

## NATIONAL TECHNOLOGY CENTERS FOR NETWORKS AND PATHWAYS

RELEASE DATE: August 10, 2004

RFA Number: RFA-RM-04-019

EXPIRATION DATE: February 23, 2005

Department of Health and Human Services (DHHS)

### PARTICIPATING ORGANIZATION:

National Institutes of Health (NIH)

(<http://www.nih.gov>)

This RFA is developed as a roadmap initiative. All NIH Institutes and Centers participate in roadmap initiatives. This RFA will be administered by the National Center for Research Resources on behalf of the NIH.

CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBERS: 93.389 (NCRR)

LETTER OF INTENT RECEIPT DATE: January 18, 2005

APPLICATION RECEIPT DATE: February 22, 2005

### THIS RFA CONTAINS THE FOLLOWING INFORMATION

- o Purpose of this RFA
- o Research Objectives
- o Mechanism(s) of Support
- o Funds Available
- o Eligible Institutions
- o Individuals Eligible to Become Principal Investigators
- o Special Requirements
- o Where to Send Inquiries
- o Letter of Intent
- o Submitting an Application
- o Peer Review Process
- o Review Criteria
- o Receipt and Review Schedule
- o Award Criteria
- o Required Federal Citations

### PURPOSE OF THIS RFA

The National Institutes of Health invites applications for NIH National Technology Centers for Networks and Pathways (TCNP). These centers will cooperate in a networked national effort to develop highly novel, integrated, and broadly applicable

proteomics technologies, to include instrumentation, biophysical methods, reagents, and infrastructure. These technologies will be specifically directed at the fundamental technological challenges inherent in acquiring quantitative information at the high anatomic resolution (subcellular) and biologically relevant timescales necessary for temporal and spatial characterization of complex biochemical pathways and molecular interactions. Beyond cataloging of proteins and their binary interactions, these methods will be directed toward quantitatively defining the dynamics of complex systems.

The establishment of the TCNPs was called for in the NIH Roadmap Initiative in 2003. TCNPs will be supported by U54 awards. The U54 awards will principally support technological innovation. However, in addition it is expected that the TCNPs will commit substantial resources to collaboration with and education of biomedical researchers, as well as the transfer of technologies to other laboratories. It is anticipated that there will be strong, vibrant interactions between the centers themselves and related individual investigator projects focused on a broad range of significant biomedical research questions. The centers should foster original and creative contributions to scientific understanding over and above that which would be obtained if each component of the center existed independently.

## RESEARCH OBJECTIVES

Proteomics experiments have consistently been characterized as falling into two broad classes, either directed at defining the physical interactions of proteins, or concerned with characterizing changes in the expression of proteins corresponding to internal or external perturbations of cells or systems. The methodological issue that has largely driven this distinction is the inherent difficulty of quantitation of individual molecules in complex systems. The distinction is artificial, since in either instance, the goal is to define the roles and functions of proteins in inherently dynamic systems, whether considered as networks of interactions or steps in a biochemical pathway.

As the results of biophysical experiments are assembled into coherent models of these systems, temporal, spatial, and quantitative resolution all become increasingly critical factors. While substantial and rapid progress has been made over the past decade in the development of analytical technologies for proteomics, the greatest successes have overwhelmingly resided in the realm of tightly bound protein complexes. In this case, definition of protein identity and interaction are the two critical analytical tasks, addressed through the creative application of molecular and cellular biological methods, often followed by separation and mass spectrometry.

While these basic technologies arguably underlie all of proteomics, and still present significant challenges, we feel it is necessary to begin a concentrated effort to develop and integrate a series of technologies orthogonal to these fundamental tools. These additional technologies should address the problems of temporal and spatial dynamics of protein function and interaction, and they should do so quantitatively. Significant NIH resources continue to be directed to fundamental separation and identification technologies. This program is meant to be largely orthogonal to those efforts,

intersecting with them and utilizing them, but not investing significantly in further development of those areas.

It will be impossible to fully define dynamic biological systems strictly on the basis of proteomic data alone. Protein interaction, modification, translocation and expression level will need to be considered in the context of gene transcription and metabolism. The same necessity for quantitative, temporal, and spatial resolution applies to these analyses. Acquisition and integration of these data are significant challenges, and substantial difficulties remain with respect to the fundamental tasks of profiling and cataloging biomolecules in complex systems. While efforts continue in development of these fundamental technologies, it is important that parallel efforts build technologies directed specifically to the dynamics of complex systems. To facilitate the development of these technologies and build infrastructure for support of biomedical research, the NIH is embarking on a program to build National Technology Centers for Networks and Pathways.

This Request for Applications (RFA) is intended to encourage development of highly sensitive tools to measure the dynamics of quantity, activity, translocation, or interactions of molecules in cells. Preference will be given to applications that have promise to be quantitative, capture information at timescales relevant to the study of pathways and networks, and that have promise to be applied at subcellular resolution. It is anticipated that approaches will be valuable which can be scaled, facilitating capture of information about a comprehensive set of molecules or with the potential for broad, flexible application to a range of specific molecules.

These issues are deliberately discussed with respect to fundamental analytical challenges, rather than in relation to specific technologies, in order to emphasize the overriding importance of surmounting these obstacles, irrespective of the analytical strategy adopted to pursue those solutions. This solicitation encourages unconventional or alternative approaches as a balanced portion of the overall center effort.

