

Part I Overview Information

Department of Health and Human Services

Participating Organizations

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

Components of Participating Organizations

National Institute of Dental and Craniofacial Research (NIDCR/NIH), (<http://www.nidcr.nih.gov>)

Title: Multidisciplinary Research On Oral Manifestations Associated With HIV/AIDS

Announcement Type

New

Program Announcement (PA) Number: PAR-05-031

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Key Dates

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Application Receipt Dates(s): September 13, 2005, 2006 and 2007

Peer Review Date(s): November/December 2005, 2006 and 2007

Council Review Date(s) : January/February 2006, 2007 and 2008

Earliest Anticipated Start Date: February/March 2006, 2007 and 2008

Additional Information To Be Available Date (Url Activation Date): Not applicable

Expiration Date: September 14, 2007

Due Dates for E.O. 12372

Not applicable.

Additional Overview Content

Executive Summary

- The primary goal of this initiative is to encourage the formation of multidisciplinary scientific teams to study the oral manifestations and complications associated with HIV/AIDS-related immunosuppression. The applicants are expected to develop a minimum of three highly integrated projects that address the existing gaps in our knowledge of the pathogenesis of the oral complications of HIV disease. The projects will be expected to be synergistic and to utilize cutting-edge approaches such as genomics, proteomics, molecular imaging and other emerging technologies to achieve their goals.
- The NIDCR intends to commit approximately \$1.3 million total cost in each of FY 2006, 2007 and 2008 to fund one new and/or competitive continuation grant per year in response to this Program Announcement.

- This PAR will use the NIH Program Project (P01) award mechanism.
- Eligible organizations include: For-profit or non-profit organizations, public or private institutions, such as universities, colleges, hospitals, and laboratories, units of State and local governments, eligible agencies of the Federal government, Domestic Institutions/Organizations only. However foreign investigators can participate as co-investigators if they can offer unusual talent, resources, populations, or environmental conditions that are not readily available in the United States or that augment existing U.S. resources and provided their participation will enhance the overall performance of the grant.
- Eligible principal investigators include any individual with the skills, knowledge, and resources necessary to carry out the proposed research. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.
- Investigators may submit more than one application as part of different collaborative groups. There should be no scientific or budgetary overlap.
- The PHS 398 application can be obtained from <http://grants.nih.gov/grants/funding/phs398/phs398.html>
- Telecommunications for the hearing impaired is available at: TTY 301-451-0088

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

Purpose:

The primary goal of this initiative is to bring together interdisciplinary scientific teams to study the oral manifestations and complications associated with HIV/AIDS-related immunosuppression. The applicants will use the Program Project (P01) grant mechanism to develop highly integrated projects that address the existing gaps in our knowledge of the pathogenesis of the oral complications of HIV disease. Regardless of the theme, projects in each multidisciplinary program will be expected to be synergistic and to utilize cutting-edge approaches such as genomics, proteomics, molecular imaging and other emerging technologies to achieve their goals. In addition it is expected that these P01 Program Projects will provide interdisciplinary career development opportunities for investigators new to the field of oral AIDS.

Background:

HIV infection continues to be a major public health problem throughout the world. The oral manifestations of HIV infection occur in 30 to 80 percent of the affected patient population. These patients are vulnerable to several oral complications, including oral tumors, oral candidiasis, oral viral infections, HIV related salivary gland disorders, mucositis and oral ulcerations of diverse etiologies. Some of these conditions are aggressive, hard to treat and can affect the quality of life of the patients. Factors that predispose the patients to the oral complications are CD4 T cell counts less than 200 cells/mm³, viral load greater than 3000 copies/ml, xerostomia, poor oral health hygiene and smoking.

Although the incidence of some of the oral lesions associated with HIV infections has been reduced after the introduction of highly active antiretroviral therapy (HAART), some did not change and others increased. For example, while there was a reduction in the incidence of oral candidiasis and oral Kaposi's sarcoma over time, there was no change in the incidence of aphthous ulcers and an increase in the incidence of salivary gland disease and oral warts. An increasing problem among patients receiving HAART is the development and

spread of drug resistant strains, which in turn leads to failure of therapy, disease progression and rebound of oral complications. The effects of HAART can not be completely explained by immune reconstitution and the reduction in the viral load. Due to exposure to a multitude of factors, the protein profile of the oral mucosa is constantly changing. Examining the effects of HAART on the oral mucosal milieu is likely to elucidate the conditions that appear conducive or protective to these lesions.

