NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 1, January1, 1982

IN THIS ISSUE:

(Continued)

HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

Index (Continued)

ANNOUNCEMENT

ORGANIZATION AND FUNCTION OF THE NIEHS

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

The National Institute of Environmental Health Sciences (NIEHS) is the principal Federal agency for biomedical research on the effects of chemical and physical environmental agents on man's health and well-being.

The NIEHS is one of the Institutes of the National Institutes of Health (NIH). The only one located outside the Washington, D.C. area, it is situated in the Research Triangle Park, North Carolina. All operations and activities of the NIEHS are conducted within the framework of the NIH, and the Extramural Program functions within the purview of the Office of Extramural Research and Training, NIH. The Institute utilizes the Division of Resarch Grants (DRG) and national advisory groups for review of grant applications. Application forms, receipt dates, publication of announcements, notices and requests for applications (RFA) follow the standard NIH format and procedures.

Following assignment of applications to the NIEHS Referral Office, Division of Research Grants, an appropriate Initial Review Group (Study Section) selected by the DRG, reviews the Regular Research Grant, Program Project Grant, and Research Career Development Grant applications.

An alternative review procedure is used for Environmental Health Sciences Center, Marine and Freshwater Biomedical Center, Institutional Training, and Mid-Career Developmental grant applications which undergo initial review by an advisory group established by the NIEHS. Secondary review of all grant applications is carried out by the National Advisory Environmental Health Sciences Council (NAEHSC). The assignment of all grant proposals to the NIEHS, regardless of type, is through the Division of Research Grants, NIH.

Additional information concerning the mission and interests of the program of the NIEHS may be obtained by contacting the Office of the Director, Extramural Programs, NIEHS, P.O. Box 12233, Research Triangle Park, North Carolina 27709, Telephone (919) 541-7723, or Program Directors for specific programs as listed below:

Dr. Robert G. Owens - Special Programs
Telephone (919) 541-7825

Dr. Edward Gardner, Jr. - Regular Research Grants
Telephone (919) 541-7724

Dr. Christopher Schonwalder - Research Manpower Development
Telephone (919) 541-7634

ANNOUNCEMENT

AVAILABILITY OF SENIOR INTERNATIONAL FELLOWSHIPS FOR 1983-84

FOGARTY INTERNATIONAL CENTER

The John E. Fogarty International Center for Advanced Study in the Health Sciences (FIC) announces the availability of senior postdoctoral research fellowships to U.S. health scientists who wish to study abroad. The purpose of these fellowships is to enhance the exchange of ideas and information in the various biomedical and behavioral disciplines. The types of activity that are supported by this program include collaboration in basic or clinical research, and the familiarization with or utilization of special techniques and equipment not otherwise available to the applicant. These programs do not provide support for brief observational visits, attendance at scientific meetings, attendance in formal training courses, or independent research projects within the host institution.

ELIGIBILITY REQUIREMENTS

Applicants must meet the following requirements:

- U.S. citizen or permanent U.S. resident;
- Doctoral degree in a clinical, biomedical or behavioral science;
- Five years or more of postdoctoral experience;
- Professional experience in the health or biomedical sciences for at least two of the last four years;
- Affiliation with a non-Federal U.S. public or private nonprofit research, clinical or educational institution.

APPLICATION AND SELECTION

Fellowship applications are reviewed once annually. The receipt date for applications to the Senior International Fellowship Program is June 1, 1982. All applications are reviewed for scientific merit by the National Institutes of Health. Fellowship awards are made for periods of three to twelve months. A fellowship can be activated within one year after receiving the Notice of Award and the starting date of the fellowship is set by mutual agreement between the applicant and the host institution.

Prospective applicants for the Senior International Fellowship Program may obtain information brochures from FIC. Only the dean or equivalent institutional official may

request fellowship applications which will be available from Januuary 15 to May 15, 1982. Information and fellowship applications are available from:

International Research and Awards Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205

For an expedient reply, please send a self-addressed label to the above address.

ANNOUNCEMENT

THE GENETIC BASIS OF AGING

NATIONAL INSTITUTE ON AGING

INTRODUCTION

This announcement supersedes three preceding announcements by the National Institute on Aging: 1) The Genetic Basis of Aging: Drosophila as a Model System, NIH Guide for Grants and Contracts Vol. 7, No. 19, December 15, 1978, pp 23-25; 2) The Genetic Basis of Aging: Protozoa as Models, NIH Guide for Grants and Contracts Vol. 8, No. 8, June 5, 1978, pp 7-9; and 3) The Genetic Basis of Aging: C. Elegans as a Model System, NIH Guide for Grants and Contracts Vol. 9, No. 2, January 25, 1980, pp 51-54.

BACKGROUND INFORMATION

The National Institute on Aging (NIA) conducts and supports biomedical, behavioral, social, and clinical research, and research training related to the processes of aging and to the diseases and other special problems and needs of the aged. Genetic analysis is a powerful tool that can be applied to research on aging and longevity.

Research on human populations and human cells are encouraged where they are appropriate. In addition, many types of studies on the genetic basis of aging and longevity require experimental animals that can be maintained under controlled conditions and manipulated according to experimental protocols. Research on the genetics of aging and longevity using mammalian models is particularly encouraged by the NIA. However, research using lower organisms is also of interest to the NIA where understanding aging is the major focus of the project, where questions will be asked that cannot be examined readily in mammals and where there is evidence for physiological processes that parallel those seen in human aging.

GOALS AND SCOPE

The purpose of this announcement is to withdraw the three previous announcements described in the Introduction. Hence, this is not an announcement of a new program. A new program announcement concerning mammalian models for genetic research on aging will be made in the future.

This program is described in the Catalog of Federal Domestic Assistance Number 13.866, Aging Research. 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 uner PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 7. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

INQUIRIES AND CORRESPONDENCE

Inquiries and correspondence should be directed to:

Dr. Richard L. Sprott
Chief
Molecular and Cellular Biology Branch
Biomedical Research and Clinical Medicine Program
National Institute on Aging
Building 31, Room 5C15
Bethesda, Maryland 20205

Telephone: 301 - 496-6402

ANNOUNCEMENT

RESEARCH GRANTS ON BRAIN DYSFUNCTION IN DISORDERS OF LEARNING

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

The Developmental Neurology Branch, Neurological Disorders Program of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), in co-sponsorship with the Human Learning and Behavior Branch, Center for Research for Mothers and Children of the National Institute of Child Health and Human Development (NICHD) encourages the submission of research grant applications (R01) on brain dysfunction in disorders of learning.

BACKGROUND

Learning disorders affect one of the largest groups of handicapped children as defined under Public Law 94-142. Estimates of incidence of unexpected school failure range from 2% to 20% of the school population. A major etiological hypothesis is the presence of subtle neurophysiological abnormalities in brain electrical activity of these children who show deficits in attention, memory, and control of motor activity, as well as in information processing. The Developmental Neurology Branch, Neurological Disorders Program (NINCDS) and the Human Learning and Behavior Branch, Center for Research for Mothers and Children (NICHD) encourage the submission of applications for the support of basic and clinical research on the neurophysiological and/or neurochemical mechanisms associated with specific and precisely defined learning disorders in children with normal intelligence, normal psychiatric status, and adequate environmental support. Similar studies of the same mechanisms in control children with normally developing cognition are also encouraged.

RESEARCH GOALS

Research grant applications should focus on brain neurophysiology and/or neurochemistry, but related research supporting this effort would be appropriate. Of particular interest are studies using evoked potential and EEG measures. Other areas of interest include neuroendocrine, metabolic and neuroradiological studies. The two primary research goals are: (1) to develop objective and reproducible diagnostic criteria for identifying homogeneous subgroups of children with learning disorders; (2) to refine neurophysiological techniques for evaluating cortical functions in these LD subgroups and in normal comparison groups. The reliability and validity of measures of brain electrical activity need to be investigated in both study and normal control groups by age, sex, type of learning task, and hemispheric specialization. Research should be directed at

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This program is described in the Catalog of Federal Domestic Assistance No. 13.852, Neurological Disorders, and 13.865, Research for Mothers and Children. 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 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

developing knowledge of the neurophysiology of learning disorders, and expanding the capability for accurate diagnosis. This research would require a multidisciplinary approach involving participation from such areas as neurophysiology, developmental neuropsychology and pediatric neurology.

MECHANISM OF SUPPORT

Support for this program will be through the regular research project grant-in-aid. Each successful applicant will plan, direct, and carry out the individual research project.