Regardless of the system under study or specific experimental approaches of proteomics, a common theme in this field is the need for synergy among three principal domains: (1) biological issues, including study design, sample collection and processing, sample complexity and prefractionation; (2) analytical chemistry, including the challenges of quantitation, maximization of separation space, and improving dynamic range; and (3) informatics, including data handling, statistical analyses, validation and curation, integration of results from multiple platforms used in the center, and development of improved tools for data analysis. These three domains should each inform the development of tools and methods in their counterpart areas. Accomplishing this goal in a climate of specialization demands a fundamentally collaborative approach. It is anticipated that investigators will assemble interdisciplinary teams from multiple laboratories.

It is not required that all participating investigators and laboratories be located either at a single institution or in the same local geographic area. However, because of the need for

integration of technologies at a fundamental level, it is considered critical that participating investigators be in a position to work closely together in an iterative manner. This is seen as particularly important for example in the effective interfacing of analytical instrumentation. These issues should be addressed in detail in the application. The project will be administered through the principal investigator and his/her institution.

The TCNPs will focus on technology development, but three features of the program will ensure that the technology developed can be applied to relevant biological problems. First, each TCNP is encouraged, though not required, to select a biological focus or model system that will provide a thematic focus or context for technology development. Second, each TCNP will support a set of Driving Biological Projects (DBPs), which will provide an internal biological context for technology development. Third, after the initial TCNPs have been funded in September 2004, NIH anticipates releasing a new program announcement that will support additional partnerships between individual investigators and these centers. These awards will leverage and complement the research activities of the U54 centers in building comprehensive technologies for molecular networks and pathways research focused around biological processes, cellular organelles, organs, or diseases. It is anticipated that the announcements for partnering projects will include both new R01's and R21's as well as competitively reviewed supplements to existing projects. These awards will be made by a variety of participating NIH ICs.

All applications in response to this announcement will be evaluated primarily for the potential of the proposed activities to address the broad challenges discussed above, where it is clear that the technology to be developed can be used to obtain the data required to elucidate and test models of a molecular network or pathway. However, it is anticipated that these challenges are too broad for a single center to address comprehensively. Investigators will be expected to clearly define the scope of their technical and biological activities.

The funding mechanism for the TCNPs will be a U54 center. Each TCNP will be required to perform or facilitate six different core functions: (1) conducting core research in technology development, (2) establishing Driving Biological Projects (DBP) to allow biomedical researchers to interact with and drive research in the TCNP, (3) providing infrastructure to biomedical researchers (hardware, software, and personnel as appropriate), (4) enhancing the training for biomedical researchers in appropriate proteomics tools and techniques, (5) disseminating newly developed tools, reagents, and techniques to the broader biomedical research community, and (6) providing formal project leadership and management to ensure that these large centers achieve their goals within the 5 to 10 year funding lifetime of the center.

The technological research in core 1 will be the largest component of a TCNP, focused on development of cutting edge technology and methods for proteomic characterization of networks and pathways.

The technological R&D component consists of investigations that are at the cutting edge of the technological field with a goal of increasing its usefulness in biomedical research.

A minimum of three technological research projects constitutes this section of the application. An element of high risk (high payoff) should be present in one or more of these projects and is appropriate for this component. It is expected that to make significant progress in this difficult area, revolutionary approaches will be necessary in many instances. When included as a component of technology development, a high-risk project should be well justified by the potential for correspondingly high returns, and should be presented in the context of an overall research plan, with appropriate discussion of the inherent risks and the alternative strategies available if the primary plan fails. Plans should balance risk within the overall goals of the project.

Conversely, in the case of technologies and methods that may be somewhat prosaic by comparison with the more revolutionary aspects of the research plan, care should be taken to describe their important contribution to the overall fabric of the Center's activities. If for example a well-established analytical method is a critical component of the technology development plan, then the manner in which it is leveraged to support novel approaches should be well delineated. The integration of methods to create a coherent analytical strategy greater than the sum of its parts is a legitimate approach.

The technological R&D projects to be conducted must be presented in detail. For each project describe the background, objectives, rationale, methods and procedures, significance, and facilities available to conduct the project. If research activities involve support at more than one location through a consortium/contractual arrangement, the application should provide a separate description, detailed budget and budget justification for the consortium/contractual component(s).

In addition to the individual technology development projects, the interrelationships of these technologies should be described, as well as plans for maximizing connectivity and synergy both in the technologies and between participating groups. These discussions should be placed in the context of the overall strategic goals of the center's research program.

Development of complex, integrated approaches to formulating networks and pathways will require a context within which methods development can proceed. Investigators should consider selection of a model system (such as a cellular process, an already characterized network or pathway where the connections are mostly known but none of the dynamic information), or define a thematic biological research topic that will serve as a framework for the technological research and development activities of the resource. It is suggested that an overarching biological theme will provide some coherence and focus for technology development, and it is encouraged, but it is not a requirement. In its absence, care must still be taken to show that the technology is biomedically relevant, the Driving Biological Projects and other collaborations will provide appropriate drivers for technology development, and that technologies will be integrated appropriately to form a coherent analytical system. Investigators should propose to tackle a problem that is both technically challenging and relevant to biomedical research. These projects should be structured to achieve their goal in a 5 to 10 year timeframe.

Through collaborations, infrastructure development, training, and dissemination, TCNPs will be expected to have a broad-based, significant impact on a variety of biological problems. However, the most important deliverables will be the state-of-the-art technology, reagents and methods for proteomics research developed in Core 1.