The incidence of salivary gland disease continues to increase despite the introduction of HAART. Patients with HIV-related salivary gland disease present with signs and symptoms similar to those of patients with Sjögren's syndrome. This condition is characterized by lymphocytic infiltration of the salivary glands and lymphoepithelial cysts of the major salivary glands. Occasionally lymphomas may develop within the salivary glands. The search for an etiology for these lymphomas is inconclusive.

The majority of HIV infections are initiated at mucosal sites. The oral mucosal tissue has been shown to be a potential route of entry in both humans and primates. HIV RNA and proteins can be detected directly in the oral mucosa, as well as in the saliva from infected subjects. However, infectious HIV virions are rarely found in the saliva, suggesting that the oral mucosa is not permissive for efficient HIV replication. The structural and environmental protective factors that make the oral mucosa more resistant to HIV replication than other mucosal sites in the body is not clear and has implications for development of vaccines. In children however, mother to child transmission of HIV, through breast feeding, constitutes a major problem for infection of newly born babies and development of reliable novel strategies to interrupt this route of transmission is of the utmost importance.

Despite the advances in HIV vaccine research, we are far from having a reliable protective HIV vaccine. Since the majority of infections occur through mucosal sites, it is logical to develop vaccines that make use of the oral mucosal lymphoid tissue as a route of inoculation. The oral mucosa is rich with immunologically functional cells, including dendritic cells, lymphocytes, monocytes/macrophages and neutrophils. Understanding the interactions of adaptive and innate immune networks will facilitate the development of new strategies to prevent and control HIV and other opportunistic infections.

Our understanding of HIV pathogenesis is far from complete as is our understanding of how other opportunistic pathogens (HHV-8, CMV, EBV, HPV and Candida) infect and cause the oral complications associated with AIDS. The ability of the oral cavity to resist HIV infection and replication while providing a site for latency for other pathogens provides a unique opportunity to dissect the differential patterns of host defenses, the mechanisms utilized by oral pathogens to evade the immune response and the mechanisms involved in reactivation of latent oral viral pathogens to cause disease. It is conceivable that polymicrobial interaction may play a role in the pathogenesis of the viral complications associated with HIV/AIDS. This can be via a virus-virus, virus-bacteria or virus-fungal interaction.

Infection of the oral tissues is influenced by environmental factors. The surface of the mucosa is covered by salivary carbohydrates, lipids and proteins, and directly interacts with the oral environment, containing bacteria, fungi, viruses, food, tobacco products, alcohol, etc. In addition, the mucosa produces or is bathed by cytokines, chemokines, antibodies and innate host factors in saliva. The exposure of the oral mucosa to many of these factors, suggest the environmental conditions that facilitate the induction of the oral lesions, are possibly multifactorial. Understanding these potential interactions in the context of HIV infection will provide insight into their influence on the pathogenesis of the AIDS related oral disorders.

Multidisciplinary studies with a common theme, addressing the pathogenesis of the oral manifestations associated with AIDS, is crucial for increasing our understanding of these disorders. The information gained can provide the basis for the development of novel diagnostic, preventive and therapeutic strategies for HIV-related oral disorders.

Scope:

The aim of this initiative is to encourage the submission of interdisciplinary research proposals with at least three (four or more are recommended) tightly integrated projects and any necessary cores that address the existing gaps in our knowledge of the pathogenesis of the oral complications of HIV infection. Integrating expertise from diversified scientific fields such as virology, immunology, pathology, molecular biology,

bioimaging, nanotechnology, systems biology, mathematical modeling and bioinformatics will facilitate the performance of cutting edge studies to advance the field.

