

# NIH GUIDE

# for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Vol. 7, No. 19, December 15, 1978

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*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.*

*Supplements, printed on yellow paper, are published by the respective awarding units concerning new projects, solicitations of sources, and requests for proposals.*

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FOGARTY INTERNATIONAL CENTER,  
SENIOR INTERNATIONAL FELLOWSHIPS

IN

SPECIAL FIELDS:

AGING

ARTHRITIS

DIABETES

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TROPICAL DISEASES

**ANNOUNCEMENT**

As part of its Senior International Fellowship Program and in cooperation with certain Institutes of the National Institutes of Health, the Fogarty International Center announces that several Senior International Fellowship awards will be allocated each year to specified fields for research and study abroad. The fields and cooperating Institutes are:

- Aging - National Institute on Aging
- Arthritis - National Institute of Arthritis, Metabolism,  
and Digestive Diseases
- Diabetes - National Institute of Arthritis, Metabolism,  
and Digestive Diseases
- Epilepsy - National Institute of Neurological and  
Communicative Disorders and Stroke
- Tropical  
Diseases - National Institute of Allergy and Infectious  
Diseases

These awards will be in addition to those made under the broad range of fields of its regular program. The number will be dependent upon the availability of special funds for this purpose and the merit of applications.

The eligibility requirements and general terms are the same as for regular Senior International Fellowships except that the following pertain for these fellowships for the initial year:

Application Deadline - March 1, 1979

Notification of Final Selection Decisions - August 1979

Fellowships may be activated at any time within 12 months of issuance of the Notice of Research Fellowship Award (PHS Form 416).

Concurrent Applications - An application for one of these special fellowships will not be accepted if the applicant has an application under concurrent consideration for a regular Senior International Fellowship. However, if an application for a special fellowship is approved but cannot be funded, upon request it may be held over for consideration in the next cycle for a regular Senior International Fellowship.

An applicant must be a U.S. citizen or permanent resident, be an experienced investigator at mid-career, hold a full-time staff position at a U.S. biomedical research or graduate level educational institution, be nominated by that institution, and have an invitation by a foreign host institution. Awards are made for periods of three to 12 months abroad and provide a stipend, travel costs, and host institution allowance. To be given particular consideration in one of the specified fields, the study proposal in the application must be clearly and directly related to that field but may range from the basic biological mechanisms to clinical aspects.

Individuals interested in being considered for these special fellowships should first familiarize themselves with the general program guidelines for Senior International Fellowships. Application kits will be sent only to offices of Deans or equivalent institutional officials upon request. In order to assure proper processing, all inquiries and application materials submitted should be clearly identified in the following manner: "SENIOR INTERNATIONAL FELLOWSHIP - SPECIAL FIELD ( \_\_\_\_\_ )."  
(Name of Field)

Further information may be obtained from:

Senior International Fellowship Program  
Scholars and Fellowships Program Branch  
Fogarty International Center  
National Institutes of Health  
Bethesda, Maryland 20014

Dr. Mark S. Beaubien  
Telephone: (301) 496-1653

ESTABLISHMENT AND AVAILABILITY OF  
PREVENTIVE CARDIOLOGY ACADEMIC AWARD  
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

**ANNOUNCEMENT**

The Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute is initiating the Preventive Cardiology Academic Award to provide a stimulus for the development of a preventive cardiology curriculum in those schools of medicine and osteopathy that do not have one and to strengthen and improve the preventive cardiology curriculum in those schools that do. Each school of medicine or osteopathy in the United States and its possessions or territories is eligible to compete for one award for a project period that does not exceed five years. The number of awards made each year will depend upon the availability of funds.

For the purposes of the Preventive Cardiology Academic Award, the term preventive cardiology is used to define the area of cardiovascular medicine having a special concern with the development of knowledge and the application of knowledge directed at the prevention of heart and vascular diseases. This includes the area of primary prevention of cardiovascular diseases in individuals who have increased risk of developing such diseases and the reduction of preventable complications or disability in persons who have developed cardiovascular disease.

This award is intended to:

- encourage the development of a high quality preventive cardiology curriculum in schools of medicine and osteopathy that will attract outstanding students to preventive cardiology research and medical practice;
- ensure superior learning opportunities in preventive cardiology;
- develop promising young faculty whose interest and training are in preventive cardiology teaching, research, and practice;
- develop superior faculty who have a major commitment to, and possess educational skills for teaching preventive cardiology;
- facilitate interchange of educational ideas and methods applicable to teaching preventive cardiology among awardees and institutions; and
- develop at the grantee institution the ability to strengthen continuously the improved preventive cardiology curriculum, with local funds, subsequent to the award.

Criteria for the Award

Competitive review of proposals will include an evaluation of the evidence of commitment of both the sponsoring institution and the head of the

cardiology division to the accomplishment of the objectives of the award as well as the qualifications, interest, and commitment of the candidate to undertake responsibility for implementing a high quality preventive cardiology curriculum. Sponsorship of the candidate must be by the head of the division responsible for the teaching and practice of cardiology in the institution. Joint appointments with other departments or schools such as Preventive Medicine, Pediatrics, or Epidemiology would be encouraged when they would lead to a meaningful enhancement of the curriculum, extend concepts of prevention to other teaching areas or enhance the candidate's professional development in preventive cardiology teaching, research, or practice.

The candidate must have sufficient clinical training or research experience in cardiology to be able to develop and implement a high quality curriculum within the institution. If the candidate's background requires further educational development, the plans to acquire this additional training should be described. Relevant training in epidemiology, clinical trials, behavioral science, or other areas could be advantageous in the broader role of the candidate in stimulating preventive cardiology concepts among other peer health professionals in the institution.

#### Provisions of the Award

The nonrenewable Preventive Cardiology Academic Award will include funds for the awardee's salary, fringe benefits, developmental funds, and actual indirect costs not to exceed 8% of total allowable direct costs.

Up to \$30,000 annually will be available to support the academic salary of the awardee who would be expected to devote the majority of his/her time and effort participating in the implementation of curricula or instructional planning in preventive cardiology for medical students. The awardee must devote at least 50 percent of his/her time and effort to the purpose of this award. The awardee may also participate in research, patient care, or administrative activities at his/her institution. The sponsoring institution may supplement salaries from non-Federal funds in accordance with local policies. Awardees should receive a salary commensurate with comparable peers.

Developmental funds may include personnel support necessary to achieve the program objectives; travel funds to enable the awardee to visit other institutions or to attend special meetings, courses or conferences designed to increase his/her knowledge and competence in the teaching/learning process related to preventive cardiology; equipment necessary as teaching aids; supplies necessary to the program objectives; and stipends for a limited number of students to extend their preventive cardiology learning experience during their elective quarter in the academic year.

#### Deadline for Receipt of Applications

Two receipt dates and start dates have been established for the Preventive Cardiology Academic Awards:

<u>Application Receipt</u>	<u>Council Review</u>	<u>Start Date</u>
February 15, 1979	May 1979	July 1, 1979
May 1, 1979	September 1979	July 1, 1980

For Additional Information

Prospective applicants are encouraged to review the Preventive Cardiology Academic Awards Guidelines dated November 1, 1978, which detail the eligibility requirements and application procedures. Requests for copies of these Guidelines and questions related to Preventive Cardiology Academic Awards should be directed to:

Dr. Max A. Heinrich, Jr.  
Manpower Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Room 5A08, Federal Building  
Bethesda, Maryland 20014

Telephone: (301) 496-1724

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NHLBI-DLD-79G-C

BRONCHIAL SECRETIONS: PHYSICAL AND CHEMICAL STUDIES

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

**ANNOUNCEMENT**

The Division of Lung Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research to study respiratory glycoproteins. The scope of this program includes studies on the isolation and characterization of the chemical structure and physical properties of respiratory mucous glycoproteins from normal human subjects and from individuals with chronic airways diseases.

This type of soliciatation (the RFA) is utilized when the Division wishes to stimulate investigator interest in a particular research area that is important to the National Program. Unlike the RFP (Request for Contract Proposals), the RFA identifies the scope of the Division's interest but does not require that the proposal conform to specified research requirements. Moreover, the RFA is supported through the customary NIH grant-in-aid and is governed by the policies for regular research grants. However, the RFA soliciatation represents a single competition, with a specified deadline for receipt of applications. All applications in response to the RFA will be reviewed by the same initial review group.

The present announcement is for a single competition with a specified deadline of March 1, 1979, for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections.

- I. BACKGROUND INFORMATION
- II. GOALS AND RESEARCH SCOPE
- III. MECHANISM OF SUPPORT
- IV. REVIEW PROCEDURES AND CRITERIA
- V. METHOD OF APPLYING
- VI. INQUIRIES

We hope this RFA and participation in this program will be of interest to you.

I. BACKGROUND INFORMATION

A. The Division of Lung Diseases

The Division of Lung Diseases, National Heart, Lung, and Blood Institute, sponsors fundamental and clinical research grants and contracts for the study of normal and abnormal function of the lung. This request for applications is intended to encourage submission of individual research grant proposals designed for the study of the isolation, structure, molecular organization, and physical properties of respiratory mucous glycoproteins from normal human subjects and their variations in individuals with chronic airways diseases.



B. Background

A wide range of human lung diseases have been described in which mucinous material accumulates in the submucosal glands, bronchi, bronchioles, or the alveoli. Increased production of mucus and the inability to clear the airways of secretions, are critical factors in the pathology of many of these diseases. Because mucous glycoproteins are the primary determinants of the rheological properties of these secretions, any alterations of these molecules resulting in changes in their rheologic properties could be responsible for widespread and damaging obstructive events.

