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The NIH Guide announces scientific
initiatives and provides policy and
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.

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NOTICES

WORLD AIDS FOUNDATION

P.T. 34; K.W. 0715008, 0745027, 0720005

The World AIDS Foundation (WAF) announces its intent to support research and education relating to AIDS in the developing world. The goal of the WAF is to facilitate information exchange and to assist developing countries to respond to the AIDS pandemic.

The Foundation is particularly interested in projects which are catalytic, and once in place could have a multiplicative effect. The WAF is specifically interested in supporting:

A) short-term, in-country training for clinicians, allied health professionals and technicians;

B) fellowships to support training for national experts;

C) development and testing of new concepts and demonstrations for preventing the spread of HIV; and

D) highly focused workshops which enhance the scientific process and transfer knowledge needed in the effort against HIV infections and AIDS.

The limit of any single funding request to WAF is \$200,000.

Application Procedures

Concept letters and applications may be prepared in English or French. Applicants should submit concept letters for initial consideration. Following review of concept proposals, applicants may be invited to submit complete proposals.

For further information please contact:

World AIDS Foundation
c/o Assistant Secretary for Health
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
U.S.A.

or

World AIDS Foundation
c/o Director
Institut Pasteur
28 Rue du Docteur Roux
75724 Paris, Cedex 15
FRANCE

NOTICES OF AVAILABILITY (RFPs AND RFAs)

ANALGESIC AND BIOCHEMICAL RESPONSES TO PERIPHERAL OPIATES IN DENTAL PAIN PATIENTS

RFP AVAILABLE: NIH-NIDR-2-90-5R

P.T. 34; K.W. 0755015, 0715148, 0715150, 0740025

National Institute of Dental Research

This acquisition is for a proposed double-blind, randomized, placebo-controlled, single center clinical trial using dental pain patients to evaluate the following hypotheses: (1) Does local administration of opioids produce a peripherally-mediated analgesia? (2) Is this analgesia due to selective activation of opiate receptors? (3) Is this analgesia associated with decreased levels of inflammatory mediators? These hypotheses will be evaluated in patients experiencing dental pain (due to acute periradicular periodontitis) requiring periodontal ligament injections with collection of pain reports and tissue perfusates for measurement of chemicals related to pain and inflammation. It is anticipated that one award will be made, covering a two-year period of performance.

RFP No. NIH-NIDR-2-90-5R will be available on or about April 20, 1990, with proposals due on or about June 1, 1990.

The RFP will be available upon written request to:

Marion L. Blevins
Contract Management Section
National Institute of Dental Research
National Institutes of Health
Westwood Building, Room 521
5333 Westbard Avenue
Bethesda, MD 20892

POSTMORTEM STUDIES OF PAINFUL PERIPHERAL NEUROPATHY: ABNORMALITIES OF NEUROPEPTIDE SYNTHESIS AND RECEPTOR REGULATION

RFP AVAILABLE: NIH-NIDR-2-90-8R

P.T. 34; K.W. 0715140, 0715150, 0765010, 0760075, 0780020

National Institute of Dental Research

This proposed acquisition is for a two-year study to determine whether painful peripheral neuropathies in humans are associated with abnormalities of spinal cord neuropeptide synthesis and neuropeptide receptor regulation. Such abnormalities have been detected in rats with an experimental version of painful peripheral neuropathy; the question addressed in this project is whether or not similar abnormalities occur in humans.

The contractor will be required to attend autopsies of tissue donors with a pre-morbid history of reflex sympathetic dystrophy or causalgia, obtain properly identified segments of the spinal cord (in some cases brainstem), and properly prepare the tissue samples for subsequent histology. The project officer will be responsible for recruiting tissue donors. The contractor must be available to travel to the autopsy sites within 1-3 hours notice from the project officer. It is anticipated that one award will be made. RFP No. NIH-NIDR-2-90-8R will be available on or about April 20, 1990, with proposals due on or about June 4, 1990.

The RFP will be available upon written request to:

Marion L. Blevins
Contract Management Section
National Institute of Dental Research
National Institutes of Health
Westwood Building, Room 521
5333 Westbard Avenue
Bethesda, MD 20892

OPERATION OF A FACILITY FOR THE STUDY OF INFECTIOUS AGENTS VACCINES AND ANTIMICROBIALS IN ADULT AND PEDIATRIC HUMAN SUBJECTS

