

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

This Funding Opportunity Announcement (FOA) is developed as a Common Fund initiative (<http://commonfund.nih.gov/>) through the NIH Office of the Director, Office of Strategic Coordination (<http://dpcpsi.nih.gov/osc/>). The FOA will be administered by a trans-NIH team led by the National Institute on Drug Abuse (<http://www.nida.nih.gov>) on behalf of the Common Fund.

Title: Developing Technologies for Improved *In Vivo* Epigenetic Imaging or Analysis (R01)

Announcement Type

New

Request for Applications (RFA) Number: RFA-RM-09-016

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](http://Grants.gov/Apply) (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)

93.310

Key Dates

Release/Posted Date: December 3, 2009

Opening Date: January 3, 2010 (Earliest date an application may be submitted to Grants.gov)

Letters of Intent Receipt Date(s): January 4, 2010

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): February 3, 2010

Peer Review Date(s): June, 2010

Council Review Date(s): August, 2010

Earliest Anticipated Start Date(s): October 1, 2010

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

Expiration Date: February 4, 2010

Due Dates for E.O. 12372

Not Applicable

Additional Overview Content

Executive Summary

- **Purpose.** The specific purpose of this FOA is to develop revolutionary technologies that will enable *in vivo* imaging or analysis of epigenetic changes. The epigenetic features of interest include epigenetic marks, modifying enzymes, effector molecules, the activities of these molecules, or other measures of chromatin state.
 - **Mechanism of Support.** This FOA will utilize the R01 grant mechanism.
 - **Funds Available and Anticipated Number of Awards.** A total of \$3.5 million in FY 2010 funds has been committed to support this FOA. The anticipated number of awards under this FOA is 7-10. Awards issued under this FOA are contingent upon the availability of funds and the submission of a sufficient number of meritorious applications.
 - **Budget and Project Period.** The budget must be commensurate with the proposed research, and the requested project period may not exceed five years. Competing renewals are not allowed.
 - **Application Research Strategy Length:** The R01 application Research Strategy section of the PHS398 may not exceed **12** pages, including tables, graphs, figures, diagrams, and charts. See [Table of Page Limits](#)
 - **Eligible Institutions/Organizations.** Institutions/organizations listed in [Section III, 1.A.](#) are eligible to apply.
 - **Eligible Project Directors/Principal Investigators (PDs/PIs).** 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 each application is scientifically distinct.
 - **Resubmissions.** Resubmission applications are not permitted in response to this FOA.
 - **Renewals.** Renewal applications are not permitted in response to this FOA.
 - **Special Date(s).** This FOA uses non-standard due dates. See [Receipt, Review and Anticipated Start Dates](#).
 - **Application Materials.** See [Section IV.1](#) for application materials.
- All applications, including resubmission, revision and renewal, submitted for due dates January 25, 2010 and beyond, must utilize the current forms and instructions.
- **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 specific purpose of this FOA is to develop revolutionary technologies that will enable *in vivo* imaging or analysis of epigenetic changes. The epigenetic features of interest include epigenetic marks, modifying enzymes, effector molecules, the activities of these molecules, or other measures of chromatin state.

Background

This initiative is funded through the NIH Common Fund, which supports cross-cutting programs that are expected to have exceptionally high impact. All Common Fund initiatives invite investigators to develop bold, innovative, and often risky approaches to address problems that may seem intractable or to seize new opportunities that offer the potential for rapid progress. This Common Fund initiative is part of a series of programs known collectively as the NIH Roadmap (<http://nihroadmap.nih.gov/>).

NIH ROADMAP EPIGENOMICS PROGRAM. Epigenomics was selected by the NIH Leadership as a Roadmap Program following a series of discussions with panels of scientific experts and stakeholders, as well as with input from the scientific community solicited via a Request for Information in the summer of 2006. These discussions indicated a growing awareness among researchers that inappropriate epigenetic changes may have profound implications for human health and disease. However, due to specific scientific gaps, our current ability to determine the extent to which this occurs is limited. This led to the establishment of the NIH Roadmap Epigenomics Program (<http://nihroadmap.nih.gov/epigenomics/>).

