

Part I Overview Information

Department of Health and Human Services

Participating Organizations

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

Components of Participating Organizations

National Center for Research Resources (NCRR), (<http://www.ncrr.nih.gov>)

National Institute of Environmental Health Sciences (NIEHS), (<http://www.niehs.nih.gov/>)

Title: Technology Development for Biomedical Applications

Announcement Type

This is a reissue of [RFA-RR-04-005](http://www.nih.gov/rr/rr04005)

Request For Applications (RFA) Number: RFA-RR-05-001

Catalog of Federal Domestic Assistance Number(s)

93.389, 93.113, 93.114

Key Dates

Release Date: February 4, 2005

Application Receipt Date(s): June 22, 2005 and October 19, 2005

Peer Review Date(s): October 2005 and February 2006

Council Review Date(s): January 2006 and May 2006

Earliest Anticipated Start Date: April 2006 and July 2006

Expiration Date: October 20, 2005

Due Dates for E.O. 12372

Not Applicable

Additional Overview Content

Executive Summary

- The purpose of this request for applications (RFA) is to invite innovative applications for (1) the development of new and improved instruments or devices, (2) the development of new methodologies using existing instruments, or (3) the development of software related to instrumentation.
- NCRR intends to commit approximately \$1 million to this program in FY 2006.
- This amount will allow the funding of five to eight new grants.
- Applications will use either the R21 or the R21/R33 mechanisms.
- Eligible organizations include for-profit or non-profit institutions, public or private institutions, units of state and local government, domestic institutions, and eligible agencies of the Federal government. Applicants from for-profit organizations are strongly encouraged to contact program staff before submitting an application.
- Eligible principal investigators include any individual with the skills, knowledge, and resources necessary to carry out the proposed research.
- There is no limit on the number of scientifically different applications from an individual or an institution.

- Application materials are available at <http://grants.nih.gov/grants/forms.htm>.
- 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

This RFA replaces PAR-03-075 and RFA-RR-04-005. Applications that were previously considered under either of those announcements should be resubmitted as revised applications. The rules for revised applications on page 16 of the 9/2004 revision of the PHS 398 form should be followed.

The purpose of this request for applications (RFA) is to invite innovative applications for (1) the development of new and improved instruments or devices, (2) the development of new methodologies using existing instruments, or (3) the development of software related to instrumentation. Any of these projects should propose tools, methodologies, or software that can be used by a wide range of biomedical or clinical researchers. Awards made for applications received in response to this announcement will employ the R21 and the R21/R33 mechanisms that are designed to support high-risk applications for which few if any preliminary findings are available. Investigators with substantial preliminary data should seek an R01 award by submitting an unsolicited application at the standard receipt date or by responding to a particular program announcement.

Questions about the suitability of applications should be addressed to program staff listed in the "Agency Contacts" section well before submission. Applications focused in the areas of biomedical imaging, sensors, biomaterials, microelectromechanical systems (MEMS), tissue engineering, and nanotechnology will be considered nonresponsive and returned without review. Investigators considering research in these areas should look at the NIBIB (<http://www.nibib.nih.gov/research/investigators.htm>) and BECON (http://www.becon.nih.gov/becon_funding.htm) web pages for funding opportunities in bioengineering research or biomedical imaging research. In addition, applications that are focused on a specific organ or disease will be considered nonresponsive and also returned without review; however, applications may use a specific organ or disease as a model system.

The proposed research may involve conceptualization, design, fabrication, and/or testing of new instruments or devices. Applications to develop new experimental techniques and protocols using existing instrumentation are also welcome. Applications to develop new software related to instrumentation are encouraged, with the exception of proposals with a primary focus in the area of medical informatics. The overall objective of applications for new instruments, techniques, or software should be the development of more powerful and more precise technology with broad applicability to biomedical research.

The primary intent of this RFA is to stimulate the development of new techniques for biomedical research that will allow scientists to achieve biomedical breakthroughs. High-risk applications are encouraged, and the innovative nature of the application is emphasized in the review criteria.