Much of the information currently available on human mucous glycoproteins has been derived from studies on ovarian cyst secretions. Only limited data are available on pulmonary secretions. This paucity of information, especially on secretions from normal human subjects, is due to practical problems such as the relative inaccessibility of lower respiratory tract, inability to quantitatively standardize the conditions for collection of secretions and the difficulties with fractionation of these heterogeneous gel-like macromolecules, which are insoluble in physiological media. Reduction of disulfides and carboxymethylation, both of which solubilize the gels, have been of some value in conjunction with affinity, ion exchange and exclusion chromatographic techniques and electrophoresis. Comparative chemical studies carried out on mucous glycoproteins isolated from tracheobronchial secretions of patients with cystic fibrosis demonstrated increased sulfation of glycoproteins in cystic fibrosis but no major differences in the peptide or oligosaccharide composition. Furthermore, histochemical observations confirmed a relative increase of sulfate groups in the epithelia of mucus-secreting cells in patients with cystic fibrosis. However, compositional and structural data are lacking for human respiratory glycoproteins from normal individuals and patients with chronic airways diseases.

II. GOALS AND RESEARCH SCOPE

The primary goal of this program is the characterization of the chemical and physical properties of normal human respiratory glycoproteins and their pathologic counterparts. Also of interest is elucidation of the interactions which result in the obstructive events observed in pathologic states.

Proposals submitted in response to this announcement should be addressed to studies on the separation, purification, structural, and physical characterization of glycoproteins from normal human respiratory mucus and comparisons with mucus from various airways diseases. Studies on pathologic material should include comparisons with samples from subjects without evidence of airways disease. Proposals may include plans to study mucins from animal sources if their similarity to human respiratory glycoproteins can be convincingly established. Each application should clearly define the rationale, background, and specific aims of the proposed studies and provide details of the methods and procedures to be used. Some possible approaches are suggested below.

A. Materials

Collection of respiratory mucus from normal individuals in amounts sufficient for analytic studies is difficult; this lack of sufficient materials has hampered progress in its characterization. There is, consequently, a need for effective methods for securing uncontaminated tracheobronchial mucus secretions from human sources, especially from normal subjects. In addition to the direct collection of the secretions, explant cultures maintained in media containing radiolabelled precursor substances can provide labelled glycoprotein materials suitable for certain analytical studies. Collection by fiberoptic bronchoscopy, lung lavage, and cell cultures offer additional approaches. Development of innovative approaches which would provide secretions useful for these studies are encouraged. Proposals should include details of the procedures planned for securing the secretory products.

B. Structural-Chemical Studies

Some approaches that are potentially useful for separation and purification of solubilized mucous glycoproteins are ion-exchange and affinity chromatography, electrophoresis and gel chromatography. Structural characterization should include demonstration of the purity of the fractions under study and of their homogeneity with respect to size, charge, antigenic determinant(s), etc. The composition and structural details of the protein backbone and the oligosaccharide side chains, including peptide sugar-linkages, disulfide bonds, amino acid and carbohydrate sequences, terminal sugars and sites and extents of sulfation and sialylation are of particular interest. Microheterogeneity with regard to the amino acid sequence or the oligosaccharide side chains of these glycoproteins needs to be evaluated to determine its biological significance.

C. Rheological and Other Physico-Chemical Studies

The abnormal viscosity of respiratory secretions in such disease states as cystic fibrosis is believed to cause many of the obstructive events observed. However, it is not known whether the altered rheological properties correlate with changes in the chemical and/or other properties of these macromolecules. The structural-chemical studies indicated above may be complemented with physical characterization of the purified glycoproteins. These studies might include molecular weights and hydrodynamic properties, sedimentation patterns, gel-filtration behavior, hydration, molecular mobility, and aggregation characteristics. Rheological properties of the purified components, either alone or in combinations, may be correlated with their chemical and other physical characteristics. Studies of interest include specific polymer-polymer and polymer-ion interactions and the variations in these interactions due to change in pH and concentrations of the other constituents. Viscometry, light

scattering, and gel permeation chromatography may also be considered. Studies of the effects of mycolytic and other pharmacologic agents on the physical characteristics of the pulmonary secretions are encouraged.

The research areas cited above are illustrations only. Proposals need not be restricted to these approaches nor is it required that they all necessarily be incorporated in a single proposal. However, it must be noted that since structural elucidation of human respiratory glycoproteins is the central goal of this program, proposals dealing solely with physical studies will not be supported unless they also include structural-chemical studies. Proposals concerned only with methodology development will likewise be unacceptable.

### III. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional 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 between investigators who participate in this program.

Although this program is included and provided for in the financial plans for fiscal year 1979, award of grants pursuant to this request for grant applications is contingent upon ultimate receipt of appropriate funds for this purpose. A variety of approaches would represent valid responses to this announcement. Accordingly, it is anticipated that there will be a range of costs among individual grants awarded. Applicants are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the total project period of this proposal must not exceed five years. At the end of the project period, renewal proposals may be submitted for competitive review. A project period start date of September 28, 1979, is anticipated.

The current policies which govern the research grant programs of the NIH will prevail.

### IV. 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 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 one already submitted to 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 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 relative to the work proposed.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a one-page letter of intent which includes a very brief synopsis of proposed areas of research and identification of any other participating institutions. This letter should be sent no later than February 1, 1979, to:

Dr. J. Sri Ram  
Division of Lung Diseases  
National Heart, Lung, and  
Blood Institute  
National Institutes of Health  
Room 6A11, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20016

The Institute requests such letters only to provide an indication of the number and scope of applications to be received. A letter of intent is not binding; it will not enter into the review of any proposal 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 the traditional research grant. The conventional presentation in format and detail for regular research grant applications should be utilized. Specific attention is directed toward 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 and 6 copies should be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Room 240, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20016

To ensure their review, applications must be received by 5:00 p.m., EST, on March 1, 1979.

A brief covering letter should accompany the original application indicating that it is submitted in response to this program announcement: NHLBI, BRONCHIAL SECRETIONS: PHYSICAL AND CHEMICAL STUDIES.

VI. INQUIRIES

Inquiries may be directed to:

Dr. J. Sri Ram  
Division of Lung Diseases  
National Heart, Lung,  
and Blood Institute  
National Institutes of Health  
Room 6All, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20016

Telephone: (301) 496-7332

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NHLBI-DLD-79G-D

RESPONSE OF THE PULMONARY ENDOTHELIUM TO INJURY,

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

**ANNOUNCEMENT**

The Division of Lung Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research to study the response of the pulmonary endothelium to injury. The scope of this program includes studies directed toward characterizing the anatomical and functional properties of pulmonary endothelium and how these properties may be altered by various types of injury and disease.

This type of solicitation (the RFA) is utilized when the Division wishes to stimulate investigator interest in a particular research area that is important to the National Program. Unlike the RFP (Request for Contract Proposals), the RFA identifies the scope of the Division's interest but does not require that the proposal conform to specified research requirements. Moreover, the RFA is supported through the customary NIH grant-in-aid and is governed by the policies for regular research grants. However, the RFA solicitation represents a single competition with a specified deadline for receipt of applications. All applications in response to the RFA will be reviewed by the same initial review group.

The present announcement is for a single competition with a specified deadline of March 1, 1979, for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections.

- I. BACKGROUND INFORMATION
- II. GOALS AND SCOPE
- III. MECHANISM OF SUPPORT
- IV. REVIEW PROCEDURES AND CRITERIA
- V. METHOD OF APPLYING
- VI. INQUIRIES

We hope this RFA and participation in this program will be of interest to you.

I. BACKGROUND INFORMATION

The pulmonary vascular endothelium is a major structural and functional component of lung tissue. The pulmonary endothelium is actively involved in storage, synthesis, and metabolism of vasoactive materials such as prostaglandins, polypeptides, and amines. There is an extensive surface on which these blood-borne substances can be metabolized, bound, or transported into tissues. In addition, the vascular endothelium maintains a nonthrombogenic surface at the interface of blood and tissues. The integrity of the endothelial

surface is, therefore, essential to the normal function of the lung, and injury can result in abnormal exchange of materials between blood and tissues, altered metabolism of vasoactive substances, and thrombus formation.

The pulmonary endothelium is particularly vulnerable to injury. A variety of mechanical or chemical insults, including radiation, drugs, hyperoxia, hypoxia, or proteolytic enzymes can cause structural derangement and loss of normal function. The response of the endothelium to a particular type of injury and the implications for development of pulmonary disease are not well understood. Damage to the pulmonary vessels by drugs or other blood-borne agents undoubtedly occurs first at the luminal surface and probably affects the metabolic transport functions of endothelium. Damage to surrounding tissues, e.g., by radiation, can result in adherence of leukocytes to endothelium and further injury due to release of proteolytic enzymes. Such injuries may affect secretory functions and also could possibly contribute to thrombus formation. Once these facts are known, it may be possible to determine how endothelial damage leads to pathologic changes in lung diseases and how various interventions can prevent or alter the magnitude of those changes. For example, the role of endothelial injury in acute adult respiratory distress syndrome, pulmonary embolism, and pulmonary hypertension still needs to be defined.

## II. GOALS AND SCOPE

The specific goal of this program is to encourage submission of individual research grant proposals to study the structural and functional properties of pulmonary endothelium and how these may be altered by various types of injury and repair. Studies should be designed to determine the specific response of the endothelium to a particular intervention, such as hypoxia, radiation, hyperoxia, drugs, or proteolytic enzymes. The proposed studies can utilize whole animal preparations, isolated lungs, organ cultures, or cell cultures. The normal functions of the endothelium, e.g., enzymatic activities, transfer properties, or secretory mechanisms, must be defined for the proposed experimental system.

A general approach might include the following topics:

### A. Alteration of Endothelial Transport Functions by Injury

It has only recently been appreciated that pulmonary endothelium is involved in the active transport of amines, drugs, and prostaglandins and that it may be an important site of drug metabolism. Additional investigations are needed to elucidate transport functions and how they are affected by changes in O<sub>2</sub> and CO<sub>2</sub>, drugs, or other interventions. It is also not known how mediators of inflammation (which may have direct effects on endothelial cells) can affect the mechanisms of uptake and metabolism. A variety of chemical agents, e.g., chemotherapeutic agents, antimicrobial agents, and herbicides, cause lung damage in man, possibly by affecting endothelial

transport mechanisms. Studies that focus upon endothelial transport function in response to these interventions should help to determine the mechanisms of lung damage.