The overarching goal of the Roadmap Epigenomics Program is to target and overcome these scientific gaps such that the role of epigenetics in disease pathogenesis can be fully understood in a wide range of common complex human diseases. Portfolio analysis revealed that although the NIH has made a substantial investment in basic epigenetic studies and the epigenetic basis of cancer, significantly less attention had been paid to the investigation of the epigenetic basis of diseases other than cancer, or to furthering genome-wide approaches to epigenetics research. Additional gaps were identified by the scientific community through a Roadmap workshop in March 2007 as well as several prior epigenetics workshops held by NIEHS, NIDA, and NCI. These included the absence of reference epigenomes for any mammalian cell type, the lack of an epigenetics-focused public data interface to facilitate the mining of epigenetic data, technological constraints that impede more rapid analysis of epigenetic

marks, and an incomplete catalog of epigenetic marks. Finally, it was necessary to encourage investigations into the epigenetic basis of diseases spanning the interests of all of the NIH Institutes and Centers. Funding opportunities for the Roadmap Epigenomics Program were developed to address these critical gaps in knowledge.

COMPONENTS OF THE NIH ROADMAP EPIGENOMICS PROGRAM. The Roadmap Epigenomics Program consists of six major components. Current funding opportunities and descriptions of funded grants within each component may be found at (<http://nihroadmap.nih.gov/epigenomics/>).

1. REFERENCE EPIGENOME MAPPING CENTERS. The Reference Epigenome Mapping Centers (REMCs) will generate reference epigenome maps of a variety of human cell types. Specific cell types to be analyzed are selected by the network of awardees with guidance from external scientific experts, and include certain human embryonic stem cells, induced pluripotent stem cells, differentiating cells, differentiated cell populations and primary cells relevant to complex human disease. These epigenomic maps will include information about DNA methylation, histone modifications, and associated non-coding RNAs. Functional correlates of these epigenetic marks, such as gene expression and chromatin accessibility (DNaseI hypersensitivity), will also be measured. The comprehensive data sets comprising this valuable community resource can be used to understand basic biological processes as well as disease mechanisms, provide insights into epigenetic and genetic disease susceptibility, and assist in the identification of potential therapeutic targets.

2. EPIGENOMICS DATA ANALYSIS AND COORDINATION CENTER. The Epigenomics Data Analysis and Coordination Center (EDACC) provides an informatics and analysis resource to assist the REMCs, as well as grantees from other components of the program, by coordinating and facilitating a common data format structure and integrative analyses of the epigenomic data. These data are being made publically available by NCBI through an Epigenetics Public Interface (see below).

3. TECHNOLOGY DEVELOPMENT IN EPIGENETICS (R01 AND R21). Although the technologies and tools necessary for epigenetic analyses are improving, there are still constraints that impede even more rapid progress. The Technology Development initiative supports the development of innovative technologies that have the potential to significantly change the way that epigenomics research can be performed in the future.

4. DISCOVERY OF NOVEL EPIGENETIC MARKS IN MAMMALIAN CELLS (R01 AND R21). The current catalog of known epigenetic marks (as well as proteins that create, remove, and "read" these marks) is likely incomplete. This initiative supports research to identify and characterize novel epigenetic marks in mammalian cells. Novel marks that can be validated as important epigenetic regulators in human cells will be considered for incorporation into the REMCs.

5. EPIGENOMICS OF HUMAN HEALTH AND DISEASE (R01). Although there has been a great deal of investigation into the epigenetic underpinnings of many types of cancer, the role of epigenetics in other diseases remains largely unstudied. This initiative supports transformative research aimed at identifying the fundamental epigenetic mechanisms underlying specific diseases, conditions of development or aging, or response to exposures (including physical, chemical, behavioral, and social factors).

6. EPIGENETIC PUBLIC INTERFACE. The National Center for Biotechnology Information (NCBI) is generating a repository and long-term data archive for the Roadmap Epigenomics Program as well as a user friendly platform for epigenomics research. It will allow researchers to access epigenomic data for normal and diseased cell types and to correlate it with other types of information, such as gene expression data. A major goal of this effort is to enable researchers with varied backgrounds to leverage epigenomic data for future scientific discoveries.