RFP AVAILABLE: NIH-NIAID-DIR-91-01

P.T. 34; K.W. 0715125, 1002045, 0740075, 0785035, 0403017

National Institute of Allergy and Infectious Diseases

The Laboratory of Infectious Diseases (LID), National Institute of Allergy and Infectious Diseases (NIAID), studies infections in humans and evaluates the effectiveness of various vaccines and antimicrobials in the prevention and treatment of these diseases. The purpose of the proposed contract is to provide a facility and volunteers to study the biology of important viruses in humans, to examine the immune response of the host to these viruses, and to test new candidate vaccines for safety, genetic stability, immunogenicity, transmissibility and protective efficacy. Studies will include administration of wild type viruses to volunteers in order to assess their virulence. Subsequently, these viruses will be used to challenge vaccinated volunteers in order to assess the extent of immunity induced by candidate vaccines. Studies with vaccines will include an evaluation of their safety, immunogenicity, transmissibility, and protective efficacy. The major infectious agents of interest to the LID include influenza A and B viruses, paramyxoviruses, rotaviruses, and other gastrointestinal viruses such as the Norwalk group of agents. This contract will meet the Institute needs for a nearby facility in which clinical and epidemiological studies on infectious agents, vaccines, other biological products, and pharmaceuticals shall be

evaluated in healthy (adult and pediatric) volunteers in collaboration with NIAID staff members. Since there will be active collaboration on a day-to-day basis between the investigators at the testing facility and NIAID scientist, the proposed contract will require that the facility be located within one (1) hour of the National Institutes of Health, Bethesda, Maryland, campus.

The Institute expects to make one award from this solicitation.

The Request for Proposals (RFP) will be available on or about April 3, 1990. Any responsible offeror may submit a proposal which shall be due by the close of business on June 4, 1990.

Requests for this RFP should be directed to:

Ms. Rosemary McCabe Hamill
Contracting Officer
Contract Management Branch
National Institute of Allergy and Infectious Diseases
Westwood Building, Room 707
5333 Westbard Avenue
Bethesda, MD 20892

Please provide this office with two self addressed labels.

CENTRALIZED PATHOLOGY UNIT FOR SICKLE CELL DISEASE

RFP AVAILABLE: RFP-NHLBI-HB-90-03

P.T. 34; K.W. 0715032, 0785165, 0755018

National Institute of Heart, Lung, and Blood

The National Heart, Lung, and Blood Institute (NHLBI) is seeking a contractor to establish a centralized laboratory to characterize and catalogue autopsy and surgical specimens and correlate pathological findings with clinical data to determine more precisely the causes of death in patients with sickle cell disease. This unit shall be a major determinant to our ability to accurately assess causes related to mortality in sickle cell disease.

RFP-NHLBI-HB-90-03 was issued on March 20, 1990, with proposals due on May 9, 1990. One (1) award is anticipated by the Government and the contract period is sixty 60 months.

To expedite requests for this solicitation, please furnish three (3) self-addressed labels with your mailing address and cite RFP-NHLBI-HB-90-03.

Requests for copies of the RFP should be sent to:

Jack E. Jackson
Contracting Officer
DBDR Contracts Section, Contracts Operations Branch
National Heart, Lung, and Blood Institute
Federal Building, Room 5C14
Bethesda, MD 20892

STUDY OF CAUSES AND COURSE OF DISABILITY IN OLDER WOMEN

RFP AVAILABLE: RFP-NIH-AG-90-08

P.T. 34, II; K.W. 0710010, 0715000, 0755030

National Institute on Aging

The Epidemiology, Demography and Biometry (EDB) Program of the National Institute on Aging (NIA) proposes to support, through a research and development contract, an epidemiologic study on the causes and course of physical disability in older women. The overall goal of this study is to screen a population of non-institutionalized women age 65 and older, to select those with moderate to severe physical disability, to comprehensively evaluate these women to gain an understanding of the diseases and conditions responsible for their disabilities, and then to follow them prospectively over a period of 3 years with twice yearly assessments. Goals for data collection shall be derived from a priori hypotheses.

For the purpose of this solicitation, disability is defined as a deviation or alteration in normal functional performance. Physical disability specifically

relates to dependence in some aspect of physical functioning. The focus of this study is on physical functioning, but other domains of functioning, such as cognitive, psychological, and social functioning, will also be assessed. These other domains of functioning will be approached as important modifiers of physical functioning and disability. In analyses, these domains of functioning will be considered as independent variables which have a potential impact on physical functioning in much the same way that underlying chronic diseases, demographics, health behaviors, and other independent variables may have such an impact. The overall approach incorporates a general goal of understanding factors involved in the loss of autonomy and the development of dependence on The Institute expects to make one award from this solicitation.

others to perform a variety of tasks which older persons want to do and usually can do given good health and vitality.

The issuance of the Request for Proposals (RFP) will be on or about April 12, 1990, and proposals will be due by the close of business on June 14, 1990.

Any responsible offeror may submit a proposal and will be considered by the Government.

Request for the RFP should be directed to:

Ms. Bonnie Keane
Contracting Officer
Research Contracts Branch
National Institutes of Health
Building 31, Room 1B44
Bethesda, MD 20892

Please provide this office with two self-addressed mailing labels.

