

# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific  
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administrative information to indi-  
viduals and organizations who need to  
be kept informed of opportunities,  
requirements, and changes in extra-  
mural programs administered by the  
National Institutes of Health.

Vol. 19, No. 39  
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SUZANNE FISHER

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## NOTICES

### PUBLIC HEALTH SERVICE - OPEN MEETING ON CONFLICTS OF INTEREST IN CLINICAL EVALUATION OF COMMERCIAL PRODUCTS

P.T. 42; K.W. 1014004

National Institutes of Health  
Alcohol, Drug Abuse, and Mental Health Administration

**SUMMARY:** The Public Health Service (PHS) recognizes the need to issue regulations addressing conflict-of-interest issues that arise when investigators conducting PHS-supported clinical evaluations of commercial products have financial interests in those products. Before proceeding with rulemaking, the PHS invites members of the public to attend a meeting to discuss principles and questions relevant to such regulations.

**DATE:** November 30, 1990, 8:30 a.m. to 4:30 p.m.

**ADDRESS:** Masur Auditorium, Clinical Center, (Building 10)  
National Institutes of Health  
9000 Rockville Pike  
Bethesda, MD 20892

#### **FOR FURTHER INFORMATION CONTACT:**

George Galasso, Ph.D.  
Associate Director for Extramural Affairs  
NIH, Building 1, Room 152  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-5356

#### **SUPPLEMENTAL INFORMATION:**

The PHS supports clinical trials that involve the evaluation of commercial products such as drugs, vaccines, and devices. The efficient transfer of these research results into commerce is essential to improve health care and economic competitiveness. In generating new knowledge about a commercial product, the PHS-supported research may affect the product's value either favorably or adversely. To the extent that participating investigators have financial interests related to commercial products they are evaluating in clinical trials, the risk of apparent or actual conflicts of interest must be addressed by the PHS and the research community it supports. Financial holdings of investigators must not influence the design, conduct, or reporting of such clinical trials.

The PHS has already issued regulations dealing with misconduct in science to protect PHS-supported biomedical and behavioral research against falsification, fabrication, plagiarism or other practices that seriously deviate from commonly accepted practices within the scientific community. PHS is considering issuance of additional rules to promote the integrity of PHS-supported clinical trials where investigators may have financial interests that could affect or give the appearance of affecting their objectivity. Before doing so, the PHS and its component agencies, the National Institutes of Health (NIH) and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) will conduct a public meeting to discuss one approach to addressing the issues involved, as well as other alternatives.

The proposed approach is outlined in this notice. In developing the outline, NIH/ADAMHA have taken into consideration the comments received on the earlier proposed Guidelines published in the NIH Guide for Grants and Contracts, Vol. 18, No. 32, September 15, 1989. The meeting will provide a forum for public comments on the proposed approach and the various issues which it attempts to address, as well as an opportunity for alternative suggestions.

The meeting will be held on November 30, 1990 in Masur Auditorium on the campus of the NIH. Registration is requested as seating is limited to approximately 500 attendees. To assure that your comments will be considered in the event that you may not be able to present them orally, written comments may be submitted at the registration desk. Interested parties may register by contacting:

Ms. Bonnie Kaps  
National Institutes of Health  
Building 31, Room 5B32  
Bethesda, MD 20892  
Telephone: (301) 402-0854  
FAX: (301) 496-0166

## DISCUSSION TOPICS - CLINICAL PRODUCT EVALUATION

### General Principles

- o Efficient transfer of research results into commerce is and will continue to be essential if the United States is to maintain and enhance health care and economic competitiveness.
- o Pertinent Federal statutes provide generally that tax-financed research institutions will give high priority to ensuring commercialization of their scientists' results wherever appropriate.
- o The research community will not maintain public confidence without rules that harmonize the national interest, institutional interests, and individual interests.
- o There is an apparent need for rules on conflict of interest that will protect the integrity of PHS-sponsored clinical trials and ensure that financial interests of investigators will not compromise the conduct or reporting of such research.
- o At the same time, the PHS must strive to ensure that procedures for protection against conflict of interest do not stifle the advancement of research and technology transfer, which are key aspects of the PHS mission.
- o The proposed approach is to address potential conflicts of interest in clinical trials of commercial products because of the near term significance for patient care.

### Proposed Approach

- o Require institutions to establish procedures that ensure that clinical trials supported by PHS are not compromised by inappropriate financial interests on the part of investigators.
- o Covered individuals would include investigators responsible for designing, conducting or reporting research and their spouses, dependents and business partners.
- o Institutions must solicit and review disclosures of financial interests of investigators who will receive PHS funding for clinical trials of commercial products and where necessary, take action to eliminate or prevent inappropriate financial interests, particularly financial interests in firms that manufacture, sell, or otherwise have property rights in the product under study.
- o A financial interest in the product under study may be approved by the institution if it is judged unlikely to compromise the design, conduct, or reporting of the study. The institution should impose requirements to minimize even perceived conflict, for example, by requiring disclosure of interests in resulting publications.
- o Investigators/institutions must disclose to the PHS all sources of support for the PHS-supported clinical trial (before the award of PHS funds and after the award when changes occur).