B. Interactions of Blood Components and Endothelium

Since the luminal surface of vessels is continually in contact with circulating blood, various humoral components and formed elements can readily influence endothelial cell function. A growing body of evidence indicates that injury to vessels or surrounding tissue results in adhesion of platelets and leukocytes to the vascular wall. The temporal sequence of these events, relative to endothelial cell injury, needs to be established. The contribution of leukocytes, platelets, and other factors to endothelial injury should be assessed. Substances such as proteolytic enzymes or prostaglandins from these cells should be identified and their role in injury defined. In addition, the role of kinins, complement, and other mediators of inflammation in the adherence of leukocytes to the pulmonary endothelium needs to be examined. Information derived from such studies should help to determine the role of the endothelium in thrombus formation and in inflammatory reactions of the pulmonary circulation.

C. Regeneration and Repair of Pulmonary Endothelium Following Injury

The normal vascular endothelium has a slow rate of turnover, but as in all tissue, there is spontaneous loss of cells and replacement. As endothelial cells die and are shed, cell replication maintains the protective barrier between blood and the vessel wall. It is important to determine the temporal sequence of cell replication and repair of injured endothelium under various experimental conditions, e.g., hyperoxia, pulmonary hypertension, etc. Since various substances from blood and blood cells can stimulate cell replication, the interaction of blood components with the processes of repair should be investigated.

The research topics presented above are intended only to indicate the scope of research that would meet the goals of this program. Investigators are not restricted to these approaches nor do they have to include all of them in a single proposal. Investigators are encouraged to consider other approaches. The emphasis of the proposal, however, must be specifically directed toward elucidating the anatomical or functional responses of the pulmonary vascular endothelium to injury and repair. The proposal should include a detailed description of the experimental intervention used to produce the injury as well as the methods used to assess endothelial damage and repair.



This program is to support only studies of pulmonary vascular endothelium. Studies of systemic vascular endothelium will not be considered an acceptable response to this announcement nor will studies of the mechanics of fluid and solute exchange associated with pulmonary edema fulfill the requirements of this request.

### III. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional 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 between investigators who participate in this program.

Although this program is included and provided for in the financial plans for fiscal year 1979, award of grants pursuant to this request for grant applications is contingent upon ultimate receipt of appropriate funds for this purpose. A variety of approaches would represent valid responses to this announcement. Accordingly, it is anticipated that there will be a range of costs among individual grants awarded. Applicants are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the total project period of this proposal must not exceed 5 years. At the end of the project period, renewal proposals may be submitted for competitive review. A project period start date of September 28, 1979, is anticipated.

The current policies which govern the research grant programs of the National Institutes of Health will prevail.

### IV. 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 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 one already submitted to 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 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 relative to the work proposed.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a one-page letter of intent which includes a very brief synopsis of proposed areas of research and identification of any other participating institutions. This letter should be sent no later than January 15, 1979:

Dr. Carol E. Vreim  
Division of Lung Diseases  
National Heart, Lung,  
and Blood Institute  
National Institutes of Health  
Room 6A03, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20016

The Institute requests such letters only to provide an indication of the number and scope of applications to be received. A letter of intent is not binding; it will not enter into the review of any proposal 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 the traditional research grant. The conventional presentation in format and detail for regular research grant applications should be utilized. Specific attention is directed toward 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.

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5333 Westbard Avenue  
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To ensure their review, applications must be received by 5:00 p.m. EST on March 1, 1979.

A brief covering letter should accompany the original application indicating that it is submitted in response to this program announcement: "RESPONSE OF THE PULMONARY ENDOTHELIUM TO INJURY."

VI. INQUIRIES

Inquiries may be directed to:

Dr. Carol E. Vreim  
Division of Lung Diseases  
National Heart, Lung, and  
Blood Institute  
National Institutes of Health  
Room 6A03, Westwood Building  
Bethesda, Maryland 20016

Telephone: (301) 496-7034

BASIC AGING PROGRAM,  
EXTRAMURAL AND COLLABORATIVE RESEARCH PROGRAM,  
NATIONAL INSTITUTE ON AGING

A D D E N D U M

The following information supplements the announcement by the National Institute on Aging originally published in the *NIH Guide for Grants and Contracts*, Vol. 7, No. 12, September 1, 1978:

Applicants responding to this announcement are instructed to type the phrase "NIA BASIC AGING PROGRAM" on the upper margin of the face page of the application.

MINORITY AGING,  
NATIONAL INSTITUTE ON AGING

**ANNOUNCEMENT**

I. BACKGROUND INFORMATION

The National Institute on Aging (NIA) was established in 1974 to conduct and support biomedical, behavioral, and social research and training related to the aging processes and the diseases and other special problems and needs of the aged.

Although research is being conducted on the psychological and social issues relevant to aging, little of this research focuses specifically on the aging of racial and ethnic minorities. Because of the dearth of research in this area, the NIA invites research grant applications on psychosocial aging of minorities. A major question to be considered is whether psychological and social response to aging is different for racial and ethnic minorities than for the white or majority population and, if so, are there different adaptive or coping responses brought to bear to deal with aging. Research on aging of minorities provides not only opportunity to learn more about subgroups and aging, their particular problems, and especially their strengths and adaptability, etc., but also by comparison provides the opportunity to learn more about aging in the majority population.

II. GOALS AND SCOPE

Research on aging is a relatively new field, and research on aging of ethnic minorities is an even newer area of concentration. Available studies on aging minorities are extremely limited and have dealt primarily with needs assessment, service delivery, and utilization. In general, life expectancy, health status, and environmental influences are less favorable for minorities than for whites; however, within the last few decades, there have been historic and cultural changes

which have no doubt had impact on the lives of minority group members and no doubt upon the aging of these members. The lack of reliable baseline data on these groups limits our ability to understand the impact of these changes on aging as well as a number of other variable such as social and environmental strain and adaptation. There is a need for research to focus on commonalities in the way in which minority groups respond to a variety of circumstances and situations in aging as well as isolating unique characteristics and response patterns.

Research is sought on socio-cultural factors which impact on differential life expectancy such as socioeconomic status, occupation, lifestyle, environmental conditions, and health care practices. Information on family structure, social networks, and problems associated with life transitions and their impact on aging of minorities is also sought. Specifically, the NIA seeks grant supported research which characterizes psychosocial aging of ethnic minorities. Several research areas are suggested below; however, support is not limited to these areas.

- A. Determination of the demographic characteristics of minority elderly, e.g., numbers, location, education, socioeconomic status, mortality trends.
- B. Studies of psychosocial and cultural characteristics of aging minorities and the impact of these characteristics on life expectancy as compared to aging majority population members. Determination of differential attitudes toward aging.
- C. Impact of diets and health status on aging, including predisposition to certain diseases.
- D. Characterization of problem solving skills and styles, particularly as responses differ from majority population responses.
- E. Research on perceptual-attentional characteristics, e.g., the selectivity of cues and events from the environment and how these vary in different ethnic groups of elderly in relation to adjustment and survival.
- F. Identification of personal strengths and other characteristics which are influential in coping with problems associated with aging.

Relevant research on aging of minorities in addition to the specific areas outlined above is welcomed by the National Institute on Aging.

### III. MECHANISM OF SUPPORT

The support of this program will be the traditional NIH grant-in-aid. Applicants are expected to plan and execute their own research programs. Support of grants pursuant to this request for applications is, of course, contingent upon ultimate receipt by NIA of appropriate funds

for this purpose. The intent is to budget funds specifically for this program.

IV. REVIEW PROCEDURES AND CRITERIA

A. Application Review

Upon receipt, applications will be assigned by the Division of Research Grants, NIH, for initial review by an appropriate Study Section. Final review will be by the National Advisory Council on Aging.

B. Review Criteria

Applications must be relevant to the goals of this announcement. The factors considered in evaluating applications are:

- scientific merit of the research design, approaches, and methodology;
- adequacy of existing and proposed facilities and resources;
- qualifications and experiences of principal investigator and proposed staff for the conduct of the proposed investigations;
- reasonableness of the subject and duration in relation to the proposed research;
- adequacy of time to be devoted by proposed project staff.

V. METHOD OF APPLYING

Use the standard research grant application form PHS 398 which is available in your institution's business office or in its central application control office. If not available at your institution, contact:

Division of Research Grants  
National Institutes of Health  
Bethesda, Maryland 20014

Telephone: (301) 496-7591

Type the phrase "MINORITY AGING" on the face page of the application. Enclose a covering letter stating that the application is in response to this announcement. Send NIA a copy (see below). Follow the instructions included with the application form PHS 398, making sure that items noted in Section IV of this announcement are covered appropriately. Forward to:

Division of Research Grants  
Room 240, Westwood Building  
5333 Westbard Avenue  
National Institutes of Health  
Bethesda, Maryland 20014

Receipt dates for research grant applications in response to this announcement are March 1, 1979, and July 1, 1979.

VI. INQUIRIES AND CORRESPONDENCE

Inquiries and correspondence should be directed to:

Associate Director for Extramural  
and Collaborative Research Programs  
National Institute on Aging  
National Institutes of Health  
9000 Rockville Pike  
Bethesda, Maryland 20014

Attention: Ms. Shirley Bagley

THE GENETIC BASIS OF AGING:

DROSOPHILA AS A MODEL SYSTEM,

NATIONAL INSTITUTE ON AGING

**ANNOUNCEMENT**

I. BACKGROUND INFORMATION

The National Institute on Aging (NIA) conducts and support biomedical, behavioral, and social research and research training related to aging processes and the diseases and other special problems and needs of the aged.

The objective of NIA-supported biomedical research is to improve the quality of life during the normal life span. To facilitate achievement of health maintenance or enhancement in the course of senescence, the NIA seeks to understand the molecular basis for senescence and longevity. Comparative studies using relatively simple organisms may provide the first insight to these basic mechanisms.

Phenotypic expression of life span is a readily predictable feature of most metazoan organisms. The genetic basis is not known for senescence. The NIA encourages the use of invertebrates, with genetic-research qualities, to study the genetic basis of senescence and longevity.

