

CLINICAL TRIAL PLANNING GRANTS FOR PEDIATRIC REHABILITATION

Release Date: November 21, 2000

RFA: HD-01-006

National Institute of Child Health and Human Development

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

National Institute of Arthritis and Musculoskeletal and Skin Diseases

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

Letter of Intent Receipt Date: December 29, 2000

Application Receipt Date: February 22, 2001

THIS RFA USES THE "MODULAR GRANT" AND "JUST-IN-TIME" CONCEPTS. IT INCLUDES DETAILED MODIFICATIONS TO STANDARD APPLICATION INSTRUCTIONS THAT MUST BE USED WHEN PREPARING APPLICATIONS IN RESPONSE TO THIS RFA.

PURPOSE

The National Center for Medical Rehabilitation Research (NCMRR) of the National Institute of Child Health and Human Development (NICHD) and National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) intend to support clinical trials of rehabilitation interventions focused on pediatric injuries and trauma, including burn wounds. In addition, the NIAMS is interested in rehabilitation interventions that are focused on chronic musculoskeletal disorders (e.g., juvenile rheumatoid arthritis and heritable disorders of connective tissue) and genetic skin disorders. The purpose of the Clinical Trial Planning Grant is to provide support for the organization of an effective research group and development of elements essential for a successful clinical trial. Applications may address the development of activities relevant to such elements as plans for recruitment of patients, experimental design and protocols, testing of procedures, data management, analysis techniques, facilities, administrative procedures, and collaborative arrangements. Detailed information regarding the rationale for the clinical trial based on preclinical and preliminary clinical research must be included in the application for the Clinical Trial Planning Grant for Pediatric Rehabilitation. The purpose of the planning grant is neither to obtain preliminary data nor to conduct studies to support the rationale for the clinical trial.

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 Request for Applications (RFA) is related to one or more priority areas. Potential applicants may obtain "Healthy People 2010" at: <http://www.health.gov/healthypeople>.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as Principal Investigators.

Clinical trial planning support is for new projects and may not be used to supplement research projects already being supported or to provide interim support of projects under review. Simultaneous submissions of both planning and regular clinical trial grant applications (R01) on the same topic will not be accepted. Only one Clinical Trial Planning Grant application from an individual Principal Investigator will be considered.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) Individual Exploratory/ Developmental Research Grant (R21) award mechanism. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. This RFA is a one-time solicitation. Applicants may apply for continuation of projects developed under this program using traditional, unsolicited grant mechanisms (e.g., R01, P01). Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures. The anticipated award date is September 2001.

Specific application instructions have been modified to reflect "MODULAR GRANT" and "JUST-IN-TIME" streamlining efforts being examined by the NIH. Complete and detailed instructions and information on Modular Grant applications can be found at <http://grants.nih.gov/grants/funding/modular/modular.htm>.

FUNDS AVAILABLE

The NICHD intends to commit approximately \$750,000 in total costs [direct plus Facilities and Administrative (F&A) costs] in FY 2001 to fund up to seven new grants in response to this RFA. The NIAMS intends to commit approximately \$250,000 in total costs [direct plus Facilities and Administrative (F&A) costs] in FY 2001 to fund two or three new grants in response to this RFA. An applicant may request a project period of one year and a budget for direct costs of up to \$75,000. Although this program is provided for in the financial plans of NICHD and NIAMS, awards pursuant to this RFA are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications.

RESEARCH OBJECTIVES

Background

Traumatic injury is the leading cause of death for children and adolescents in the United States. Age is a significant epidemiological factor because the causes of the injury differ according to the developmental stage of the individual. Overall, accidents are the largest cause of morbidity and mortality during childhood. Accidents and violence are the most frequent causes of death in five- to 18-year-old children. Traumatic Brain Injury (TBI) alone has an incidence of 90/100,000 with the majority of these individuals experiencing long-term disability.

With technical advances in medicine and emergency services, the number of children surviving their injuries has increased, but consequently so have the disabilities and long-term effects on quality of life. Long-term care for such children extends beyond the rehabilitation facilities and touches all aspects of their lives. Children with disability require attention to allow them to continue in school, maximize their participation in social and family activities, and develop into productive, healthy adults. Their conditions are managed by a variety of rehabilitation interventions including physical therapy, medication, and the provision of adaptive equipment such as prostheses, orthoses, and wheelchairs. Although these interventions are widely used, very little systematic information exists regarding the effectiveness of many of them.

Although disorders in adults and children may be similar in causality, diagnosis, and treatment, it is the wide range of developmental phenomena that distinguishes the rehabilitation of infants, children, and adolescents from that of adults. The developmental process forms the template for establishing appropriate interventions and rehabilitation goals. However, the identification of objective and effective rehabilitation interventions is complicated not only by the adaptation and

recovery processes taking place at different stages following the injury, but also by the additional uncertainties of the process of biological maturation.