In the context of this solicitation, technology development should be interpreted broadly to encompass all aspects from proof of principle of an innovative idea through development of practical instruments and systems. It is anticipated that as innovative technology is developed, to the extent possible, it will be optimized and brought to bear in application to challenging biomedical research problems. It will be considered appropriate to balance evolutionary technology development, the refinement and optimization of current technologies, with the more challenging development of revolutionary new approaches.

In core 2, an applicant will propose a minimum of 4 projects that address cutting edge biological questions within the thematic biological research topic of the Center. The projects will involve collaborations with biomedical researchers who would use proteomic approaches under development in the TCNP. It is not essential that the biomedical researchers have expertise in analytical chemistry or proteomics, but each DBP must have a question that will drive one or more specific research projects in core 1. That linkage must be made explicit in the description of each DBP.

The defining characteristic of Driving Biological Projects are that they should provide both a driver and a test-bed for the technological research and development carried out in core 1. They should be hard problems whose solution requires the technology being developed in the center. Interactions with these projects should serve to ensure that the research carried out in core 1 has direct relevance to biomedical research.

These projects will be at different degrees of maturity. Some will require funding through the center, but others will not. The Center will function as an incubator for biological projects, allowing for a means to begin cutting edge projects for which no outside funding is yet available. These collaborations will last for at most three years without separate funding. It is anticipated that some DBPs will begin during the first year, while others may be phased in over the lifetime of the award. If appropriate, the PI and collaborating researchers must present plans to use these DBPs as a foundation for the collaborators to compete for independent funding for continuation of the work. Plans must also be presented to select additional DBPs in an ongoing manner as these are completed.

Whether the projects are funded through the center or not, they should be described in the proposal under Core 2. If separate funding is already available, that should be made explicit, including the grant number if it is NIH funding. It is anticipated that independently funded biological projects, either pre-existing or matured DBPs, will form strong continuing interactions with the TCNPs.

It is expected that a substantial number of the DBPs in core 2 will come from outside the institution(s) that make up the Center. It is expected that the Center will have a national scope and impact.

It is anticipated that technologies proposed in applications will be at different stages of maturity, both among and between centers. It therefore may be appropriate that the proposed function of a DBP collaboration may be limited at least initially to helping the center appropriately define a specific problem.

The new tools, reagents, and methods that are being developed are likely to require substantial infrastructure to implement them. Core 3 will provide that infrastructure. This infrastructure will be used to develop appropriate components and to provide the biomedical community with access to these components. It is appropriate to request hardware, software, and associated personnel in this core.

It is expected that demand may outstrip available resources. Specific plans should be presented for the following: ongoing selection and prioritization of new DBPs, other biological collaborative projects, and routine service work.

The NIH's long-term goals in proteomics recognize the need to develop a new generation of multi-disciplinary scientists. The twofold training mission of a TCNP should be described in core 4: Each center should develop mechanisms for ensuring that graduate students and postdoctoral fellows receive broad, relevant training beyond the specific contributions they make to the infrastructure and research projects of the center. In addition, there should be plans for workshops, training courses, or other mechanisms to train the larger biomedical research community about the new tools and techniques that the TCNP is developing.

The focus of core 5 is to disseminate new discoveries, reagents, methods and technology to the biomedical community and to participate in an effort to develop standards for data sharing and integration. Publications and a genuinely useful web site are excellent ways to broadcast some of the discoveries of the TCNP, but those routes may not be sufficient to inform biomedical investigators who require guidance in pursuing solutions to their questions. Innovative plans to disseminate discoveries to the biomedical community should be presented in core 5. It is also appropriate to discuss how hardware, analytical methods, or software will be made available to the community in this core and to justify possible restrictions. Finally, where appropriate, plans to make data sets and databases available on a continuing basis should be presented. The development of data standards and ontologies is extremely important for sharing and communicating data and information. It is expected that multiple TCNPs will participate actively in an effort to develop standards for data sharing and integration.

It is essential to provide appropriate project leadership and management for these large centers. In core 6 the investigator should describe management plans. Investigators are strongly encouraged to consider proposing a project manager for the TCNP. The investigators should undertake a planning process and document an action plan.

Elements of an action plan include determining which cores will be established; establishing overall policies and procedures for management of cores and Center resources. In addition, outcome measurements should be determined and include how progress on action plans will be measured. In addition to a project manager, it is expected that the TCNP will interact with an advisory panel to the program, selected by investigators and program staff after awards are made. This committee will meet on an at least an annual basis to review progress and offer advice. NIH Program directors will attend these meetings. The application should NOT include the names of potential members of a proposed center's External Advisory Committee if it chooses to form one.

Multiple institutes and centers at NIH continue to support programs to develop centers in proteomics. Recipients of those awards or contracts are welcome to apply for the U54 centers in this announcement. It is anticipated that in those cases, the U54 application may be tailored to complement the center's existing mission while addressing the additional unique features of this program. No preference will be given either to recipients or non-recipients of previous proteomics center awards or contracts.

#### MECHANISM OF SUPPORT

This RFA will use the NIH U54 award mechanism. As an applicant you will be solely responsible for planning, directing, and executing the proposed project. This RFA is a one-time solicitation. Future unsolicited, competing-continuation applications based on this project will compete with all investigator-initiated applications and will be reviewed according to the customary peer review procedures. The anticipated award date is September, 2005.

This RFA uses just-in-time concepts. It also uses the non-modular budgeting formats. This program does not require cost sharing as defined in the current NIH Grants Policy Statement at [http://grants.nih.gov/grants/policy/nihgps\\_2001/part\\_i\\_1.htm](http://grants.nih.gov/grants/policy/nihgps_2001/part_i_1.htm).