The relationship between specific developmental stages of an organism and subsequent senescence and longevity is not understood. This may be of particular significance should the genetic control be the programming of a developmental sequence and the eventual senescence secondary to genetic program, i.e., an expression of a decay in one or more systems of the organism subsequent to development.

The proposed program emphasizes investigations pertaining to, but not limited to, the following areas in Drosophila genetics:

- A. Population genetics to elucidate evolutionary strategies and selection pressures which establish longevity patterns in wild and experimental populations of Drosophila.
- B. Isolation of developmental and longevity mutants which show promise for identification of specific gene products with key relationships to events determining longevity and senescence.
- C. Identification and/or development of mutants or strains that can be used in somatic mosaic studies with the potential to provide knowledge on the genetic control of senescence and longevity.
- D. Transplantation studies, which enable a differential expression of genetic factors related to senescence and longevity.



- E. Cell, tissue, and organ culture studies of *Drosophila* complementary to the program on the genetic basis of senescence and longevity.
- F. Research on the biology of *Drosophila* at the molecular, biochemical, and physiological levels to complement genetic studies of longevity and senescence.

## II. GOALS AND SCOPE

Goals of NIA incorporated in this announcement are to understand the genetic basis for longevity and senescence in *Drosophila*: that is, the specific genes, their products, and the function of those products that most directly relate to control of longevity and, if appropriate, to the senescence phenomenon. Anticipated findings are not expected to relate, necessarily, to senescence in mammals but should lead to more precise scientific inquiry of aging in mammals.

## III. MECHANISM OF SUPPORT, FUNDING

The support for this program will be via the traditional NIH research project grant. Applicants are expected to plan and execute their own research programs. Support of grants pursuant to this announcement is contingent upon ultimate receipt of appropriate funds for this purpose.

## IV. REVIEW PROCEDURES AND CRITERIA

### A. Application Review

Upon receipt, applications will be assigned by the Division of Research Grants to an initial review group for scientific merit review and to an appropriate Institute or Division for final review by their National Advisory Council/Board.

### B. Review Criteria

Applications must be relevant to the goals of this announcement. The factors considered in evaluating applications are:

- scientific merit of the research design, approaches, and methodology;
- adequacy of existing and proposed facilities and resources;
- qualifications and experiences of the principal investigator and proposed staff for the conduct of the proposed investigations;
- rationale of the subject and duration of the project in relation to the proposed research.

V. METHOD OF APPLYING

A. Application Procedure

Use the standard research grant application form PHS 398. If the institution's business office or central application control office does not have this form, an individual copy may be requested by writing to:

Office of Grants Inquiries  
Division of Research Grants  
National Institutes of Health  
Bethesda, Maryland 20014

Telephone: (301) 496-7441

Type the phrase "NIA DROSOPHILA GENETICS PROGRAM" in the upper right hand corner of the face page of the application. Enclose a covering letter stating that the application is in response to this announcement. Send the NIA a copy (see below).

Follow the instructions with the application form PHS 398 making sure that items noted in Section IV of this announcement are covered appropriately. Forward to:

Division of Research Grants  
Room 240, Westwood Building  
5333 Westbard Avenue  
National Institutes of Health  
Bethesda, Maryland 20014

Receipt dates for research grant applications in response to this announcement are no later than: March 1, July 1, and November 1.

VI. INQUIRIES AND CORRESPONDENCE

Inquiries and correspondence should be directed to:

Basic Aging Program  
Extramural and Collaborative  
Research Program  
National Institute on Aging  
National Institutes of Health  
Bethesda, Maryland 20014

Telephone: (301) 496-9350

MACULAR DISEASE

RESEARCH GRANT APPLICATIONS SOUGHT BY THE RETINAL

AND CHOROIDAL DISEASES PROGRAM

OF THE NATIONAL EYE INSTITUTE

**ANNOUNCEMENT**

The National Eye Institute's Retinal and Choroidal Diseases Program maintains continuing interest in abnormalities associated with the macular region of the retina which include loss of central visual acuity and depressed color vision. Collectively, these pathological conditions are referred to as macular degenerations and constitute an area of exceptional importance in terms of disease processes and resultant vision loss, as well as in scientific interest and research opportunity. With our present state of knowledge, degenerative disorders of the macula can neither be prevented nor cured and are considered to be one of the most difficult visual disease problems to manage clinically. Until more information is obtained about disease mechanisms, little more can be done for the patient than observe the development of macular degenerations, limit therapy to symptomatic measures, and localize the disease process on an anatomical basis.

The purpose of this announcement is to emphasize the need for new and more comprehensive interdisciplinary studies to increase our fundamental knowledge base with respect to the structure and physiology of this region of the retina as well as the etiology and pathogenesis of its disorders. Examples of research areas identified by the National Advisory Eye Council in its recent report entitled Vision Research - A National Plan requiring further investigation include:

1. The temporal events in the pathogenesis of early and late onset of macular diseases need further study. Information on biochemical, physiological, and anatomical changes in the retina, retinal pigment epithelium, Bruch's membrane, and retinal and choroidal vasculature needs to be correlated in terms of the disease process.
2. The macular region is predisposed to degenerative changes, and laboratory studies of differences between central and peripheral retinal structure and functions are needed to better understand the increased susceptibility of the macular region to disease.

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This announcement is made under authority of Section 451 of the Public Health Service Act as amended (42 CH. 6A, subch. III). National Eye Institute research grants are administered in accord with law, regulation, and policy as described in the *Public Health Service Grants Policy Statement*, October 1, 1976 [DHEW Publication (OS) 77-50,000] and Addendum [DHEW Publication (OS) 77-50,000-A].

3. The maintenance of photoreceptor metabolism and of intra- and intercell membrane-barriers are essential in order to avoid retinal edema and abnormal accumulation of fluids under the retina which may lead to loss of visual acuity, retinal detachment, and ensuing blindness. Further research efforts are needed to address the relationship between the neural retina and blood-retinal barriers.
4. Angiogenic factor(s) may exist and have a role in choroidal and retinal neovascularization. There is need for cell biologists to develop isolation and bioassay procedures in order to study the factor(s).
5. Chemicals, drugs, and systemic medications should be evaluated to learn if they have a high affinity for the retinal structures and may alter membrane physiology and photoreception. Studies are needed to address the sites of action of these agents in the visual system and reasons for high affinity of certain of these agents for ocular tissues. Efforts are also encouraged for studies on the mechanism of action and nature of the toxic changes produced by these agents in the macular region as a means of studying specialized regions of the retina.

#### APPLICATION SUBMISSION AND REVIEW

Submission of research grant applications addressing these fundamental problems is encouraged. It is expected the fundamental studies will eventually impact upon improved prevention and control of macular diseases.

National Institutes of Health peer review procedures will be followed for all responses to this announcement. Applicants must use the regular research grant application form PHS 398 which is available at institutional central application control offices. Please identify grant application submitted in response to this announcement by writing at the top of the face sheet of the application "SUBMITTED IN RESPONSE TO NEI PROGRAM ANNOUNCEMENT ON MACULAR DISEASE". The completed application should be mailed to:

Division of Research Grants  
Room 240, Westwood Building  
National Institutes of Health  
Bethesda, Maryland 20016

where it will then be assigned for consideration and review according to the NIH referral guidelines for research grants. The scientific quality and the technical merit of all applications will be evaluated by a National Institutes of Health Study Section and by the National Advisory Eye Council. Approved applications will compete for available funds with all other approved applications assigned to the National Eye Institute. Potential applicants are encouraged to communicate with National Eye Institute staff early in the process of preparing applications.

Application receipt dates are March 1, July 1, and November 1 of each year. Applications received after any one receipt date are considered and reviewed together with those received by the next receipt date. The earliest possible award date is approximately nine months after receipt date.

Preliminary drafts of proposals and other inquiries regarding this announcement and the report Vision Research - A National Plan may be addressed to:

Retinal and Choroidal Diseases Program  
Scientific Programs Branch  
National Eye Institute  
National Institutes of Health  
Bethesda, Maryland 20014

NONHUMAN PRIMATES AVAILABLE



The National Institutes of Health has established several supply sources of nonhuman primates. These sources were established to assure a supply of animals for National Institutes of Health (NIH) and Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) supported projects. Animals available from these sources in the near future are as follows:

Rhesus monkeys - Macaca mulatta

- 100 females - domestically bred, over 1 year of age, 1.5 - 3.5 kg  
Price - \$474
- 150 males - domestically bred, over 1 year of age, 1.5 - 3.5 kg  
Price - \$474
- 200 females - domestically bred, less than 1 year of age, under 1.5 kg  
Price - \$384
- 200 males - domestically bred, less than 1 year of age, under 1.5 kg  
Price - \$384
- 30 adult females - wild caught, nonbreeders but otherwise healthy  
Price \$474

Cynomolgus monkeys - Macaca fascicularis

- 10 females - domestically bred, over 1 year of age, 1.5 - 2.5 kg  
Price - \$315
- 15 males - domestically bred, over 1 year of age, 1.5 - 2.5 kg  
Price - \$315
- 30 females - domestically bred, less than 1 year of age, under 1.5 kg  
Price - \$225
- 35 males - domestically bred, less than 1 year of age, under 1.5 kg  
Price - \$225

Squirrel monkeys - Saimiri sciureus

- 10 males - domestically bred of Colombian stock, over 1 year of age,  
500 - 700 grams - Price - \$240
- 10 males - domestically bred of Colombian stock, less than 1 year of age,  
350 - 500 grams - Price \$200
- 10 females - domestically bred of Bolivian stock, over 1 year of age,  
500 - 700 grams - Price - \$240
- 10 males - domestically bred of Bolivian stock, over 1 year of age,  
500 - 700 grams - Price - \$240
- 12 females - domestically bred of Bolivian stock, less than 1 year of age,  
350 - 500 grams - Price - \$200
- 12 males - domestically bred of Bolivian stock, less than 1 year of age,  
350 - 500 grams - Price - \$200
- 11 females - domestically bred of Guyanan stock, over 1 year of age,  
500 - 700 grams - Price - \$240
- 7 males - domestically bred of Guyanan stock, over 1 year of age,  
500 - 700 grams - Price - \$240
- 39 adult females - wild caught, Guyanan animals, excess breeders  
Price - \$100

Except for the wild caught animals, the dates of birth and the sex are available upon request. Unless specifically requested otherwise, rhesus monkeys, but not the squirrel monkeys, will be vaccinated against measles. Requests for special handling, specimens, and procedures will be considered.