### Issues

- o The overarching issue is how best to protect the integrity of research while promoting technology transfer.
- o Should the basic regulatory approach a) require disclosure and allow flexibility for institutions to take appropriate action, b) state specific prohibitions, or c) require disclosure and decisions on appropriateness by the funding agency?
- o To what extent should conflict of interest rules applicable to Federal employees, including those applicable to NIH/ADAMHA study

section members, serve as a model in developing the proposed requirements? (See 45 C.F.R. Part 73.)

- o Are there regulatory frameworks not specific to PHS (e.g., Federal Securities Laws) that are applicable to the topic? o Who are the most appropriate parties to determine a conflict of interest?
- o Should all forms of financial interests be reviewed, for example, equity, salary, other payment for services, honoraria, and gifts?
- o Are there minimal levels of financial interests which would not create an actual or apparent conflict of interest?
- o Should PHS require submission and approval of institutional policies in order to ensure consistency and provide technical assistance where necessary?
- o Should PHS require disclosure to the funding agency of approved financial interests, if any?
- o Should there be a requirement for public disclosure of financial interests, for example, in publications?
- o Should there be disclosure of the investigators' financial interests as part of the document seeking the research subjects' informed consent to participation in clinical trials? (In this regard, see the decision in Moore v. Regents of University of California, 271 Cal. Rpt. 146, 793 P2d 475, 19 USPQ2d 1753 California Supreme Court, July 9, 1990).
- o Should institutional financial interests be considered?
- o What should the remedies be for violations?

#### CONFLICT OF INTEREST

Clinical Evaluation of Products  
November 30, 1990  
Masur Auditorium, Clinical Center, NIH  
Public Meeting

- 8:30-9:00 Introduction and Opening Remarks
- 9:00-10:30 Presentations  
9:00-10:00 Four Presenters - 15 minutes each  
10:00-10:30 General questions and answers
- 10:30-11:00 Coffee
- 11:00-12:30 Comments from the audience concerning all aspects of this issue including, but not limited to:
- General Policy - Basic regulatory approach; responsibilities of PHS and institutions; reporting and disclosures of financial interests; resolution of conflicts of interest.
- Restrictions - Types of financial interests; minimal levels; waivers.
- Remedies and Sanctions - Federal oversight and role with respect to institutions; enforcement against investigators.
- Audience comments - 3-5 minutes each.
- 12:30-1:30 Lunch.
- 1:30-2:45 Comments continued.
- 2:45-3:15 Coffee.
- 3:15-4:15 Comments continued.
- 4:15 Conclusion.

NATIONAL INSTITUTES OF HEALTH AND THE FOOD AND DRUG ADMINISTRATION NATIONAL WORKSHOPS ON "PROTECTION OF HUMAN SUBJECTS"

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

I. SOUTHEAST WORKSHOP

DATES: December 6-7, 1990

WORKSHOP SITE:  
The Hotel Nikko Atlanta  
3300 Peachtree Road  
Atlanta, GA 30305

SPONSORS:  
Emory University School of Medicine  
1440 Clifton Road  
Atlanta, GA 30322

Moorehouse School of Medicine  
720 Westview Drive, S.W.  
Atlanta, GA 30310

REGISTRATION CONTACT:  
Office of Continuing Medical Education  
Emory University School of Medicine  
1440 Clifton Road, N.E.  
(107 WHSCAB)  
Atlanta, GA 30322  
Telephone: (404) 727-5695

TOPIC: "Protection of Human Subjects in Research: Difficult Bioethical Issues"

II. SOUTHWEST WORKSHOP

DATES: February 4-5, 1991

WORKSHOP SITE:  
Meridien Hotel  
50 Third Street  
San Francisco, CA 94103

SPONSOR:  
University of California at San Francisco  
Box 0400  
San Francisco, CA 94143

REGISTRATION CONTACT:  
Ms. Phyllis Colbert  
Workshop Contact Person  
University of California at San Francisco  
Box 0400  
San Francisco, CA 94143  
Telephone: (415) 476-1881

TOPIC: "The Use of Human Subjects in Research: AIDS as a Model of Complexity"

III. MIDEAST WORKSHOP

DATES: March 4-5, 1991

WORKSHOP SITE:  
Friday Center  
Laurel Hill Parkway  
Chapel Hill, NC 27599-1020

SPONSORS:  
University of North Carolina at Chapel Hill  
300 Bynum Hall  
Chapel Hill, NC 27599-4100