Current constraints on clinical researchers make the complex and time-consuming process of planning Phase III clinical trials problematic, especially in the fields of medical rehabilitation, where there is not a well-established clinical research infrastructure. These planning grants will provide a mechanism for early peer review of the rationale and design of the potential clinical trial, and provide successful applicants resources to assist development of detailed clinical trial study plans and collaborations.

Research Scope

The range of activities that may be supported by this Clinical Trial Planning Grant includes:

1. Development of a detailed experimental design, including: translation of the clinical question into a statistical hypothesis; determination of the sample size and duration of the trial; selection of endpoint(s) and data to be collected; creation of inclusion/exclusion criteria.
2. Development of specific protocols, including: patient selection and informed consent procedures; randomization and masking procedures; data collection techniques; treatment administration and dose/quantity measurements; follow-up and quality control procedures.
3. Development of detailed plans for patient recruitment and retention, including women and minority individuals, and plans for recruitment outreach.
4. Identification of other personnel necessary to perform the proposed research, including statisticians, data managers, and study coordinators.
5. Identification of the physical resources necessary to perform the proposed research, including clinical space and equipment which is accessible to subjects and researchers with disabilities.
6. Selection of specific methods of data analysis.
7. Evaluation of models of the rehabilitation treatment process, including: involvement of various professional disciplines, team approaches, and treatment settings; coordination of health care systems and resources.

Research Topics

It is hoped that these Planning Grants will help to facilitate clinical trial projects in areas of research need relevant to the National Center for Medical Rehabilitation Research (NCMRR), NICHD, and to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Examples of research areas within the scope of the RFA include, but are not limited to, the following:

- o development and evaluation of rehabilitation interventions and new treatment strategies to improve the functional outcome in children following traumatic injury;
- o evaluations of interventions to improve the functional mobility of children with chronic disability including physical therapy, medication, prosthetics and orthotics, electrical stimulation, and other physical modalities;
- o evaluations of interventions to improve functional mobility of children with chronic musculoskeletal disorders, burn wounds, and genetic skin disorders, including physical therapy, medication, electrical stimulation, and other physical modalities;
- o evaluation of interventions including medication, cognitive rehabilitation, and memory prosthetics to improve the cognitive functioning of children with disabling conditions;
- o evaluation of interventions to prevent and/or ameliorate secondary conditions with a higher prevalence among children with physical disabilities.

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification are provided 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 research involving human subjects should read the UPDATED "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research," published in the NIH Guide for Grants and Contracts on August 2, 2000

(<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html>);

a complete copy of the updated Guidelines are available at http://grants.nih.gov/grants/funding/women_min/guidelines_update.htm. The revisions relate to NIH defined Phase III clinical trials and require: a) all applications or proposals and/or protocols to 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) all investigators to report accrual, and to conduct and report analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of NIH 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. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

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," published in the NIH Guide for Grants and Contracts, March 6, 1998, and available on the Internet at: <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>.

Investigators also may obtain copies of these policies from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

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. Reviewers are cautioned that their anonymity may be compromised when they directly access an Internet site.

LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the

identities of other key personnel and participating institutions, and the 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 NICHD staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent to Dr. Beth Ansel at the address listed under INQUIRIES, below, by December 29, 2000.

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 4/98) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research, on the Internet at <http://grants.nih.gov/grants/funding/phs398/phs398.html>, and from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301-435-0714, E-mail: Grantsinfo@nih.gov.

Application Instructions

The modular grant concept establishes specific modules in which direct costs may be requested as well as a maximum level for requested budgets. Only limited budgetary information is required under this approach. The just-in-time concept allows applicants to submit certain information only when there is a possibility for an award. It is anticipated that these changes will reduce the administrative burden for the applicants, reviewers, and NIH staff. The research grant application form PHS 398 (rev. 4/98) is to be used in applying for these grants, with the modifications noted below.

For responses to this RFA, Modular Grant applications will request direct costs in \$25,000 modules, up to a total direct cost request of \$75,000 for one year. The total direct costs must be requested in accordance with the program guidelines and the modifications made to the standard PHS 398 application instructions described below:

o FACE PAGE: Items 7a and 7b should be completed, indicating Direct Costs (in \$25,000 increments up to a maximum of \$75,000) and Total Costs [Modular Total Direct plus Facilities and Administrative (F&A) costs] for the initial budget period. Items 8a and 8b should be completed indicating the Direct and Total Costs for the entire proposed period of support, identical to the figures in Items 7a and 7b for this RFA.

o DETAILED BUDGET FOR THE INITIAL BUDGET PERIOD: Do not complete Form Page 4 of the PHS 398. It is not required and will not be accepted with the application.

o BUDGET FOR THE ENTIRE PROPOSED PERIOD OF SUPPORT: Do not complete the categorical budget table on Form Page 5 of the PHS 398. It is not required and will not be accepted with the application.

o NARRATIVE BUDGET JUSTIFICATION: Prepare a Modular Grant Budget Narrative page. (See <http://grants.nih.gov/grants/funding/modular/modular.htm> for sample pages.) At the top of the page, enter the total direct costs requested for the project year. This is not a Form Page.

o Under Personnel, list ALL project personnel, including their names, percent of effort, and roles on the project. No individual salary information should be provided. However, the applicant should use the NIH appropriation language salary cap and the NIH policy for graduate student compensation in developing the budget request.