CLINICAL UNITS FOR ASYMPTOMATIC CARDIAC ISCHEMIA PILOT STUDY

RFP AVAILABLE: RFP NIH-NHLBI-HV-90-08

P.T. 34; K.W. 0715040, 0745070, 0785210, 0755015

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute will do a study to determine the efficacy and safety of the three different treatment strategies in reducing cardiac ischemia in patients with coronary artery disease (CAD). Patients will be randomly assigned to usual symptom-guided medical care; stepped maximal, ambulatory ECG-directed, medical therapy; or mechanical revascularization (angioplasty and/or surgery). The principal endpoint for these comparisons is a reduction of ambulatory ECG-documented ischemia. To accomplish this objective this program proposes to recruit 10-12 Clinical Units with access to sufficient numbers of patients with documented CAD and positive exercise stress test. Outcomes of assigned treatment such as non-fatal MI, type and frequency of revascularization, hospitalization for unstable angina, change in both myocardial perfusion and left ventricular function assessed by radionuclide scintigraphy, and mortality will be monitored for all patients in all treatment groups. It will be necessary to enroll 600 patients or approximately 60 patients per Clinical Unit. The expectation of this study is determination of the safety and efficacy of treatment of cardiac ischemia in patients with documented CAD. Methodology to be considered includes contrast coronary angiography and radionuclide scintigraphy (both myocardial perfusion and left ventricular function). Definition of specific data to be collected, methods of collection, and management of the data are necessary, as well as proposed criteria to evaluate and interpret the results in close collaboration with the Clinical Coordinating Center. This incrementally funded contract will be awarded for 36 months.

This is not a Request for Proposals. RFP NHLBI-HV-90-08 was released on March 10, 1990, with proposals due on or about April 30, 1990. Ten (10) to twelve (12) awards are anticipated by the Government. Your written request should include three (3) labels, self-addressed with your mailing address, and must cite RFP No. NHLBI-HV-90-08.

Request for copies of the RFP should be sent to the following address:

Sharon M. Kraft, Contract Specialist
HLVD Contracts Section, Contracts Operations Branch, DEA
National Heart, Lung, and Blood Institute
Federal Building, Room 4C04
National Institutes of Health
Bethesda, MD 20892
Telephone: (301) 496-6838

Note: This announcement is published for information purposes. It appeared in the Commerce Business Daily on March 8, but did not make the NIH Guide for prompt publication. NHLBI was unable to extend the date that responses are due.

STEM CELLS FOR ENGRAFTMENT: BLOOD CELLS FOR TRANSFUSION

RFA AVAILABLE: HL-90-06-B

P.T. 34; K.W. 0750010, 0780015, 0710070, 1002008, 0760020

National Heart, Lung, and Blood Institute

Application Receipt Date: August 1, 1990

The Blood Diseases and Blood Resources Branches of the Division of Blood Diseases and Resources (DBDR), National Heart, Lung, and Blood Institute (NHLBI), announce the availability of a Request for Applications (RFA) on the above subject. Copies of the RFA are currently available from staff of the NHLBI. Awards will be made to foreign institutions only for research of very unusual merit, need, and promise.

This special program will support research on the development and utilization of in vitro culture systems for stem cells. This research will help to gain basic insights into the control of hematopoiesis and stem cell engraftment and to produce stem cells and other specific cell populations that might be useful in transplantation and transfusion therapies.

The support mechanism for this FIVE-year program will be the traditional individual research grant (R01). Although approximately \$1,500,000 (for direct plus indirect costs) for this program is included in the financial plans for fiscal year 1991, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. The specific number of awards to be funded depends on the merit and scope of the applications received and the availability of funds.

Requests for copies of the RFA may be addressed to:

Alan S. Levine, Ph.D.
Chief, Blood Diseases Branch, DBDR
National Heart, Lung, and Blood Institute
Federal Building, Room 5A12
Bethesda, MD 20892
Telephone: (301) 496-5911
FAX: (301) 496-9940

or

Milton J. Hernandez, Ph.D.
Health Scientist Administrator
Blood Resources Branch, DBDR
National Heart, Lung, and Blood Institute
Federal Building, Room 504
Bethesda, MD 20892
Telephone: (301) 496-1537
FAX: (301) 496-9940

RESEARCH ON THE MOLECULAR BASIS OF CYSTIC FIBROSIS

RFA AVAILABLE: DK-90-09

P.T. 34; K.W. 0765035, 0755030, 0790005, 1013004, 0755020

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: June 15, 1990
Application Receipt Date: August 1, 1990

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Cystic Fibrosis Foundation (CFF) invite investigator-initiated research grant applications to define and characterize the molecular pathophysiology of cystic fibrosis (CF) and the membrane transport processes associated with the etiology and pathogenesis of CF.

Applications submitted to the NIH will be reviewed according to normal NIH peer review procedures. Applications judged meritorious but not funded by the NIH may be submitted by the applicant, along with the NIH-prepared summary statement, to the CFF for possible funding by the Foundation.