Investigators in nonprofit institutions who wish to obtain animals from the above groups for use in biomedical and behavioral projects are invited to submit requests for them. The requests in letter form should indicate the source of support for the using project and, if supported by NIH or ADAMHA, the title and number of the grant or contract. The request should also include a specification of the animals required, including number, age, sex, or other special characteristics, and state what, if any, requirement there will be to obtain animals from captive bred sources in future years. Such requirements for future supply from captive bred sources will be honored whenever feasible. The entire request should not exceed one typewritten page. It should be addressed to:

Dr. Charles McPherson  
Chief  
Animal Resources Branch  
Division of Research Resources  
Room 5B59, Building 31  
National Institutes of Health  
Bethesda, Maryland 20014

Priority will be given to requests for use on NIH and ADAMHA supported projects received prior to March 1, 1979, and after that all requests will be honored on a first-come/first-served basis.

The price indicated for each animal includes shipping costs. These funds will be paid directly to the contractor supplying the animals and will be credited to the NIH supported breeding program to provide partial support for the breeding colonies.

PROTECTION OF HUMAN SUBJECTS



Title 45, Code of Federal Regulations, Part 46, PROTECTION OF HUMAN SUBJECTS, has been amended by an interim final regulation. The interim final regulation adds a new element to the definition of Informed Consent in 46.103(c) as follows:

"(7) With respect to biomedical or behavioral research which may result in physical injury, an explanation as to whether compensation and medical treatment is available if physical injury occurs and, if so, what it consists of or where further information may be obtained. This subparagraph will apply to research conducted abroad in collaboration with foreign governments or international organizations absent the explicit nonconcurrence of those governments or organizations."

The interim final regulation, which will become effective on January 2, 1979, and accompanying explanations appeared in the *Federal Register*, Vol. 43, No. 214, Friday, November 3, 1978, at 51559. Copies of the *Federal Register* notice and an explanation have been sent to the 5,000 names on the Office for Protection from Research Risks mailing list. Additional copies of the reprint and explanation are available from Doris McGuire, telephone (301) 496-7541, or through the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Maryland 20014.

The interim final regulation is to become effective in advance of public comment and without prior notice. However, public comment is requested on the policy of including advice on the availability or nonavailability of compensation and medical treatment for injuries resulting from research and on the specific amendment.

The regulation is not intended to require compensation nor to change existing law. The intent is only to give the prospective subject information which he or she may use in deciding whether to participate.

For the present, the Office for Protection from Research Risks offers the following advice on the implementation of this amendment:

- All new research proposals and competing renewals reviewed by Institutional Review Boards after January 2, 1979, shall utilize the definition of informed consent as amended.
- After the above date, if a research subject who is part of an ongoing research project asks about compensation or treatment for physical injury, then that individual is entitled to receive correct and complete information on the matter.
- The institution must designate an individual or official from whom information on the availability of compensation or treatment can be obtained.



- Section 46.103(c) (7) refers only to research in collaboration with foreign governments and international organizations, not to institutions in foreign countries.
- Suggested wording for consent forms: "I understand that in the event of physical injury resulting from the research procedures, (state what is available, e.g., 'medical treatment for injuries or illness is available'/'only acute/immediate/essential medical treatment [including hospitalization]is available'/'monetary compensation is available for wages lost because of injury'; or what is not available, e.g., 'financial compensation is not available, but medical treatment is provided free of charge,' etc.)."

The Secretary of Health, Education, and Welfare requests comments from you and your colleagues on the interim final regulations, Informed Consent - Definition Amended to Include Advice on Compensation. Your response should be forwarded to:

Director  
Office for Protection from  
Research Risks  
National Institutes of Health  
Bethesda, Maryland 20014

within 60 days of this publication notice. A prompt reply is necessary.

Questions on the regulation and its implementation should be directed to:

Charles MacKay, Ph.D.  
Deputy Director  
Office for Protection from  
Research Risks  
National Institutes of Health  
Bethesda, Maryland 20014

Telephone: (301) 496-7005

DISTRIBUTION AND UTILIZATION OF PRIMATE MODELS

FOR

ATHEROSCLEROSIS AND HYPERTENSION

**NOTICE**

The Division of Heart and Vascular Diseases, NHLBI, is supporting through contracts a program to breed and model nonhuman primates for studies of atherosclerosis and hypertension. This program was prompted by the growing evidence of the value of the nonhuman primate as a model of choice for studies into the pathophysiology of atherosclerosis, hypertension, cerebrovascular disease, and dyslipoproteinemia; the impending shortages in nonhuman primates from import sources; and the knowledge that colony reared animals can provide a better characterized animal for study.

Since 1975, six species of nonhuman primates have been under resource and model development: Baboons and African green, rhesus, squirrel, patas, and stump-tailed monkeys. A seventh species was introduced in the Fall of 1977: the cynomolgus monkey. The animals and their colony reared progeny are maintained in modelled regimens as well as in control groups. In addition to the effort supported by the DHVD Primate Model Program, each resource site possesses distinctive ancillary aspects valuable to many of the potential users of the resource colonies. A brochure describing the specific aspects of the individual sites and the species and modelling is in preparation. See the Table attached for a general outline of species and modelling available from existing primate resources and the address of the resource directors who may be contacted for further information.

We are presently entering the utilization phase of the effort and are inviting requests to use the available resources - requests from the atherosclerosis, hypertension, and cardiovascular research community, in particular, as well as the scientific community at large. Priority will be given to NHLBI and NIH supported grantees, but meritorious requests from others will be entertained where possible, given the limited number of animals which will be available for utilization.

The resource program is designed to allow maximum utilization without compromising the breeding colony or modelling procedures. The following criteria developed by the Federal Interagency Primate Steering Committee will be considered as basic elements in evaluating any request for utilization of the animals.

1. That the research proposed can be done best with primates, i.e., that no other known system or other kind of animal could produce comparable results.
2. That the species of primate proposed is the most appropriate and that some other more plentiful species would not be adequate.
3. That the number of primates proposed is the minimum that will produce acceptable scientific results.

4. That the primates will not be sacrificed during or at the end of the study except in those cases requiring termination as part of the investigation.
5. That, if autopsy is deemed necessary, positive action will be taken to share tissue when feasible.

In general, requests are likely to fall within three areas of use. For descriptive purposes these categories have been designated as:

- o Category 1 - i.e., drawing blood samples, collecting urine samples, studies with minimal or no perturbation.
- o Category 2 - i.e., metabolic, dietary, surgical studies, or such long term studies which do not compromise the animal's future role in the resource.
- o Category 3 - i.e., procedures of such a nature that the animal's future role in the colony setting is compromised - the animal has clearly decreased or no value for other experiments in the future; terminal studies.

These three general types of use will require varying degrees of review. Two Use Panels will review requests on the basis of (a) scientific merit, (b) program relevance, (c) specific need for captive reared animals, (d) practicality of performing studies at the resource site, and (e) in those cases where animals are transferred, documented ability of the applicant institution to house and care for primates properly. (An institutional assurance, accepted by the Office for Protection from Research Risks, NIH, will provide such documented ability, as will accreditation by the AAALAC. See *NIH Guide for Grants and Contracts*, Vol. 7, No. 17, November 10, 1978.)

Each contractor will establish an On-site Use Review Panel comprised of the appropriate contract staff and outside consultants, as necessary. In addition there will be a DHVD Use Review Panel comprised of NHLBI and NIH staff, expert consultants, and the Project Officer as Executive Secretary.

Routine use requests in Category 1 will be reviewed/approved by the contractor in conjunction with the On-site Use Review Panel, utilizing customary merit criteria.

Category 2 studies will be reviewed/approved by the contractor in conjunction with the On-site Use Review Panel. In certain cases these requests may be referred to the Project Officer and the DHVD Use Review Panel.

Category 3 use requests will be reviewed collaboratively by the contractor, the Project Officer, and the DHVD Use Review Panel.

Procedures to be employed in the use of the resource, such as animal care, veterinary care, quarantine, necropsies, operating room use, data management, etc., and the cost of these procedures will also be considered in the review of requests to use the resource.

Multiple use of animals, such as sharing body tissues and fluids when an animal is terminated and concurrent studies, will be given highest priority when feasible.

Any appeal of requests for routine or non-invasive use denied at the contractor level may be addressed to the Project Officer and the NHLBI's Use Review Panel.

It is emphasized that users of the resource must at least share the cost of such use. Funds received from users shall be credited to the contract to help pay the costs of developing and maintaining the resource.

The requests, in letter form, should include the title and number of the NHLBI/NIH grant supporting the research or other support as appropriate, the names of the major coinvestigators (if any), a short description of the research project, a specification of the animals required including number, age, sex, or other special characteristics, if animals are to be studied at resource site or transferred. The entire request should not exceed two typewritten pages, and when appropriate should be addressed to the specific resource contact. A copy of this request should also be sent to Ms. Nanci C. Briggs, Project Officer, National Institutes of Health, National Heart, Lung, and Blood Institute, Room 4C16, Federal Building, Bethesda, Maryland 20014.

If an investigator needs more information about the resources to plan a proposal, he may write the Director of each program directly for additional information.

Also, requests of a general nature should be addressed to Ms. Briggs for referral coordination. The investigator will be notified in writing of the outcome of his/her request.

This is an announcement of the limited availability of primates from the resources maintained by the National Heart, Lung, and Blood Institute.  
IT IS NOT A REQUEST FOR APPLICATIONS FOR RESEARCH GRANTS.

