institutions/Organizations.** Institutions/organizations listed in [Section III, 1.A.](#) are eligible to apply.
- **Eligible Project Directors/Principal Investigators (PDs/PIs).** Include Individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution/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.
- **Number of PDs/PIs.** More than one PD/PI (i.e., multiple PDs/PIs), may be designated on the application.
- **Number of Applications.** Applicants may submit more than one application, provided that each application is scientifically distinct.
- **Resubmissions.** Applicants may submit a resubmission application, but such application must include an Introduction addressing the previous peer review critique (Summary Statement). See new NIH policy on resubmission (amended) applications ([NOT-OD-09-003](#), [NOT-OD-09-016](#)).
- **Renewals.** Applicants may submit a renewal application.
- **Application Materials.** See [Section IV.1](#) for application materials.
- **General Information.** For general information on SF424 (R&R) Application and Electronic Submission, see these Web sites:
 - SF424 (R&R) Application and Electronic Submission Information: <http://grants.nih.gov/grants/funding/424/index.htm>
 - General information on Electronic Submission of Grant Applications: <http://era.nih.gov/ElectronicReceipt/>
- **Hearing Impaired.** Telecommunications for the hearing impaired are available at: TTY: (301) 451-5936

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

Purpose

The purpose of this FOA is to encourage research that will advance our understanding of how Apolipoprotein E, lipoprotein receptors and CNS lipid homeostasis influence brain aging, brain repair and neurodegeneration. The ultimate goal of this funding initiative is to elucidate the molecular mechanisms by which the Apolipoprotein E e4 allele confers increased AD risk and exerts its negative pharmacogenetic effect on various AD therapeutic modalities. If successful this effort will facilitate the process of developing Apolipoprotein E e4-directed AD therapeutics and prevention strategies. To this end we invite multidisciplinary and interdisciplinary research at multiple levels of analysis in animal models and in humans. We encourage collaborations between AD and neurobiology of aging experts, and scientists with expertise in lipid biology, developmental biology, epigenetics, and evolutionary biology.

Background

The Apolipoprotein E e4 allele of the Apolipoprotein E gene is the strongest risk factor for late onset AD identified to date; in contrast, the Apolipoprotein E e2 allele is associated with reduced AD risk. In spite of the fact that the discovery of Apolipoprotein E as an AD risk factor gene was made more than 15 years ago, the mechanisms by which Apolipoprotein E4 exerts its risk-factor activity remain elusive. Most importantly, despite the enormous impact of the Apolipoprotein E e4 allele on AD burden, small molecule therapeutics that would neutralize the negative impact of Apolipoprotein E e4 are presently lacking.

In the last decade a growing body of epidemiological and experimental evidence suggests that disrupted lipid metabolism (in the periphery and in the CNS) plays an important role in AD pathogenesis. Little is known however about how disrupted lipid homeostasis in the periphery may impact lipid homeostasis in the CNS and consequently brain function. In spite of the fact that multiple aspects of lipid dysregulation have been observed in AD, we know very little about the triggers of this dysregulation in the course of aging or about the mechanisms by which lipid dysregulation may impact multiple neurodegenerative processes.

In August 2008, NIA's Division of Neuroscience convened a multidisciplinary workshop entitled: "The Role of Apolipoprotein E in Brain Aging and Alzheimer's Disease". Leading experts in AD and neurobiology of aging research from academia as well as from the biotech and pharmaceutical industries evaluated the current state of knowledge about the biology of Apolipoprotein E and lipoprotein receptors with an emphasis on their role in normal brain aging and in AD and discussed advances and challenges in the drug discovery arena aimed at Apolipoprotein E as a therapeutic target. The workshop participants put forth a number of new ideas regarding research directions and pointed to a real gap in the current understanding of the role that brain lipids and ApoE play in normal brain aging as well as a lack of ApoE-targeted AD therapeutics. The

identified knowledge gaps and opportunities served as a basis for this funding initiative. The ultimate goal of this funding opportunity is to encourage an integrative, multidisciplinary approach that will inform the search for successful therapeutic interventions that will neutralize the negative impact of ApoE e4 and advance the discovery and development of early biomarkers of neurodegeneration related to lipid metabolism.

Research Scope

This FOA encourages multidisciplinary and interdisciplinary research to elucidate the role of Apolipoprotein E, lipoprotein receptors and CNS lipid homeostasis on brain aging and on the transition to neurodegeneration in AD and other neurodegenerative disorders. We strongly encourage studies that aim to identify new therapeutic targets for the treatment of AD and other age-related neurodegenerative conditions. Research spanning multiple levels of analysis and multiple species (from mice to man) is particularly encouraged. Also of great interest are projects that aim to use lipidomics, various types of imaging and other cutting edge technologies to identify and develop early biomarkers of neurodegeneration related to lipid metabolism.