Examples of topics include, but are not limited to:

- Studies of host genetic factors and markers that are associated with susceptibility and progression of HIV-associated orally relevant microbes and opportunistic pathogens (HPV, EBV, KSHV, CMV, etc.);
- Studies on the changes of the composition of the saliva in HIV disease and AIDS-associated oral complications. This may include studies that will identify signature patterns that are of predictive, diagnostic and prognostic value;
- Studies on the changes in the oral microbiota and their contribution to the oral complications associated with HIV disease. These studies may explore the role of polymicrobial interactions in triggering the oral complications associated with HIV disease and/or identify the qualitative and quantitative patterns of the oral flora that induce disease.
- Studies that will determine the host and/or environmental factors that will facilitate infection of oral epithelial cells with oral opportunistic pathogens;
- Studies on oral mucosal immunity, including approaches to enhance innate and adaptive immunity; novel approaches for interfering with oropharyngeal transmission of opportunistic pathogens in the context of immunosuppression; and novel approaches for HIV vaccine development that make use of the oral or nasopharyngeal tissues for inoculation. This may include the design of new antigens, adjuvants and vaccine delivery methods that elicit long lasting protective immune responses;
- Studies to determine the immunological mechanisms that are involved in viral-induced oral malignancies and tumors, in the context of HIV infection;
- Studies to determine the viral reservoirs and anatomic sites for viruses associated with oral complications of HIV disease (EBV, CMV, HSV, KSHV, HPV, etc.) and the site of their shedding in the oral cavity. This may include studies that will investigate the mechanisms of latency and factors that trigger the switch of the virus from latent to lytic replication in HIV infection;
- Studies on the oral complications associated with the prolonged use of HAART in patients with HIV including etiology, host susceptibility, early detection and prevention;
- Studies on salivary gland complications in HIV infection, including basic research on etiology, pathogenesis, epidemiology and prevention;

Each program project is expected to provide an excellent environment for training of graduate students, postdoctoral fellows and other health professionals. This initiative is not designed to support clinical trials. However, the use of clinical samples from patients is allowable and encouraged. The applicants are encouraged to contact the designated Program official at least six weeks prior to submission.

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

Section II. Award Information

1. Mechanism of Support

This funding opportunity will use the Program Project (P01) award mechanism. Program Project grants support broadly based, multi-disciplinary research programs that have a well-defined, central research focus or objective. An important feature is that the interrelationships of the individual scientifically meritorious projects will result in a greater contribution to the overall program goals than if each project were pursued individually. The program project grant consists of a minimum of three interrelated individual research projects (four or more are recommended) that contribute to the program objective. This type of award also can provide support for certain common resources (cores). Such resources should be utilized by two or preferably more projects within the program project. The total project period may not exceed five years. As an applicant, you will be solely responsible for planning, directing, and executing the proposed project.

This funding opportunity uses the just-in-time budget concepts. It also uses the non-modular budget format described in the PHS 398 application instructions (see <http://grants.nih.gov/grants/funding/phs398/phs398.html>). A detailed categorical budget for the "Initial Budget Period" and the "Entire Proposed Period of Support" is to be submitted with the application.

2. Funds Available

- The NIDCR intends to commit approximately \$1.3 million total costs in each of FYs 2006, 2007 and 2008.
- The NIDCR intends to fund one grant per year (new and/or competitive continuation grant) in response to this PAR. An applicant may request a project period of up to 5 years.
- The expected amount of an individual award is \$750,000 to \$850,000 direct costs. 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 NIDCR provide support for this program, awards pursuant to this PAR are contingent upon the availability of funds and the receipt of meritorious applications.
- The anticipated starting date for these awards will be February/March of each of the three years.

Facilities and administrative costs requested by consortium participants are not included in the direct cost limitation, see <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-004.html>.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

You may submit (an) application(s) if your organization has any of the following characteristics:

- For-profit organizations
- Non-profit organizations
- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State government
- Units of local government
- Eligible agencies of the Federal government
- Domestic Institutions only.

However, foreign investigators can participate as co-investigators if they can offer unusual talent, resources, populations, or environmental conditions that are not readily available in the United States or that augment existing U.S. resources and provided their participation will enhance the overall performance of the grant.

1.B. Eligible Individuals

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution 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 programs.

2. Cost Sharing or Matching

Cost sharing is not required.

The most current Grants Policy Statement can be found at:
http://grants.nih.gov/grants/policy/nihgps_2003/nihgps_Part2.htm#matching_or_cost_sharing

3. Other-Special Eligibility Criteria

There is no limit on the number of applications an institution can submit. However, an investigator can only be a principal investigator on one application.

Section IV. Application and Submission Information

1. Address to Request Application Information

The PHS 398 application instructions are available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. Applicants must use the currently approved version of the PHS 398. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088.