NHLBI-SUPPORTED PRIMATE RESOURCES

Institution		African Green	Baboon	Cyno	Patas	Rhesus	Squirrel	Stump Tail
Bowman Gray School of Med. Wake Forest University Winston-Salem, N.C. 27103	Chronic Ather.* Control*			X	X			X
Dr. Thomas B. Clarkson	Arterio. Susceptible Arterio. Resistant					X X		
Hahnemann Med. College 235 North 15th Street Philadelphia, Pa. 19102	Spontaneous Hyper.* Controls*	X X						
Dr. E. T. Angelakos								
Harvard Medical School New England Regional Primate Research Center One Pine Hill Drive Southborough, Mass. 01772	Spontaneous Hyper.* Controls*			X X				
Dr. J. Alan Herd								
Litton Bionetics 5516 Nicholson Lane Kensington, Md. 20795	Chronic Athero.* Controls*	X X			X X	X X	X X	X X
Dr. David Martin								
Southwest Foundation P.O. Box 28147 8838 West Commerce Street San Antonio, Texas 78284	Controls* Chronic Athero.* Hypertension*		X X X					
Dr. Henry McGill								

\*Progeny available from modelled and control colonies

TABLE

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA  
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

**ANNOUNCEMENT**

*LEGIONNAIRES' DISEASE*

I. INTRODUCTION

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for research in the ongoing problem of Legionnaires' Disease (LD). There is a growing body of information about LD, yet many critical gap areas in our knowledge of this disease remain. It is of crucial importance that these information gaps be bridged so that medical and health care professionals will be better prepared to study and to deal with the diagnosis, prevention, and treatment of this disease.

Our present knowledge indicates that LD is primarily an acute, febrile disease that often presents as a severe pneumonia. It is now known that the putative causal organism is a fastidious, gram-negative bacterium, showing no close relationship to other gram-negative bacteria. Serologic and cultural data have linked this bacterium, or others very similar to it, to earlier recorded outbreaks of a severe pneumonia-like disease for which no specific cause could be found at that time. It has now been reported that LD is also found in patients within the hospital setting; rise in antibody titer has also been noted in hospital employees. The disease can therefore be considered as a potential nosocomial infection. As a result of this newer information, debilitated or immunosuppressed patients may now be considered at greater risk of acquiring this disease.

In addition to the widely-reported and more spectacular epidemics, such as occurred in Philadelphia, Pennsylvania; in Bloomington, Indiana; and elsewhere, it is now recognized that sporadic cases are quite common. Cases of the disease have been reported from nearly a dozen countries; it is entirely possible that, as our diagnostic techniques improve, sporadic cases may well be identified worldwide.

As a result of the growing recognition of the importance of LD, a symposium on this disease was held at the Center for Disease Control (CDC), Atlanta, on November 13-15, 1978, sponsored jointly by CDC, the NIAID, and the World Health Organization (WHO). The symposium conferees discussed every aspect of the disease problem, from the clinical illness, through epidemiology, to diagnostic and therapy methods. The conference proceedings will be published in the Annals of Internal Medicine.

## II. RESEARCH SCOPE

In an effort to stimulate and broaden the scope of research in the U.S. on this disease problem, the NIAID is inviting applications from interested researchers who are highly motivated either to expand their ongoing research to include studies on LD or to initiate entirely new research problems in LD. The areas of research interest of the NIAID are broad and can include any or all of the following general categories (these are not listed in any specific priority order):

- A. Clinical disease manifestation; therapy;
- B. Pathology;
- C. Biology of the causal organism - cultural characteristics, biochemical properties, ultrastructure and morphology, antigenic relationships and antigen composition; the ecological niche of the causal organism;
- D. Animal model systems; pathogenesis;
- E. Role of toxic or other virulence factors;
- F. Immunology and host-parasite interactions; cellular immune responses, humoral immunity and the role of antibody;
- G. Epidemiology - host range, methods of spread, nosocomial infections, contributing factors;
- H. Diagnostic methods - serological, cultural, and other techniques.

## III. APPLICATION PROCESS

Research grant proposals submitted to the NIH will be reviewed by the normal NIH peer review system, i.e., initial review by an appropriate Study Section and final review by an Advisory Council. Funding of approved grant proposals will be based on priority scores as recommended by the reviewing groups as well as the availability of funds.

Applications, on form PHS 398, should be forwarded to:

Division of Research Grants  
National Institutes of Health  
Room 240, Westwood Building  
Bethesda, Maryland 20014

Receipt dates will be the same as for all new research grant proposals to the NIH, i.e., March 1, July 1, and November 1 of each calendar year.

For further information on this program or related research programs  
of the NIAID, please contact:

Milton Puziss, Ph.D.  
Chief  
Bacteriology and Virology Branch  
MIDP, NIAID  
National Institutes of Health  
Room 738, Westwood Building  
Bethesda, Maryland 20014

Telephone: (301) 496-7728



REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NHLBI-DHVD-79G-G

HYPERTENSION SPECIALIZED CENTERS OF RESEARCH

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

**ANNOUNCEMENT**

I. INTRODUCTION

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute announces a national competition to establish a limited number of SPECIALIZED CENTERS OF RESEARCH (SCOR) devoted to HYPERTENSION.

The objective of the Institute in renewing this program is to focus resources, facilities, and manpower on particular problems and to expedite the development and application of new knowledge essential for improved diagnosis, treatment, and prevention of hypertension.

II. BACKGROUND

United States Public Health Service surveys indicate that there are at least 35 million Americans who have hypertension. This represents over 15% of the adult population, with the prevalence among the black population near 30%.

Hypertension is a major contributing factor to cardiovascular death and disease. It is associated with a reduced life expectancy due to an increase in frequency of stroke, heart attack, heart failure, and kidney failure. Although the detection and control of hypertension continue to increase primarily through greater public awareness and more widespread use of diet and drug therapy, the identification of the underlying cause in the great majority of cases of hypertension is still unknown. Because so many people are affected by hypertension and because of the potential for serious complications, it would be especially desirable to prevent it. An increased emphasis on fundamental research is needed to accomplish this.

III. OVERVIEW

A thorough understanding of the etiology and pathogenesis of hypertension will be required to achieve its effective treatment and prevention. The objective of the Hypertension SCOR program is to expedite the development and application of new knowledge essential for improved diagnosis, treatment, and prevention of hypertension. Each SCOR research program should represent a multidisciplinary approach to either fundamental research or clinical research, or preferably an interactive combination of fundamental and clinical research, focused on particular problems dealing with one or more types of hypertension (including labile, mild, essential, malignant, primary aldosteronism, renal, and other secondary forms).

Although the research programs will vary as a function of local talent, interest, and resources, each SCOR should have a central theme to which all individual projects should relate. The following are examples of such topics: renal and endocrine factors contributing to the development and maintenance of essential or secondary hypertension; pathophysiology of vascular smooth muscle resulting from hypertensive disease or vasoactive agents; the kidney as a regulator of arterial pressure - including the renin-angiotensin-aldosterone system and its interaction with sympathetic nervous system; the role of the central nervous system in hypertension; the relationship of vasoactive systems such as kallikrein-kinin, prostaglandin, and other lipid materials to etiology of hypertension; juvenile hypertension; epidemiological and clinical studies of genetic, constitutional, and environmental factors related to hypertension; and interrelationships of cardiovascular dynamics, fluid compartment volumes, and sodium balance. This list is not to be regarded as complete or exclusive.

This third competition for Hypertension SCORs represents an open competitive continuation of the present extramural program which currently has an annual funding base of \$4.4 million. This is not a commitment to expend any or all of these funds, but it is anticipated that on the order of five or more Hypertension SCORs might be supported. It should be emphasized that there is no necessary relationship between the cost and size of a SCOR and the quality of scientific research to be carried out.

#### IV. CHARACTERISTICS OF A SPECIALIZED CENTER OF RESEARCH

##### A. Description

A SCOR should be an identifiable organizational unit within the sponsoring institution. Each applicant organization will be expected to propose its own program based on local interests and resources. The research program should consist of a planned attack upon problems associated with etiology, pathogenesis, prevention, diagnosis, or treatment of hypertension.

Each SCOR will identify specific objectives that will represent the primary theme of the proposed hypertension research. A SCOR may address several objectives provided that the resultant combination can be shown to be related directly to the primary theme. The relationship of each project to the theme of the overall SCOR proposal will be given considerable attention in the review of the proposal. Funds may also be requested to support core resources.

-Facilities must be available for the primary needs of the SCOR and must require no more than moderate modification. Funds for new construction are not available. The applicant institution must be willing to make a long-term commitment of physical resources and staff necessary for development and operation of the SCOR. Also the participating staff must be outstanding, experienced, and willing to make a long-term commitment.

## 1. Mechanisms of Support

Although the support mechanism for SCORs will be the grant-in-aid, it will differ from other research grants both in its emphasis on goal orientation and in the degree of coordination by the National Heart, Lung, and Blood Institute (NHLBI). While it is expected that the SCOR will plan, direct, and execute its own research program, it must also be responsive to the identified needs of the NHLBI both as to program content and direction. Applicants may request support for a period of five years.

(The Hypertension SCORs should not be confused with the National Research and Demonstration Centers that the NHLBI supports. A Research and Demonstration Center includes research, demonstration, and education elements, while the emphasis of a SCOR is on research.)

A SCOR differs from a program project in that the area for research (i.e., hypertension) is identified by the NHLBI as well as by the closer coordination of the program by the NHLBI staff as discussed below.

Although this third solicitation for Hypertension SCORs is included and provided for in the financial plans for Fiscal Year 1981, support of grants pursuant to this request for applications is contingent upon ultimate receipt of appropriated funds for this purpose. The current program represents an ongoing effort involving four grants which have a total annual funding base of approximately \$4.4 million (including overhead). It is not possible to predict the level of future funding at this time. This will be influenced by the amount of funds available to the Division, by the overall merit of proposals, and by their relevance to the program goal. 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.