Examples of research areas of interest include but are not limited to the following:

- Understand the role that Apolipoprotein E and lipoprotein receptors play in the course of normal brain aging and how ApoE-isoform specific signaling via these receptors impacts various aspects of cognitive aging. Of particular interest are the mechanisms by which ApoE influences synaptic plasticity, innate immunity, CNS bioenergetics, age-related myelin breakdown and microvascular remodeling.
- Identify common pathogenic mechanisms mediated by Apolipoprotein E across neurodegenerative disorders.
- Understand the isoform-specific effects of Apolipoprotein E on Amyloid beta-associated and Amyloid beta-independent pathogenic mechanisms in AD and determine if and how these pathways interact.
- Identify new therapeutic targets related to the mechanisms by which Apolipoprotein E e4 confers greater risk for late onset AD.
- Understand the mechanisms by which Apolipoprotein E e2 reduces AD risk.
- Identify the underlying mechanisms of the pharmacogenetic effect of Apolipoprotein E on various AD therapeutics.
- Apply a lifecourse approach to examine how the isoform specific effects of Apolipoprotein E on brain development influence various aspects of cognitive aging.
- Apply an epigenetic approach to understand the mechanisms by which genetic and environmental factors interact in different populations to modulate the negative effects of the Apolipoprotein E e4 allele on brain aging.
- Understand how CNS lipid homeostasis changes during aging and during different stages of neurodegeneration.
- Determine the mechanisms by which lipid dysregulation in the CNS influences cognitive aging and the transition to neurodegeneration in AD.

- Understand the impact of chronic changes in circulating cholesterol on lipid homeostasis in the CNS and on other processes associated with cognitive aging and neurodegeneration.
- Determine how cholesterol transport between glial cells and neurons changes during brain aging and in response to different types of brain injury.
- Understand the mechanisms underlying myelin breakdown during aging and elucidate the role of myelin breakdown in cognitive aging and AD pathogenesis.

See [Section VIII, Other Information - Required Federal Citations](#), for policies related to this announcement.

Section II. Award Information

1. Mechanism of Support

This FOA will use the R01 award mechanism. The Project Director/Principal Investigator (PD/PI) will be solely responsible for planning, directing, and executing the proposed project.

This FOA uses “Just-in-Time” information concepts (see [SF424 \(R&R\) Application Guide](#)). It also uses the modular as well as the non-modular budget formats (see <http://grants.nih.gov/grants/funding/modular/modular.htm>). Specifically, a U.S. organization submitting an application with direct costs in each year of \$250,000 or less (excluding consortium Facilities and Administrative [F&A] costs) should use the PHS398 Modular Budget component.

U.S. applicants requesting more than \$250,000 in annual direct costs and all foreign applicants must complete and submit budget requests using the Research & Related Budget component.

2. Funds Available

The total amount of funding for this FOA is expected to be \$2.5 million during fiscal year 2010. Future year amounts will depend on annual appropriations. It is anticipated that four to seven awards will be funded through this FOA;

- Awards will be limited to no more than five years.

Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Although the financial plans of the IC(s) provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds.

Facilities and Administrative (F&A) costs requested by consortium participants are not included in the direct cost limitation, see [NOT-OD-05-004](#).

NIH grants policies as described in the [NIH Grants Policy Statement](#) will apply to the applications submitted and awards made in response to this FOA.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

The following organizations/institutions are eligible to apply:

- Public/State Controlled Institutions of Higher Education
- 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
- 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)
- Small Businesses
- For-Profit Organizations (Other than Small Businesses)
- State Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribally Designated Organizations
- County Governments
- City or Township Governments
- Special District Governments
- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- U.S. Territory or Possession
- Indian/Native American Tribal Governments (Other than Federally Recognized)
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Organizations)

1.B. Eligible Individuals

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the PD/PI 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.

More than one PD/PI (i.e., multiple PDs/PIs), may be designated on the application for projects that require a "team science" approach and therefore clearly do not fit the single-PD/PI model. Additional information on the implementation plans and policies and procedures to formally allow more than one PD/PI on individual research projects is available at http://grants.nih.gov/grants/multi_pi. All PDs/PIs must be registered in the NIH electronic Research Administration (eRA) Commons prior to the submission of the application (see <http://era.nih.gov/ElectronicReceipt/preparing.htm> for instructions).