OBJECTIVES

It is the intention of the NIDDK and the CFF to stimulate research on the CF defect(s) by support of meritorious applications proposing:

- o To study processes involved in the expression and/or over-expression of the normal or mutant products of the CF gene.
- o To study the role of the CFTR protein, or other relevant membrane proteins, in biochemical and physiological events related to defective ion transport in CF.
- o To elucidate the mechanisms by which aberrant control of ion transport pathways in epithelial cells leads to the pathophysiology of CF.
- o To develop appropriate model systems for studying the regulation of defective cellular processes in CF.
- o To study epithelial cell membrane associated proteins other than CFTR, such as components of transport systems or signal transduction systems, with relevance to understanding the mechanism of the defective ion transport in CF.
- o To apply novel biophysical approaches to structural studies of membrane transport systems, or their components, or their crystals as they pertain to understanding the defective ion transport in CF.
- o To identify and characterize potential therapeutic agents capable of modulating the transport defect in CF.
- o To develop and characterize techniques of gene transfer into cells specifically useful in studying and/or ultimately in correcting the transport defect in CF.

MECHANISM OF SUPPORT

The National Institutes of Health (NIH) will provide support for this program through the regular research project grant (R01). Those grants funded by the CFF will follow CFF guidelines. The CFF support will be limited to three years duration with a maximum of eight percent indirect costs.

Applications submitted to the NIH in response to this Request for Applications (RFA) that are judged scientifically meritorious but not funded by the NIDDK may be submitted by the applicant to the CFF for consideration for funding.

The NIDDK and the CFF each plan to support approximately five to seven applications submitted in response to this solicitation; however, the specific number to be funded will depend upon the overall merit, the scope of the applications received, and availability of funds.

REVIEW PROCEDURES AND CRITERIA

Upon receipt, applications will be reviewed (initially) by the Division of Research Grants (DRG) for completeness. Applications also will be reviewed by NIDDK staff for their responsiveness to the objectives of this RFA. If an application submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted.

The National Heart, Lung, and Blood Institute also has an interest in supporting areas of research covered by this RFA. Should a question of program overlap arise for a given application, the DRG Referral Guidelines will prevail in the institute assignment of the applications.

Applications in response to this RFA will be reviewed on a nationwide basis and in accord with the usual NIH peer review procedures. Review criteria

include the extent of relevance and/or contribution of the proposed research to the overall goals and objectives of the RFA.

METHODS OF APPLYING

Letter of Intent

Prospective applicants are encouraged to submit an optional one-page letter of intent, which includes the title of the proposed project and identification of all participating institutions. This letter should be received no later than June 15, 1990, and should be sent to the program representative listed under Inquiries.

Format for Applications:

Applications should be submitted on Form PHS 398 (rev. 10/88), which is available from an applicant institution's Office of Sponsored Research or from the NIH Division of Research Grants. To identify the application as a response to this RFA, check "yes" on item two of page one of the application and enter the title "The Molecular Basis of Cystic Fibrosis" and the RFA Number DK-90-09.

Application Procedure:

The original and four copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

Two additional copies of the application must be sent under separate cover to:

Review Branch
National Institute of Diabetes and Digestive and Kidney Diseases, NIH
Westwood Building, Room 406
Bethesda, MD 20892

Inquiries:

For further information, investigators are encouraged to contact:

Nancy Lamontagne, Ph.D.
Director, Cystic Fibrosis Program
Division of Diabetes, Endocrinology, and Metabolic Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 607
Bethesda, MD 20892
Telephone: (301) 496-4980

This program is described in the Catalog of Federal Domestic Assistance No. 13.847, Diabetes, Endocrinology, and Metabolic Diseases. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations most specifically at 42 CFR Part 52 and CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

SEXUALLY TRANSMITTED DISEASES COOPERATIVE RESEARCH CENTERS

RFA AVAILABLE: AI-90-03

P.T. 04; K.W. 0715182, 0710030, 0715125, 0404000, 0785035, 0403004

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: August 1, 1990
Application Receipt Date: October 10, 1990

The Sexually Transmitted Diseases (STD) Branch of the Division of Microbiology and Infectious Diseases (DMID) of the National Institute of Allergy and Infectious Diseases (NIAID) invites grant applications for the establishment of a network of Sexually Transmitted Diseases Cooperative Research Centers (STD CRCs). The CRCs will provide a multi-disciplinary, systematic, sustained approach to sexually transmitted diseases research. The intent of this

approach is to bridge the basic research, and clinical and epidemiologic research arenas; to facilitate intervention-oriented behavioral research for prevention and control of STDs; to foster interaction with both local medical and lay communities; to develop potential sites for future multi-center clinical trials; and to provide opportunities for interaction, dialogue and planning among STD investigators through STD Branch coordination of regularly scheduled workshops.

RESEARCH OBJECTIVES AND SCOPE

The purpose of this RFA is to stimulate exceptionally high quality, multi-disciplinary, collaborative STD research efforts. This will be accomplished by collaborations among the disciplines from the basic research, clinical and epidemiological, and behavioral arenas. Interdisciplinary collaborations should both link disciplines within a single arena (e.g., molecular biology and immunology) and reach across to link disciplines in different arenas (e.g., microbiology and social/clinical psychology). In addition to the importance of utilizing a multi-disciplinary approach, specific programmatic requirements are as follows:

DEFINITION OF RESEARCH SCOPE: Research must focus on a minimum of three STD pathogens or syndromes, each of which should be approached through multi-disciplinary collaborations. STD CRC applications must include at least two projects that link disciplines within a single arena and at least one project that links disciplines in two different arenas. Applications must therefore include a minimum of three research projects. Applicants are strongly encouraged, however, to propose three or more projects linking disciplines within a single arena and two or more projects linking disciplines across two different arenas for a total of at least five projects.