Shaw University  
118 E. South Street  
Raleigh, NC 27611

REGISTRATION CONTACT:  
Mr. Al Dawson  
Director  
Friday Center  
Laurel Hill Parkway  
C. B. 1020  
Chapel Hill, NC 27599-1020  
Telephone: (919) 962-1106

TOPIC: "Problems in Interpreting the Federal Code for the Protection of Human Subjects"

#### IV. MIDWEST WORKSHOP

DATES: April 11-12, 1991

WORKSHOP SITE:  
Hyde Park Hilton  
4900 Lake Shore Drive  
Chicago, IL 60615

SPONSORS:  
University of Chicago  
970 East 58th Street  
Chicago, IL 60637

Chicago State University  
95th Street at King Drive  
Chicago, IL 60628

REGISTRATION CONTACT:  
Mr. Arnold L. Aronoff  
Associate Director  
Faculty and Administrative Services  
University Research Administration  
University of Chicago  
970 East 58th Street  
Chicago, IL 60637  
Telephone: (312) 702-8669

TOPIC: "Cultural Diversity, Ethics, and Research: A Workshop on Human Subject Protections"

NIH/FDA have planned national human subject protections workshops in other parts of the United States. For further information regarding these workshops contact:

Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
9000 Rockville Pike  
Bldg. 31, Room 5B43B  
Bethesda, MD 20892  
Telephone: (301) 496-8101

NOTICES OF AVAILABILITY (RFPs AND RFAs)

PRODUCTION AND DELIVERY OF SCHISTOSOMA MANSONI

RFP AVAILABLE: RFP-NIH-NIAID-DIR-91-24

P.T. 34; K.W. 0780005

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases has a requirement for the production and delivery of adult worms, sporocysts, and cercariae of *Schistosoma mansoni*. The successful offeror must be able to deliver worms and cercariae to the NIH campus within one hour after they have been harvested. Approximately 6,000 mature *S. mansoni* shall be required each week. When different isolates are requested at the same time, the total number of worms and/or mice perfused per week for the worms will not exceed 6,000 worms or the number of mice needed to obtain 6,000 adult worms (60 mice). Approximately 1,000,000 cercariae shall be required each week. Cercariae, eggs, and sporocysts shall be live upon receipt. One fixed-priced award is contemplated. It is anticipated that this contract will be awarded for one year with four one-year options to continue this contract. Any contract awarded will be subject to DHHS regulations regarding the use of animals in research. Any responsible source may submit a proposal which shall be considered by the Government.

RFP-NIH-NIAID-DIR-91-24 will be issued on or about October 29, 1990. Proposals will be due forty-five days thereafter.

To receive a copy of this RFP, please supply this office with a request in writing and two self-addressed mailing labels addressed to the office listed below:

Ms. Grace A. Bruce  
Contract Specialist  
Contract Management Branch, NIAID  
National Institute of Allergy and Infectious Diseases  
Westwood Building, Room 707  
5333 Westbard Avenue  
Bethesda, MD 20892

This advertisement does not commit the Government to make an award.

PROTECTIVE EFFECTS OF PATTERNED ELECTRICAL STIMULATION ON THE DEAFENED AUDITORY SYSTEM

RFP AVAILABLE: NIH-NIDCD-91-01

P.T. 34; K.W. 0715050, 0745047

National Institute on Deafness and Other Communication Disorders

The National Institute of Deafness and Other Communication Disorders (NIDCD), NIH, has a requirement to evaluate the possibility that chronic electrical stimulation of selected portions of the auditory system can maintain the anatomical and physiological viability of deafferented auditory nerve axons and their cell bodies in a manner compatible with future implantation of a functional auditory prosthesis.

Past studies supported by NIDCD and its predecessor, the National Institute of Neurological and Communicative Disorders and Stroke, have supported the development of essentially all aspects of auditory prostheses. These have included the evaluation of the safety of chronic implantation and electrical stimulation of the cochlea. For the most part, these components were designed for permanent implantation in adults. Recently the NIDCD, through the Neural Prosthesis Program, has supported studies of problems that are unique to implants in children. Specifically, the effects of head growth and recurrent otitis media have been evaluated in young animals.

Recently, research in deafened kittens has suggested that spatially and temporally patterned electrical stimulation with multielectrode cochlear implants does indeed provide selective protection to auditory ganglion cells and their axons in the cochlea. The purpose of this proposed study is to confirm this effect and, if real, to optimize it. It is possible that this could lead to a method of extracochlear stimulation for protection of the deaf human cochlea in the period between the diagnosis of deafness and the



implantation of a cochlear implant. This is especially appealing in the young deaf child where a delay in implantation may be desirable.

The contractor will be required to come to Bethesda yearly to present progress on their work at the Neural Prosthesis Workshop sponsored by the Neural Prosthesis Program.

It is anticipated that one award will be made under this RFP for a three-year period.