The decision of whether to apply for a grant with a single PD/PI or multiple PDs/PIs grant is the responsibility of the investigators and applicant organizations and should be determined by the scientific goals of the project. Applications for grants with multiple PDs/PIs will require additional information, as outlined in the instructions below. The NIH review criteria for approach, investigators, and environment have been modified to accommodate applications involving either a single PD/PI or multiple PDs/PIs. When considering the multiple PD/PI option, please be aware that the structure and governance of the PD/PI leadership team as well as the knowledge, skills and experience of the individual PDs/PIs will be factored into the assessment of the overall scientific merit of the application. Multiple PDs/PIs on a project share the authority and responsibility for leading and directing the project, intellectually and logistically. Each PD/PI is responsible and accountable to the grantee organization, or, as appropriate, to a collaborating organization, for the proper conduct of the project or program, including the submission of required reports. For further information on multiple PDs/PIs, please see http://grants.nih.gov/grants/multi_pi.

2. Cost Sharing or Matching

This program does not require cost sharing as defined in the current [NIH Grants Policy Statement](#).

3. Other-Special Eligibility Criteria

Number of Applications. Applicants may submit more than one application, provided that each application is scientifically distinct.

Resubmissions. Applicants may submit a resubmission application, but such application must include an Introduction addressing the previous peer review critique (Summary Statement). Beginning with applications intended for the January 25, 2009 official submission due date, all original new applications (i.e., never submitted) and competing renewal applications will be permitted only a single amendment (A1). See new NIH policy on resubmission (amended) applications ([NOT-OD-09-003](#), [NOT-OD-09-016](#)). Original new and competing renewal applications that were submitted prior to January 25, 2009 will be permitted two amendments (A1 and A2). For these

“grandfathered” applications, NIH expects that any A2 will be submitted no later than January 7, 2011, and NIH will not accept A2 applications after that date.

Renewals. Applicants may submit a renewal application.

Section IV. Application and Submission Information

To download a SF424 (R&R) Application Package and SF424 (R&R) Application Guide for completing the SF424 (R&R) forms for this FOA, use the “Apply for Grant Electronically” button in this FOA or link to <http://www.grants.gov/Apply/> and follow the directions provided on that Web site.

A one-time registration is required for institutions/organizations at both:

- Grants.gov (http://www.grants.gov/applicants/get_registered.jsp) and
- eRA Commons (<http://era.nih.gov/ElectronicReceipt/preparing.htm>)

PDs/PIs should work with their institutions/organizations to make sure they are registered in the NIH eRA Commons.

Several additional separate actions are required before an applicant can submit an electronic application, as follows:

1) Organizational/Institutional Registration in [Grants.gov/Get Registered](http://www.grants.gov/GetRegistered)

- Your organization will need to obtain a [Data Universal Number System \(DUNS\) number](#) and register with the [Central Contractor Registration \(CCR\)](#) as part of the Grants.gov registration process.
- If your organization does not have a Taxpayer Identification Number (TIN) or Employer Identification Number (EIN), allow for extra time. A valid TIN or EIN is necessary for CCR registration.
- The CCR also validates the EIN against Internal Revenue Service records, a step that will take an additional one to two business days.
- Direct questions regarding Grants.gov registration to:
[Grants.gov Customer Support](#)
Contact Center Phone: 800-518-4726
Business Hours: M-F 7:00 a.m. - 9:00 p.m. Eastern Time
Email support@grants.gov

2) [Organizational/Institutional Registration in the eRA Commons](#)

- To find out if an organization is already Commons-registered, see the "[List of Grantee Organizations Registered in NIH eRA Commons](#)”

- Direct questions regarding the Commons registration to:
eRA Commons Help Desk
Phone: 301-402-7469 or 866-504-9552 (Toll Free)
TTY: 301-451-5939
Business hours M-F 7:00 a.m. – 8:00 p.m. Eastern Time
Email commons@od.nih.gov

3) Project Director/Principal Investigator (PD/PI) Registration in the NIH eRA Commons: Refer to the [NIH eRA Commons System \(COM\) Users Guide](#).

- The individual(s) designated as PDs/PIs on the application must be registered also in the NIH eRA Commons. In the case of multiple PDs/PIs, all PDs/PIs must be registered **and be assigned the PI role** in the eRA Commons prior to the submission of the application.
- Each PD/PI must hold a PD/PI account in the Commons. Applicants should not share a Commons account for both an Authorized Organization Representative/Signing Official (AOR/SO) role and a PD/PI role; however, if they have both a PD/PI role and an Internet Assisted Review (IAR) role, both roles should exist under one Commons account.
- When multiple PDs/PIs are proposed, all PDs/PIs at the applicant organization must be affiliated with that organization. PDs/PIs located at another institution need not be affiliated with the applicant organization, but must be affiliated with their own organization to be able to access the Commons.
- This registration/affiliation must be done by the AOR/SO or his/her designee who is already registered in the Commons.

Both the PD(s)/PI(s) and AOR/SO need separate accounts in the NIH eRA Commons since both are authorized to view the application image.