CLINICAL FACILITY: In order to bridge the basic research and clinical arenas, STD CRCs must offer a strong clinical facility with accessible patient populations that are appropriate to answering STD research questions. Adolescents, inner city minority groups, and antenatal, family planning and STD clinic patients are examples of potentially relevant populations. To further integrate clinical and basic biomedical research initiatives, it is also permissible for projects to include post-residency personnel who spend a maximum of one third of their time in clinical activities related to the research focus of the project.

Applications must also include at least one of the following components. It should be emphasized, however, that no single application is expected to include all of these components. Other creative approaches may be proposed in addition to, but not instead of, these components.

INCLUSION OF A STRONG, INNOVATIVE, BEHAVIORAL COMPONENT TO STD CRC RESEARCH PROJECTS: STD CRCs, because of their multi-disciplinary approach, are in a unique position to design and evaluate behavioral interventions by examining microbiologic as well as behavioral outcomes.

OUTREACH ACTIVITIES TO THE LAY AND THE LOCAL MEDICAL COMMUNITIES: Outreach activities 1) may be nonhealth-care facility based, 2) should usually focus on non-patient populations, and 3) must include an evaluation component.

LONG-TERM, ONGOING COLLABORATIONS WITH FOREIGN INSTITUTIONS IN DEVELOPING COUNTRIES: Proposals for development of long-term, ongoing collaborations between STD CRCs and foreign institutions in developing countries will be considered. The collaboration not only must be beneficial to the foreign country, but also must offer the potential for collection of STD data which are pertinent to U.S. populations and which could not be generated as effectively in the United States.

An optional component which may also be helpful in achieving STD CRC research goals is a developmental funds pool:

DEVELOPMENTAL FUNDS FOR NEW INVESTIGATOR OR PILOT PROJECTS: Within budget proposals, applicants may request developmental funds for new investigator projects or pilot projects. It is hoped that this type of support may be used for objectives such as the rapid, "pilot" exploration of new ideas and approaches, the generation of preliminary data for traditional NIH grant applications, or the development of new "programs."

In designing specific projects, applicants are encouraged to consider research proposals which focus on important, yet underserved, areas of STD investigation. Areas and organisms of particular interest include: Sequelae of STDs in women, genital ulcer disease, and human papillomavirus (hpv) infection.

STD VACCINE DEVELOPMENT also continues to be an important priority. Ongoing basic research directed towards vaccine development, particularly for pathogens such as *N. gonorrhoeae*, *T. pallidum*, and herpes simplex virus type 2 (HSV-2) are research areas of interest. In order to make critical advances in this area, functional collaborations between immunologists and microbiologists focused on pathogenesis will be extremely important.

WORKSHOP PARTICIPATION: Successful applicants will be expected to participate in regularly scheduled workshops that will be held at least twice yearly to share STD research advances; to discuss STD research needs and opportunities; and to develop new collaborative protocols which may include multi-center studies.

MULTI-CENTER TRIALS: Because the STD CRCs will form the nucleus of a network of high-quality STD research environments, STD CRC applicants are strongly encouraged to be receptive to future participation in the development of multi-center trials.

Applicants are urged to give added attention where feasible and appropriate to the inclusion of females and of minorities in study populations for STD CRCs. If either females or minorities are not included in a given study, a clear rationale for their exclusion should be provided.

MECHANISM OF SUPPORT

Awards will be made as COOPERATIVE AGREEMENTS. These are interactive assistance relationships in which an ongoing collaborative relationship exists between the NIAID staff and the investigative team. The NIAID anticipates making two to four awards as a result of this RFA. The final number of awards to be made is dependent upon the availability of funds. It is estimated that the initial year's direct and indirect costs will not exceed \$1.2 million for each award. Awards will be made for a project period of up to five years. The earliest possible award date is July 1, 1991.