APPLICATION AND REVIEW PROCEDURES

Applications should be prepared on Form PHS 398 (Revised 5/80) following instructions contained in the application kit. Application kits are available from most institutional business offices, or may be obtained from the Division of Research Grants, at the address given below.

Applications must be responsive to the program announcement and the goals of NINCDS and NICHD. They will be judged on scientific merit and program relevance in accordance with NIH policy and procedures involving peer review. An initial review will be made by the appropriate study section of the Division of Research Grants. A second level of review will be made by the National Advisory Neurological and Communicative Disorders and Stroke Council or by the National Advisory Child Health and Human Development Council depending on Institute assignment of the application.

Deadline dates for the receipt of applications are March 1, July 1, and November 1.

The phrase "Prepared in response to NINCDS and NICHD program announcement for research on brain dysfunction in disorders of learning" should be typed across the top of the first (face) page of the application. The original and six copies of the application should be mailed to:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

One copy of the application is to be sent to each of the addresses below. Also, for further information applicants may contact:

Sarah H. Broman, Ph.D.
Acting Chief, Mental Retardation and Learning
Disorders Section
Developmental Neurology Branch
Neurological Disorders Program
National Institute of Neurological and
Communicative Disorders and Stroke
Federal Building, Room 8C-06
7550 Wisconsin Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-6377

Norman A. Krasnegor, Ph.D.
Chief, Human Learning and Behavior Branch
Center for Research for Mothers and Children
National Institute for Child Health and
Human Development
Landow Building, Room 7C-18
7910 Woodmont Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-6591

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NHLBI-DLD-82G-B

SPECIALIZED CENTERS OF RESEARCH IN ADULT RESPIRATORY FAILURE

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

I. BACKGROUND

The Division of Lung Diseases of the National Heart, Lung, and Blood Institute invites new or competitive renewal applications for grants to support Specialized Centers of Research (SCOR) for basic and clinical investigations addressed to Adult Respiratory Failure. In addition to the Adult Respiratory Failure program, the Division currently supports SCOR programs in Chronic Obstructive Lung Diseases, Fibrotic and Immunologic Interstitial Lung Diseases, Pediatric Pulmonary Diseases, and Pulmonary Vascular Diseases.

This SCOR program complements other programs supported by the Division. It fosters a concerted research effort that involves basic disciplines but has a major emphasis on clinical problems relevant to the prevention, diagnosis, and management of adult respiratory failure. Special features of the SCOR grant are the following:

- It provides the opportunity for investigators with mutual or complementary interests to engage in interdisciplinary research focused on problems of adult respiratory failure as identified in this announcement.

- While clinical aspects of the disease must be the primary emphasis, the center program must include fundamental studies. The basic research must be clearly related to the disease focus, and must contribute, directly or indirectly, to the elucidation of mechanisms underlying the disease process, or to better diagnosis, management, or prevention of the disease. The SCOR grant may include projects designed to accelerate the transfer of knowledge gained from research to its use in medical practice.

- Each center must have a well-delineated organizational structure and administrative mechanism to ensure a productive research effort that will further the stated goals of the grant.

- Inherent in the SCOR program is the special interaction between all the centers, which is coordinated by the Division of Lung Diseases. The Division will provide advice and guidance to meet the goals of the Division's National Program as well as the goals of the SCOR grant. To these ends, the Division will provide, as part of the grant, funds specifically allocated for SCOR coordination. This makes it possible for investigators in different centers to

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This program is described in the Catalog of Federal Domestic Assistance No. 13.838, Lung Diseases. Grants will be awarded 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 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

meet and discuss problems of mutual interest and to engage in workshops addressed to specific facets of the SCOR program.

- The Division's SCOR program and each SCOR grant undergo periodic evaluation. Also, reports of progress are prepared for the information of the Pulmonary Diseases Advisory Committee and the National Heart, Lung and Blood Advisory Council.

Because of the size and complexity of a SCOR, prospective applicants are urged to take advantage of the opportunity to consult with the staff of the Division of Lung Diseases early in the preparation of the application (See Section V).

II. RESEARCH GOALS AND SCOPE

To be acceptable for the Adult Respiratory Failure SCOR competition, the focus of an application must be on adult respiratory distress syndrome that can be associated with such conditions as trauma, fat embolism, near-drowning, aspiration, drug overdose, sepsis, pneumonia, and other acute illnesses. The SCOR will not support investigations of acute respiratory failure that results from progression of such chronic pulmonary disorders as asthma, chronic bronchitis, or emphysema, in which prolonged pulmonary damage and respiratory insufficiency precede acute respiratory failure. This program also excludes neonatal respiratory distress syndrome.

The overall goal of the Division of Lung Diseases for the adult respiratory failure program is to improve the diagnosis, management, and prevention of the disease through the better understanding of the structural, biochemical, immunologic, and physiologic mechanisms and structural changes associated with acute lung injury. Therefore, a SCOR should be planned so the knowledge gained from fundamental investigations will be relevant to the clinical studies of the natural history of the disease, its diagnosis, treatment, and prevention.

The primary focus of the clinical and fundamental research projects that comprise the SCOR program should be the elucidation of the mechanisms of acute lung injury which result in adult respiratory failure, the mechanisms of lung repair, and the means by which therapeutic interventions can prevent progressive damage or accelerate repair processes.

A proposed SCOR may include pilot studies to test innovative approaches for diagnosis or therapy, but support will be provided only for the preliminary phases of such studies and not for large scale clinical evaluations. Costs for research patients may be charged only insofar as they result from the purely research aspects of care and if they clearly relate to the requirements of the proposed research.

To be responsive to this announcement, the proposed SCOR must include the following:

1. Clinical investigations addressed to the etiologies, natural history, diagnosis, treatment, or prevention of adult respiratory failure;*

* A given SCOR need not address all of the above problems but must address some from both items 1 and 2.

2. Fundamental investigations of the mechanisms of acute lung injury, sites of damage, processes involved in progression and repair of the injury, or alterations in lung function associated with acute lung injury;*

3. A clinical core unit that will provide a patient population for the clinical studies; and

4. A well-delineated plan for a mutually supportive interaction between investigators involved in the clinical and the fundamental research aspects of the proposed SCOR.

III. MECHANISM OF SUPPORT

The support mechanism will be the grant-in-aid. Thus, all policies and requirements which govern the grant programs of the PHS will prevail, including the requirement for cost sharing. However, it will differ from other research grants in its degree of goal orientation and in the degree of direct participation by the National Heart, Lung and Blood Institute. While it is expected that the investigators of the individual SCORs will plan, direct, and execute their own research program, any substantive modifications in that program must be mutually agreed upon by the National Heart, Lung and Blood Institute. Ongoing evaluation will include periodic visits to the SCOR institutions and review of formal progress reports.

Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work, a schedule for completion of the work, or an outline of the phases or segments into which the proposed program can be logically divided. Awards will be for a maximum 5 year period; a December 1, 1983, start date should be requested.

Although this solicitation will be included and provided for in the fiscal plans for Fiscal Year 1984, support of grants pursuant to this request for applications is contingent upon receipt of appropriated funds for this purpose. The current Adult Respiratory Failure SCOR program involves three grants which have a total annual funding base of approximately two million dollars (including indirect costs). At this time, it is not possible to predict whether future funding will be above or below this level. The final allocation of funds to this program will be influenced by the total amount of funds available to the Division, by the overall merit of proposals, and by their relevance to the program goals. A variety of approaches would be responsive to this announcement; accordingly, it is anticipated that there will be a range of costs among individual grants awarded.

IV. REVIEW PROCEDURES AND CRITERIA

The merit review of these applications will be conducted by the National Heart, Lung, and Blood Institute. Primary review will be conducted by a group of consultants specifically convened for this purpose. Secondary review will be by the National Heart, Lung and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the May 1983 meeting of the Council.

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* A given SCOR need not address all of the above problems but must address some from both items 1 and 2.

The review criteria include:

- The scientific merit of each research project and the relation of the project to the overall goals of the center;
- The technical merit and justification of each core unit;
- The accomplishments and progress to date, particularly for renewal applications;
- The qualifications, experience, and commitment of the investigators responsible for the research projects or core units and their ability to devote adequate time and effort to the program; and
- The appropriateness of the budget for the proposed projects and core units.