Several of the steps of the registration process could take four weeks or more. Therefore, applicants should immediately check with their business official to determine whether their organization/institution is already registered in both Grants.gov and the [Commons](#). The NIH will accept electronic applications only from organizations that have completed all necessary registrations.

1. Request Application Information

Applicants must download the SF424 (R&R) application forms and the SF424 (R&R) Application Guide for this FOA through Grants.gov/Apply.

Note: Only the forms package directly attached to a specific FOA can be used. You will not be able to use any other SF424 (R&R) forms (e.g., sample forms, forms from another FOA), although some of the "Attachment" files may be useable for more than one FOA.

For further assistance, contact GrantsInfo -- Telephone 301-435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY:Â (301) 451-5936

2. Content and Form of Application Submission

Prepare all applications using the SF424 (R&R) application forms and in accordance with the SF424 (R&R) Application Guide for this FOA through [Grants.gov/Apply](https://www.grants.gov/apply).

The SF424 (R&R) Application Guide is critical to submitting a complete and accurate application to NIH. Some fields within the SF424 (R&R) application components, although not marked as mandatory, are required by NIH (e.g., the *“Credential”* log-in field of the *“Research & Related Senior/Key Person Profile”* component must contain the PD/PITMs assigned eRA Commons User ID). Agency-specific instructions for such fields are clearly identified in the Application Guide. For additional information, see *“Frequently Asked Questions”* Application Guide, [Electronic Submission of Grant Applications](#).

The SF424 (R&R) application has several components. Some components are required, others are optional. The forms package associated with this FOA in [Grants.gov/APPLY](https://www.grants.gov/apply) includes all applicable components, required and optional. A completed application in response to this FOA includes the data in the following components:

Required Components:

SF424 (R&R) (Cover component)
Research & Related Project/Performance Site Locations
Research & Related Other Project Information
Research & Related Senior/Key Person
PHS398 Cover Page Supplement
PHS398 Research Plan
PHS398 Checklist
PHS398 Modular Budget or Research & Related Budget, as appropriate (See [Section IV.6.](#), *“Special Instructions,”* regarding appropriate required budget component.)

Optional Components:

PHS398 Cover Letter File
Research & Related Subaward Budget Attachment(s) Form

Foreign Organizations (Non-domestic [non-U.S.] Entities)

NIH policies concerning grants to foreign (non-U.S.) organizations can be found in the NIH Grants Policy Statement at:

http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPs_Part12.htm#_Toc54600260.

Applications from Foreign organizations must:

- Request budgets in U.S. dollars;
- Prepare detailed budgets for all applications (that is, complete the Research & Related Budget component of the SF424 (R&R) application forms “not the PHS398 Modular Budget component”(see [NOT-OD-06-096](#));
- Not include any charge-back of customs and import fees;
- Comply with the format specifications, which are based upon a standard U.S. paper size of 8.5” x 11” within each PDF;
- If appropriate, request funds for up to 8% Facilities and Administrative (F&A) costs (excluding equipment) (see [NOT-OD-01-028](#), March 29, 2001);
- Comply with Federal/NIH policies on human subjects, animals, and biohazards; and
- Comply with Federal/NIH biosafety and biosecurity regulations (see [Section VI.2.](#), “Administrative and National Policy Requirements”)

Proposed research should provide special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions in other countries that are not readily available in the United States (U.S.) or that augment existing U.S. resources.

SPECIAL INSTRUCTIONS

Applications with Multiple PDs/PIs

When multiple PDs/PIs are proposed, NIH requires one PD/PI to be designated as the "Contact" PI, who will be responsible for all communication between the PDs/PIs and the NIH, for assembling the application materials outlined below, and for coordinating progress reports for the project. The contact PD/PI must meet all eligibility requirements for PD/PI status in the same way as other PDs/PIs, but has no other special roles or responsibilities within the project team beyond those mentioned above.

Information for the Contact PD/PI should be entered in item 15 of the SF424 (R&R) Cover component. All other PDs/PIs should be listed in the Research & Related Senior/Key Person component and assigned the project role of “PD/PI.” Please remember that all PDs/PIs must be registered in the eRA Commons prior to application submission. **The Commons ID of each PD/PI must be included in the “Credential” field of the Research & Related Senior/Key Person component. Failure to include this data field will cause the application to be rejected.**

All projects proposing Multiple PDs/PIs will be required to include a new section describing the leadership plan approach for the proposed project.

Multiple PD/PI Leadership Plan: For applications designating multiple PDs/PIs, a new section of the research plan, entitled “Multiple PD/PI Leadership Plan” [Section 14 of the Research Plan Component in the SF424 (R&R)], must be included. A rationale for

choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and the research project should be described, and should include communication plans, process for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PDs/PIs and other collaborators.