INTEGRATION OF THE PROGRAM COMPONENTS. The Roadmap Epigenomics Program is integrated on multiple levels. Regular meetings between the REMC, EDACC, and NCBI teams enable these groups to coordinate and standardize their efforts in generating genome-wide epigenetic information, as well as for verifying and releasing this data through the EDACC and NCBI. Data produced by all components of the program will be made available through the Epigenetics Public Interface. An external scientific panel provides scientific advice and guidance throughout the life of the program. A yearly Roadmap Epigenomics Program Investigators Meeting will assemble investigators from all components of the program fostering collaboration and cross-fertilization of ideas. In addition to the efforts already described, monoclonal antibodies against up to 50 epigenetic targets nominated by the scientific community are being produced to provide standardized, low-cost reagents to the public. Finally, workshops will be held periodically to identify needs in specific areas of epigenetics research as they arise, as well as to help integrate the efforts of the Roadmap Epigenomics Program with other international and US epigenetics efforts.

Objectives

The objective of the Technology Development in Epigenetics Initiative is to stimulate the development of revolutionary epigenetic technologies as part of the Roadmap Epigenomics Program. We are specifically interested in revolutionary technologies rather than evolutionary changes to currently existing technologies. Transforming technologies are needed to enable researchers to monitor epigenetic events related to development and disease.

Each human cell type is believed to have a distinct epigenomic profile, which may be altered in a disease state. Therefore, clinical diagnosis of diseases with a significant epigenetic component requires the ability to monitor the epigenetic state of specific tissues/cell types. Tissues such as blood or skin are readily available for this analysis, however in the case of diseases impacting the brain, heart, bone, and other organs it may be difficult or impossible to obtain the appropriate tissue/cell type for epigenetic analysis. Currently the technologies available to determine the epigenetic state of tissues *in vivo* are extremely limited. The specific purpose of this FOA is to develop revolutionary technologies that will enable *in vivo* imaging or analysis of epigenetic changes. The epigenetic features of interest include epigenetic marks, modifying enzymes, effector molecules, the activities of these molecules, or other measures of chromatin state.

Areas of interest include but are not limited to:

- The development of technologies and associated optical probes, radiotracers, or ligands for the *in vivo* imaging of epigenetic modifications or modifying enzymes or epigenetic effector molecules.
- Imaging technologies for monitoring epigenetic modifications or modifying enzymes at a cellular, tissue, or organ level in living organisms.
- Technologies that enable *in vivo* determination of the epigenetic state of human tissues that are not readily available (brain, heart, bone, etc).

Researchers may propose to develop their technology in any *in vivo* system. We are looking for high impact research in this scientific target area. Applications addressing low impact, incremental improvements to current technologies are not of interest. Applications that propose to use a new technology primarily to test specific scientific hypotheses are advised to submit investigator-initiated applications rather than to submit to this FOA. Applicants should pay close attention to the review criteria for special requirements concerning the significance of the project to the epigenetics research community and project innovation. In all cases, the proposed budget should be commensurate with the research proposed. Upon receipt, applications will be evaluated for completeness by the Center for Scientific Review and for responsiveness by program staff in the NIH Roadmap Epigenomics Workgroup. Incomplete and/or non-responsive applications will be administratively withdrawn without review and will not be considered for funding. A sustained investment in the development of epigenetics technologies will lead to significant advances in our ability to measure and monitor epigenetic modifications *in vivo*. In the long term, advances in these areas will enhance our ability to investigate, diagnose and ameliorate human disease with a significant epigenetic component.

Evaluation

As part of good program management, NIH assesses the implementation and effectiveness of its programs using evaluation tools and techniques. Grantees may be asked to provide information for program evaluation purposes, both locally and at the national level. Such information may be used in evaluations of the Technology Development projects, as well as the "Mid-Course" review of the entire Roadmap Epigenomics Program. Note that the Roadmap Epigenomics Program Mid-Course evaluation will be directed by the Epigenomics Working Group (EWG). Applicants are advised to review the additional details on evaluation that are provided in Section IV.6. Application and Submission Information, "Other Submission Requirements."

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) must 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

- **Funds Available.** A total of \$3.5 million in FY 2010 funds has been committed to support this FOA.
- **Anticipated Number of Awards.** The anticipated number of awards under this FOA is 7-10. Awards issued under this FOA are contingent upon the availability of funds and the submission of a sufficient number of meritorious applications.
- **Budget and Project Period.** The requested budget must be commensurate with the work proposed. The proposed project period may not exceed 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)
- Other(s):
 - Eligible Agencies of the Federal Government
 - Faith-based or Community-based 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 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. 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 each application is scientifically distinct.

Resubmissions.

Resubmission applications are not permitted in response to this FOA.

Renewals.

Renewal applications are not permitted in response to this FOA.

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.