The NIH U54 is a cooperative agreement award mechanism in which the Principal Investigator retains the primary responsibility and dominant role for planning, directing, and executing the proposed project, with NIH staff being substantially involved as a partner with the Principal Investigator, as described under the section "Cooperative Agreement Terms and Conditions of Award". The initial period of support for a U54 center will be five years. NIH may reissue this RFA and allow competitive renewals for a second period of up to five years. If competing segments of a U54 award are shorter than five years, grantees may apply for more than one renewal, but no center will receive more than ten years total of NIH funding.

#### FUNDS AVAILABLE

The participating ICs intend to commit approximately \$7.4 million in FY 2005 to fund 2 to 3 new centers in response to this RFA. An applicant should request a project period of 5 years. The budget (direct costs) may not exceed \$2 million per year. Indirect costs associated with subcontracts will not be counted as direct costs when determining

compliance with the above ceiling (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-040.html>). Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size of each award will also vary. Although the financial plans of the ICs provide support for this program, awards pursuant to this RFA are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications.

## ELIGIBLE INSTITUTIONS

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

- o Public or private institutions, such as universities, colleges, hospitals, and laboratories
- o Eligible agencies of the Federal government
- o Domestic Institutions
- o Foreign institutions may participate through subcontracts.

## INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

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.

## SPECIAL REQUIREMENTS

Applicants are encouraged to contact program staff well in advance of the letter of intent submission date, in order to discuss the proposed research program, budget, organization of the center, and its potential biomedical impact. These contacts help to assure that applicants have a clear understanding of current program policies and priorities, especially with respect to any special situations, such as the inclusion of consortia, subcontracts, etc. It will also allow staff to assess responsiveness to this RFA and provide appropriate guidance as needed. Programmatic guidance from NIH staff does not imply pre-review or approval of the science proposed.

Principal investigators and key personnel as appropriate are expected to participate in an annual meeting in the Washington, DC area. Funds for travel to the meeting should be requested in the budget.

The annual progress report for the U54 award will use the standard 2590 form. In addition, to the basic information in that form, the annual progress report for the U54 centers will be more involved. Additional information in the progress report will include both the progress made in the center as well as the relationship between the center and the individual investigator awards. Details of the U54 progress report are spelled out in the notice of grant award and in the Terms and Conditions section of this RFA. Applications

for U54 centers should contain appropriate personnel to collect the needed information and to prepare this progress report.

Because of the complexity of the TCNP, program staff from NIH will likely want to visit periodically to conduct an administrative site visit. U54 centers should be prepared for annual visits and should budget appropriately (including travel for collaborators and other necessary costs).

The complexity of these centers necessitates a project manager(s). U54 centers should budget appropriately for these manager(s). One of the review criteria for these centers will be the qualifications of these project managers as well as whether the institution has an appropriate career pathway for these individuals. Because of their important role, it is recommended that the project manager be listed as one of the key personnel.

A principle underlying this program is that substantial benefits in technology development and biological problem solving will accrue through successful integration of the biological, analytical, and informatics domains of the center. The application should articulate a specific organizational plan. This plan should describe anticipated interactions between key personnel in support of the overarching goals of the resource. It should also maximize synergy between the component technologies. Ultimately, a successful center will function as a coherent whole, rather than a collection of individual technological capabilities. In cases where geographically distributed collaboration is essential, the management plan should include provisions for teleconferencing or videoconferencing as appropriate. The applicant may include these provisions in the budget if appropriate.

To address the joint interests of the government in the availability of, and access to, the results of publicly funded research, NIH requires applicants who respond to this RFA to propose detailed plans for sharing the research resources generated through the grant. It is expected that the resources to be shared include all materials developed in projects funded under the RFA. A reasonable time frame for release of materials should be specified in the application and will be considered during the review of the plan for sharing.

It is expected that the investigator's data and biomaterials sharing plan will include the access to biomaterials and methods not currently available to the wider scientific community. In other words, plans for the development of resources for use by the biomedical community should have the appropriate timeliness and milestones. For example software development should include plans and timeliness for alpha testing, beta testing, production release, interface development, bug reporting, integration with other codes, extension to multiple platforms, etc.

Data sharing will be as important as software sharing for many National Programs. All awards made under this RFA are subject to the Final NIH Statement on Sharing Research Data (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>).

The scientific review group will evaluate the adequacy of the proposed plan for sharing and data access. Comments on the plan and any concerns will be presented in an administrative note in the Summary Statement. The adequacy of the plan will be considered by NIH program staff and will be important in determining whether the grant shall be awarded. The sharing plan approved by program staff, after negotiation with the applicant when necessary, will become part of the terms and conditions of the award. NIH program staff will evaluate the compliance with the sharing plan and scientific progress in the non-competing continuation of the grant award application.

## INTELLECTUAL PROPERTY RIGHTS

NIH is interested in ensuring that the research resources developed through this RFA become readily available to the research community. With regard to patentable research results, such as genetically encoded reporters, cell lines, and vectors, the NIH expects applicants who respond to this RFA to develop a plan addressing if, or how, they will exercise their intellectual property rights while making available to the broader scientific community research resources produced in projects funded under this RFA. This is expected to include an elaboration of the applicant's anticipated plans to generate, or not generate, patents and/or exclusive or non-exclusive licensing of biomaterials and other patentable subject matter created in projects funded under this RFA. This plan should be consistent with the applicant's institution's policies on intellectual property rights.