If budget allocation is planned, the distribution of resources to specific components of the project or the individual PDs/PIs should be delineated in the Leadership Plan. In the event of an award, the requested allocations may be reflected in a footnote on the Notice of Award (NoA).

Applications Involving a Single Institution

When all PDs/PIs are within a single institution, follow the instructions contained in the SF424 (R&R) Application Guide.

Applications Involving Multiple Institutions

When multiple institutions are involved, one institution must be designated as the prime institution and funding for the other institution(s) must be requested via a subcontract to be administered by the prime institution. When submitting a detailed budget, the prime institution should submit its budget using the Research & Related Budget component. All other institutions should have their individual budgets attached separately to the Research & Related Subaward Budget Attachment(s) Form. See Section 4.8 of the SF424 (R&R) Application Guide for further instruction regarding the use of the subaward budget form.

When submitting a modular budget, the prime institution completes the PHS398 Modular Budget component only. Information concerning the consortium/subcontract budget is provided in the budget justification. Separate budgets for each consortium/subcontract grantee are not required when using the Modular budget format. See Section 5.4 of the Application Guide for further instruction regarding the use of the PHS398 Modular Budget component.

3. Submission Dates and Times

See [Section IV.3.A.](#) for details.

3.A. Submission, Review, and Anticipated Start Dates

Opening Date: September 5, 2009 (Earliest date an application may be submitted to Grants.gov)

Application Due Date(s): Standard dates apply, please see <http://grants.nih.gov/grants/funding/submissionschedule.htm>

AIDS Application Due Date(s): Standard dates apply, please see

<http://grants1.nih.gov/grants/funding/submissionschedule.htm#AIDS>

Peer Review Date(s): Standard dates apply, please see

<http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward>

Council Review Date(s): Standard dates apply, please see

<http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward>

Earliest Anticipated Start Date(s): Standard dates apply, please see

<http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward>

3.A.1. Letter of Intent

Not applicable

3.B. Submitting an Application Electronically to the NIH

To submit an application in response to this FOA, applicants should access this FOA via http://www.grants.gov/applicants/apply_for_grants.jsp and follow Steps 1-4. Note:

Applications must only be submitted electronically. **PAPER APPLICATIONS WILL NOT BE ACCEPTED.**

3.C. Application Processing

Applications **may** be submitted on or after the opening date and **must** be successfully received by Grants.gov no later than **5:00 p.m. local time** (of the applicant institution/organization) on the application due date(s). (See [Section IV.3.A.](#) for all dates.) If an application is not submitted by the due date(s) and time, the application may be delayed in the review process or not reviewed.

Once an application package has been successfully submitted through Grants.gov, any errors have been addressed, and the assembled application has been created in the eRA Commons, the PD/PI and the Authorized Organization Representative/Signing Official (AOR/SO) have two weekdays (Monday – Friday, excluding Federal holidays) to view the application image to determine if any further action is necessary.

- If everything is acceptable, no further action is necessary. The application will automatically move forward to the Division of Receipt and Referral in the Center for Scientific Review for processing after two weekdays, excluding Federal holidays.
- Prior to the submission deadline, the AOR/SO can “Reject” the assembled application and submit a changed/corrected application within the two-day viewing window. This option should be used if it is determined that some part of the application was lost or did not transfer correctly during the submission process, the AOR/SO will have the option to “Reject” the application and submit a Changed/Corrected application. In these cases, please contact the eRA Help Desk to ensure that the issues are addressed and corrected. Once rejected, applicants should follow the instructions for correcting errors in Section 2.12, including the requirement for cover letters on late applications. The “Reject” feature should also be used if you determine that warnings are applicable to your application and need to be addressed now. Remember,

- warnings do not stop further application processing. If an application submission results in warnings (but no errors), it will automatically move forward after two weekdays if no action is taken. Some warnings may need to be addressed later in the process.
- If the two-day window falls after the submission deadline, the AOR/SO will have the option to “Reject” the application if, due to an eRA Commons or Grants.gov system issue, the application does not correctly reflect the submitted application package (e.g., some part of the application was lost or didn’t transfer correctly during the submission process). The AOR/SO should first contact the [eRA Commons Helpdesk](#) to confirm the system error, document the issue, and determine the best course of action. NIH will not penalize the applicant for an eRA Commons or Grants.gov system issue.
 - If the AOR/SO chooses to “Reject” the image after the submission deadline for a reason other than an eRA Commons or Grants.gov system failure, a changed/corrected application still can be submitted, but it will be subject to the [NIH late policy](#) guidelines and may not be accepted. The reason for this delay should be explained in the cover letter attachment.
 - Both the AOR/SO and PD/PI will receive e-mail notifications when the application is rejected or the application automatically moves forward in the process after two days.