This is not a Request for Proposals. RFP No. NIH-NIDCD-91-01 will be issued on or about October 26, 1990, with responses due December 21, 1990.

To receive a copy of the RFP, please submit a written request to the following address, and supply this office with two (2) self-addressed mailing labels:

Contracting Officer  
Contracts Management Branch, DEA  
National Institute of Neurological Disorders and Stroke, NIH  
Federal Building, Room 901  
7550 Wisconsin Avenue  
Bethesda, MD 20892

Attention: RFP No. NIH-NIDCD-91-01

All responsible sources may submit a proposal which shall be considered by the Government.

#### CLINICAL COORDINATING CENTER FOR A CHILDHOOD ASTHMA MANAGEMENT PROGRAM

RFP AVAILABLE: NHLBI-HR-90-12

P.T. 34, AA; K.W. 0715013, 0785035, 0755018

National Heart, Lung, and Blood Institute

The purpose of this solicitation is to establish a clinical coordinating center for a collaborative study of a Childhood Asthma Management Program (CAMP). The objective of this program is to determine, in a population of 5-9 year old children with asthma, if regular use of either of two types of anti-inflammatory medications (inhaled corticosteroids or cromolyn sodium), compared to regular bronchodilator medication and to each other, results in greater lung function and less bronchial hyperresponsiveness over a five-year period. The program will require a clinical coordinating center (CCC) to collect data from approximately 8 participating clinical centers, each studying a minimum of 132 children with asthma aged 5-9 years, including 44 from minority groups, e.g., Blacks, Hispanics and Native Americans, over a 6 1/2 year period. The coordinating center will be responsible for: (1) coordinating and participating in the development, preparation, and maintenance of the study protocol, reporting forms, and manual of operations, and printing and distribution of these documents; (2) designing a system for collection and management of data with feedback systems for quality control; (3) arranging and attending meetings of the principal investigators from each clinical center, and taking and distributing minutes of the meetings; (4) developing procedures for standardization of pulmonary function testing; (5) coordinating and training appropriate staff in implementing study interventions, including administration of medications, health education protocols, and procedures for measurement of pulmonary function; (6) training clinical center staff in entering data through a distributed data entry system, if appropriate, and completion of study forms; (7) randomizing subjects to treatment groups and monitoring subject recruitment; (8) assuring prompt accumulation, entry, and editing of study data; (9) communicating with the clinical centers concerning missing, delayed, incomplete, or erroneous data; (10) obtaining and processing laboratory reports, if appropriate; (11) storing blood samples from subjects and obtaining appropriate analyses; (12) preparing statistical reports on a quarterly basis and, as needed, to monitor study progress, quality of data, clinical center performance; (13) submission of weekly recruitment reports to the Project Officer; (14) interacting with the Project Officer on issues relating to study design, study conduct, and data analysis; (15) analyzing data from the beginning of data collection through the end of the study; (16) completing analysis of study data; and (17) assisting in the preparation of scientific reports for publication and presentation.

This announcement is not a request for proposal (RFP). It is anticipated that RFP NHLBI-HR-90-12 will be available on or about November 1, 1990, with proposals due on February 28, 1991. Copies of the RFP may be obtained by

submitting a written request along with three (3) self-addressed mailing labels to:

Pamela S. Randall  
National Heart, Lung and Blood Institute, NIH  
Contracts Operations Branch, DEA  
Westwood Building, Room 654  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7334

The Institute expects to make one award from this solicitation.

MINORITY FELLOWSHIPS FOR DOCTORAL AND/OR POSTDOCTORAL TRAINING IN NEUROSCIENCES

RFA AVAILABLE: MH-91-01

P.T. 22, FF; K.W. 0720005, 1002030

National Institute of Mental Health

Application Receipt Date: January 10, 1991

The Minority Fellowship Program (MFP) of the National Institute of Mental Health is designed to facilitate the entry of minority students into mental health careers with the long-term goal of increasing the number of minority scientists trained at the doctoral and postdoctoral levels to conduct research and teach in the neurosciences.

Three awards will be made for national programs to be administered by professional associations, academic institutions, or other eligible organizations, or by any combination of the foregoing. Domestic public or private nonprofit institutions and professional and scientific organizations may apply.

The National Institute of Mental Health will accept applications on the receipt date of January 10, 1991. Applications received after this date will be returned without review. It is estimated that approximately \$750,000 is available in fiscal year 1992 for three MFPs for Doctoral and Postdoctoral Training in the Neurosciences.