2. Content and Form of Application Submission

Applications must be prepared using the most current PHS 398 research grant application instructions and forms. Applications must have a Dun and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the universal identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at <http://www.dnb.com/us/>. The D&B number should be entered on line 11 of the face page of the PHS 398 form.

The title and number of this funding opportunity must be typed on line 2 of the face page of the application form and the YES box must be checked.

3. Submission Dates and Times

Applications must be mailed on or before the receipt date described below ([Section IV.3.A](#)). Submission times N/A.

3.A. Receipt, Review and Anticipated Start Dates

Letters of Intent Receipt Date(s): August 14, 2005, 2006 and 2007
Application Receipt Dates(s): September 13, 2005, 2006 and 2007
Peer Review Date(s): November/December 2005, 2006 and 2007
Council Review Date(s) : January/February 2006, 2007 and 2008
Earliest Anticipated Start Date: February/March 2006, 2007 and 2008

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 Principal Investigator
- 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 at the beginning of this document.

The letter of intent should be sent to:

H. George Hausch, Ph.D.
Division of Extramural Activities
National Institute of Dental and Craniofacial Research
45 Center Drive,
Building 45 Room 4AN-44F
Bethesda, MD 20892-6402
Telephone: (301) 594-2904
Fax: (301) 480-8303
Email: George.Hausch@nih.gov

3.B. Sending an Application to the NIH

Applications must be prepared using the PHS 398 research grant application instructions and forms as described above. Submit a signed, typewritten original of the application, including the checklist, and three signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or regular mail)
Bethesda, MD 20817 (for express/courier service; non-USPS service)

At the time of submission, two additional copies of the application and all copies of the appendix material must be sent to:

H. George Hausch, Ph.D.
Division of Extramural Activities
National Institute of Dental and Craniofacial Research
45 Center Drive
Building 45, Room 4AN-44F
Bethesda, MD 20892-6402
Telephone: (301) 594-2904
Fax: (301) 480-8303
Email: George.Hausch@nih.gov

3.C. Application Processing

Applications must be **received on or before the application receipt date(s)** described above ([Section IV.3.A.](#)). If an application is received after that date, it will be returned to the applicant without review. Upon receipt, applications will be evaluated for completeness by CSR and responsiveness by the NIDCR.

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. The NIH will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an application already reviewed, but such application must include an Introduction addressing the previous critique.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight (8) weeks.

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. The Grants Policy Statement can be found at <http://grants.nih.gov/grants/policy/policy.htm> (see also [Section VI.3. Reporting](#)).

6. Other Submission Requirements

Supplemental Instructions

The applicants should include an Overview of the synergistic interactions that will be achieved through the establishment of multi-disciplinary teams, the utilization of novel approaches and the integration of the various projects.

The following page limitations will apply:

Overview describing the Program Project synergy -five pages

Cores - ten pages

Individual projects - 25 pages (Research Plan sections a-d of the PHS398 form)

Appendix- All essential information must be in the submitted application. Use the instructions for the appendix detailed in the PHS 398 except that no more than five manuscripts previously accepted for publication may be included per individual project. All components of the appendix should be single sided and unbound.

No corrections or updated information will be accepted after the application has been submitted.

Special Requirements

Grantees will meet annually at or near NIH, Bethesda, MD, to share results, to ensure that the NIDCR has a coherent view of the advances in the field, and to have an opportunity for collective problem solving among investigators. Applicants should budget for travel in their requested budget for the principal investigator and Project leaders to attend the annual meeting.

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 must carry out the following steps:

- 1) Contact the IC program staff at least 6 weeks before submitting the application, i.e., as you are developing plans for the study;
- 2) Obtain agreement from the IC staff that the IC will accept your 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 investigator-initiated new (type 1), competing continuation (type 2), competing supplement, or any amended or revised version of these grant application types. Additional information on this policy is available in the NIH Guide for Grants and Contracts, October 19, 2001 at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html>.

Plan for Sharing Research Data

The precise content of the data-sharing plan 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 may wish to 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.

Applicants requesting more than \$500,000 in direct costs in any year of the proposed research must include a plan for sharing research data in their application. The funding organization will be responsible for monitoring the data sharing policy (http://grants.nih.gov/grants/policy/data_sharing).

The reasonableness of the data sharing plan or the rationale for not sharing research data may 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.

Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm and http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600131). Investigators responding to this funding opportunity should include a plan for sharing research resources addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing plan and any related data sharing plans will be considered by Program staff of the funding organization when making recommendations about funding applications. 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. Reporting](#).