Upon receipt, applications will be evaluated for completeness by the Center for Scientific Review, NIH. Incomplete applications will not be reviewed.

There will be an acknowledgement of receipt of applications from Grants.gov and the [Commons](#). The submitting AOR/SO receives the Grants.gov acknowledgments. The AOR/SO and the PI receive Commons acknowledgments. Information related to the assignment of an application to a Scientific Review Group is also in the Commons.

Note: Since email can be unreliable, it is the responsibility of the applicant to check periodically on their application status in the Commons.

The NIH will not accept any application in response to this FOA that is essentially the same as one currently pending initial merit review unless the applicant withdraws the pending application. The NIH will not accept any application that is essentially the same as one already reviewed. However, the NIH will accept a resubmission application, but such application must include an Introduction addressing the critique from the previous review.

4. Intergovernmental Review

This initiative is not subject to [intergovernmental review](#).

5. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement.

Pre-award costs are allowable. A grantee may, at its own risk and without NIH prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new or renewal award if such costs: 1) are necessary to conduct the project, and 2) would be allowable under the grant, if awarded, without NIH prior approval. If specific expenditures would otherwise require prior approval, the grantee must obtain NIH approval before incurring the cost. NIH prior approval is required for any costs to be incurred more than 90 days before the beginning date of the initial budget period of a new or renewal award.

The incurrence of pre-award costs in anticipation of a competing or non-competing award imposes no obligation on NIH either to make the award or to increase the amount of the approved budget if an award is made for less than the amount anticipated and is inadequate to cover the pre-award costs incurred. NIH expects the grantee to be fully aware that pre-award costs result in borrowing against future support and that such borrowing must not impair the grantee's ability to accomplish the project objectives in the approved time frame or in any way adversely affect the conduct of the project. See NIH Grants Policy Statement

http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part6.htm.

6. Other Submission Requirements

PD/PI Credential (e.g., Agency Login)

The NIH requires the PD(s)/PI(s) to fill in his/her Commons User ID in the "PROFILE" Project Director/Principal Investigator section, "Credential" log-in field of the "Research & Related Senior/Key Person Profile" component.

Organizational DUNS

The applicant organization must include its DUNS number in its Organization Profile in the eRA Commons. This DUNS number must match the DUNS number provided at CCR registration with Grants.gov. For additional information, see "Frequently Asked Questions" Application Guide, [Electronic Submission of Grant Applications](#).

PHS398 Research Plan Component Sections

Page limitations of the PHS398 Research Plan component must be followed as outlined in the SF424 (R&R) Application Guide. While each section of the Research Plan component needs to be uploaded separately as a PDF attachment, applicants are encouraged to construct the Research Plan component as a single document, separating sections into distinct PDF attachments just before uploading the files. This approach will enable applicants to better monitor formatting requirements such as page limits. All

attachments must be provided to NIH in PDF format, filenames must be included with no spaces or special characters, and a .pdf extension must be used.

All application instructions outlined in the SF424 (R&R) Application Guide are to be followed, incorporating "Just-in-Time" information concepts.

Specific Instructions for Applications Requesting \$500,000 (direct costs) or More per Year

Applicants requesting \$500,000 or more in direct costs for any year (excluding consortium F&A costs) must carry out the following steps:

- 1) Contact the IC program staff at least 6 weeks before submitting the application, i.e., as plans are being developed for the study;
- 2) Obtain agreement from the IC staff that the IC will accept the application for consideration for award; and,
- 3) Include a cover letter with the application that identifies the staff member and IC who agreed to accept assignment of the application.

This policy applies to all new, renewal, revision, or resubmission applications. See [NOT-OD-02-004](#), October 16, 2001.

Appendix Materials

Applicants **must** follow the specific instructions on Appendix materials as described in the SF424 (R&R) Application Guide (See <http://grants.nih.gov/grants/funding/424/index.htm>).

Do not use the Appendix to circumvent the page limitations of the Research Plan component. An application that does not comply with the required page limitations may be delayed in the review process.

Resource Sharing Plan(s)

NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. If the final data/resources are not amenable to sharing, this must be explained in the Resource Sharing section of the application (see http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm.)

(a) *Data Sharing Plan*: Regardless of the amount requested, investigators are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible. Applicants are encouraged to discuss data-sharing plans with their NIH program contact (see [Data-Sharing Policy](#) or <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>.)

(b) *Sharing Model Organisms*: Regardless of the amount requested, all applications where the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organisms and related resources or state appropriate reasons why such sharing is restricted or not possible (see [Sharing Model Organisms Policy](#), and [NOT-OD-04-042](#).)