Applicants are encouraged to contact Institute staff before applying for an award:

Stanley F. Schneider, Ph.D.  
Associate Director for Research Training and Career Development  
Division of Basic Brain and Behavior Sciences  
National Institute of Mental Health  
5600 Fishers Lane  
Rockville, MD 20852  
Telephone: (301) 443-4347

MOLECULARLY TARGETED APPROACHES TO ANTIVIRAL THERAPY DEVELOPMENT

RFA AVAILABLE: AI-91-01

P.T. 34; K.W. 0740012, 1002008, 1002045

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: November 28, 1990  
Application Receipt Date: January 17, 1991

The National Institute of Allergy and Infectious Diseases (NIAID) invites grant applications for research that applies an understanding of the molecular biology of virus replication and pathogenesis to the development of antiviral agents that are targeted to inhibit specific viral functions. Therapeutic and prophylactic agents (other than vaccines) that specifically inhibit virus replicative functions without interfering with normal cellular processes are likely to provide significant clinical benefits with minimal toxicity. Research on any virus that is a human pathogen or that serves as a model for a human pathogen, except for human immunodeficiency virus (HIV) and/or other retroviruses, is an appropriate subject for a proposal. Research on HIV antiviral agents is the subject of a separate initiative.

## RESEARCH GOALS AND SCOPE

The purpose of this Request for Applications (RFA) is to stimulate research in the development of novel molecularly targeted approaches to antiviral therapy. This includes strategies for both the design of novel specific agents and development of methods for selective drug delivery. The strategies proposed should involve a molecular rationale for anticipated antiviral activity without significant concomitant cellular and/or organism toxicity. The preparation and testing of derivatives of previously identified nucleoside analogue antiviral agents does not constitute a novel approach. Investigators will choose the virus and system they prefer for these studies, but the selected virus should either be a clinically important human pathogen or serve as a model for a human viral pathogen. Possible choices include, but are not limited to: hepatitis B, C, and D virus, papillomavirus, cytomegalovirus, herpes simplex virus, varicella zoster virus, influenza viruses, respiratory syncytial virus, parainfluenza, rotavirus, coxsackievirus, and rhinovirus. The development of agents inhibitory to HIV and other retroviruses is the focus of a separate RFA and, therefore, proposals to target HIV will not be accepted in response to this initiative.

## MECHANISM OF SUPPORT

Award(s) will be made as Cooperative Agreements. These are assistance relationships with substantial involvement of NIAID staff. Universities, medical colleges, hospitals, and laboratories or other public, private, or for-profit institutions are eligible.

This RFA is a one-time solicitation. NIAID anticipates making ten to fifteen awards as a result of this RFA. However these anticipated awards are dependent upon receipt of a sufficient number of applications of high scientific merit and upon the availability of funds. The earliest possible award date is June 1, 1991. It is the intent of NIAID to fund a group of proposals that will ensure that a variety of approaches and virus systems will be investigated.

## INQUIRIES

Investigators seeking information relevant to this RFA should contact Dr. Catherine Laughlin at the address below. Requests for copies of the complete RFA and questions regarding review procedures should be addressed to Dr. Preble at the address below.

Dr. Olivia Preble  
Chief, Microbiology and Immunology Review Section  
Program and Project Review Branch  
National Institute of Allergy and Infectious Diseases  
National Institutes of Health  
Westwood Building, Room 3A10  
Bethesda, MD 20892  
Telephone: (301) 496-8208

Dr. Catherine Laughlin  
Chief, Antiviral Research Branch  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
Westwood Building, Room 753  
Bethesda, MD 20892  
Telephone: (301) 496-8285

## CARDIOVASCULAR DEVICE-CENTERED INFECTIONS

RFA AVAILABLE: HL-90-09-H

P.T. 34; K.W. 0715040, 0740035, 0715125

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: December 3, 1990  
Application Receipt Date: January 14, 1991

The Devices and Technology Branch of the Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI), NIH, and the Section of Bioengineering and Environmental Systems, National Science Foundation (NSF), announce the availability of a Request for Applications (RFA) on the above subject. Applications are invited for support of interdisciplinary research on the mechanisms, prevention, and treatment of infections developing in and around permanently implanted cardiovascular

devices such as total artificial hearts, ventricular assist devices, and prosthetic heart valves.

Molecular approaches to the life sciences and medical sciences and new engineering techniques are encouraged. These may deal with the nature of the molecular interaction between bacterial surface components, the biomaterial surface, and molecules mediating bacterial adhesion, growth, and colonization on biomaterials. Other approaches based on recent advances in molecular and computational biology are encouraged. Research utilizing NSF support must have a substantive bioengineering component. The engineering contribution may include mathematical modeling, instrumentation, tissue engineering, or any other engineering approach that may relate to cardiovascular device-centered infections. Research projects involving human subjects, animal models, or other experimental approaches may be focused on: (1) the etiology, pathogenesis, and natural history of device-centered infections, including the relationship to thromboembolism; (2) elucidation of possible predisposing factors for their development; and/or (3) potential approaches to improved prevention and treatment of such infections.

In any studies involving human subjects, women and minority individuals should be included in the study population; otherwise a clear rationale for their exclusion must be provided in the application. Minority institutions are encouraged to apply, and other institutions are encouraged to establish collaborative arrangements with minority institutions.