METHOD OF APPLYING

A copy of the complete RFA should be obtained before beginning the application process. For further information, or to receive a copy of the complete RFA, please contact:

Dr. Judith N. Wasserheit
Chief, Sexually Transmitted Diseases Branch
Division of Microbiology and Infectious Diseases
Westwood Building, Room 749
NIAID, National Institutes of Health
Bethesda, MD 20892
Telephone: (301) 402-0443

Prospective applicants are asked to submit, by August 1, 1990, a short letter of intent that includes a descriptive title and the names and affiliation(s) of proposed key investigators for each of the proposed research projects. Letters of intent should be sent to Dr. Olivia Preble at the following address:

Dr. Olivia Preble
Acting Chief, Microbiology and Immunology Review Section
Program and Project Review Branch
Westwood Building, Room 3A-10
NIAID, National Institutes of Health
Bethesda, MD 20892
Telephone: (301) 496-8208

ONGOING PROGRAM ANNOUNCEMENTS

RESEARCH CAREER AWARDS IN THROMBOSIS

PA: PA-90-01

P.T. 34; K.W. 0715040, 0785035, 0745020, 0745070, 0404000

National Heart, Lung, and Blood Institute

The objective of the Research Career Awards in Thrombosis is to support the professional development of individuals who can serve expanding and evolving research, teaching, and clinical requirements in the area of thrombosis and thromboembolic disorders. This announcement emphasizes the need for increased

research training in this area and encourages individuals to submit applications for support using the three existing research career development awards sponsored by the NHLBI: Physician Scientist Award (PSA) (K11); Clinical Investigator Award (CIA) (K08); and Research Career Development Award (RCDA) (K04).

Applications submitted in response to this announcement will be brought to the attention of the National Heart, Lung, and Blood Advisory Council and or another appropriate Council and will receive consideration for support by the appropriate Institute.

BACKGROUND

Thromboembolic events give rise to serious clinical disease and contribute significantly to the nation's health care burden. Both thrombosis and atherosclerosis are important factors in cardiovascular disease. In 1987, they accounted for almost one million deaths. In addition, 150,000 persons in the United States died of cerebrovascular disease, the third leading cause of death in 1987. The economic burden of cardiovascular diseases in 1984 was an estimated \$110 billion. It is further estimated that six million episodes of venous thrombosis occur annually accounting directly for 10,000 hospital deaths due to pulmonary embolism. In all, the impact of thromboembolism and thromboembolic disorders on mortality and morbidity is impressive.

Substantial progress has been made towards understanding the basic mechanisms operating in thrombosis, the impact of thromboembolic phenomena on organ systems, and the techniques needed to prevent and treat thrombosis. Specific areas of progress include molecular and cellular pathology of thrombosis, biochemistry of coagulation and fibrinolysis, biology of vessel growth, endothelial cell function and vascular reactivity, the blood-vessel interface, and the interaction of cellular components with the vascular endothelium, thus contributing to the development of thrombosis. Therapeutic options are now available for the management of thrombosis and other treatment modalities are under development. Prevention of thrombosis and thromboembolic disorders, development of more effective therapies, and the appropriate choice of treatment demands a thorough understanding of all these facets of the subject.

The major strides which have taken place in basic and clinical understanding of thrombosis suggest that an unprecedented opportunity exists for major improvements in the way patients with these disorders are managed. In addition, the enormous health and economic impact of arterial and venous thrombosis argues strongly for giving this area increased attention. This announcement is prompted by the need to provide increasing numbers of basic and clinical investigators in the area of thrombosis and thromboembolic disorders, so that rapid and effective progress in the area can be made.

Candidates submitting research career development proposals in response to this program announcement should focus on topics such as those listed below:

- o basic research projects that lead to better understanding of mechanisms in thrombosis and thromboembolic disorders;
- o clinical research projects that will improve the detection of high-risk patients and prevent thrombosis;
- o applied research projects that lead to improved diagnosis and therapeutic approaches to thrombosis;
- o effective, safe monitoring techniques for patients undergoing anti-thrombotic therapy; or
- o studies that deal with the logistical, economic, social, and behavioral aspects of thrombosis and thromboembolic disease.

Individual training programs that offer research and career development opportunities in all areas related to thrombosis and thromboembolic disorders are welcomed. If candidates do not possess skills in research design and biostatistics, the applicant should consider including these training areas in the plan. The background training of candidates for these research training programs may have been in hematology, cardiology, surgery, orthopedics, radiology, clinical pharmacology, pathology, or epidemiology.

MECHANISMS OF SUPPORT

The three support mechanisms for these Research Career Awards in Thrombosis are summarized in this announcement and provide for several levels of career development. Detailed guidelines for each of the three support mechanisms can be obtained from your business office, from the Division of Research Grants, NIH, (301) 496-7441, or from Dr. Fann Harding, Division of Blood Diseases and Resources, (301) 496-1817. Only citizens and non-citizen nationals are eligible for support under these programs.

A. PHYSICIAN-SCIENTIST AWARD - PSA (K11)

Provides 3-5 years of support based on previous experience of the applicant. A full two-phase award may be requested by physicians inexperienced in research to undertake 5 years of special study in basic science with a supervised research experience. Newly trained clinicians are encouraged, during Phase I of the award, to develop independent research skills and experience in a fundamental science which can be applied, during Phase II, towards problems in thrombosis and thromboembolic disorders. Investigators having some research experience may elect to apply for Phase II only of the PSA.