Applicants are reminded that funding recipients must not enter into any agreements with third parties that are inconsistent with the terms and conditions of their NIH award, if awarded, and must revise any agreements with third parties that are inconsistent with the terms and conditions of an NIH award to remain in compliance with such NIH award.

The majority of transfers to not-for-profit entities should be implemented under terms no more restrictive than the Uniform Biological Materials Transfer Agreement (UBMTA). In particular, recipients are expected to use the Simple Letter Agreement (SLA) provided at [http://ott.od.nih.gov/NewPages/RTguide\\_final.html](http://ott.od.nih.gov/NewPages/RTguide_final.html), or another document with no more restrictive terms, to readily transfer unpatented tools developed with NIH funds to other recipients for use in NIH-funded projects. If the materials are patented or licensed to an exclusive provider, other arrangements may be used, but commercialization option rights, royalty reach-through, or product reach-through rights back to the provider are inappropriate. Similarly, when for-profit entities are seeking access to NIH-funded tools for internal use purposes, recipients should ensure that the tools are transferred with the fewest encumbrances possible. The Simple Letter Agreement may be expanded for use in transferring tools to for-profit entities, or simple internal use license agreements with execution or annual use fees may be appropriate.

Applicants also are reminded that the grantee institution is required to disclose each subject invention to NIH within two months after the inventor discloses it in writing to grantee institutional personnel responsible for patent matters. The awarding institute reserves the right to monitor awardee activity in this area to ascertain if patents

or patent applications on protocols, cell lines, vectors, or other patentable subject matter are adversely affecting the goals of this RFA.

As noted earlier, Principles and guidelines for recipients of NIH research awards on obtaining and disseminating biomedical research resources can be found at [http://ott.od.nih.gov/NewPages/RTguide\\_final.html](http://ott.od.nih.gov/NewPages/RTguide_final.html).

## COOPERATIVE AGREEMENT TERMS AND CONDITIONS OF AWARD

The following Terms and Conditions will be incorporated into the award statement. The following special terms of award are in addition to, and not in lieu of, otherwise applicable OMB administrative guidelines, HHS grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies:

1. The administrative and funding instrument used for this program will be the U54, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH scientific and/or programmatic involvement with the awardees is anticipated during performance of the activities. Under the cooperative agreement, the NIH purpose is to support and/or stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role. The NIH purpose is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and designated NIH Science Officers.

### 2. PI Rights and Responsibilities

The PI will coordinate project activities scientifically and administratively at the awardee institution. The PI will have primary responsibility for defining the details for the projects within the guidelines of this RFA (RFA RM-04-019), and for performing all scientific activities. The PI will agree to accept the close coordination, cooperation, and participation of the NIH Science Officer(s), Molecular Pathways and Network Steering Committee (MPANSC) and Molecular Pathways and Network Scientific Panel (MPANSP) in those aspects of scientific and technical management of the project as described below. Specifically, the PI will:

- o Determine experimental approaches, design protocols, direct experiments, and work cooperatively to set project milestones, in consultation with the Molecular Pathways and Network Steering Committee (MPANSC).
- o Release data according to the approved plans for sharing research resources generated through the award, and publish results, as agreed upon by the Molecular Pathways and Network Steering Committee (MPANSC).

- o Submit periodic progress reports in a standard format, as agreed upon by Molecular Pathways and Network Steering Committee (MPANSC).
- o Accept and implement the common guidelines and procedures approved by Molecular Pathways and Network Steering Committee (MPANSC) and Molecular Pathways and Network Scientific Panel (MPANSP).
- o Share with other Molecular Pathways and Network facilities research resources, tools, and data of interest to those facilities, as directed by MPANSC and MPANSP.
- o The PI and other critical staff should participate in MPANSC meetings held in the metropolitan Washington, DC area at least twice per year.

### 3. NIH Program Staff Responsibilities

The NIH Science Officer(s) will have substantial scientific/ programmatic involvement during the conduct of this activity through technical assistance, advice, and coordination above and beyond normal program stewardship for grants. This includes functioning as a peer with the PIs, facilitating the partnership relationship between NIH and the facilities funded under this RFA, helping to maintain the overall scientific balance in the program commensurate with new research and emerging research opportunities, and ensuring that the activities of the centers are consistent with the missions of the participating Institutes.

The role of NIH will be to facilitate and not to direct activities. It is anticipated that decisions will be reached by consensus of the PIs and that NIH staff will be given the opportunity to offer input to this process as members of MPANSC.

Specifically, the NIH Science Officer(s) will:

- o Provide relevant scientific expertise and overall knowledge.
- o Participate with other MPANSC members in the group process of setting research priorities and milestones, deciding optimal research approaches and protocol designs, and contributing to the adjustment of research protocols or approaches as warranted.
- o Provide information about ongoing NIH-supported research and resource collections.
- o Attend MPANSC meetings as one voting member, and assist to develop operating guidelines, quality control procedures, and consistent policies for dealing with recurrent situations that require coordinated action. The Science Officer(s) must be informed of all major interactions of members of MPANSC. The MPANSC will be responsible for preparing within 30 days a concise summary of each MPANSC meeting.
- o Serve as scientific liaison between the awardees and other NIH program staff.

- o Assist in promoting the centers to the scientific community at large.
- o Assist in developing timetables for the wide distribution of biomaterials and data to the scientific community.
- o Coordinate the activities of facilities to ensure the efficient long-term storage and timely release of biomaterials and data to the wider scientific community.
- o Help determine the most appropriate mechanisms for storage and distribution of biomaterials and data to the scientific community, i.e., storage and distribution by one of the facilities funded under this RFA and/or by another NIH-funded facility.
- o Retain the option to recommend re-allocating NIH support among awardees, as scientific goals evolve.
- o Participate in data analyses and, where warranted, co-authorship of papers resulting from projects funded under this RFA.