REVIEW OF THE CENTER AS AN INTEGRATED EFFORT

The review criteria include:

- The significance and the importance of the research to the programmatic goals of the SCOR announcement;
- The multidisciplinary scope of the center and the coordination and interrelation of the research projects and core units;
- The leadership and scientific stature of the program director and his or her commitment and ability to devote adequate time and effort to the program;
- The participation of an effective number of responsible experienced investigators;
- The academic and physical environment in which the research would be conducted, including the availability of space, equipment, patients, and the potential for interaction with scientists from other departments and other institutions;
- The internal arrangement for quality control of on-going research, the allocation of funds, day-to-day management, communication and cooperation between the investigators involved in the program, and contractual agreements;
- The presence of an administrative and organizational structure that would facilitate attainment of the proposed objective of the program;
- The institutional commitment to the requirements of the program; and
- The appropriateness of the budget to the proposed program.

REVIEW OF THE PROPOSED CENTER BY THE NATIONAL HEART, LUNG, AND BLOOD ADVISORY COUNCIL

Factors considered in this review include:

- o The results of the initial review for scientific and technical merit;
- o The significance of the research program to the adult respiratory failure program;
- o National needs; and
- o Policy and budgetary consideration.

V. METHOD OF APPLYING

SPECIFIC GUIDELINES FOR PREPARATION OF AN APPLICATION FOR A SPECIALIZED CENTER OF RESEARCH ARE AVAILABLE UPON REQUEST. PROSPECTIVE APPLICANTS ARE URGED TO WRITE FOR THESE GUIDELINES EARLY IN THE PLANNING STAGE.

To the extent possible, the Division of Lung Diseases is prepared to discuss plans for developing a SCOR proposal with prospective applicants. However, to provide effective guidance, the Division must receive a draft that is complete with regard to all substantive sections. These include description of SCOR goals, detailed presentations of projects and cores, description of organization and administrative plans, detailed budgets for each project and core and biographical data for all participating investigators.

Inquiries about preparation of applications should be addressed to:

Carol E. Vreim, Ph.D.
Chief, Interstitial Lung Diseases Branch
Division of Lung Diseases
National Heart, Lung, and Blood Institute
Westwood Building, Room 6A05
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7034

To provide an estimate of the nunmber of applications, for purposes of planning the review, prospective applicants should submit a brief letter of intent (not to exceed two pages) no later than July 1, 1982, describing the proposed goals of the SCOR, types of projects to be included, names of responsible investigators with academic titles, and an estimate of the level of funding (direct costs) required. Letters of intent are not binding.

Letters of intent should be sent to:

Charles Turbyfill, Ph.D.
Chief, Centers and Special Projects Review Section
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building, Room 553A
5333 Westbard Avenue
Bethesda, Maryland 20205

Application form PHS 398 should be used. Forms may be obtained from the institution's application control office or from the Division of Research Grants, NIH.

The completed application and 24 copies should be delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

Two additional copies should be mailed to the Division of Lung Diseases, NIH.

Applications must be received by September 15, 1982.

A brief covering letter should accompany the application indicating that the proposal is being submitted in response to this Request for Applications NHLBI-DLD-82G-B.

Consequences of Lack of Responsiveness to the RFA or Late Submission

Applications submitted in response to this request will be reviewed by NHLBI staff to determine responsiveness to the criteria for a Specialized Center of Research. Those applications that are judged not responsive, or are not received by September 15, 1982, will not be accepted for review and will be returned to the applicant.

Timetable

Letters of intent should be submitted no later than July 1, 1982.

The original and 24 copies of the completed application should be submitted to the Division of Reserch Grants, NIH not later than September 15, 1982. Two additional copies should be submitted to the Division of Lung Diseases.

The final review of applications by the National Heart, Lung, and Blood Advisory Council will be completed by May 28, 1983.

Applicants will be notified of the outcome of the review by June 1983.

Initiation of awards will not be before December 1, 1983.

Much has been learned about the role of the "accessory" muscles of respiration during normal (non-fatigued) breathing. The intercostals and abdominal muscles are activated even at rest during inspiration to stiffen the rib cage and to keep the diaphragm at a more nearly optimal length. During exercise, other accessory muscles are activated to help the diaphragm with the increased load. Little is known, however, about the mechanics of the lung and chest wall during progressive fatigue. Discoordinate rib cage and abdominal motion has been observed, but the muscles involved, their fatigue limits, and the pressures that they generate require further study. In addition, such basic characteristics of respiratory muscle function as force-velocity and force-length responses under, for example, various regimens of stimulation, alterations of nutrient supply, or disease states, are not well known and require further study.

Diseases affecting lung function are known to have an effect on respiratory muscle structure and function. For instance, the diaphragm is known to operate at a shorter, less efficient length in patients suffering from emphysema when lung hyperinflation is present. Such patients, if adequately nourished, have been found at autopsy to have diaphragms that are thicker than those of people with normal lungs; this thickening may help compensate for the disadvantage of operating at a shorter length. The morphology and fatigue characteristics of such diaphragms need to be understood more completely. Similar fatigue studies are also required in neonates who have immature respiratory systems as well as in patients with altered lung mechanics due to fibrotic diseases or asthma. Even the oxygen cost of breathing and changes in efficiency of the respiratory muscles are not well described in many disease states including respiratory failure. Thus, animal studies involving immature lungs or lungs with experimentally induced and well characterized changes in lung elastic or resistive properties should yield useful data on respiratory muscle fatigue.

IV. MECHANISM OF SUPPORT

The support mechanism for this program will be the regular NIH grant-in-aid; successful applicants will plan and execute their own research program. Upon initiation of the program, the Division of Lung Diseases will sponsor periodic workshops to encourage exchange of information among investigators who participate in this program. Prospective grantees should include in their grant applications a statement indicating their willingness to participate in such information exchange activities.

Although this program is included in the financial plans for Fiscal 1982, award of grants pursuant to this request for grant applications is contingent upon receipt of appropriated funds for this purpose. It is anticipated that four to six proposals will be supported under this program. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded. Although interdisciplinary approaches are encouraged, grant applications should be tightly focused; it is not the intent of this request to solicit proposals for large multidisciplinary studies (program projects) encompassing a variety of essentially independent research projects. Applicants are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award period for this proposal must not exceed 3 years. At the end of the initial award period, renewal proposals may be submitted for further competitive review through the regular grant mechanism. It is anticipated that support will begin on September 30, 1982.

The current policies and requirements which govern the research grant programs of the National Institutes of Health will prevail, including the requirement for cost sharing.

V. REVIEW PROCEDURES AND CRITERIA

Upon receipt, applications will be reviewed for their responsiveness to the specific objectives described in this announcement. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to submit it for consideration in the traditional grant program of the NIH. Initial technical merit review will be arranged by the Division of Research Grants (DRG). Secondary review will be undertaken by the National Heart, Lung, and Blood Advisory Council.

If a proposal 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. Simultaneous submission of identical applications will not be allowed.

The factors to be considered in the scientific merit evaluation of each application will be identical to those used in traditional NIH research grant application evaluation, including an assessment of the importance of the proposed research problem; the novelty and originality of the approach; the training, experience, and research competence or promise of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed.

VI. METHOD OF APPLYING

1. Letter of Intent

Prospective applicants are asked to submit a brief letter of intent which would include a synopsis of the proposed research as well as the names of other institutions which might collaborate on the project. Such letters are requested only to obtain an indication of the number and scope of applications to be received. A letter of intent is not a requirement for application, nor is it binding, and information provided in the letter will not enter into the review of any application subsequently submitted.

The letter of intent should be received by February 15, 1982, addressed to Dr. Everett E. Sinnett, Division of Lung Diseases, NHLBI, National Institutes of Health, Westwood Building, Room 6A03, Bethesda, Maryland 20205.

2. Format for Applications

Applications should be submitted on the standard research grant application form, PHS-398 (Revised 5/80), which may be obtained at the applicant's institution business or research office or by contacting the Division of Research Grants, Office of Grants Inquiries, Room 449, Westwood Building, Bethesda, Maryland 20205, phone (301) 496-7591. The conventional presentation in format and detail for regular research grant applications should be utilized.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NHLBI-DLD-82G-C

STRUCTURAL AND FUNCTIONAL CHANGES ASSOCIATED WITH RESPIRATORY MUSCLE FATIGUE

NATIONAL HEART, LUNG AND BLOOD INSTITUTE

I. BACKGROUND

Although fatigue of respiratory muscles has long been thought to contribute to respiratory failure, the extent to which ventilatory muscle fatigue is involved in respiratory disability and failure is still not well-documented. Nevertheless, it appears likely that when the mechanisms involved in such fatigue are more thoroughly understood, effective means for detection, prevention, and treatment of fatigue may be identified and significant improvements made in the care and treatment of persons with a variety of lung disorders.