(c) *Genome-Wide Association Studies (GWAS)*: Regardless of the amount requested, applicants seeking funding for a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. A genome-wide association study is defined as any study of genetic variation across the entire genome that is designed to identify genetic associations with observable traits (e.g., blood pressure or weight) or the presence or absence of a disease or condition. For further information see Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (go to [NOT-OD-07-088](#), and <http://grants.nih.gov/grants/gwas/>.)

Foreign Applications (Non-domestic [non-U.S.] Entities)

Indicate how the proposed project has specific relevance to the mission and objectives of the NIH/IC and has the potential for significantly advancing the health sciences in the United States

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process.

2. Review and Selection Process

Applications submitted for this funding opportunity will be assigned on the basis of established PHS referral guidelines to the ICs for funding consideration.

Applications that are complete will be evaluated for scientific and technical merit by (an) appropriate scientific review group(s) in accordance with NIH peer review procedures (<http://grants1.nih.gov/grants/peer/>) using the review criteria stated below.

As part of the scientific peer review, all applications will:

- 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 a priority score;
- Receive a written critique; and
- Receive a second level of review by the appropriate national advisory council or board.

Applications submitted in response to this funding opportunity will compete for available funds with all other recommended applications. 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.

The mission of the NIH is to support science in pursuit of knowledge about the biology and behavior of living systems and to apply that knowledge to extend healthy life and reduce the burdens of illness and disability. As part of this mission, applications submitted to the NIH for grants or cooperative agreements to support 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 five core review criteria, and additional review criteria (as applicable for the project proposed).

Core Review Criteria. Reviewers will consider each of the five review criteria below in the determination of scientific and technical 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? 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?

Investigator(s). Are the PD/PIs, collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, 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?

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?

Approach. Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? 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?

If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

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

Additional Review Criteria. As applicable for the project proposed, reviewers will consider **the following additional items in the determination of scientific and technical merit, but will not give separate scores for these items.**

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

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials.

Inclusion of Women and Minorities. When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders.

Vertebrate Animals. The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia.

Resubmission Applications. When reviewing a Resubmission application (formerly called an amended application), 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.

Renewal Applications. When reviewing a Renewal application (formerly called a competing continuation application), the committee will consider the progress made in the last funding period.

Revision Applications. When reviewing a Revision application (formerly called a competing supplement application), 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.

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.

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

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

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).

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.

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 (http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm); 2) Sharing Model Organisms (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html>); and 3) Genome Wide Association Studies (GWAS) (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html>).

3. Anticipated Announcement and Award Dates

Not Applicable

Section VI. Award Administration Information

1. Award Notices

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 NIH eRA [Commons](#).

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the [NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General](#).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization. The NoA signed by the grants management officer is the authorizing document. Once all administrative and programmatic issues have been resolved, the NoA will be generated via email notification from the awarding component to the grantee business official.

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. See [Section IV.5.](#), "Funding Restrictions."

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the *NIH Grants Policy Statement* 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](#) and [Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities](#).

3. Reporting

When multiple years are involved, awardees will be required to submit the [Non-Competing Continuation Grant Progress Report \(PHS 2590\)](#) annually and financial statements as required in the [NIH Grants Policy Statement](#).

A final progress report, invention statement, and Financial Status Report are required when an award is relinquished, when a recipient changes institutions, or when an award is terminated.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research (program), peer review, and financial or grants management issues:

1. Scientific/Research Contact:

Suzana S. Petanceska, Ph.D.
Division of Neuroscience
National Institute on Aging
7201 Wisconsin Avenue, Suite 350
Bethesda, MD 20892-9205
Telephone: (301) 496-9350
FAX: (301) 496-1494
Email: petanceskas@mail.nih.gov

2. Peer Review Contact(s):

Not Applicable

3. Financial/Grants Management Contact:

Ms. Linda Whipp
National Institute on Aging

Grants and Contracts Management Office
7201 Wisconsin Avenue, Suite 2N212
Bethesda, MD 20892-9205
Telephone: (301) 496-1472
FAX: (301) 402-3672
Email: whipl@nia.nih.gov

Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:

Recipients of PHS support for activities involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (<http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf>) as mandated by the Health Research Extension Act of 1985 (<http://grants.nih.gov/grants/olaw/references/hrea1985.htm>), and the USDA Animal Welfare Regulations (<http://www.nal.usda.gov/awic/legislat/usdaleg1.htm>) as applicable.

Human Subjects Protection:

Federal regulations (45 CFR 46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>).