- o Award is made to an institution on behalf of a candidate whose primary sponsor is an accomplished basic science investigator who will provide guidance for the entire award period.
- o Selection is by national competition.
- o Training support is for up to 5 years for full-time effort. Phase I entails 2 or 3 years of creative and detailed basic science learning experience; Phase II entails 2 or 3 years of intensive research activity under general guidance of a qualified sponsor.
- o Salary is up to \$40,000 per year plus fringe benefits for 100 percent effort.
- o During Phase I, up to 10 percent of the primary sponsor's salary and commensurate fringe benefits may be requested.
- o Research support may be requested in an amount not to exceed \$10,000 per year and increasing to \$20,000 per year in Phase II.
- o Salary supplementation from non-federal sources is allowable.
- o Indirect costs of 8 percent of total direct costs, exclusive of tuition, fees, and equipment expenditures, or actual rate, whichever is less, may be requested.
- o Awardees must inform the NIH for each of five years following the completion of the award about academic status, publications, and research grants and contracts received.
- o PSA application may not be submitted concurrently with other development awards, such as CIA, RCDA, FIRST Award, or Academic Award; however, the awardee is encouraged to apply for research support during the period of the award.
- o Use application form PHS 398 (Rev. 10/88) with special PSA instructions.

B. CLINICAL INVESTIGATOR AWARD - CIA (K08)

Provides support for a period of career development of 3-5 years for individuals with the M.D. degree or other professional doctorates. The objective is to encourage the development of basic, clinical, and behavioral research skills. Candidates with previous research experience may apply for an abbreviated program of development. Applicants will usually have not less than 3 years of postdoctoral clinical training nor more than seven years of total postdoctoral clinical and research experience by the time an award is made.

- o Award is made to an institution on behalf of a candidate who has an appropriate sponsor willing to assume responsibility and provide guidance for candidate's research program.
- o Selection is by national competition.
- o Salary is up to \$40,000 per year plus fringe benefits.
- o Research support is provided in an amount not to exceed \$10,000 per year.
- o Training period is for 3-5 years for full-time effort.
- o Salary supplementation from non-federal funds is allowable.
- o Indirect costs of 8 percent of total direct costs or actual rate, whichever is less, may be requested.

- o Awardees must inform the NIH for each of five years following the completion of the award about academic status, publications, and research grants and contracts received.
- o CIA applications may not be submitted concurrently with other development awards, such as PSA, RCDA, FIRST Award, or Academic Award. CIA awardees are, however, encouraged to apply for research support during the period of the award.
- o Use application form PHS 398 (Rev. 10/88) with special CIA instructions.

C. RESEARCH CAREER DEVELOPMENT AWARD - RCDA (K04)

Supports investigators who have demonstrated outstanding research potential. Provides salary support only for investigators who normally have 5 years of postdoctoral experience at the time of application, including 2 years of experience as an independent investigator with independent peer-reviewed support. Support must be available to carry out the research project for which the RCDA salary is provided. This award may not substitute for other sources of research support since the objective is to provide relief from responsibilities that prevent full-time (not less than 80 percent basic, clinical, or behavioral research) pursuit of an academic research career. New investigators and well-established investigators are not eligible for this Award.

- o Candidate is nominated by and an award is made to an institution on behalf of the candidate.
- o Selection is by national competition.
- o Salary is up to \$50,000 per year plus fringe benefits.
- o Award period is 5 years.
- o Salary supplementation from non-federal funds is allowable.
- o Indirect costs of 8 percent of total direct costs or actual rate, whichever is less, may be requested.
- o RCDA applications may be submitted concurrently with a regular research grant application but must not be submitted concurrently with other career development awards, such as PSA, CIA, FIRST Award, or Academic Award.
- o Use application form PHS 398 (Rev. 10/88) with RCDA instructions.

APPLICATION SUBMISSION AND REVIEW

The receipt dates are the traditional NIH dates: February 1, June 1, and October 1 for Council review October, February, and May, respectively. The PSA and CIA applications will be reviewed by the NHLBI Research Manpower Review Committee or other appropriate Institute review committees. RCDA applications will be reviewed for scientific merit through the regular NIH peer review system in the Division of Research Grants.

Applications submitted in response to this announcement should be identified by typing P.A./Research Career Awards in Thrombosis PA-90-01 on line 2 of the face page.

For the PSA and CIA the original and four copies of the application should be mailed to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

Two copies of the application should be mailed to:

Fann Harding, Ph.D.
National Heart, Lung, and Blood Institute
Division of Blood Diseases and Resources
Federal Building, Room 5A08
Bethesda, MD 20892
Telephone: (301) 496-1817

For the RCDA, submit the original and six copies of the application to DRG at the address above.

The programs of the Division of Blood Diseases and Resources of the National Heart, Lung, and Blood Institute are identified in the Catalog of Federal Domestic Assistance, number 13.839. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency Review.

INVESTIGATIONS INTO THE BIOLOGY OF THE RENAL MICROVASCULATURE

PA: PA-90-02

P.T. 34; K.W. 0785095, 1002004, 1002008, 0785050, 1002019, 0765035, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases

The Division of Kidney, Urologic and Hematologic Diseases (DKUHD) of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) announces the availability of an ongoing Program Announcement (PA) on the above subject.