The most direct definition for ventilatory muscle fatigue is failure of task performance. Inability to continue voluntary hyperpnea at a specified level, to tolerate inspiratory resistive loading, or to generate specific pressures at the airway or across the diaphragm during resistive loading have served as criteria for ventilatory muscle fatigue. Accompanying the development of fatigue is a shift in the electromyogram (EMG) power spectrum (the distribution of power versus frequency). Finally, changes in respiratory patterns are seen in circumstances associated with fatigue or with EMG changes.

The exact physiological, morphological, and biochemical causes of fatigue in respiratory muscles, and the changes associated with fatigue, have not been explored. Although our understanding of skeletal muscle fatigue has progressed considerably over the past decade, largely through the study of isolated limb muscles, the respiratory system has several features that make it difficult to extrapolate this knowledge to the respiratory muscles. First, the activation of the muscles is under both voluntary and involuntary control, and knowledge about neural control of breathing during fatigue is at best very limited. Second, the diaphragm, the principal muscle of respiration, receives its blood supply largely over the surface of the muscle rather than through the muscle mass itself and thus is less liable to interruptions in the supply of oxygen and nutrients during a contraction. The biochemistry of diaphragmatic fatigue and its responsiveness to pharmacologic therapy may therefor be different from fatigue in other muscles. Third, the diaphragm is aided in its function by intercostal and accessory muscles that may, as the diaphragm reaches its limits of endurance, take on some or all of the burden of ventilation, thus "resting" the diaphragm and postponing the advent of ventilatory failure. The ability of the accessory muscles to cope with such demands and the neural mechanisms involved in such a shift of muscular activation have received little attention.

This program is described in the Catalog of Federal Domestic Assistance, No. 13.838, Lung Diseases. Grants will be awarded 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 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

II. GOALS AND SCOPE

The specific goal of this program is to encourage collaboration between researchers in different disciplines and fields for the purpose of elucidating basic mechanisms of respiratory muscle fatigue. Thus, to be responsive to this RFA, interdisciplinary efforts (such as between researchers in the disciplines of physiology, biochemistry or morphology) or intradisciplinary approaches (such as between neuro- and respiratory physiologists) are required. The studies should be based on common goals and must be designed to test a specific hypothesis or a few closely related hypotheses.

Physiological as well as biochemical, morphologic, and neurologic aspects of fatigue in the normal respiratory system, the influence of various lung diseases and associated changes in lung and chest wall mechanics on muscle fatigue, and the neural control of breathing during fatigue are examples of areas of research that will be supported under this announcement. Studies may include whole animal or isolated muscle preparations. If the latter are used, care should be taken to ensure that the studies are relevant to an in vivo situation. Although it is expected that proposals will be primarily addressed to animal studies, human studies may also be included if clearly related to elucidation of basic mechanisms of fatigue. Basic research, such as investigations of lung and chest wall mechanics or central and peripheral neural control and transmission, may be proposed if the intent is to correlate the studies with an understanding of fatigue mechanisms, but the major emphasis must be on the latter.

Although the importance of overall nutritional status on respiratory muscle structure and function is recognized, studies dealing with whole body nutrition as an independent variable will not be considered responsive to this announcement. In addition, methodological studies aimed at developing or improving clinical means of detection of respiratory muscle fatigue, and clinical studies on prevention (e.g., respiratory muscle training) and treatment (e.g., optimal use of ventilators, drugs, etc., in cases where fatigue has resulted in the patient's inability to maintain adequate gas exchange) of respiratory muscle fatigue, while of importance, will not be supported by this RFA.

III. EXAMPLES OF RESEARCH TOPICS

The research topics presented below serve as examples of research areas that would meet the goals of this program. The topics mentioned are not intended to be all inclusive and are not presented in any order of priority. Investigators are encouraged to consider other relevant topics and approaches that would lead to an understanding of respiratory muscle fatigue.

With other skeletal muscles, it has been demonstrated that fatigue can be the result of a failure at one of several sites. Central fatigue would be characterized by a failure of the central nervous system to provide sufficient neural stimuli to maintain the required muscle output. Fatigue can occur due to depletion of neuro-transmitters, either at a ganglionic site or at the neuromuscular junction. Finally, numerous biochemical disturbances, such as inadequate supply of energy-producing substrates or the accumulation of wastes, can result in a failure of contraction at the cellular level. Few studies have been done to identify the critical site(s) of fatigue in respiratory muscles. These have dealt with a few aspects of diaphragmatic metabolism, but have not identified a specific metabolite or metabolic pathway that may be considered rate limiting and therefore a cause of fatigue. It is important to identify which link in the muscle activation pathway may be the weakest and under what conditions it or a different link may be expected to fail.

3. Application Procedure

The completed application and 24 copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications must be received by April 15, 1982.

The face page of the application must indicate that it is submitted in response to this program announcement: RFA-NHLBI-DLD-82G-C, "Structural and Functional Changes Associated with Respiratory Muscle Fatigue."

4. Timetable

Letter of Intent due ..... February 15, 1982
Applications to Division of
Research Grants due ..... April 15, 1982
NHLB Advisory Council Review ..... September, 1982
Initiation of awards not before .....September 30, 1982

VII. INQUIRIES

Inquiries may be directed to Dr. Everett E. Sinnett, Division of Lung Diseases, NHLBI, National Institutes of Health, Westwood Building, Room 6A03, Bethesda, Maryland 20205. Telephone: (301) 496-7171.

REQUEST FOR RESEARCH GRANT APPLICATION: RFA NIH-NHLBI-82G-E

IDENTIFICATION OF CELLS IN ATHEROSCLEROTIC PLAQUES

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 1, 1982

The National Heart, Lung, and Blood Institute (NHLBI) invites applications for research grants, to be initiated during FY 1982, to develop and apply improved methods, particularly biochemical and marker methods, which in conjunction with morphology can 1) improve the accuracy and ease of identification of normal and abnormal cells in atherosclerotic plaques, and 2) assess the specific characteristics of cells at various stages of plaque development. The present RFA is for a single competition, with the deadline specified above..

BACKGROUND INFORMATION

For many decades attempts have been made to identify the changes in the arterial wall and the cells involved in the development of atherosclerotic lesions. It is not always possible to identify different types of cells with certainty. There is a great deal of variation among lesions including both the kinds and proportions of cells present and the particular stages of cellular differentiation that may be found. A detailed and accurate appreciation of the identity and range of phenotypic characteristics of such cells should greatly enhance our understanding of the pathogenesis of atherosclerotic plaques.

Study of the role of vascular cells in atherogenesis has suggested that atherosclerosis may involve the reaction of the vessel wall to cycles of injury-repair in which monocytes, leukocytes, platelets, macrophages, smooth muscle cells, fibroblasts and endothelial cells play a part.

RESEARCH GOALS AND SCOPE

The cells associated with atherosclerotic plaques have been designated in many ways. Some are designated according to cell type, others by purely descriptive terms without assignment to a cell type or origin although particular properties and characteristics may be described. Normally differentiated cells are easily recognized, but differentiation is commonly unusual and recognition of cell types is often difficult or impossible. The goal of this RFA is to elicit applications which hold substantial promise of significantly advancing the state of the art for one or more aspects of the identification of cell types, detection and quantification of their biochemical activity and functions in different stages of differentiation and in different kinds of plaques.

This program is described in the Catalog of Federal Domestic Assistance, number 13.837, Heart and Vascular Diseases Research. 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 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Healt' Systems Agency Review.

There is the possibility of improving methods and markers, or finding new markers to identify properties and characteristics of cells in or derived from plaque. Some of these technical improvements relate to biochemical, immunological or physical methods, some can assess function, and all can be associated with morphology. However, this RFA is not directed to research that is primarily morphological. While the ultimate interest is in human atherosclerosis, animal lesions and cell culture models can provide valuable information.

MECHANISM OF SUPPORT

The support mechanism for this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute--with the concurrence of its National Advisory Council--wishes to stimulate investigator interest in a particular research problem that is important to its program.

The RFA identifies the scope of the Institute's interest but does not require that the application to be submitted conform to a specific protocol. Thus it is expected that each successful applicant will plan, direct, and carry out his or her research proposal within the general scope or frame of reference. As with any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that the general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a specific program need.

Applicants are requested to furnish their own estimates of the time required to achieve the specific objectives of the proposed work, but the total project period should not exceed three years in duration; a September 30, 1982 start date should be requested.

REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with one another. Primary review will be conducted by an Initial Review Group composed in the main of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September 1982 meeting of the Council.