For some high-risk applications, it may be appropriate to use only the R21 mechanism to generate preliminary data. For applications with two distinct phases where the high-risk portion of the research occurs early, the R21/R33 mechanism is appropriate. As a simple example, consider an applicant who had developed a new material that might be used to fabricate a lens. The R21 portion of such a research plan would be the fabrication and testing of the lens. At the end of the R21 portion of the application, the Principal Investigator would propose a set of quantitative milestones that the new lens would have to achieve. Such quantitative

milestones might deal with the focal length, field of view, and aberrations of the lens. Once the lens had been made, the R33 phase of the research could be to incorporate this lens into a working microscope. At the end of a successful R21/R33 award, it is expected that there be a working instrument or new technique. Since the R21/R33 award cannot be renewed, it is not suitable for establishing a long-term research project in a particular area. Investigators should not propose to test a biological hypothesis as the R33 phase of an application.

Examples of new tools and techniques that are responsive to this RFA include optical spectroscopy, mass spectrometry, electrophoresis and other separation techniques, microscopy, lasers and optics, X-ray tools and techniques, nuclear magnetic resonance spectroscopy, bioreactors and other forms of cell culture, centrifugation, proteomics, genomic sequencing, functional genomics, comparative genomics, microarrays, and human sequence variation (e.g., genotyping). This list is not exhaustive, but investigators outside of these areas are strongly encouraged to contact program staff to ensure that their applications are responsive.

This program announcement is similar to the "Instrument Development for Biological Research" program in the Directorate for Biological Sciences at the National Science Foundation (http://www.nsf.gov/publications/pub_summ.jsp?ods_key=nsf98119). The major difference between the two programs is that instrumentation for the conduct of disease-oriented research is specifically excluded from the NSF program. Some instrument development proposals could be considered either under this program announcement or by NSF. Applicants are encouraged to contact program staff at either NSF or NIH to identify the best program for the application.

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

Section II. Award Information

1. Mechanism(s) of Support

This funding opportunity will use the R21 and R21/R33 award mechanisms. Applications under this program announcement will use either the combined R21/R33 mechanism or the R21 mechanism alone. Applications using just the R33 mechanism will not be considered. An application using the R21 mechanism alone is appropriate when the possible outcomes of the proposed research are unclear; under these conditions, it would not be reasonable to propose quantitative milestones or describe the R33 phase of the research. Applicants are encouraged to contact program staff with any questions about the appropriate mechanism.

For the R21 phase of the application, direct costs are limited to a maximum of \$125,000 per year for no more than three years. The combined R21/R33 application is limited to five years, including a maximum of three years for the R33 phase.

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

NCCR intends to commit approximately \$1 million dollars in FY 2006 to fund five to eight new grants in response to this RFA. An applicant may request a project period of up to five years for an R21/R33 application and up to three years for an R21 application. The budget for direct costs in the R21 phase cannot exceed \$125,000. The budget for direct costs in the R33 phase cannot exceed \$500,000 without permission from program staff.

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 NCRR provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications.

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, however applicants from for-profit organizations should contact program staff prior to submitting an application
- 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

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

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

Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The applicant can choose to submit either an R21 application, or a combined R21/R33 application. The advantage of the combined R21/R33 mechanism is that it offers a seamless transition between the exploratory phase and the development phase of a project. Transition from the R21 to the R33 is dependent on completion of negotiated milestones. Once these milestones have been achieved, the investigator will submit a progress report to program staff. Upon determination that the milestones have been accomplished, the R33 phase can begin.

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

3.A. Receipt, Review and Anticipated Start Dates

Application Receipt Dates(s): June 22, 2005 and October 19, 2005

Peer Review Date(s): October 2005 and February 2006

Council Review Date(s): January 2006 and May 2006

Earliest Anticipated Start Date: April 2006 and July 2006

3.A.1. Letter of Intent

Prospective applicants do not need to submit a letter of intent.