## 2. Relationship to the National Heart, Lung, and Blood Institute

The award of a SCOR grant will establish a special collaborative relationship between the NHLBI and the grantee institution. To accomplish this, a scientific program officer will be designated by the NHLBI to work closely with the staff of the SCOR. The staff member will advise the SCOR about the Institute's research goals and will participate in decisions affecting the level of support, rebudgeting of funds, initiation of new projects, etc. The program officer will coordinate plans for special projects of mutual interest to the Institute and the SCOR and will also coordinate activities among all Hypertension SCORs. The program officer will make regular visits to each SCOR to evaluate progress and to provide assistance in administrative matters.

B. Operational Aspects

1. Responsibility of the SCOR Director

The SCOR director should be a respected scientist who can provide strong, effective scientific and administrative leadership. The director will be responsible for the organization and operation of the SCOR and for communication with the NHLBI on all scientific and operational matters.

2. Within a SCOR

Each SCOR will be responsible for developing an individualized research program that reflects local interest, talents, and resources. The research program for each SCOR will be evaluated annually by an internal review board consisting jointly of staff members and other expert consultants not part of that SCOR program. This board will advise the SCOR Director of its assessment of progress on current projects and conduct an initial review of new initiatives. Although SCOR grantees will work within the workscope of the approved program, they will be encouraged to pursue promising leads including pilot studies. The incorporation of a new project into the SCOR program will be considered by the NHLBI and its advisors for final action.

The interaction of scientists from various disciplines within a SCOR must be more than a casual one brought about by a mutual interest in "hypertension." The active collaboration of the various investigators on projects of mutual interest is a necessity for an effective SCOR. In addition, the nature of the SCOR concept will be greatly enhanced if all investigators are aware of the activities of the entire program. To meet this need, each SCOR should plan to have seminars in which staff members describe their own current research activities or relevant work by other investigators.

3. Relationship between SCORs

An active collaboration between the Hypertension SCORs is one of the more important concepts of the NHLBI SCOR program. To accomplish this goal, SCOR directors will meet twice a year to review progress, discuss common interests and problems, and plan collaborative efforts. One additional meeting a year will be attended by key SCOR staff, and other invited investigators having mutual scientific interests.

The SCORs also will be encouraged to hold workshops on topics of mutual interest to SCOR grantees. The workshops, although planned by the SCOR staff, will provide an opportunity to invite other scientists carrying out hypertension research relevant to

SCOR activities. A workshop could be initiated by a SCOR or by the NHLBI. The workshops and meetings will help the NHLBI assess current problems, accomplishments, and needs in hypertension research. They will also enable interested members of the scientific community to participate in and be kept abreast of SCOR activities.

## V. METHOD OF APPLYING

### A. Letter of Intent

The NHLBI should receive a letter of intent not later than the close of business on March 3, 1979, from all prospective applicants. The Institute requests such letters in order to have a reasonable estimate of the number of applications to be expected and to begin planning for the review. A letter of intent is not binding and will not enter into the review of any proposal subsequently submitted. The letter should briefly describe the SCOR's overall approach.

Letters should be addressed to:

Dr. Charles L. Turbyfill  
Review Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Room 553, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20014

### B. Format for Applications

Proposals for Specialized Centers of Research should be submitted on form PHS 398, using the format outlined below.

1. Title Page: The title should be "Hypertension Specialized Center of Research."
2. Table of Contents: This should afford quick reference to specified budgets, sections, etc., of the application.
3. Introduction: This should be an outline of the proposed research objective(s) of the SCOR's central theme and how all individual components of the program relate directly to this theme.
4. Research Projects: Each proposed research activity should be detailed separately with its requested budget. For clinical investigation projects, the criteria for selecting patients for the study should be included, as well as the anticipated number of patients to be studied annually.

For experimental projects, the hypotheses on which they are based, their relevance to the clinical studies (if any are proposed) and to the SCOR's goals, and how their progress will affect other SCOR activities, should be stated.

The relevance of each project to the SCOR's central theme should be clearly described. The means of integrating activities and data from specific projects with those of other projects should also be explained.

Any "core" activities or "centralized" laboratories (i.e., those shared by several or all investigators) should be described to show how they will support the proposed research. Core budgets must also be provided in detail.

The proposal for each project and core facility must be described in sufficient detail for experts to assess its merit.

#### Format for Individual Projects

Title:

Responsible Investigator: Include other primary contributing professionals.

Specific Aim: Include hypotheses to be tested.

Method of Procedure: Detailed methodology needs to be submitted only when it departs from standard practice. However, in all instances there should be sufficient information to show the investigator's grasp of the proposed methodology and an understanding of its possible problems or limitations.

Significance: This section should indicate how results obtained will be relevant to the SCOR's primary theme and integrated with other projects in the SCOR.

Previous Work by Responsible Investigators:

Related Ongoing Research: To be funded from sources other than the SCOR.

Previous Work by Others: Summary, including literature references.

#### 5. Facilities

- a. Describe facilities available to the SCOR.
- b. For any proposed alterations or renovations, include line drawings to demonstrate feasibility, adequacy, and relationship to other relevant facilities. (No funds for new construction will be available.)

- c. Describe the geographic distribution of space and personnel comprising the SCOR. Geographic proximity is desirable, but not mandatory.
6. Central Instrumentation and Data Management
  - a. Describe major items of equipment available.
  - b. Describe and justify needs for major equipment in terms of research to be accomplished.
7. Patient Availability (if clinical studies are proposed)

The patient population, community physician cooperation, etc., should be outlined and documented.
8. Organization and Administration
  - a. Describe the administrative relationships of the proposed SCOR within the sponsoring institution.
  - b. Indicate the department or office of the university which will have administrative responsibility for the SCOR through its director.
  - c. Describe the relationship of the SCOR with other departments or research groups (Centers, Institutes, etc.).
  - d. Specify the arrangements for appointing a replacement SCOR Director if the need should arise.
  - e. Describe the internal and external procedures for monitoring the proposed research and providing ongoing quality control and scientific review.
  - f. Describe the organizational framework of the SCOR itself.
  - g. Illustrate lines of responsibility in the SCOR for:
    - o administrative matters
    - o planning and conduct of research
    - o patient care (if applicable).
9. Other Research Support

List all active, pending, or planned research support of all participants. While more than one source of support might be applied toward an investigator's research, duplication of funding for a given project is not allowed. Support to be relinquished should be clearly designated.

10. Budget: The budget must be presented as follows:  
(See NOTE on budget categories)

- a. Detailed first year budget for each proposed research or core project. This should precede the relevant project proposal. A summary budget for all years of requested support should also be included.

If collaborative efforts or "purchased services" are anticipated, all costs associated with the third party participation (including any applicable indirect costs) should be itemized under the "Other Direct Costs" budget category. For details, please refer to *The NIH Guide for Grants and Contracts*, Vol. 4, No. 8, September 19, 1975, or contact NHLBI staff.

- b. Detailed composite budget for all requested support for the first year.
- c. Summary budget, by category only, for all years of requested support. [Budgets (b.) and (c.) above, should be placed before the textual description of the SCOR proposal.]

NOTE: Budget Categories

- A. Personnel - List professional and non-professional personnel using the format indicated in the application.
- B. Consultant Services
- C. Equipment - (a) Purchase; (b) Rental
- D. Supplies
- E. Hospitalization Costs (if applicable)
- F. Outpatient Costs (if applicable)
- G. Travel - Support for both domestic and foreign travel may be requested by the applicant. However, grant funds for foreign travel may be expended only upon specific prior approval by the NHLBI. Sufficient travel funds should be budgeted to cover the cost of SCOR meetings. (See section IV.B.3. "Relationship between SCORs")
- H. Alterations and Renovations - A maximum of \$75,000 may be requested during the entire project period.
- I. Publication Costs
- J. Other Direct Costs

11. Biographical Sketches:

Each investigator participating in the SCOR should supply a biographical sketch and selected bibliography. Complete bibliographies may be requested at the time of review but need not be included in the application.



12. Appendices

If a facet of the proposal requires further detailed description, it may be placed in an appendix. However, appendices should be kept to an absolute minimum.

C. Submission of Proposals

The original and twenty-four copies of the full SCOR application must be received by June 8, 1979. Applications should be sent to:

Division of Research Grants  
National Institutes of Health  
Room 240, Westwood Building  
Bethesda, Maryland 20014

The material should be clearly identified as a proposal for a Hypertension Specialized Center of Research. A covering letter should accompany the application indicating that it is submitted in response to this announcement. A copy of the covering letter should be sent to Dr. Turbyfill (see address given in paragraph V.A.-"Method of Applying - Letter of Intent").

VI. CRITERIA FOR SCIENTIFIC REVIEW

The applications for Specialized Centers of Research solicited in this announcement will be evaluated in national competition with each other. Initial review will be conducted by a primary review group of predominantly non-Federal consultants with selected scientific expertise and may involve a site visit. 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 February 1980 meeting of the Council.

The criteria for evaluation listed, in order of importance, will include:

- A. The scientific merit of the SCOR's primary research objective (central theme), its importance to hypertension research, and rationale for the planned attack on the designated problems.
- B. The scientific merit of each individual project (i.e., the questions proposed, the research design, the methodology, and the analysis and interpretation of data) and the project's relationship to the central theme of the overall proposal.
- C. Willingness to work cooperatively with other SCORs and the NHLBI (See IV. A.2 and B.3)

- D. The administrative leadership ability of the SCOR Director, the research competence of all professional personnel, particularly the SCOR Director.
- E. The Institutional arrangements for:
  - 1. internal and external quality control of ongoing research
  - 2. allocation of funds
  - 3. day-by-day management
  - 4. SCOR seminar programs.
- F. The amount requested in relation to proposed research program.
- G. Institutional commitment to SCOR goals.
- H. The academic and physical environment in which the research will be conducted.
- I. The Institutions' arrangements for:
  - 1. providing continuity for the program
  - 2. fiscal responsibility in handling awarded funds.