The major factors to be considered in evaluating each application are given below:

- The relevance and significance of the proposed approach to the goals described in this announcement.
- The scientific merit of the proposal: the methodology, the research design, the plan for analysis and interpretation of data.
- The research experience and competence of the applicant(s) to carry out the proposed investigations.
- Adequacy of time/effort to be devoted to the project by investigators and technical staff.
- Adequacy of collaborative arrangement(s) if applicable.
- Adequacy of facilities and resources for the proposed research.
- Justification for the proposed budget in relation to the scope of the project.

METHOD OF APPLYING

A. LETTER OF INTENT

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research to

Dr. Charles Turbyfill
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
5333 Westbard Avenue
Bethesda, MD 20205

This letter should be received no later than February 15, 1982.

The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. FORMAT FOR APPLICATION

Applications should be submitted on form PHS 398, the application form for a regular research grant. This form is available at the applicant's institutional office of sponsored research or from the Office of Grants Inquiries, Division of Research Grants, NIH. The conventional format of research grant applications should be utilized ensuring that the points identified under "Review Procedures and Criteria" are addressed.

C. APPLICATION PROCEDURE

The completed application and thirty (30) copies thereof should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications must be received by April 1, 1982. Applications not received by this deadline will be considered ineligible for this competition but after discussion with the applicant, may be considered as a regular research grant application which meets the usual July 1, 1982 deadline. If an application is judged to be non-responsive to this announcement, the applicant will be contacted to determine if he or she wishes to have the proposal returned or reviewed as an application for a regular research grant. Due dates are as follows:

Letter of Intent	February 15, 1982
Application Due	April 1, 1982
Grant Start Date	September 30, 1982

PLEASE NOTE
The outside of the mailing package and the top of the face page of the application should be labeled: "Response to RFA NIH-NHLBI-82G-E"

FUNDING

Although this program is included and provided for in the Institute's financial plans for FY 1982, awards are contingent upon ultimate allocation of appropriated funds for this purpose. It is expected that up to $700,000 for total costs will be available for the first year to support approximately five grant awards.

IDENTIFICATION OF CONTACT POINTS

Inquiries may be directed to Dr. Edwin C. Gangloff, Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute, Federal Building, Room 4C-12, Bethesda, Maryland 20205; Telephone (301) 496-1978.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-82G-F

ANALYSIS OF THE ROLE OF GENETIC AND DEVELOPMENTAL FACTORS IN THE ETIOLOGY AND PROGRESSION OF ESSENTIAL HYPERTENSION

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 1, 1982

The National Heart, Lung, and Blood Institute (NHLBI) invites applications for grants from interested investigators for studies on the role of genetic and developmental factors in the etiology and progression of essential hypertension. The proposed studies would seek, as their major objective, to investigate the effects of genetic, prenatal and/or postnatal factors on the development of "essential hypertension" through the use of animal models.

Grants are awarded only to nonprofit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Heart and Vascular Disease Research Program. Applicants funded under the RFA are supported through the customary NIH grant-in-aid, in accordance with PHS policies applicable to Research Project Grants, including cost sharing. However, the RFA solicitation represents a single competition, with a specified deadline for receipt of applications. All applications received in response to the RFA will be reviewed by the same National Institutes of Health (NIH) Initial Review Group.

It is important to call attention to the fact that the RFA application differs from that for the regular research grant in that it is requested that a letter of intent to submit an application be sent by February 15, 1982, and that the applications be received by the April 1, 1982 deadline. More detailed instructions are provided under Section V, Method of Applying.

I. BACKGROUND INFORMATION

A. The Behavioral Medicine Program

As a component of the Clinical Application and Prevention Program of the Division of Heart and Vascular Diseases, the Behavioral Medicine Branch is responsible for support of biobehavioral research activities related to cardiovascular health and disease issues. To this end, the branch seeks to foster collaboration between the biomedical and behavioral science communities on research problems of mutual concern. The scope of the research supported by the branch extends from basic studies on central nervous system - cardiovascular system interaction to health

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Disease Research. 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 A-95 Clearinghouse or Health Systems Agency review.

promotion/disease prevention issues. Focusing on basic research using animal models, the investigations to be supported through this RFA are intended as a primary step in identifying the separate as well as the interactive contributions of genetic and early environmental factors to the development of essential hypertension.

B. Historical Perspective

Hypertension has been brought to the forefront of medical attention by recent studies; the benefits derived from eliminating even mildly increased blood pressures in humans have been demonstrated. Efforts to prevent and treat hypertension, however, have been hampered by a lack of knowledge concerning its etiology. Genetic, dietary, environmental and psychological factors have all been implicated. Epidemiological studies in human populations have demonstrated familial aggregation of hypertension, differences in blood pressure based on dietary practices, and in fact, have implicated both heredity and environment as causal factors for development of hypertension.

Systematic studies of the effects of heredity and environment have been lacking, although there have been notable successes with animal models in selective breeding for hypertension. These efforts have resulted in strains of animals which show marked propensity to develop hypertension spontaneously or under dietary (salt) stress.

The roles of the intrauterine environment, maternal behavior and heredity have not been systematically investigated to determine their relative contributions to the development of essential hypertension. Eating habits, dietary preference, activity, sensitivity to psychological stress, and autonomic responsivity all appear to play some part in this process. Techniques are now available to identify, describe and quantify the relative roles of genetic, intrauterine and maternal factors in the development of neural, cardiovascular and behavioral dysfunctions that could produce high blood pressure.

II. RESEARCH GOALS AND SCOPE

Investigation of the roles of genetic and developmental factors is thus appropriate, using animal models as a basis for understanding possible parallel contributions of genetic or environmental factors in essential hypertension in humans. For illustrative purposes, some general areas of relevant research effort are listed below. Other areas or methodologies may occur to the applicant which would be appropriate to the objectives. New concepts and approaches are encouraged. In all instances, the perceived relationship and importance of the proposed work to the improved understanding of genetic and developmental factors in hypertension should be made explicit.

Embryo transplantation and cross fostering between genetically selected strains of animals are among the techniques that could provide the methodological basis for such proposals. A genetically homogeneous strain of animals predisposed to hypertension can provide the embryos to be transplanted into a normal strain and vice versa. Offspring can either remain with the mother who has carried and delivered them or can be cross fostered to another mother of a similar or dissimilar strain. Physical, psychological, and physiological stressors can be introduced at

various stages of embryonic developmenmt. By combining these approaches, the contribution of heredity, maternal behavior and intrauterine environment to the subsequent development of hypertension can be described.

Such a systematic approach can provide the basis for a series of investigations oriented toward the elucidation of the various risk factors for the development of hypertension. Examples of risk factors which may be investigated include, but are not limited to, dietary preferences, exercise, sodium intake, increased susceptibility and cardiovascular responsivity to psychological stress, or alterations in renal blood flow and subsequent hormonal activity in response to stress.

Applications should identify the hypothesis and clearly outline the questions proposed for investigation. The description of the proposed studies should include the research design and methodology, including procedures for the analysis and interpretation of data.

Potential applicants should review their research proposals in the context of the enunciated program goals and review criteria to reassure themselves that their application is truly responsive; if the relevance and responsiveness of a research proposal to these goals and criteria are tenuous, the application should be considered for submission as a regular research grant application. It should be recognized that the existence of a targeted program and the distribution of a request for grant applications does not preempt the topic from the regular research grant program.

Because this program is one in which the various elements have relevance to one another and may depend upon each other, free communication is expected between the participants. In the preparation of the budget for the grant application, applicants should request travel funds for one, two-day research conference each year, most likely to be held in Bethesda, Maryland.

III. MECHANISMS OF SUPPORT

The support mechanism for this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute--with the concurrence of its National Advisory Council--wishes to stimulate investigator interest in a particular research problem that is important to its program. The RFA solicitation represents a single competition with one specified deadline for receipt of application. All applications in response to an RFA are reviewed by the same initial review group usually for a designated amount of funds or number of awards.

The RFA identifies the scope of the Institute's interest but does not require that the proposal conform to a specific protocol. Thus it is expected that each successful applicant will plan, direct, and carry out the research program. As with any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that this general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a special program need.

Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work and an outline of the phases or

segments into which the proposed project can be logically divided. The total project period should not exceed three years in duration; a September 30, 1982 starting date for the project should be requested.

Although this announcement is included and provided for in the financial plans for Fiscal Year 1982, support of grants pursuant to this Request for Applications is contingent upon ultimate receipt of appropriated funds for this purpose. The total annual funding level for the program is estimated at $300,000. A variety of approaches would be responsive to this solicitation; accordingly, it is anticipated that there will be a range of costs among the individual grants awarded. It is anticipated that 5 to 6 awards will be made if a sufficient number of high quality applications is received; this should be considered in the preparation of the scope of work and budget.