For Consortium/Contractual costs, provide an estimate of total costs (direct plus F & A), rounded to the nearest \$1,000. List the individuals/organizations with whom consortium or contractual arrangements have been made, the percent effort of all personnel, and the role on the project. Indicate whether the collaborating institution is foreign or domestic. The total cost for a consortium/contractual arrangement is included in the overall requested modular direct cost amount. Include the Letter of Intent to establish a consortium.

o BIOGRAPHICAL SKETCH: The Biographical Sketch provides information used by reviewers in the assessment of each individual's qualifications for a specific role in the proposed project, as well as to evaluate the overall qualifications of the research team. A biographical sketch is required for all key personnel, following the instructions below. No more than three pages may be used for each person. A sample biographical sketch may be viewed at: <http://grants.nih.gov/grants/funding/modular/modular.htm>.

- Complete the educational block at the top of the form page;
- List position(s) and any honors;
- Provide information, including overall goals and responsibilities, on research projects ongoing or completed during the last three years;
- List selected peer-reviewed publications, with full citations.

o CHECKLIST: This page should be completed and submitted with the application. If the F&A rate agreement has been established, indicate the type of agreement and the date. All appropriate exclusions must be applied in the calculation of the F&A costs for the budget period.

o The applicant should provide the name and telephone number of the individual to contact concerning fiscal and administrative issues if additional information is necessary following the initial review.

Submission Instructions

The RFA label available in the PHS 398 (rev. 4/98) application form must be stapled to the bottom of the face page of the application and must display the RFA number HD-00-025. A sample RFA label is available at <http://grants.nih.gov/grants/funding/phs398/label-bk.pdf>. Please note this is in the pdf format. 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.

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
BETHESDA, MD 20817 (for express/courier service)

At the time of submission, two additional copies of the application should be sent to:

L. R. Stanford, Ph.D.
Director, Division of Scientific Review
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 5E03F, MSC 7510
Bethesda, MD 20892-7510
Bethesda, MD 20854 (for express/courier service)

Applications must be received by February 22, 2001. If an application is received after that date, it will be returned to the applicant without review.

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. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by CSR and for responsiveness to this RFA by NICHD and NIAMS. Incomplete and/or non-responsive applications will be returned to the applicant without further consideration.

Applications that are complete and responsive to the RFA will be reviewed for scientific and technical merit by a review group convened by the NICHD, in cooperation with the NIAMS, in accordance with the review criteria stated below. As part of the initial merit review, all applications will receive a written critique and may undergo a process in which only those applications deemed to have the highest scientific merit will be discussed, assigned a priority score, and receive a second level review by the National Advisory Child Health and Human Development Council and/or the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council.

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 discuss the following aspects of the application 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 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.

(1) 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?

(2) Approach. Are the conceptual frameworks, 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?

(3) Innovation. Does the project employ novel concepts, approaches or method? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

(4) 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)?

(5) 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?

In addition to the above criteria, in accordance with NIH policy, applications also will be reviewed with respect to the following:

o The adequacy of plans to include both genders, minorities and their subgroups, and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects also will be evaluated.

o The reasonableness of the proposed budget and duration in relation to the proposed research.

o The adequacy of the proposed protection for humans, animals, and the environment, to the extent they may be adversely affected by the project proposed in the application.

Schedule

Letter of Intent Receipt Date: December 29, 2000

Application Receipt Date: February 22, 2001

Peer Review Date: June/July 2001
Council Review: September 2001
Earliest Anticipated Start Date: September 2001

AWARD CRITERIA

Funding decisions will be based on scientific and technical merit as determined by peer review, program balance and need, and the availability of funds.

INQUIRIES

Inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Beth M. Ansel, Ph.D., CCC-SLP
Director, Clinical Practices Research Program
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 2A03, MSC 7510
Bethesda, MD 20892-7510
Telephone: (301) 402-2242
FAX: (301) 402-0832
E-mail: Beth_Ansel@nih.gov

James S. Panagis, M.D., M.P.H.
Director, Orthopaedics Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
6500 Center Drive, Room 5AS-37K, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-5055
FAX: (301) 480-4543
E-mail: jp149d@nih.gov

Direct inquiries regarding fiscal matters to:

Ms. Mary Ellen Colvin

Grants Management Branch
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 8A17H, MSC 7510
Bethesda, MD 20892-7510
Telephone: (301) 496-1304
FAX: (301) 402-0915
E-mail: mc113b@nih.gov

Ms. Melinda Nelson
Grants Management Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
6500 Center Drive, Room 5AS-49F, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-3535
FAX: (301) 480-5450
E-mail: mn23z@nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.929 and 93.846. Awards are made under authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and administered under NIH grants policies and Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant and contract recipients to provide a smoke-free workplace and promote the non-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.

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