Registration:

Appropriate registrations with Grants.gov and eRA Commons must be completed on or before the due date in order to successfully submit an application. **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 with both [Grants.gov](http://www.grants.gov/) and the [Commons](http://era.nih.gov/). All registrations must be complete by the submission deadline for the application to be considered "on-time" (see 3.C.1 for more information about on-time submission).

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](http://www.duns.com/) and register with the [Central Contractor Registration \(CCR\)](http://www.ccr.gov/) 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](http://www.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](http://era.nih.gov/)

- To find out if an organization is already Commons-registered, see the "[List of Grantee Organizations Registered in NIH eRA Commons.](http://era.nih.gov/era-commons-registered-organizations)"
- 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](http://era.nih.gov/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 NIH 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 PDs/PI(s) and AOR/SO need separate accounts in the NIH eRA Commons since both are authorized to view the application image.

Note: The registration process is not sequential. Applicants should begin the registration processes for both Grants.gov and eRA Commons as soon as their organization has obtained a DUNS number. Only one DUNS number is required and the same DUNS number must be referenced when completing Grants.gov registration, eRA Commons registration and the SF424 (R&R) forms.

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](http://www.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: (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://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/PI's 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://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% administrative 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", 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.

Applications Involving Federal Agencies

The requests from federal agencies, including the NIH intramural program, will not include any salary and related fringe benefits for career, career conditional or other federal employees (civilian or uniformed service) with permanent appointments under existing position ceilings or any costs related to administrative or facilities support (equivalent to Facilities and Administrative costs).

In general, the budget requests will be limited to the incremental costs required for carrying out the proposed work. These costs may include salary for staff to be specifically hired under a temporary appointment for the project, consultant costs, equipment, supplies, travel, and other items typically listed under Other Expenses. While support for extramural collaborators may be requested in a separate grant application, funds can be requested for services by an external investigator or contractor as a subcontract/consortium including the applicable indirect (F&A costs) of the contractor/collaborating institution.

Justification must be provided for all requested support and for the Federal employees who will be committed to the project although no funds are requested in the application.

Applicants should indicate the number of person-months devoted to the project, even if no funds are requested for salary and fringe benefits.

3. Submission Dates and Times

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

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

Opening Date: January 3, 2010 (Earliest date an application may be submitted to Grants.gov)

Letters of Intent Receipt Date(s): January 4, 2010

Application Due Date(s): February 3, 2010

Peer Review Date(s): June 2010

Council Review Date(s): August 2010

Earliest Anticipated Start Date(s): October 1, 2010

3.A.1. Letter of Intent

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed research.
- Name, address, and telephone number of the PD(s)/PI(s).
- Names of other key personnel.
- Participating institutions.
- Number and title of this funding opportunity.

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed in [Section IV.3.A.](#)

The letter of intent should be sent to:

John Satterlee, Ph.D.
Roadmap Epigenomics Program Co-coordinator
National Institute on Drug Abuse/NIH
Division of Basic Neuroscience and Behavioral Research
6001 Executive Blvd., Rm 4264
Bethesda, MD 20892
Telephone: (301)-443-1887
Email: satterleej@nida.nih.gov

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

3.C.1 Submitting On-Time

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. All applications must meet the following criteria to be considered "on-time":

- All registrations must be complete prior to the submission deadline
- The application must receive a Grants.gov tracking number and timestamp (or eRA help desk ticket confirming a system issue preventing submission) by 5:00 p.m. local time on the submission deadline date.
- Any system identified errors/warnings must be corrected and the submission process completed within the "error correction window."

Please visit http://era.nih.gov/electronicReceipt/app_help.htm for detailed information on what to do if Grants.gov or eRA system issues threaten your ability to submit on time.

Submission to Grants.gov is not the last step – applicants must follow their application through to the eRA Commons to check for errors and warnings and view their assembled application!

3.C.2 Two Day Window to Correct eRA Identified Errors/Warnings

Once an application package has been successfully submitted through Grants.gov, NIH provides applicants a two day *error correction window* to correct any eRA identified errors or warnings before a final assembled application is created in the eRA Commons. The standard error correction window is two (2) business days, beginning the day after the submission deadline and excluding weekends and standard federal holidays. All errors must be corrected to successfully complete the submission process. Warnings will not prevent the application from completing the submission process.