Unless specifically stated to the contrary herein, all policies and requirements which govern the grant program of the PHS apply, including the requirement for cost sharing.

IV. REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with each other. Primary review will be conducted by an Initial Review Group composed primarily of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September, 1982 meeting of the Council.

The major factors considered in evaluating each applications will be:

1. The scientific merit of the application, that is, the questions proposed for study, the research design and approaches, the methodology, and the analysis and interpretation of data.

2. The likelihood of arriving at meaningful and useful data to accomplish the goal of this solicitation.

3. The research experience and competence of the staff to carry out the proposed investigations and the time they will devote to the program.

4. The adequacy of existing and proposed facilities and resources.

5. The organizational and administrative structure of the proposed program.

6. The evidence of institutional commitment to the program.

7. The cost of the proposed research.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research and identification

of any other participating institutions. This letter should be sent no later than February 15, 1982 to:

Dr. Charles L. Turbyfill
Review Branch
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building, Room 553
5333 Westbard Avenue
Bethesda, MD 20205

The Institute requests such letters for the sole purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. Format for Applications

Applications should be submitted on form PHS 398, the application form for a regular research grant. This form is available at the applicant's institutional control office or from the Division of Research Grants, NIH. The conventional format of research grant applications should be utilized, ensuring that the points identified under "Review Procedures and Criteria" (see Section IV above) are fulfilled. Specific attention is directed towards the inclusion of a statement indicating the willingness of the applicant to work cooperatively with other participants in the program and with the National Heart, Lung, and Blood Institute.

C. Application Procedure

The completed application ans six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, MD 20205

An additional twenty (20) copies of the application should be sent or delivered to:

Processing Section
Review Branch, Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building, Room 5A15
5333 Westbard Avenue
Bethesda, MD 20205

To ensure their review, applications must be received by April 1, 1982. Applications not received by this deadline will be considered ineligible and, after discussion with the applicant, may be considered as a regular research grant application. Concerning applications that are determined to be nonresponsive to this announcement, applicants will be contacted to determine if they wish to have the proposal returned or reviewed as a regular research grant.

The outside of the mailing package and the top of the face page of the applications should be labeled "Response to RFA NIH-NHLBI-DHVD-82G-F."

Applications will be accepted and reviewed as follows:

Application Receipt	Initial Review	Council Review	Start Date
April 1	June	September	September 30

VI. IDENTIFICATION OF CONTACT POINTS

Inquiries may be directed to:

Dr. Sonja B. Haber
Behavioral Medicine Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 604
Bethesda, Maryland 20205

Telephone: (301) 496-9380

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

RFA-NIH-NHLBI-DHVD-82G-H

MECHANISMS OF CALCIFICATION OF PROSTHETIC MATERIALS IN THE CARDIOVASCULAR SYSTEM

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 15, 1982

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research leading to a better understanding of the mechanisms of calcification of implanted cardiovascular prostheses.

Calcification of tissue valves in humans impairs their performance and thereby necessitates their replacement; this problem occurs more frequently in children than in adults. Calcification of the flexing elastomeric surfaces of implanted circulatory support devices is a frequent occurrence in calves and often necessitates termination of the experiment. The events which initiate this calcification process are unknown. The purpose of this special program is to stimulate research in this area. It is anticipated that a variety of approaches and expertise could be brought to bear on the solution of this problem. Among the disciplines and expertise which may be appropriate are calcium metabolism, immunology, hematology, pathology, surgery, veterinary medicine, and the physical, chemical and engineering sciences.

The Institute will use the grant-in-aid as the support mechanism, but it will differ from other research grants both in its goal orientation and in the expectation that grantees will exchange information and develop collaborations related to the research supported by this program. The present announcement is for a single competition with a specified deadline of April 15, 1982 for receipt of applications. It is open to all interested investigators, including those who are already the recipients of research grants from the NHLBI. Applications should be prepared and submitted in accordance with the aim and requirements described in the following sections.

I. BACKGROUND

A. The Biomaterials Program

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute has the responsibility to support research which leads to the design or improvement of prosthetic devices for the cardiovascular system. Within this framework, the biomaterials program supports research and development of biocompatible materials suitable for cardiovascular prostheses. Such cardiovascular prostheses may either support or replace a portion of the host

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This program is described in the Catalog of Federal Domestic Assistance, Number 13.837, Heart and Vascular Diseases Research. 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 CF Part 74. This program is not subject to A-95 Clearinghouse of Health Systems Agenc Review.

system which does not function adequately to meet physiologic needs. Basic and applied research in the design and function of heart valves, vascular grafts, intra-aortic balloons, ventricular assist devices and the total artificial heart has been supported through grant and contract programs of the Division of Heart and Vascular Diseases, particularly through the Devices and Technology Branch.

B. Historical Perspective

In the last decade, more than 60,000 xenograft valves have been implanted in adults and children. Recent data indicate that these valves may calcify at a greater rate than natural valves, particularly in the juvenile population. At the same time, it has been noted in experimental systems in calves that not only xenograft valves, but also the elastomeric flexing surfaces of circulatory support devices calcify within a period of a few months. Calcification of other types of cardiovascular prostheses has also been noted, including vascular grafts and materials in the perivascular space. In these situations, the consequences may be impaired physiologic function, failure of the prosthesis, and difficult surgical access when reoperation is required.

On the one hand, calcification is impairing clinical status of valve recipients and on the other it affects experimental progress. The relationship of these two situations is unknown, but is presumed to be related to similar underlying mechanisms. At the moment, there are only a few research studies devoted specifically to unravelling the mechanism and etiology of this process. Since the problem could have a serious impact on clinical care of heart valve recipients and could potentially limit the longevity of circulatory assist devices, additional effort to delineate the mechanisms of the process is necessary.

II. RESEARCH GOALS AND SCOPE

The proposed research should address the evaluation of a hypothesis concerning the mechanism of calcification of cardiovascular prostheses. The test system might be in vitro or in vivo; the role of blood or materials, or both, might be investigated. Ideally, the proposed hypothesis should be tested in a system in which the proposed variable can be manipulated independently and its change can be documented in order to test and verify the hypothesis. Clinical or experimental prosthetic devices may be used or, with adequate justification, an appropriate test configuration may be used. However, it is outside the scope of this RFA to support work for extensive development of new devices.

The role of circulating blood components in initiating or exacerbating the calcification process remains to be defined. Blood proteins, lipoproteins, or cells may contribute to the process, as well as inorganic ions, such as calcium and phosphate. It appears that calcification is related to blood-materials interactions and there is an assumption that it may be a consequence of thrombotic events. Studies which would define such relationships are within the scope of this RFA.

Calcification appears to be most severe on flexing surfaces of cardiovascular devices and therefore may be related to mechanical strain and/or stress. At flexing sites with a strain greater than 20%, injury to either the prosthetic surface or the absorbed biological layer has been noted at sites of frank calcification. The relationship of calcification to stress or the rate of stress/strain development has not been determined. Other factors which can be controlled in the prosthetic design, such as micro- and macro-flow profiles, bulk properties, surface chemistry

or morphology have not been evaluated for possible contribution to the initiation of calcification of tissue or synthetic materials. Studies of such factors are appropriate to this RFA.

For an in vivo experiment, the species and age of the animal model should be clearly specified and justified. The appropriate animal model to predict long-term performance of cardiac devices in adults and children remains to be identified.

Calcification of biological or synthetic cardiovascular prostheses was not recognized as a problem until after extensive experience in humans or long-term implantation in certain animal species. There is a clear need for tests which will predict calcification prior to such late animal or clinical experience. Several types of in vitro systems have been proposed to mimic the calcification process in humans. The validity of these systems remains to be demonstrated. In all studies, it is important to demonstrate that when calcification is observed, it is due to an intrinsic process rather than as a consequence of infection.

It is anticipated that a variety of approaches and expertise could be brought to bear on the solution of this problem. Among the disciplines and expertise which may be appropriate are calcium metabolism, immunology, hematology, pathology, surgery, veterinary medicine, and the physical, chemical and engineering sciences. Each research program supported by this mechanism should have a very focused approach to answer the proposed hypothesis rather than an all-encompassing approach with multiple projects. Domonstrated expertise in the methodologies proposed is advantageous. The roles of all personnel should be clearly identified. If collaborative or subcontracting arrangements are proposed, the effort and justification for all such personnel and other budget items should be specified; all subcontracting arrangements should include authorized signatures from the subcontracting facility which indicate their commitment to the proposed research should a grant be awarded. A clear time plan for staging experiments, plans for integrating experimental results at each stage, the types of controls which will be used for all parameters to be studied, the numbers of replicate experiments required for meaningful interpretation of results, and criteria for acceptance or rejection of the hypothesis should be specified.