BACKGROUND

Intrarenal microcirculatory forces are responsible for formation of filtrate at the glomerulus, reabsorption of fluid by the peritubular capillaries, and maintenance of the hyperosmotic environment in the kidney medulla. Accordingly, mechanisms that regulate these forces in the renal vascular beds are of paramount importance to the kidney's homeostatic function. Acting on the hydrodynamic force derived from the heart, the smooth muscle cells of these microcirculatory systems respond to neural, hormonal, and intrinsic stimuli to maintain an appropriate blood flow through each "nephrovascular" unit and an optimal hydrostatic pressure within the glomerular capillaries.

In recent years considerable attention has been focused on the renal microvasculature in attempts to gain insight into the function of such difficult to explore entities such as the macula densa and the juxtaglomerular apparatus. A growing body of evidence suggests that the renal microvasculature is the site of the integrative regulatory mechanisms involved in the kidney's homeostatic mechanisms. In addition, disturbances in the microvasculature at all levels in the kidney, and particularly in the glomerulus, appear to underlie several important renal disorders. Therefore, it is the objective of this PA to encourage increased research activity directed toward the elucidation of the renal microvasculature.

RESEARCH GOALS AND SCOPE

This special grant program will support both fundamental and clinical research. An emphasis of this initiative, however, is to foster extensive collaboration between individuals in the basic sciences, including biochemistry, cell biology, embryology, endocrinology, genetics, molecular biology, pathology, pharmacology, renal physiology and pathophysiology. It is the intent of this solicitation to engage investigators with diverse research interests but who wish to apply their technologies and expertise in elucidating and extending the current understanding of the renal microvasculature. To that end the following are some of the objectives of this solicitation that are being encouraged:

- o Development of model culture systems that maintain the in vivo phenotype of the cells involved in microcirculation and filtration, i.e., epithelial and endothelial cells from various nephron segments, mesangial cells, etc.;
- o Studies to identify molecular components participating in cell-cell and cell-matrix interactions in normal and disease states;
- o Studies aimed at defining in vivo roles for specific cytokines, growth factors and eicosanoid or other mediators in physiologic microvascular responses and in human renal diseases and animal models of renal disease, especially through techniques identifying in situ production, local release and/or verifiable action of specific mediators. Also, develop in vivo methods for the assessment of intracellular signalling events critical to vascular control systems and elaboration of growth factors;

Beyond description of mediators, additional approaches may address consequences for the local renal microvasculature arising from over-expression of individual mediators as might occur with transgenic animal models, retroviral expression, or other methods.

o Studies of the roles of coagulation, fibrinolytic, complement and other mediator systems in specific models of glomerular injury;

The above are examples only and should not be viewed as all inclusive.

MECHANISMS OF SUPPORT

Support for this program will be through the grant-in-aid and will be governed by the current policies of grant programs of the National Institutes of Health (NIH). New applications may be submitted for the traditional, investigator-initiated research project grant (R01) and First Independent Research Support and Transition (FIRST) Awards (R29). Under these mechanisms, the applicants will plan, direct, and conduct the research programs. The project period during which the research will be conducted should adequately reflect the time required to accomplish the stated goals and be consistent with the policy for grant support. Support will be provided up to five years (renewable for subsequent periods) subject to the availability of funds and progress achieved.

Research grant applications may be submitted by both nonprofit and profit-making organizations and institutions, State and local governments and their agencies, and eligible agencies of the Federal government.

APPLICATION AND REVIEW PROCEDURES

The Division of Research Grants, NIH, serves as a central point for receipt of applications for most discretionary PHS grant programs. Applications in response to this announcement will be assigned to an Initial Review Group (IRG) in accordance with established PHS Referral Guidelines. The IRGs, consisting primarily of non-Federal scientific and technical experts, will provide the peer review for scientific merit of the proposed research, potential significance of the research findings, adequacy of methodology, availability of necessary facilities, and the qualifications of the research team. A secondary review will be by an appropriate National Advisory Council that will consider the Institute's mission, policy and program relevance to its research needs.

Applications must be submitted using Form 398 (rev. 10/88), "Application for Public Health Service Grant", available in the business or grants office of most academic or research institutions, or from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Bethesda, MD 20892. In order to assure proper identification of the application, line 2 of the application form should state "Renal Microvasculature Program Announcement, PA-90-02" and check the "YES" box.

The first receipt date for applications will be June 1, 1990, with Initial Review Group review in September-October 1990 and Advisory Council review January-February 1991. The earliest requested begin-date should be April 1, 1991. Thereafter, the regular NIH receipt dates for grant applications will pertain: October 1, February 1 and June 1 of each year.

The original and six copies of the application are to be sent to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

Prior to submitting applications, applicants are encouraged to contact:

M. James Scherbenske, Ph.D.
Renal Physiology/Cell Biology Program Director
DKUHD/NIDDK
Westwood Building, Room 621
Bethesda, MD 20892
Telephone: (301) 496-7458