#### NIH Program Director

NIH will appoint a Program Director who will have responsibility for normal program oversight and stewardship of the award. The Program Director may also serve as the designated Science Officer. The Program Director will:

- o Have the option to recommend withholding support to a participating institution if technical performance requirements are not met.
- o Carry out continuous review of all activities to ensure objectives are being met.
- o Appoint the MPANSC Chair based on a recommendation from MPANSC committee members.
- o Serve as a non-voting member of MPANSC if not also participating as a Science Officer.

Serve as administrative liaison to MPANSP, attending MPANSP meetings as a non-voting member, to help coordinate activities of facilities funded under this RFA other NIH molecular pathways and network initiatives. The Program Director(s) will also coordinate the activities of facilities funded under this RFA with other US and international efforts.

#### 4. Collaborative Responsibilities - MPANSC Functions

**MOLECULAR PATHWAYS AND NETWORK STEERING COMMITTEE (MPANSC):**  
A committee that is the main governing board of all of the molecular pathways and

network facilities funded under this RFA, and the committee through which the NIH interacts and collaborates with the facilities. Voting membership includes the NIH Science Officers(s) (one vote total), the PI of each awarded cooperative agreement, and three scientists with relevant expertise who are not affiliated with any of the funded projects.

NIH will interact and collaborate with the facilities principally through the MPANSC. After appointment by NIH, the Science Officer(s) will schedule the first meeting and set the agenda, following which the Chair of MPANSC will rotate among the PIs and will be responsible for developing meeting agendas and chairing meetings. MPANSC will meet at least twice per year, but may use video or teleconferencing rather than face-to-face meetings, at the discretion of the committee members. Additional MPANSC members may be added by action of MPANSC. Other NIH staff may attend MPANSC meetings, when their expertise is required for specific discussions.

MPANSC will coordinate the activities of the centers and the exchange of information and biomaterials with the wider scientific community.

MPANSC will discuss scientific progress, make recommendations regarding how the centers achieve their scientific goals. MPANSP recommendations will be addressed by MPANSC.

#### 5. Molecular Pathways and Networks Scientific Panel (MPANSP)

**MOLECULAR PATHWAYS AND NETWORK SCIENTIFIC PANEL (MPANSP):** A committee that is advisory to NIH. MPANSP ensures coordination among TCNP projects funded under this RFA and evaluates their progress in relation to the evolving goals for trans-NIH initiatives on proteomics, molecular pathways and networks.

MPANSP will use its knowledge of the activities of all of the participating facilities to ensure adequate investigation, communication and sharing, and to avoid redundant activities. It will advise NIH with respect to the coordination of all activities that involve molecular networks and pathways. MPANSP will evaluate and make recommendations regarding the coordination of the activities of the facilities that are funded by the molecular pathways and networks initiative, and other related activities such as computation and data management that may be developed in the future.

It will be the responsibility of MPANSP to make recommendations that will lead to exchanging research tools, research resources, adopting common policies on data sharing, creating compatible databases, and other activities that will make these facilities of maximal utility to the scientific community. MPANSP will also recommend standards for data format and nomenclature, as well as develop common guidelines and procedures for deposition of the primary data.

The committee will consist of about 10 scientists (advisors) who are not affiliated with any of the molecular pathways and network centers.

They will be appointed by NIH. These advisors will be selected for their broad expertise in relevant topics. MPANSP will meet at least once each year. A schedule for subsequent meetings will be prepared at the first meeting.

NIH will select one member to be the committee chair, after considering MPANSP's recommendations. The chair will schedule the first meeting, will be responsible for developing meeting agendas and chairing the meetings. Additional MPANSP members may be added by an action of the original MPANSP members. The MPANSC Chair and Science Officer(s) will attend MPANSP as non-voting members and will act as representatives of MPANSC. Other NIH staff and MPANSC members may attend MPANSP meetings, when their expertise is required for specific discussions.

## 6. Milestones and Evaluations

The progress of the TNCPs will be reviewed annually by the NIH Program Director(s) and MPANSP to assure that satisfactory progress is being made in achieving the project objectives. During the first year of funding, and during subsequent years if deemed necessary by the Program Director, reviews may be more frequent. Should problems arise in the conduct of the study, the NIH Program Director may require that the awardee submit quarterly reports on progress and fiscal matters.

The progress report will have two components. The first will be the standard NIH progress report (Form 2590). The second will be a more specialized report that will go to the NIH Science Officer(s) and the NIH Program Director. This specialized report should be included as an attachment to the standard progress report. The contents of the report may be changed according to programmatic needs, based on discussion between NIH program officials, the PI and MPANSC.

The awardees' yearly milestones will be provided to MPANSC and MPANSP. It is expected that the milestones should be adjusted annually at the award anniversary dates, both to incorporate a group's scientific accomplishments and progress in the field in general, as well as to reflect MPANSC and MPANSP recommendations. Following the evaluation of milestones, NIH program staff may recommend augmenting any project or reducing or withholding funds for any project that substantially fails to meet its milestones or to remain state-of-the-art.