III. MECHANISM OF SUPPORT

The support mechanism of this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute--with the concurrence of its National Advisory Council--wishes to stimulate investigator interest in a particular research problem that is important to its program. The RFA solicitation represents a single competition with one specified deadline for receipt of application with all applications to be reviewed by the same initial review group. Although this announcement is included and provided for in the financial plans for FY 1982, support of grants pursuant to this Request for Applications is contingent upon ultimate receipt of appropriated funds for this purpose. The total annual funding level for the program is estimated at $650,000. A variety of approaches would be responsive to this solicitation; accordingly, it is anticipated that there will be a range of costs among the individual grants awarded. It is anticipated that 5 to 7 awards will be made if a sufficient number of high quality applications is received; this should be considered in the preparation of the scope of work and budget. The total project period should not exceed thre years in duration; funds for those projects to be supported by this program will b awarded on September 30, 1982.

The RFA identifies the scope of the Institute's interest but does not require that the application conform to a specific protocol. Thus it is expected that each successful applicant will plan, direct, and carry out the research program. Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work and an outline of the phases or segments into which the proposed project can be logically divided.

As with any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that this general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a specific program need. Ongoing evaluation may include periodic staff visits and the review of formal progress reports. In addition, it is anticipated that participants will exchange information and identify opportunities for collaboration. Applicants should request support to attend an annual two-day research meeting for this purpose; such a meeting would most likely be held in Bethesda, Maryland.

Unless specifically stated to the contrary herein, all policies and requirements which govern the grant program of the PHS apply, including the requirement for cost sharing.

IV. REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with each other. Primary review will be conducted by an Initial Review Group composed primarily of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September, 1982 meeting of the Council.

The major factors considered in evaluating each application will be:

1. The scientific merit of the application to elucidate the mechanisms of calcification of prosthetic materials in the cardiovascular system; that is, the proposed hypothesis, the research design and approaches, the methodology, and the analysis and interpretation of data.

2. The research experience and competence of the staff, including all collaborating investigators, to carry out the proposed investigations and the justification for the effort they will devote to the program.

3. The adequacy of existing and proposed facilities and resources, including proposed subcontractors.

4. The organizational and administrative structure of the proposed program, including timing of experiments and interrelationship and integration of subprojects.

5. Willingness to work cooperatively with other participants in the program.

6. Justification for the cost of the proposed research.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research and identification of any other participating institutions. This letter should be received no later than February 15, 1982 and addressed to:

Dr. Charles L. Turbyfill
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building, Room 553
5333 Westbard Avenue
Bethesda, MD 20205

The Institute requests such letters for the sole purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. Format for Applications

Applications should be submitted on form PHS 398, the application form for a regular research grant. This form is available at the applicant's institutional office of sponsored research or from the Division of Research Grants, NIH. The conventional format of research grant applications should be utilized, ensuring that the points identified under "Review Procedures and Criteria" (see Section IV above) are fulfilled. In order to identify the application as a response to this RFA, check "yes" on Item 2 of the application face page with the tital MECHANISMS OF CALCIFICATION OF PROSTHETIC MATERIALS IN THE CARDIOVASCULAR SYSTEM and the RFA number NHLBI-DHVD-82G-H. Specific attention is directed towards the inclusion of a statement indicating the willingness of the applicant to exchange information with other participants in the program.

C. Application Procedure

The top of the face page of the applications and the outside of the mailing package should be labeled "Response to RFA NIH-NHLBI-DHVD-82G-H". The completed application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, MD 20205

To ensure their review, applications must be received by April 15, 1982. Applications not received by this deadline will be considered ineligible and, after discussion with the applicant, may be considered as a regular research grant application. If an application which is essentially identical has already beer submitted to NIH for review, it must be withdrawn before the new application is accepted. Authors of applications that are considered to be nonresponsive to this

announcement will be contacted to determine if they wish to have the application returned or reviewed as a regular research grant.

Applications will be accepted and reviewed as follows:

Application Receipt	Initial Review	Council Review	Start Date
April 15, 1982	June	September	September 30, 1982

VI. IDENTIFICATION OF CONTACT POINTS

Inquiries may be directed to:

Dr. Frances A. Pitlick
Devices and Technology Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 312
Bethesda, MD 20205

Telephone: (301) 496-1586

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA
RFA-NIH-NHLBI-82G-G

IMAGE ENHANCEMENT TECHNIQUES FOR VISUALIZATION OF CORONARY ARTERIES AND CORONARY BYPASS GRAFTS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 15, 1982

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research involving image enhancement techniques to improve visualization of coronary arteries and coronary bypass grafts. Images of such arteries, their walls, and plaques encroaching upon lumens are often of poor quality and often the image is not clearly visualized because of background noise. The major thrust of this special grant program is to improve image quality by developing better image enhancement techniques. Among disciplines which may be appropriate in this research are mathematics, computer science, pattern recognition, and clinical expertise such as cardiology and radiology.

The Institute will use the grant-in-aid as the support mechanism, but it will differ from other research grants both in its goal orientation and in the expectation that grantees will exchange information and develop collaborations related to the research supported by this program. The present announcement is for a single competition with a specified deadline of April 15, 1982 for receipt of applications. It is open to all interested investigators, including those who are already the recipients of research grants from the NHLBI. Applications should be prepared and submitted in accordance with the aim and requirements described in the following sections. Section V of this announcement specified the method for applying.

I. BACKGROUND INFORMATION

A. The Diagnostic Instrumentation Program

The Devices and Technology Branch of the Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute has the responsibility for the design and administration of programs for research and development of diagnostic instruments applied to the heart and vascular system. The program fosters the development of new knowledge and the translation of results into methods which will have clinical application. A major component of this program is the research and development of instruments for detecting and quantifying atherosclerotic lesions in arteries. Imaging techniques have been especially emphasized. Several projects in this area are supported by grants as a result of investigator-initiated applications. In addition, targeted programs initiated by the Institute have led to support of a number of contracts in the same scientific area.

This program is described in the Catalog of Federal Domestic Assistance, No. 13.837, Heart and Vascular Diseases Research. 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 A-95 Clearinghouse of Health Systems Agency review.

B. Historical Perspective

The areas of research currently supported by research grants include x-ray radiography techniques for studying cardiac structure and function, ultrasonic techniques for studying blood flow, and imaging methods for assessing atherosclerotic lesions. For several years, targeted programs for visualization of atherosclerotic lesions have been supported through research and development contracts. In 1977 several contracts were awarded for research and development of noninvasive methods for imaging arteries using ultrasound and x-ray techniques. The most recent contract awards were in later 1980 for research and development for noninvasive techniques for detection and quantification of atherosclerotic lesions in peripheral and coronary arteries. The eight contracts presently active include four which involve intravenous subtraction angiography, three involving ultrasound B-scan imaging, and one involving nuclear magnetic resonance imaging. In each of these contracts, emphasis is on detecting lesions in deep lying arteries, including coronary arteries.

II. RESEARCH GOALS AND SCOPE

This RFA is intended to encourage grant applications for research to improve image enhancement techniques applicable to images of coronary arteries and coronary bypass grafts.

Several instrumentation techniques which may be applied to imaging atherosclerotic lesions in arteries include ultrasound B-scanning, intravenous subtraction radiography, nuclear magnetic resonance, positron emission tomography, and nuclear medicine methods using radioisotopes. The image quality for each of these techniques is generally inferior to that obtained with intra-arterial angiography. Only when image enhancement techniques are applied can the images obtained approach the quality desired. These image enhancement techniques appear to be reasonably effective when applied to images of carotid or femoral arteries. Intravenous subtraction radiography, ultrasound B-scanning, and nuclear magnetic resonance are techniques which appear promising for coronary artery imaging. Instrument research now being supported by NHLBI indicates that detection of lesions in coronary arteries in humans will be possible using one or more of these less invasive techniques. The problems of close proximity to blood-filled ventricles, distance from arteries to skin surface, motion effects and small lumen diameter, among others, are factors which will contribute to the decreased quality of the resultant images. Additional research in image processing and enhancement techniques may extend present knowledge so as to allow a significant improvement in image quality. A desirable outcome would be that these improved techniques be generally applicable to images regardless of whether they are derived from x-ray, ultrasound, or other instrumentation.