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:

Linda Duffy, Ph.D.
Office of Review
National Center for Research Resources
6701 Democracy Boulevard, MSC 4874
Bethesda, MD 20892-4874
Bethesda, MD 20817 (for express/courier service)

Using the RFA Label: The RFA label available in the PHS 398 application instructions must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at: <http://grants.nih.gov/grants/funding/phs398/labels.pdf>. Personal deliveries of applications are no longer permitted.

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 the CSR and responsiveness by the program staff in NCCR. Incomplete and non-responsive applications will not be reviewed.

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. Below indicate that should submit revised applications.

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](#)).

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

The incurrence of pre-award costs in anticipation of a competing or non-competing award imposes no obligation on NIH either to make the award or to increase the amount of the approved budget if an award is made for less than the amount anticipated and is inadequate to cover the pre-award costs incurred. NIH expects the grantee to be fully aware that pre-award costs result in borrowing against future support and that such borrowing must not impair the grantee's ability to accomplish the project objectives in the approved time frame or in any way adversely affect the conduct of the project. See NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part6.htm.

6. Other Submission Requirements

SPECIFIC INSTRUCTIONS FOR REVISED APPLICATIONS

Applications that were submitted in response to PAR-03-075 or RFA-RR-04-005 should be submitted as revised applications to this RFA. Follow the instructions for revised applications in the PHS 398 form.

SPECIFIC INSTRUCTIONS FOR APPLICATIONS REQUESTING \$500,000 OR MORE PER YEAR

Applications requesting \$500,000 or more in direct costs for any year must include a cover letter identifying the NIH staff member at NCRR who has agreed to accept assignment of the application.

Applicants requesting more than \$500,000 must carry out the following steps:

- 1) Contact program staff at least six weeks before submitting the application, i.e., as you are developing plans for the study;
- 2) Obtain agreement from the program staff that NCRR will accept your application for consideration for award; and,
- 3) Identify, in a cover letter sent with the application, the staff member who agreed to accept assignment of the application.

SPECIFIC INSTRUCTIONS FOR THE APPENDIX

The only items that may be included in the appendix are original glossy photographs or color images of gels, micrographs, etc., provided that a black and white photocopy of the same size is included within the research plan.

SPECIFIC INSTRUCTIONS FOR PREPARATION OF THE R21 APPLICATION WHEN SUBMITTED WITHOUT THE R33 PHASE

1. On the Face Page of the application:

Item 2. Check the box marked "YES" and type the number and title of this RFA.

Item 7a: DIRECT COSTS REQUESTED FOR INITIAL PERIOD OF SUPPORT

For the R21 application, direct costs are limited to a maximum of \$125,000 per year for a maximum of three years. R21 budgets can only exceed this cap to accommodate F&A costs of subcontracts to the project.

2. On Page 2 in the Description:

As part of the description, identify concisely the fundamental research and/or technology or tool to be developed, its innovative nature, its relationship to presently available capabilities, and its expected impact on biomedical research.

3. On the Budget page:

The application should provide a detailed budget for Initial Budget Period (form page 4), as well as a budget for the entire proposed period of support (form page 5). All budgets should include a written justification. The modular budget format is not to be used.

4. In the Research Plan:

The research plan for an R21 application is limited to 15 pages.

Item a: Specific Aims.

Specific aims that the applicant considers to be scientifically appropriate for the relevant phases of the project must be presented. Research that develops new technologies or tools is likely to require the application of principles from fields such as analytical chemistry, mathematics, physics, and engineering. Clear statements of the underlying principles should be made within this section.

Item b: Background and Significance

Elaborate on the innovative nature of the proposed research. Clarify how the fundamental tools or technologies to be developed in this project will result in a significant improvement over existing approaches. Explain the potential of the proposed technology for having an impact on a compelling area of biomedical research. Clearly identify how the project, if successful, would result in new capabilities for biomedical research, the immediacy of the opportunity, and how any proposed technologies or tools would differ from existing technologies or tools.

Item c: Preliminary Studies

While preliminary data are not required for submission of the R21 phase, this section should provide current thinking or evidence in the field that substantiates the feasibility of the R21 phase. If the applicant does have preliminary data, it should be presented in this section. This item should not be included in the R33 portion of the application.