Section V. Application Review Information

1. Criteria

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 program priorities

Applications will be evaluated according to the standard criteria for scientific merit.

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 to the NIDCR.

Appropriate scientific review groups convened by the NIDCR in accordance with the standard NIH peer review procedures (<http://www.csr.nih.gov/refrev.htm>) will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score
- Receive a written critique
- Receive a second level of review by the National Advisory Dental & Craniofacial Research Council.

The goals of NIH supported research are to advance our understanding of biological systems, to improve the control of disease, and to enhance health. In their written critiques, reviewers will be asked to comment on each of the following criteria in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, weighting them as appropriate for each application. Note that an application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

1. Significance. Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

2. Approach. Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

3. Innovation. Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

4. Investigators. Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

5. Environment. Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

2.A. Additional Review Criteria:

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the priority score:

Administration: Are, for example, equipment calibration and maintenance, personnel oversight, internal communication, and synergistic interactions between investigators adequately addressed? Will there be an external review committee?

Multidisciplinary Research: Is the Program comprised of collaborative efforts between individuals from different scientific disciplines?

Integration of Projects: Are the proposed projects and cores well integrated?

Utilization of Contemporary Technologies: Are state of the art technologies applied to the exploration of the selected topic?

Training Environment: Does the Program provide an environment conducive to the training of graduate students, postdoctoral fellows and other health professionals?

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the five items described under Section F of the PHS Form 398 research grant application instructions will be assessed.

2.B. Additional Review Considerations

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research. The priority score should not be affected by the evaluation of the budget.

2.C. Sharing Research Data

Data Sharing Plan: The reasonableness of the data sharing plan or the rationale for not sharing research data may 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. The funding organization will be responsible for monitoring the data sharing policy. http://grants.nih.gov/grants/policy/data_sharing.

2.D. Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (See the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps/part_ii_5.htm#availofr and http://ott.od.nih.gov/RTguide_final.html). Investigators responding to this funding opportunity should include a sharing research resources plan addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing plan will be considered by Program staff of the funding organization when making recommendations about funding applications. Program staff may negotiate modifications of the data and resource sharing plans with the awardee before recommending funding of an application. The final version of the data and resource sharing plans negotiated by both will become a condition of the award of the grant. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590). See [Section VI.3. Reporting](#).

3. Anticipated Announcement and Award Dates

The applicants will learn about the priority score of their applications one week after the assigned date for the review. They will also receive a summary statement of the reviewer's comments within eight weeks of review.

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, the Principal Investigator will also receive a written critique called a Summary Statement.

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 (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part4.htm).

A formal notification in the form of a Notice of Grant Award (NGA) will be provided to the applicant organization. The NGA signed by the grants management officer is the authorizing document.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NGA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs. See Also [Section IV.5. Funding Restrictions](#).

The NGA will be sent via email to the administrative official whose name is listed in Block 12 on the Face Page of the Form PHS 398.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the notice of grant award. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part4.htm) and Part II Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part9.htm).

The following Terms and Conditions will be incorporated into the award statement and will be provided to the Principal Investigator as well as to the appropriate institutional official, at the time of award.

2.A. Cooperative Agreement Terms and Conditions of Award

Not applicable.

3. Reporting

Awardees will be required to submit the PHS Non-Competing Grant Progress Report, Form 2590 annually (<http://grants.nih.gov/grants/funding/2590/2590.htm>) and financial statements as required in the NIH Grants Policy Statement.

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, peer review, and financial or grants management issues:

1. Scientific/Research Contacts:

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Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:

Recipients of PHS support for activities projects 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 (45CFR46) 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 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.

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 http://grants.nih.gov/grants/policy/nihgps_2003/index.htm). All investigators submitting an NIH application or contract proposal, beginning with the October 1, 2004 receipt date, 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.

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 new PHS Form 398; 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-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. Applications that do not provide this information will be returned without review.

Public 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 public 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 PA 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.

Standards for Privacy of Individually Identifiable Health Information:

The Department of Health and Human Services (DHHS) 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 DHHS 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. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

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 PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.healthypeople.gov/>.

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 or Health Systems Agency review. 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 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 NIH Grants Policy Statement can be found at <http://grants.nih.gov/grants/policy/policy.htm>.

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/>.