Since coronary artery imaging using techniques other than intra-arterial angiography is in such an early stage of development, it is not possible to be precise regarding image quality. However, it appears that coronary artery images are and will continue to be "noisier" by a factor of five to ten as compared with carotid artery images. Included in the proposals should be the investigator's estimate of the expected level of improvement which may be achieved with the proposed image enhancement techniques. Also included should be quantitative methods for expressing image quality and plans for validation of the proposed technique. Validation should be directly related to demonstrating the improved diagnostic quality of coronary artery or coronary bypass graft images.

Investigators are encouraged to apply techniques which have been used in related high technology fields, e.g., space exploration, high altitude photography. Research and development in these areas may be partially or wholly applicable. Collaborative arrangements with profit-making institutions are possible through subcontrcts.

Applications are invited for any combination of theoretical studies, software development, phantom studies, studies in laboratory animals, or in the clinical setting. Proposals involving multidisciplinary research efforts are encouraged. Some of the disciplines that may be appropriate in this research include mathematics, pattern recognition, computer science, and clinical expertise, such as cardiology and radiology. New concepts and approaches are encouraged. In all instances, the perceived relationship and importance of the proposed work to the improved understanding of image processing and enhancement as related to coronary arteries and coronary bypass grafts should be made explicit.

The proposed research should be dedicated to improving quality of images which are obtainable using current technology. THERE IS NO INTENTION OF SUPPORTING MAJOR INSTRUMENT RESEARCH OR DEVELOPMENT. Applicants should include in their proposals evidence of previous feasibility studies, if applicable, as well as plans for evaluating the performance of the proposed image enhancement techniques.

Potential applicants should review their research proposals in the context of the enunciated program goals and review criteria to reassure themselves that their application is truly responsive. If it is not clearly responsive or the relevance and responsiveness of a research proposal to these goals and criteria are tenuous, the application should be considered for submission as a regular grant application. It should be recognized that the existence of a targeted program and the distribution of a request for grant applications does not preempt the topic from the regular research grant program.

Because this program is one in which the various elements have relevance to one another and may depend upon each other, free communication is expected among the participants. It is anticipated that participants will exchange information and identify opportunities for collaboration. In the preparation of the budget for the grant application, applicants should request travel funds for one, two-day research meeting each year, most likely to be held in Bethesda, Maryland.

III. MECHANISMS OF SUPPORT

The support mechanism for this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute-with the concurrence of its national advisory council-wishes to stimulate investigator interest in a particular research problem that is important to its program. The RFA solicitation represents a single competition with one specified deadline for receipt of applications. All applications in response to an RFA are reviewed by the same initial review group usually for a designated amount of funds or number of awards.

The RFA identifies the scope of the Institute's interest but does not require tha the proposal conform to a specific protocol. Thus it is expected that eac successful applicant will plan, direct, and carry out the research program. As with

any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that this general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a specific program need. Ongoing evaluation may include periodic visits and the review of formal progress reports.

Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work and an outline of the phases or segments into which the proposed project can be logically divided. The total project period should not exceed three years in duration. A September 30, 1982 starting date for the project should be requested.

Although this announcement is included and provided for in the Institute's financial plans for Fiscal Year 1982, support of grants pursuant to this Request for Applications is contingent upon ultimate receipt of appropriated funds for this purpose. The total annual funding level for the program is estimated at $450,000. A variety of approaches would be responsive to this solicitation; accordingly, it is anticipated that there will be a range of costs among the individual grants awarded. It is anticipated that 4-6 awards will be made if a sufficient number of high quality applications is received; this should be considered in the preparation of the scope of work and budget.

Unless specifically stated to the contrary herein, all policies and requirements which govern the grant program of the PHS apply, including the requirements for cost sharing.

IV. REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with one another. Primary review will be conducted by an Initial Review Group composed primarily of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September 1982 meeting of the Council.

The major factors considered in evaluating each application will be:

1. The scientific merit of the application, that is, the theoretical basis for the proposed methodology, its implementation, and the analysis of its performance in improving image quality.

2. The level of improvement of image quality likely to be achieved and the proposed methods for quantifying image quality.

3. The proposed methods for validating how the described technique improves diagnostic quality of images of coronary arteries and coronary bypass grafts.

4. The research experience and competence of the staff to carry out the proposed investigations and the time they will devote to the program.

5. The adequacy of existing and proposed facilities and resources.

6. In applications containing more than one project, the integration of various projects into an effective total program.

7. The organizational and administrative structure of the proposed program, with a clear description of the responsibilities of each of the participating individuals.

8 Willingness to work cooperatively with other participants in the program.

9. Justification for the cost of the proposed research.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research and identification of any other participating institutions. This letter should be received no later than February 15, 1982, and sent to:

Dr. Charles L. Turbyfill
Review Branch, Division of Extramural Affairs
National Institutes of Health
Westwood Building, Room 553
5333 Westbard Avenue
Bethesda, Maryland 20205

The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. Format for Applications

Applications should be submitted on form PHS 398, the appliction form for a regular research grant. This form is available at the applicant's institutional office of sponsored research or from the Division of Research Grants, NIH. The conventional format of research grant applications should be utilized, ensuring that the points identified under "Review Procedures and Criteria" (see Section IV, above) are fulfilled. To identify the application as a response to this RFA, check "yes" on Item 2 of the application with the title IMAGE ENHANCEMENT TECHNIQUES FOR VISUALIZATION OF CORONARY ARTERIES AND CORONARY BYPASS GRAFTS and the RFA number NHLBI-DHVD-82-G-G. Specific attention is directed towards the inclusion of a statement indicating the willingness of the applicant to work cooperatively with other participants in the program.

C. Application Procedure

The completed application and thirty (30) copies thereof should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Building
Bethesda, Maryland 20205

To ensure their review, application must be received by April 15, 1982. Applications not received by this deadline will be considered ineligible and, after discussion with the applicant, may be considered as a regular research grant application. Concerning applications that are non-responsive to this announcement, applicants will be contacted to determine if they wish to have the proposal returned or reviewed as a regular research grant.

The outside of the mailing package and the top of the face page of the applications should be labeled "Response to RFA NIH-NHLBI-DHVD-82-G-G."

Applications will be accepted and reviewed as follows:

Application Receipt	Initial Review	Council Review	Start Date
April 15	June	September	September 30

VI. IDENTIFICATION OF CONTACT POINTS

Inquiried may be directed to:

Dr. Alan S. Berson
Devices and Technology Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 312
Bethesda, Maryland 20205

Telephone: (301) 496-1586

ANNOUNCEMENT

FUNDING NOTICE

Congress and the President have agreed on a third Continuing Resolution affecting spending by agencies of the Federal Government during Fiscal Year (FY) 1982. The Resolution provides spending authority for the National Institutes of Health (NIH) until March 31, 1982, by which time a regular appropriation or a fourth Continuing Resolution must be enacted if NIH is to continue normal operations.

The Continuing Resolution requires NIH to achieve a 4 percent reduction in overall obligations under each of its appropriations from the lower of the proposed House or Senate levels, in contrast to the previous (second) Continuing Resolution which required a 12 percent reduction from the President's March, 1981 request for FY 1982 appropriations. Although detailed funding plans have yet to be developed, NIH expects to issue both new and continuation grant awards with an average 4 percent reduction between now and March 31, 1982. Partial restoration of reductions in previous FY 1982 awards that were based on the second Continuing Resolution will be made to bring them to comparable levels. These restorations will be made as soon as workload permits but in no case later than the end of February, 1982. The funds available for research and development contracts will also be reduced. Within this overall framework, there will be modest variations to accommodate the needs of individual award situations.

The current Continuing Resolution also will entail a reduction of approximately 4 percent in the funds for research training. The number of trainees NIH can support will be reduced by 3-4 percent. The institutional allowance associated with individual fellowships will be $3,000; the corresponding allowance for institutional fellowship awards (training grants) will be up to $2,500 per postdoctoral trainee and $1,500 per predoctoral trainee. Indirect cost reimbursement will remain at 8 percent of total allowable direct costs. There will be no change in the $2,000 allowance for individual fellowships at Federal institutions.

Awardees whose grants have a January 1 continuation start date, or whose competing award has been approved for a January 1 start date, may reasonably expect to receive reduced awards in line with the spending levels authorized by the Continuing Resolution. Awards will probably arrive late because of delayed preparation and slowdowns in holiday mail service. They will, however, be effective for the period beginning January 1, 1982.

NIH will publish additional notices as the details of FY 1982 funding plans are developed.

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