Item d: Research Design and Methods

Follow the instructions in the PHS 398 form.

5. Milestones:

Applications using the R21 mechanism without the R33 phase need not include milestones.

SPECIFIC INSTRUCTIONS FOR PREPARING A COMBINED R21/R33 PHASED INNOVATION AWARD APPLICATION

The R21/R33 Phased Innovation Award application must be submitted as a single application with one face page. Although it is submitted as a single application, it should be clearly organized into two phases. To accomplish a clear distinction between the two phases, applicants should submit Sections a-d (Specific Aims, Background and Significance, Preliminary Studies, Research Design) for the R21 phase, then the milestones, and then sections a and d (Specific Aims, Research Design) for the R33 phase. The Form 398 Table of Contents should be modified to show the sections for each phase as well as the milestones. There is a page limit of 25 pages for the composite research plan. Section a-d of the R21 research plan must not exceed 15 pages. The milestones, and the a and d sections for the R33 application can take, at most, an additional 10 pages. The clarity and completeness of the R21/R33 application with regard to specific goals and feasibility milestones are critical. The presentation of milestones that are not sufficiently scientifically rigorous or quantitative to allow program staff to assess progress in the R21 phase will be considered in evaluating the approach as proposed by the investigator.

The combined R21/R33 application must include the specific aims for each phase and the quantitative milestones that would justify transition to the R33 phase. Applications must include a specific section labeled Milestones following the Research Plan of the R21 phase. Milestones should be well described, quantifiable and scientifically justified. A discussion of the milestones relative to the progress of the R21 phase and the implications of successful completion of the milestones for the R33 phase should be included. The Milestones section should be indicated in the Table of Contents. Applications lacking this information, as determined by the NIH staff, will be returned to the applicant without review.

Prior to funding an application, the Program Director will contact the applicant to discuss the proposed milestones and any changes suggested by the review panel as indicated in the Summary Statement. The Program Director and the applicant will negotiate and agree on a final set of milestones. These will be the basis

for judging the success of the R21 work. For funded applications, the Principal Investigator will submit a progress report to the program upon completion of the R21 milestones. Receipt of this progress report will trigger a review that will determine whether or not the R33 should be awarded. The release of R33 funds will be based on successful completion of negotiated scientific milestones, program priorities, and on the availability of funds.

1. On the Face Page of the application:

Item 2. Check the box marked "YES" and type the number and title of this RFA.

Items 7 and 8: Costs Requested

For the R21 phase of the application, direct costs are limited to a maximum of \$125,000 per year for no more than three years. R21 budgets can only exceed this cap to accommodate F&A costs of subcontracts to the project. The combined R21/R33 application is limited to five years in duration, and the R33 phase may not exceed three years in duration.

2. On Page 2 in the Description:

As part of the description, identify concisely the fundamental research and/or technology or tool to be developed, its innovative nature, its relationship to presently available capabilities, and its expected impact on biomedical research.

3. On the Budget pages:

The application should provide a detailed budget for Initial Budget Period (form page 4) for the first year of the R21 phase and a second detailed budget (form page 4) for the first year of the R33 phase. Form page 5 should be used to provide a budget for the entire proposed period of support. Form pages should indicate which years are R21 and which are R33. All budgets should include a written justification. The modular budget format should not be used.

4. In the Research Plan:

Item a: Specific Aims.

Specific aims must be presented which the applicant considers to be scientifically appropriate for the relevant phases of the project. Research that develops new technologies or tools is likely to require application of principles from fields such as analytical chemistry, mathematics, physics, and engineering. Clear statements of the underlying principles should be made within this section.

Item b: Background and Significance

Elaborate on the innovative nature of the proposed research. Clarify how the fundamental tools or technologies to be developed will result in a significant improvement over existing approaches. Explain the potential of the proposed technology for having an impact on a compelling area of biomedical research. Clearly identify how the project, if successful, will result in new capabilities for biomedical research, the immediacy of the opportunity, and how any proposed technologies or tools differ from existing technologies or tools. This item should not be included in the R33 portion of the application.