Data and Safety Monitoring Plan:

Data and safety monitoring is required for all types of clinical trials, including physiologic toxicity and dose-finding studies (Phase I); efficacy studies (Phase II); efficacy, effectiveness and comparative trials (Phase III). Monitoring should be commensurate with risk. The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risks to the participants (â€œNIH Policy for Data and Safety Monitoring,â€ *NIH Guide for Grants and Contracts*, <http://grants.nih.gov/grants/guide/notice-files/not98-084.html>).

Sharing Research Data:

Investigators submitting an NIH application seeking \$500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible (http://grants.nih.gov/grants/policy/data_sharing). Investigators should seek guidance from their institutions, on issues related to institutional policies and local institutional review board (IRB) rules, as well as local, State and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

Policy for Genome-Wide Association Studies (GWAS):

NIH is interested in advancing genome-wide association studies (GWAS) to identify common genetic factors that influence health and disease through a centralized GWAS data repository. For the purposes of this policy, a genome-wide association study is defined as any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight), or the presence or absence of a disease or condition. All applications, regardless of the amount requested, proposing a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. Data repository management (submission and access) is governed by the Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, [NIH Guide NOT-OD-07-088](#). For additional information, see <http://grants.nih.gov/grants/gwas/>

Sharing of Model Organisms:

NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants.nih.gov/grants/policy/model_organism/index.htm). At the same time the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding pursuant to the Bayh-Dole Act (see the [NIH Grants Policy Statement](#)). Beginning October 1, 2004, all investigators submitting an NIH application or contract proposal are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

Access to Research Data through the Freedom of Information Act:

The Office of Management and Budget (OMB) Circular A-110 has been revised to provide access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are: (1) first produced in a project that is supported in whole or in part with Federal funds; and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this funding opportunity in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

Inclusion of Women And Minorities in Clinical Research:

It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research" (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html>); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the SF424 (R&R) application; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

Required Education on the Protection of Human Subject Participants:

NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>.

Human Embryonic Stem Cells (hESC):

Criteria for Federal funding of research on hESCs can be found at <http://stemcells.nih.gov/index.asp> and at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html>. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (<http://escr.nih.gov/>). It is the responsibility of the applicant to provide in the project description and elsewhere in the application as appropriate, the official NIH identifier(s) for the hESC line(s) to be used in the proposed research.

NIH Public Access Policy Requirement:

In accordance with the NIH Public Access Policy, *investigators funded by the NIH must submit or have submitted for them to the National Library of Medicine's PubMed Central* (see <http://www.pubmedcentral.nih.gov/>), *an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication.* The NIH Public Access Policy is available at (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html>). For more information, see the Public Access webpage at <http://publicaccess.nih.gov/>.

Standards for Privacy of Individually Identifiable Health Information:

The Department of Health and Human Services (HHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the HHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (<http://www.hhs.gov/ocr/>) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html>.

URLs in NIH Grant Applications or Appendices:

All applications and proposals for NIH funding must be self-contained within specified page limitations. For publications listed in the appendix and/or Progress report, Internet addresses (URLs) or PubMed Central (PMC) submission identification numbers must be used for publicly accessible on-line journal articles. Publicly accessible on-line journal articles or PMC articles/manuscripts accepted for publication that are directly relevant to the project may be included **only** as **URLs** or **PMC submission identification numbers** accompanying the full reference in either the Bibliography & References Cited section, the Progress Report Publication List section, or the Biographical Sketch section of the NIH grant application. A URL or PMC submission identification number citation may be repeated in each of these sections as appropriate. There is no limit to the number of URLs or PMC submission identification numbers that can be cited.

Healthy People 2010:

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This FOA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.health.gov/healthypeople>.

Authority and Regulations:

This program is described in the Catalog of Federal Domestic Assistance at <http://www.cfda.gov/> and is not subject to the intergovernmental review requirements of Executive Order 12372. 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 Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the [NIH Grants Policy Statement](#).

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and

discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Loan Repayment Programs:

NIH encourages applications for educational loan repayment from qualified health professionals who have made a commitment to pursue a research career involving clinical, pediatric, contraception, infertility, and health disparities related areas. The LRP is an important component of NIH's efforts to recruit and retain the next generation of researchers by providing the means for developing a research career unfettered by the burden of student loan debt. Note that an NIH grant is not required for eligibility and concurrent career award and LRP applications are encouraged. The periods of career award and LRP award may overlap providing the LRP recipient with the required commitment of time and effort, as LRP awardees must commit at least 50% of their time (at least 20 hours per week based on a 40 hour week) for two years to the research. For further information, please see: <http://www.lrp.nih.gov/>.

[Weekly TOC for this Announcement](#)
[NIH Funding Opportunities and Notices](#)

Office of
Extramural
Research
(OER)

National Institutes of
Health (NIH)
9000 Rockville Pike
Bethesda, Maryland
20892

Department of
Health
and Human
Services (HHS)