It is anticipated that up to five awards will be made under this program. The specific number to be funded will, however, depend on the merit and scope of the applications received and on the availability of funds. A letter of intent is requested by December 3, 1990, and the deadline for receipt of applications is January 14, 1991. The earliest award date for successful applicants will be in July 1, 1991. Awards will be made to foreign institutions only for research of very unusual merit, need, and promise. Potential applicants should contact either of the individuals designated below for the full RFA document, which includes instructions for the submission of applications:

Paul Didisheim, M.D.  
National Heart, Lung, and  
Blood Institute  
Federal Building, Room 312  
7550 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-1586

Norman Caplan  
National Science Foundation  
1800 G Street  
Washington, D.C. 20550  
Telephone: (202) 357-7955

#### CLINICAL TRIAL PLANNING GRANT FOR DIGESTIVE AND NUTRITIONAL DISEASES

RFA AVAILABLE: DK-91-02

P.T. 34; K.W. 0755015, 0715085, 0715135, 0710095

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: January 22, 1991

#### PURPOSE

The Division of Digestive Diseases and Nutrition of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) invites applications for Planning Grants (R21) to support the development of single center or multicenter clinical trials in digestive and nutritional diseases. Areas of particular importance include obesity, inflammatory bowel disease, irritable bowel syndrome, helicobacter pylori, primary biliary cirrhosis, and sclerosing cholangitis. It is anticipated that three planning grant awards will be made.

#### BACKGROUND

Recent advances in basic biomedical research have provided new insights into the pathogenesis of many nutritional and digestive diseases. These advances have led to new possibilities for therapeutic interventions in these diseases. New therapies or interventions are best evaluated in prospective, randomized controlled clinical trials. However, the planning, design, conduct, and analysis of clinical trials are difficult. Each step in the process requires major commitment of effort and time, financial support, and multidisciplinary expertise. As a consequence, opportunities can be lost to identify and rigorously evaluate important new therapeutic possibilities.

In the area of digestive diseases and nutrition there are several diseases or conditions that warrant studies of new therapeutic interventions. Digestive and nutritional diseases or conditions of importance for which there are currently no satisfactory long-term therapies include severe obesity, inflammatory bowel disease, irritable bowel syndrome, primary biliary cirrhosis, and sclerosing cholangitis. These are important conditions that affect many Americans and cause considerable morbidity and mortality. Primary biliary cirrhosis, for example, is an autoimmune disease of the liver that largely affects women and leads slowly but inexorably to cirrhosis and death from liver failure. Primary biliary cirrhosis is the leading single indication for liver transplantation in adults. Despite these features, there is currently no therapy of proven benefit for primary biliary cirrhosis. In recent years, several small clinical trials in primary biliary cirrhosis have reported some benefit of several agents including ursodeoxycholic acid, chlorambucil, cyclosporine A, methotrexate, prednisone, and colchicine. While results from several of these studies have been promising, they have not been convincing enough to provide firm guidance for therapy of patients with this important disease. It is obvious, however, that one or several of these agents could be adequately evaluated in a proper, large, multicenter randomized controlled trial.

Clinical Trial Planning Grants have been designed to aid investigators in designing clinical trials in important areas of digestive and nutritional diseases. These Planning Grants will support the development of a clinical trial research plan. This grant also provides a means for early peer review of the rationale and need for the trial.

#### OBJECTIVES AND SCOPE

The overall goal of this Request for Applications (RFA) is to encourage experienced clinical investigators in digestive diseases to undertake prospective, randomized, controlled, single-center or multicenter trials in the treatment of digestive and nutritional diseases.

The NIDDK Clinical Trial Planning Grant has been designed to help support the extensive planning that should precede any well-designed single-center or multicenter trial. The grant provides a mechanism for early peer review of the rationale and need for the trial as well as support for the development of a detailed Manual of Procedures. In addition, a limited number of patients can be recruited to test the operational aspects of the trial.

It is expected that this Planning Grant RFA will be followed by a program announcement within twelve months from the funding of grants in response to this initial RFA, for applications to perform single-center or multicenter clinical trials. Applications in response to this latter announcement will be required to provide detailed information regarding the rationale, experimental design, protocols and procedures, analytical techniques, facilities and environment, adequacy of the proposed administrative procedures, and collaborative arrangements for the trial. A well documented Manual of Procedures will also need to be part of the latter submission. The actual funding of a single or multicenter clinical trial will be contingent in part on the excellence and feasibility of the proposed trial, programmatic needs, and on the availability of designated funds.