Item c: Preliminary Studies

While preliminary data are not required for submission of the R21 phase, this section should provide current thinking or evidence in the field that substantiates the feasibility of the R21 phase. If the applicant does have preliminary data, it should be presented in this section. This item should not be included in the R33 portion of the application.

Item d: Research Design and Methods

Follow the instructions in the PHS 398 form. Applicants should also address plans to make the products, tools, or technologies forthcoming from this research available to the relevant biomedical research user community.

5. In the Milestones section:

For combined R21/R33 applications, a specific section labeled Milestones must be included following the Research Design and Methods of the R21 phase. Milestones should be well described, quantifiable, and scientifically justified. Applicants should write the milestones assuming that a scientifically literate non-expert will use them to evaluate the progress that has been achieved. Milestones should not be simply a restatement of the specific aims or a timeline. The milestones section should be indicated in the Table of Contents. Applications lacking this information will be returned to the applicant without review.

For funded applications, peer review is not likely between the two phases of the project. When the R21 milestones have been achieved, the Principal Investigator must submit a progress report. Receipt of this progress report will elicit a review to determine whether or not the R33 should be awarded. The release of R33 funds will be based on successful completion of milestones, program priorities, and on the availability of funds.

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

2. Review and Selection Process

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the program staff in NCCR. Incomplete and/or non-responsive applications will not be reviewed.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by NCCR in accordance with the review criteria stated below.

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 appropriate national advisory council or board.

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? To what degree does the proposed research support the needs of the targeted biomedical research community?

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? What is the time frame for developing the proposed approaches, tools, or technologies? Is this time frame suitable for meeting the relevant biomedical research community's needs?

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:

- For R21/R33 proposals, are the milestones quantitative? Will a scientifically literate non-expert be able to determine whether the milestones have been achieved?
- For R21/R33 proposals, are the proposed milestones appropriate for judging the success of the R21 work?
- For R21/R33 proposals, are the proposed milestones appropriate in determining whether the R33 phase should be awarded?

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#availofrr and http://ott.od.nih.gov/newpages/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

Not applicable

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. Notices of Grant Award will be transmitted electronically to registered email-enabled institutions. Otherwise, NGAs will be sent to the grantee Signing Official via US Mail.

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](#).

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).

2.A. Cooperative Agreement Terms and Conditions of Award

Not applicable

3. Reporting

Prior to funding an application, the Program Director will contact the applicant to discuss the proposed milestones and any changes suggested by the review panel as indicated in the Summary Statement. The Program Director and the applicant will negotiate and agree on a final set of milestones. These will be the basis for judging the success of the R21 work. For funded applications, the Principal Investigator will submit a progress report to the program upon completion of the R21 milestones. Receipt of this progress report will trigger a review that will determine whether or not the R33 should be awarded. The release of R33 funds will be based on successful completion of negotiated scientific milestones, program priorities, and on the availability of funds.

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:

Gregory K. Farber, Ph.D.
Division of Biomedical Technology
National Center for Research Resources
6701 Democracy Boulevard, MSC 4874
Bethesda, MD 20892-4874
Telephone: (301) 435-0778
FAX: (301) 480-3659
Email: farberg@mail.nih.gov

Dr. David M. Balshaw, Ph.D.
Center for Risk and Integrated Sciences
National Institute of Environmental Health Sciences
111 TW Alexander Drive
PO Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-2448
FAX: (919) 541-4937
Email: balshaw@niehs.nih.gov

2. Peer Review Contacts:

Linda C. Duffy, Ph.D.
Office of Review
National Center for Research Resources
6701 Democracy Boulevard, MSC 4874
Bethesda, MD 20892-4874
Telephone: (301) 435-0810
FAX: (301) 480-3660
Email: duffy1@mail.nih.gov

3. Financial or Grants Management Contacts:

Mary Niemiec
Team Leader
Office of Grants Management
National Center for Research Resources
6701 Democracy Boulevard, MSC 4874
Bethesda, MD 20892-4874
Telephone: (301) 435-0842
FAX: (301) 480-3777
Email: mn20z@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 (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.

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.