## 7. Arbitration Process

Any disagreements that may arise in scientific or programmatic matters within the scope of the award between recipients and the NIH may be brought to arbitration. This special arbitration procedure in no way affects the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulation at 45 CFR Part 16. An Arbitration Panel will help resolve both scientific and programmatic issues that develop during the course of work that restrict progress. The Arbitration Panel will be composed of three members: a designee of MPANSC chosen without the NIH staff voting, one NIH designee, and a third designee

with expertise in the relevant area who is chosen by the other two (in the case of an individual disagreement, the first member is chosen by the individual awardee rather than by MPANSC).

#### WHERE TO SEND INQUIRIES

We encourage inquiries concerning this RFA 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:

o Direct your questions about scientific/research issues to:

Douglas M. Sheeley, Sc.D.  
Division of Biomedical Technology  
National Center for Research Resources  
6701 Democracy Boulevard, Room 968  
Bethesda, MD 20892-4874  
Telephone: (301) 594-9762  
FAX: 301-480-3659  
Email: [sheeleyd@mail.nih.gov](mailto:sheeleyd@mail.nih.gov)

o Direct your questions about peer review issues to:

Sally Ann Amero, Ph.D.  
Chief, Bioengineering Sciences and Technologies IRG  
Center for Scientific Review, National Institutes of Health  
6701 Rockledge Drive, Room 4190, MSC 7826  
Bethesda, MD 20892 (20817 for courier deliveries)  
Telephone: 301-435-1159  
FAX: 301-480-4042  
Email: [TCNPReview@nih.gov](mailto:TCNPReview@nih.gov)

o Direct your questions about financial or grants management matters to:

Ms. Mary Niemiec  
Office of Grants Management  
National Center for Research Resources  
6701 Democracy Boulevard, Room 1036  
Bethesda, MD 20892-4874  
Telephone: (301) 435-0842  
FAX: 301-480-3777  
Email: [niemiecm@mail.nih.gov](mailto:niemiecm@mail.nih.gov)

## LETTER OF INTENT

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

- o Descriptive title of the proposed research
- o Name, address, and telephone number of the Principal Investigator
- o Names of other key personnel including those involved with the Driving Biological Projects and other collaborations
- o Participating institutions
- o Number and title of this RFA

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 (and the subsequent application itself) should NOT include the names of potential members of a proposed center's External Advisory Committee if it chooses to form one.

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:

Douglas M. Sheeley, Sc.D.  
Division of Biomedical Technology  
National Center for Research Resources  
6701 Democracy Boulevard, Room 968  
Bethesda, MD 20892-4874  
Telephone: (301) 594-9762  
FAX: 301-480-3659  
Email: [sheeleyd@mail.nih.gov](mailto:sheeleyd@mail.nih.gov)

Applicants are strongly encouraged to send the letter of intent by e-mail.

## SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). 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.dunandbradstreet.com/>. The D&B number should be entered on line 11 of the face page of the PHS 398 form. The PHS 398 document is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: [GrantsInfo@nih.gov](mailto:GrantsInfo@nih.gov).

## SUPPLEMENTARY INSTRUCTIONS

It is recognized that the proposals in response to this RFA will be longer and more complex than many other NIH proposals. In order to ensure effective review, the Research plan should be divided into sections according to the cores defined below, and separate page limits should be observed for each section as described below. See the RFA sections on RESEARCH OBJECTIVES and SPECIAL REQUIREMENTS for additional application instructions for the cores.

The U54 center will be required to have six cores: (1) conducting core research in technology development, (2) establishing Driving Biological Projects (DBP) to allow biomedical researchers to interact with and drive research in the TCNP, (3) providing infrastructure to biomedical researchers (hardware, software, and personnel as appropriate), (4) enhancing the training for biomedical researchers in appropriate tools and techniques, (5) disseminating newly developed tools and techniques to the broader biomedical research community, and (6) providing formal project leadership and management to ensure that these large National Programs achieve their goals within the 5 to 10 year funding lifetime of the center.

Form Pages 4-5: The budget should be completed as described in the instruction sheet for Application for a Public Health Service Grant (Form PHS 398). Applications should contain an overall detailed budget, and projections for the entire project period of five years. Budgets containing the same level of detail, also on form page 4, should be supplied for the following: Each of the technology development projects contained in Core 1, each of the driving biological projects in Core 2, and if not redundant with these two categories, for each consortium or subcontract agreement. Separate budgets should also be included for each of Cores 3, 4, 5, and 6.

The budget pages should be presented together. The budget justification should be organized by budget section.

The budget justification beginning on PHS Form Page 5 should include a detailed justification for key personnel. As part of the justification, the percent effort that all staff are spending on each core should be specified. For example, a particular postdoctoral fellow might spend 75% effort on core 1 and 25% effort on one of the DBPs in core 2.

A detailed justification should also be supplied for equipment over \$25,000 requested for the TCNP. Details of the physical location for this equipment should be provided. Existing equipment should also be described.

A detailed budget justification should also be provided for contractual or consortium arrangements. Use continuation pages as needed.

Biographical sketches must be included together in one section, according to the PHS 398 instructions, rather than within the research plans of individual projects. They should be organized for easy reference.

Section 9, Research Plan D: We request that all applicants use the following format for the Research Plan:

A. Program Introduction: A general narrative describing the goals, overall significance, theme, general research plan, and preliminary studies. Describe the interrelation and synergy between different components and cores. Describe the quality control and oversight. We recommend the use of a diagram to describe the plan for communication. This section may not exceed 25 pages.