#### ELIGIBILITY REQUIREMENTS

All applicants must be qualified nutritionists, gastroenterologists, hepatologists, or surgeons with the demonstrated ability to recruit adequate numbers of patients. Applicants for a Planning Grant for a multicenter clinical trial must have demonstrated expertise in the many complex features of conducting a multicenter study. All applicants are responsible for obtaining and maintaining the appropriate Investigational New Drug Application from the Food and Drug Administration and the appropriate assurance and certification from their Institutional Review Boards for Human Subjects. Only costs that are not usual costs for the normal care of patients entered in the trial may be requested as research costs to the grant application.

Some of the factors upon which review of single center or multicenter Planning Grant applications will be evaluated are the following: rationale for the proposed clinical trial; experimental design including identification of appropriate primary and secondary outcomes of the trial; preliminary experimental procedures and plans for patient participation; preliminary plans for quality control and data analysis; and patient recruitment potential. Planned preliminary studies and the professional credentials of the organizers and participating centers should be included. Estimates of patient numbers have to be based on the best estimates of the expected differences in measured end points between control and treatment groups.

The NIH places special emphasis on the need for inclusion of minorities and women in studies of diseases which disproportionately affect them and also requires that applicants give added attention, where feasible and appropriate, to their inclusion in other clinical studies. For proposed population-based studies that include neither women nor minorities, a clear rationale for not including them must be provided. In attempting to include either group in a particular study, attention must be paid to such issues as research design and sample size.

#### TERMS OF THE AWARD

Applications for single or multicenter clinical trial Planning Grants should request up to 1 year duration and a maximum of \$50,000 in direct cost. Examples of the allowed uses of these funds include: paying travel expenses of clinicians, biostatisticians, epidemiologists, and other essential personnel who assist in the preparation of the Manual of Procedures; supporting preliminary studies to refine trial procedures and document recruitment potential; paying for secretarial assistance and office supplies; and providing consultant fees for biostatisticians, but not generally for other scientific personnel. Three Planning Grants may be awarded. Funding decisions will be based in part on relative merit recommendation of the Initial Review Group (IRG) and in part on programmatic needs as determined by the National Diabetes and Digestive and Kidney Diseases Advisory Council and by the staff of the Division of Digestive Diseases and Nutrition. The award of applications submitted in response to this RFA is contingent on the actual availability of funds and receipt of applications deemed worthy of support by the accepted NIH peer review process.

#### REVIEW PROCEDURES

All applications submitted in response to this RFA will be evaluated for scientific and technical merit by an IRG convened for this purpose by the Division of Extramural Activities, NIDDK. There will be a single receipt date of January 22, 1991. Applications received after that date will be returned. Earliest funding will be December 1991.

#### METHOD OF APPLYING

Potential applicants should write or phone the individual listed below for the full RFA document.

Tommie S. Tralka  
Director, Clinical Trials Program  
Division of Digestive Diseases and Nutrition  
Westwood Bldg., Rm 3A-15  
5333 Westbard Ave.  
Bethesda, MD 20892  
Telephone: (301) 496-9717

#### ONGOING PROGRAM ANNOUNCEMENTS

##### MINORITY HIGH SCHOOL STUDENT RESEARCH APPRENTICE PROGRAM

PA: PA-90-35

P.T. 44, FF; K.W. 0710030

National Center for Research Resources

Application Receipt Date: November 30, 1990

This is a re-issuance of the announcement published in the NIH Guide for Grants and Contracts dated September 18, 1990, Vol. 19, No. 35.

##### BACKGROUND AND OBJECTIVES

The National Center for Research Resources (NCRR), National Institutes of Health (NIH), currently plans to continue and expand the Minority High School Student Research Apprentice Program in 1991. The purpose of the program is to provide minority high school students with a meaningful experience in various aspects of health-related research in order to stimulate their interest in careers in science.

In FY 1991, in addition to encouraging institutions to apply for an increased number of apprentices, the program is including a high school science teacher initiative. This new program extension will allow teachers who are members of

a minority group, or who teach a significant number of minority students, to participate in a summer research project in order to update their knowledge and skills in modern research tools and techniques. Such a hands-on research experience should strengthen teaching skills and provide teachers the opportunity to bring back to the classroom a sense of the excitement of research, which should stimulate students to pursue scientific careers. A longer range goal is to establish year round links between science teachers, secondary school students, and biomedical researchers.

Please note, however, that expansion of the program in FY 1991 is contingent on the availability of appropriated funds. Thus, allocations may be reduced below the requested amount. Upon recommendation of the National Advisory Research Resources Council, the Center will give preference in making awards to those institutions that can support a summer program having a "critical mass" of at least five or six students.

#### ELIGIBILITY

Eligible institutions are those that were awarded grants during the latest complete Federal fiscal year 1990 from either the Biomedical Research Support Grant (BRSR) Program or the Minority Biomedical Research Support (MBRS) Program. ALL ELIGIBLE INSTITUTIONS, INCLUDING THOSE NOT CURRENTLY FUNDED, ARE STRONGLY ENCOURAGED TO APPLY. Only one application for the Apprentice Program may be submitted by a component of an institution that is the recipient of both the BRSR and MBRS awards.