Please note that the following caveats apply:

- Initial application submission must be “on-time.”
- The AOR/institutions is expected to enforce that application changes made within the error correction window are restricted to those necessary to address system-identified errors/warnings. NIH may reject any application that includes additional changes.
- Proof of “on-time” submission (e.g., Grants.gov timestamp and tracking number) and description of all changes made within the window must be documented in the PHS 398 Cover Letter component of the application.

3.C.3 Viewing an Application in the eRA Commons

Once any eRA identified 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 assembled application before it automatically moves forward to NIH for further processing.

- 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 weekdays.

Upon receipt, applications will be evaluated for completeness by the CSR and responsiveness by the IC. Incomplete and/or non-responsive 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 the application status in the Commons.

The NIH will not accept any application in response to this funding opportunity that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, when a previously unfunded application, originally submitted as an investigator-initiated application, is to be submitted in response to a funding opportunity, it is to be prepared as a NEW application. That is, the application for the funding opportunity must not include an “Introduction” describing the changes and improvements made, and the text must not be marked to indicate the changes from the previous unfunded version of the application.

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 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 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 the [NIH Grants Policy Statement](#)).

6. Other Submission Requirements

To accelerate progress in the field of epigenomics, grantees will be expected to participate actively and openly in at least one grantee meeting per year. Substantial information sharing is critical to the program, so how an applicant plans to achieve this would be considered as a term and condition of the award; failure to openly share information will be considered in continued funding consistent with achieving the goals of the program. It is understood that some information developed under the grants will be proprietary and cannot be shared immediately without damaging the commercialization potential of the technology. Applicants should describe their plans for participating in the grantee meetings and for managing the intellectual property concerns in the context of those meetings and other opportunities for information sharing. Other investigators in the field (i.e., not supported under this program) may be invited to participate in these workshops, but their agreement to share information substantially will be a prerequisite to their participation. Applicants must budget funds for travel of the PD/PI and up to one additional investigator to attend an annual investigators’ meeting in Washington D.C.

This initiative is part of a broader program in Epigenomics funded as part of the NIH Roadmap. In order to fulfill requirements for oversight of the Epigenomics Program as a whole, NIH staff may have to present status reports on individual initiatives to coincide with NIH Office of the Director time frames. Thus, in addition to the annual progress report required at the time of submission of the noncompeting continuation application, awardees may be required to submit additional progress updates at a time to be determined by NIH. Program staff will use information from reports, site visits, etc. to evaluate each grantee’s progress and the success of the overall program. Progress will also be evaluated with the assistance of external advisors at the annual meeting and at the mid-course review of the entire Roadmap Epigenomics Program.

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

The Research Strategy section of the **R01** application may not exceed **12** pages, including tables, graphs, figures, diagrams, and charts. See [Table of Page Limits](#).

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

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. 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/>.)

Roadmap Epigenomics Program Data and Resource Sharing

To achieve the goals of this program, projects funded by this RFA are expected to share technological advances and research data. For example, depending on the precise nature of the project, sharing can take place in various ways. Examples of such approaches are described in greater detail in the sections that follow and are consistent with achieving the goals of this program. The PIs of funded projects will be expected to share technological advances and information with other PIs funded by the Roadmap Epigenomics Program through active and open participation in at least one grantee meeting per year. The PIs of funded projects will also be expected to share technological advances and information with epigenetics researchers as a whole and thus need to give thought to an appropriate intellectual property management plan necessary to facilitate this sharing.

The precise content of data sharing plans will vary, depending on the data being collected and how the investigator is planning to share the data. Applicants who are planning to share data should describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement. References to data sharing may also be appropriate in other sections of the application.

As described above, all applicants are expected to include a plan for sharing research data in their application. The data sharing policy is available at http://grants.nih.gov/grants/policy/data_sharing. All investigators responding to this funding opportunity should include a description of how final research data will be shared, or explain why data sharing is not possible.

The reasonableness of data sharing plans or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. Program staff will be responsible for overseeing the data sharing policy and for assessing the appropriateness and adequacy of proposed data-sharing plans. Applicants are encouraged to discuss data sharing plans with their program contact prior to submitting their applications.