B. Research Design and Methods Each of the six cores should be described. Use separate headings for each of these cores. It is recommended that each project in cores 1 and 2 be broken into four sections: A. Specific Aims; B. Background and Significance; C. Preliminary Work; D. Project Design and Methods. The content of Cores 3, 4, 5, and 6 may be structured however the applicant deems appropriate, but each core must be presented separately.

Each project within Core 1 may not exceed 25 pages. Each project within Core 2 may not exceed 10 pages. Cores 3, 4, 5, and 6 may each not exceed 25 pages. These page limits are not additive. That is, unused pages from one section may not be used to exceed the stated page limits for another section.

The remaining sections follow in order according to PHS 398 guidelines, viz, Human Subjects Research, Vertebrate Animals, etc.

Please observe the restrictions on appendix materials laid out in the PHS 398 instructions. Only ten items may be submitted for the entire application.

**USING THE RFA LABEL:** The RFA label available in the PHS 398 (rev. 5/2001) application form 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>.

**SENDING AN APPLICATION TO THE NIH:** Submit a signed, typewritten original of the application, including the Checklist, and five 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  
Bethesda, MD 20817 (for express/courier service)

**APPLICATION PROCESSING:** Applications must be received on or before the application receipt date listed in the heading of this RFA. If an application is received after that date, it will be returned to the applicant without review.

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

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

#### PEER REVIEW PROCESS

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the ICs. Incomplete and unresponsive 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 NIH in accordance with the review criteria stated below. As part of the initial merit review, all applications will:

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

#### REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to evaluate the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. The

scientific review group will address and consider each of the following criteria in assigning the application's overall score, weighting them as appropriate for each application.

- o Significance
- o Approach
- o Innovation
- o Investigator
- o Environment

The 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.

**SIGNIFICANCE:** Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

**APPROACH:** Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

**INNOVATION:** Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

**INVESTIGATOR:** Is the investigator 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 (if any)?

**ENVIRONMENT:** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

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

Some of the cores for the TCNPs have specific additional review criteria.

**CORE 1:** The criteria listed above will be applied to evaluation of each project within Core 1. In addition, the following factors will be considered. This solicitation seeks to build a program in which a significant fraction of the effort is aimed at developing highly novel technologies that have the potential to provide quantitative information at high anatomic resolution (subcellular) and biologically relevant timescales needed to elucidate

the function of molecular pathways and networks. This RFA therefore encourages the inclusion of the more challenging development of revolutionary new approaches as a component of the application. The degree of novelty and potential impact of these technologies will be important review criteria. The degree to which the technologies proposed are integrated into a coherent overall strategy will also be an important factor.

**CORE 2:** Do the investigators have appropriate plans to obtain support for the DBPs after their support from the TCNP has terminated? Does each DBP act as a test-bed and/or driver for the technology development proposed in Core 1?

**CORES 1-2:** Will the work proposed in these cores help establish an integrated approach to characterization of pathways and networks? Is the proposed work essential to establishing this approach?

**CORE 3:** Are the infrastructure requests adequate to meet the demands that are likely to come from biomedical researchers?

**CORES 4 and 5:** Will the proposed training and dissemination tools help create a new group of multi-disciplinary or interdisciplinary investigators?

**CORE 6:** The reviewers will be asked to address the proposed management of the project. Will the proposed management structure allow the TCNP to achieve its goals? Does the institution have an appropriate career path for the project manager? Is the mechanism to terminate old DBPs and choose new ones adequate? Will the plans to incorporate individual investigator awards work?

Reviewers will be instructed to consider all six components of the project as important, even if a particular component is only a relatively small part of the budget. For example outreach and training, while not as costly as the core development of the technologies, is considered to be critically important for the TCNP to have the appropriate impact on biomedical research.

**SOFTWARE AVAILABILITY:** Does the plan for distributing the software reasonable allow wide and easy access? Are any fee structures appropriate?

**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 criteria included in the section on Federal Citations, below).

**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. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria in the sections on Federal Citations, below).

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 398 research grant application instructions (rev. 5/2001) will be assessed.

#### ADDITIONAL REVIEW CONSIDERATIONS

##### Sharing Research Data

Applicants requesting \$500,000 or more in direct costs in any year of the proposed research must include a data-sharing plan in their application. The reasonableness of the data sharing plan or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data-sharing plan into the determination of scientific merit or priority score.

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

#### RECEIPT AND REVIEW SCHEDULE

Letter of Intent Receipt Date: January 18, 2005  
Application Receipt Date: February 22, 2005  
Peer Review Date: June 2005  
Council Review: September 2005  
Earliest Anticipated Start Date: September 2005

#### AWARD CRITERIA

Award criteria that will be used to make award decisions include:

- o Scientific merit (as determined by peer review)
- o Availability of funds
- o Programmatic priorities

#### REQUIRED FEDERAL CITATIONS

ANIMAL WELFARE PROTECTION: 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). The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risk to the participants. (NIH Policy for Data and Safety Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: <http://grants.nih.gov/grants/guide/notice-files/not98-084.html>).

**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 - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html>); a

complete copy of the updated Guidelines are available at

[http://grants.nih.gov/grants/funding/women\\_min/guidelines\\_amended\\_10\\_2001.htm](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 applications 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 RESEARCH INVOLVING HUMAN SUBJECTS:** The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects 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 that is available at

<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. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, 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 (see <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](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 applications 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 RFA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.health.gov/healthypeople>.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance at <http://www.cfda.gov/> and is not subject to the intergovernmental review requirements of Executive Order 12372 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.

---

[Return to Volume Index](#)

[Return to NIH Guide Main Index](#)

---



Department of Health  
and Human Services



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