Students eligible for support under this program are those who (1) identify themselves as minority (i.e., Black, Hispanic, American Indian, Alaskan Native, Pacific Islander, or Asian); (2) are U.S. citizens or have a permanent visa; and (3) are enrolled in high school during the 1990-91 academic year. (Students who will graduate from high school in 1991 are eligible, as is a student who participated in a previous year provided he/she is still enrolled at the high school level.)

#### MECHANISM OF SUPPORT

The mechanism of support for this program will be the NIH grant-in-aid (S03). Awards will be for one year. Awards will be effective March 1, 1991, contingent upon availability of appropriated funds. Support will be provided at a level of \$2,000 for each student apprentice and \$5,000 for each high school science teacher. Funds for ONE high school science teacher may be requested for EACH FIVE students requested and multiples thereof. No indirect costs will be paid. Direct support must be as salary; stipends are not allowed. Funds allocated may also be utilized for supplies, extending the research experience, or if adequate funds exist, for the addition of a student apprentice. However, funds from these grants may only be used for the costs of the apprentice program. The Program Director is responsible for the recruitment and selection of the apprentices, as well as the high school science teachers, and assignment of each to an appropriate investigator.

#### Students:

Recruitment and selection of students should emphasize factors including the students' motivation, ability, scholastic aptitude, and accomplishments. In addition, consideration should be given to science teachers' recommendations and, where possible, the degree of parental commitment. Assignments should be made to investigators involved in health-related research who are committed to increasing the high school student's understanding of research and the technical skills needed.

#### Teachers:

Recruitment and selection criteria should include: experience and teaching responsibilities, level of interest in participating in a research program, expected impact on their teaching programs, ability to stimulate minority students to pursue scientific careers, and future plans for continued interaction with the research institution.

#### METHOD OF APPLYING

Eligible institutions should submit an application consisting of no more than (a) a letter stating the justification for the number of student and teacher positions requested (preference will be given to those institutions with a demonstrated commitment and a documented history of encouraging students to pursue scientific careers); together with (b) the original and one signed and completed copy of the Grant Application Form, PHS 398 (Rev. 10/88) face page, page 4 "Detailed Budget for First 12-Month Budget Period Direct Costs Only," and checklist page only. The required pages of the PHS 398 application form

should be completed according to instructions provided in the PHS 398 (Rev. 10/88) kit except for the following:

Face Page:

Item 1 - Leave blank.

Item 2 - Check the box marked "YES" and indicate the announcement title as "Minority High School Student Research Apprentice Program, PA-90-35."

Items 4, 5, 7b, 8, and 10 - Not applicable; do not complete.

Item 6, Dates of entire proposed project period - Enter 91-03-31 through 92-02-29.

Item 7a - Insert the total dollar amount of the request, which is the sum, from application page 4, of the number of student positions requested times \$2,000 per student and \$5,000 per teacher.

Item 14, Organizational component to receive credit towards a Biomedical Research Support Grant - Use this space to enter the code and the BRSG component and/or MBRS grant numbers on which eligibility for this Minority High School Student Research Apprentice Program application are based (no credit will be given for the S03 application).

Page 4, "Detailed Budget for First 12-Month Budget Period Direct Costs Only" - Using ONLY the Other Expenses category, enter on separate lines the number of students requested at \$2,000 per student and the number of high school science teachers requested at \$5,000 per teacher. Not more than one teacher position may be requested for each five student positions requested. Enter the sum of the amounts requested for each under the "TOTALS" column for the Other Expenses category and under "Total Direct Costs for First 12-Month Budget Period" at the bottom of the page.

The original and one copy of the signed Program Director's report and each student and teacher report should be submitted with the renewal application by November 30 in order that the data contained in these reports can be used by NCRR to decide about policies and future funding for the Minority High School Student Research Apprentice Program. These reports should also be submitted at the same time even if renewal support is not requested.

In any event, all reports including the Financial Status Report must be submitted to the NIH by the grantee institution no later than May 31, 1991, unless an extension of the budget period end date has been authorized in writing.

Mail the completed application by the November 30, 1990, firm deadline for receipt of applications to:

Office of Grants and Contracts Management  
National Center for Research Resources  
National Institutes of Health  
Westwood Building, Room 849  
5333 Westbard Avenue  
Bethesda, MD 20892\*\*

Inquiries can be made of Dr. Marjorie A. Tingle at the above address or by calling (301) 496-6743.

This program is described in the Catalog of Federal Domestic Assistance, No. 13.337, Biomedical Research Support. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (a)(3); Public Law 78-410 (42 USC 241) as amended, and administered under PHS grant policies and Federal Regulations 45 CFR 74 and the Guidelines for Minority High School Student Research Apprentice Program. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:

5333 Westbard Avenue  
Bethesda, Maryland 20816