As the Roadmap Epigenomics Program is a community resource program, NIH expects that not only data, but also resources generated during the course of the program should be made rapidly available to the research community and that sharing plans should follow the same principles and spirit as the proposed rapid data release policy. The applicant should provide specific plans for resource sharing and distribution in the application. The reasonableness of the data sharing plans will be assessed by the reviewers. However, reviewers will not factor the proposed resources sharing plan into the determination of scientific merit or the priority score. The adequacy of the resources sharing plans will be considered by the funding organization when making recommendations about funding applications. The presence of a resources sharing plan will be part of the terms and conditions of the award. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590, <http://grants.nih.gov/grants/funding/2590/2590.htm>. See Section VI.3. Award Administration Information, "Reporting."

Intellectual Property Management Plan

Certain research plans will require collaboration and coordination between investigators at different institutions, some of whom may not be NIH funding recipients and who may have pre-existing intellectual property obligations to third parties. It is anticipated that commercial embodiments of the results of such research may incorporate single inventions shared by several institutions, or multiple inventions each from a separate institution. Therefore, prior to funding, grant applicants are expected to address, for example, how they will coordinate patent prosecution and licensing activities, if necessary, to enable a licensee to access the bundle of intellectual property needed to take a product to market on commercially viable terms. Suggested strategies include: (1) assigning intellectual property rights to related inventions to an invention management firm; (2) designating one organization to take the lead on patenting and licensing related inventions; and (3) agreeing in advance that if multiple parties are to independently license related inventions, the total of stacked royalties will not exceed a predetermined percentage rate. The technology transfer/ intellectual property management/licensing officer or equivalent of the PI's institution is expected to submit an intellectual property management plan, including at least those elements above. Alternatives to the suggested strategies, which accomplish the same goals, will be considered. Intellectual property management plans are a just-in-time requirement and do not need to be included in the grant application but plans will be required before a grant can be awarded. The applicant's institution should avoid exclusively licensing those inventions that are research tools unless either: (1) the field of use of the exclusive license is restricted to commercial use; or (2) the exclusive licensee will make the research tool available on reasonable terms. Applicants are directed to the NIH policy on the dissemination of biological research resources ("research tools") at http://grants.nih.gov/grants/intell-property_64FR72090.pdf.

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

Review Process

Applications that are complete and responsive to this FOA will be evaluated for scientific and technical merit by an appropriate peer review group convened by **CSR** and 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 an impact/priority score;
- Receive a written critique; and
- Receive a second level of review by the appropriate national advisory council or board.

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/priority 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? Will the proposed project significantly enable *in vivo* imaging or analysis of epigenetic changes? Is the potential advance resulting from the proposed work exceptional?

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? Is the project original or revolutionary? Is the hypothesis and/or the proposed methodology unconventional and exceptionally innovative? Does the proposed technological development represent a major leap beyond the current state of the art?

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, Minorities, and Children. When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children.

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.

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/priority 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>).

Selection Process

Applications submitted in response to this FOA will compete for available funds with all other recommended applications submitted in response to this FOA. The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.
- Compliance with data and resource sharing policies.

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

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(s):

John Satterlee, Ph.D.
 Roadmap Epigenomics Program Co-coordinator
 National Institute on Drug Abuse/NIH
 Division of Basic Neuroscience and Behavioral Research
 6001 Executive Blvd., Rm 4264
 Bethesda, MD 20892
 Telephone: (301)-443-1887

Email: satterleej@nida.nih.gov

Lisa Helbling Chadwick, Ph.D.
 Division of Extramural Research and Training
 National Institute of Environmental Health Sciences (NIEHS)
 530 Davis Drive
 PO 12233, Mail Drop K3-15
 Research Triangle Park, NC 27707
 Telephone: (850) 727-7218
 Fax: (919) 541-0462
 Email: chadwickL@niehs.nih.gov

2. Peer Review Contact(s):

Richard Panniers, Ph.D.
 Center for Scientific Review
 Division of Molecular and Cellular Systems
 6701 Rockledge Drive
 Room 2198, MSC 7840
 Bethesda, Maryland 20892-7840
 Telephone: (301) 435-1741
 FAX: (301) 480-1988
 Email: Pannierr@csr.nih.gov

3. Financial/Grants Management Contact(s):

Carol Alderson
 Deputy Chief Grants Management Officer
 National Institute on Drug Abuse/NIH
 6101 Exec Blvd, MSC 8403
 Bethesda, MD 20892
 301-443-6710
 Email: Ca10h@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 ("NIH Policy for Data and Safety Monitoring," *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.

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.

Inclusion of Children as Participants in Clinical Research:

The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects (<http://grants.nih.gov/grants/funding/children/children.htm>).

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-09-116.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/>.

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