VII. TIMETABLE FOR REVIEW

- A. Deadline for receipt of letters of intent: March 3, 1979.
- B. Deadline for receipt of applications: June 8, 1979.
- C. Primary review of applications by a SCOR Ad Hoc Scientific Merit Review Committee: July 1979.
- D. Site visits (if required) and collection of additional information will be held between September and November of 1979 and then a second meeting of the SCOR Ad Hoc Scientific Merit Review Committee will be held.
- E. Secondary review by the National Heart, Lung, and Blood Advisory Council: February 7-9, 1980.  
Applicants may expect to be advised of the Council's decision on their proposal about February 18, 1980.
- F. Project beginning date: December 1, 1980.

VIII. INQUIRIES

Questions regarding the Hypertension SCOR Program should be addressed to:

Hypertension and Kidney Diseases Branch  
National Heart, Lung, and Blood Institute  
Federal Building  
National Institutes of Health  
Bethesda, Maryland 20014

Telephone: (301) 496-1857

The staff will strive to provide consultation to all who desire it regarding preparation of the application or on any other matter relevant to the SCOR Program. However, the inability to provide staff consultation cannot justify extension of the deadline for receipt of applications or any other special consideration.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NHLBI-DHVD-79G-F

STUDIES ON THE EFFECTS OF HYPERTENSION AND

VASOACTIVE AGENTS ON THE VASCULATURE,

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

**ANNOUNCEMENT**

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research on mechanisms linking increased blood pressure and vasoactive agents to vascular damage, reflected as abnormal vascular structure or function. The research could involve a large variety of studies that might serve to define these mechanisms.

This type of request (the RFA) is utilized when the Division wishes to stimulate investigator interest in a particular research area that is important to the Institute's National Program. Unlike the RFP (Request for Proposals), the RFA identifies the scope of the Division's interest but does not require that proposals conform to narrowly specified research protocols, requirements, or methodology. Support will be provided through the customary NIH grant-in-aid but it differs from other research grants in its goal orientation. While it is expected that each of the successful applicants will plan, direct, and execute his/her own research program, that program and any substantial modifications must be mutually agreed upon by the participant and the National Heart, Lung, and Blood Institute.

The present RFA is for a single competition with a specified deadline of April 6, 1979, for receipt of applications. The review of all applications in response to this RFA will be arranged by the NIH Division of Research Grants. Applications should be prepared in accordance with the aims and requirements which are described in the following sections. This RFA does not in any way interfere with the freedom of investigators to apply for regular research grants in the customary manner in this or in related fields of investigation; however, two identical applications cannot be under consideration at the same time. Funded applications will be administered by the Hypertension and Kidney Diseases Branch of the Division of Heart and Vascular Diseases.

The announcement's information is outlined as follows:

I. PROGRAM SPECIFICATIONS

- A. Background Information
- B. Goal and Scope
- C. Mechanism of Support

II. METHOD OF REVIEW AND CRITERIA FOR REVIEW

- A. Review Procedures
- B. Review Criteria

III. METHOD OF APPLYING

- A. Letter of Intent
- B. Application Format
- C. Application Procedure

If you have any questions related to this announcement, you should contact Mr. Armando Sandoval of the Hypertension and Kidney Diseases Branch, NHLBI, telephone: (301) 496-1857.

We hope that this RFA and participation in the program will be of interest to you.

I. PROGRAM SPECIFICATIONS

A. Background Information

The Hypertension Research Program of the Division of Heart and Vascular Diseases supports multifaceted approaches to the problem of hypertension. Through grants and contracts, it supports investigations on many research aspects of hypertension, e.g., behavioral, circulatory, endocrine, neural, renal, etc. The projects range from studies of blood pressure regulation to development of diagnostic and therapeutic measures. While the effects of hypertension and vasoactive agents on the vasculature are presently being investigated with a variety of approaches, there is a need for new insights into the mechanisms linking increased blood pressure and/or vasoactive agents to vascular damage.

Experiments in this area have revealed a number of structural and functional differences in hypertensive and normotensive vasculatures which have been interpreted as vascular damage caused by the hypertensive state. There is a considerable amount of literature relating vascular injury to high arterial pressure. In general, many of the vascular complications of hypertension approximately parallel the level and duration of blood pressure, and hypertension appears to interact with other risk factors in inducing vascular injury. A lowering of blood pressure will, for the most part, ameliorate or prevent the development of some of the vascular changes from hypertension. However, since the structure and function of the normal blood vessel or of its damaged counterpart are not well understood, the mechanisms involved have not been defined and little is known of the specific mechanisms by which hypertension may injure the vasculature and enhance atherogenesis, or how antihypertensive therapy impacts on this process.

With respect to vasoactive agents, the concept that substances such as angiotensin II, catecholamines, kinins, and prostaglandins influence vascular permeability and induce vascular lesions in hypertension is not a new one. Recently though, interest in this relationship has been stirred by studies suggesting that elevated angiotensin II can be vasculotoxic. A need exists to delineate the effects on the vasculature of both naturally-occurring substances, such as hormones, as well as other agents such as hypertensive and antihypertensive drugs.

There are also recent studies which have linked immunological changes to hypertension, vasoactive agents, and vascular damage. However, cause and effect relationships have not been firmly determined.

It is our hope that definition of the multiple adverse effects of hypertension and of vasoactive agents on the vasculature will lead to a better understanding of one of the major consequences of this public health problem.

#### B. Goal and Scope

The goal of this RFA is to focus research efforts on mechanisms linking hypertension and vasoactive agents to vascular damage.

Since relatively little is known about these mechanisms, the scope of this RFA is flexible in order to accommodate a variety of proposals that would be potentially responsive. In the light of this goal, suitable models of hypertension (including man) may be used; the injury-prone (including atherosclerosis-prone) portions of the vasculature may be investigated, and attempts should be made to define and quantitate the "damage" or "injury" observed. All types of hypertension may be studied. Investigation could range from measurement of bulk properties of the vessel (e.g., the thickness of the arterial wall) to measurements of specific chemical components (e.g., calcium in the regulation of contraction), and it may be concerned with the vascular endothelium, the cells and cell products of the intima or media, or the integrated structure and function of the vessel. It may apply to large or small arteries or arterioles but studies limited to the vasculature of the heart are not appropriate. A variety of disciplinary approaches are possible. If the effects of drugs are to be studied, the main thrust of the proposal should concentrate on mechanisms linking hypertension and vasoactive agents to vascular damage. Since this is a very complex research area, interdisciplinary collaborations are encouraged. A proposal should reflect the research strengths of the investigator(s) rather than attempt to explore all conceivable parameters.

#### C. Mechanism of Support

The support mechanism for this program will be the grant-in-aid. It will differ from the usual research grants in its goal

orientation. While it is expected that each successful applicant will plan, direct, and execute his/her own research program, the program and any substantial modifications in it must be mutually agreed upon by the participant and the National Heart, Lung, and Blood Institute.

Although this program is included and provided for in the financial plans for fiscal year 1980, award of grants pursuant to this request is contingent upon the ultimate receipt of appropriated funds for this purpose. A variety of approaches would represent valid responses to this announcement; accordingly, it is anticipated that there will be a range of costs among individual grants awarded. However, this request is not intended for the support of proposals that would ordinarily be considered Program Projects or Centers. Applicants are requested to furnish their own estimates of the time required (up to 3 years) to achieve the objectives of the proposed research project. The earliest starting date that can be requested is September 30, 1979. Near the end of the project period, renewal proposals for further investigations may be submitted for competitive review. Current policies and regulations which govern research grants of the NIH will prevail.

## II. METHOD OF REVIEW AND CRITERIA FOR REVIEW

### A. Review Procedures

Upon receipt, applications will be reviewed for their responsiveness to the specific objectives described in the 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 research grant program of the NIH.

The initial review of applications will be arranged by the NIH Division of Research Grants. Proposals in response to this solicitation will be reviewed on a nationwide basis in competition with each other. Initial review will be conducted by a 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 results of the competition as soon as possible after the September 1979 meeting of the Council.

### B. Review Criteria

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

- The relevance and significance of the proposed approach to the goal described in this announcement.
- The scientific merit of the proposal: the questions proposed for study, the research design, the methodology, the analysis, and interpretation of data.

- The research experience and competence of the applicants to carry out the proposed investigations, including expertise in the disciplines that the study may require.
- Adequacy of time (effort) to be devoted to the project by investigators and technical staff.
- Adequacy of collaborative arrangement(s) if applicable.
- Adequacy of existing and proposed facilities and resources.
- The costs in relation to the scope of the project.

### III. METHOD OF APPLYING

#### A. Letter of Intent

Prospective applicants are asked to submit a one page letter of intent which includes a brief synopsis of the proposed area(s) of research. This letter should be sent no later than January 12, 1979, to:

Dr. Charles L. Turbyfill  
Review Branch  
Division of Extramural Affairs  
National Heart, Lung, and  
Blood Institute  
National Institutes of Health  
Room 553, Westwood Building  
Bethesda, Maryland 20014

The Institute requests such letters only to provide an indication of the number and scope of applications to be received. A letter of intent is not binding, it will not enter into the review of any proposal subsequently submitted, and it is not a requirement for application.

#### B. Application Format

Applications should be submitted on form PHS 398, the application form for the traditional research grant. The conventional presentation in format and detail for regular research grant applications should be used, ensuring that the points identified under the Review Criteria are fulfilled. A statement from collaborators (if any) indicating their willingness to work and interact in the project should be included.

#### C. Application Procedure

The receipt date for application is before 5:00 p.m. EST on April 6, 1979. The original and twenty-four (24) copies of the application should be sent or delivered to:



Division of Research Grants  
National Institutes of Health  
Room 240, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20014

The words "RESPONSE TO RFA NIH-NHLBI-DHVD-79G-F" must be typed in bold letters across the top of the face page of the application.

It is important that a brief covering letter accompany the application indicating that it is in response to this RFA - Studies on the Effects of Hypertension and Vasoactive Agents on the Vasculature. A copy of the covering letter should be sent to:

Hypertension and Kidney Diseases Branch, DHVD  
National Heart, Lung, and Blood Institute  
National Institutes of Health  
Federal Building  
Bethesda, Maryland 20014