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

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

Have You Moved?

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

DELAY IN IMPLEMENTATION OF NCI PROGRAM PROJECT GUIDELINES

In order to provide adequate time for applicants to use the revised National Cancer Institute (NCI) Program Project Guidelines (announced in the August 19, 1983, NIH Guide to Grants and Contracts) in the development of their grant applications, implementation of these guidelines will begin with applications received for the February 1984 receipt deadline, rather than the October 1983 deadline as previously announced.

A copy of the guidelines will be forwarded to all program project grantees and will be available upon request from:

Referral Officer
Grants Review Branch
Division of Extramural Activities
National Cancer Institute
2115 East Jefferson Street
Room 401
Rockville, Maryland 20205
NOTICE

GUIDELINES FOR DEMONSTRATION AND EDUCATION RESEARCH GRANTS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The National Heart, Lung, and Blood Institute (NHLBI) announces the availability of Guidelines for Demonstration and Education Research Grants.

The intent of the NHLBI in issuing these guidelines is to provide advice to members of the scientific community interested in applying for demonstration and education research grants in the cardiovascular, pulmonary, and blood areas. These guidelines (1) define the concept of demonstration and education research, (2) describe the relationship of demonstration and education research to other phases of the spectrum of biomedical research, (3) describe the general characteristics of a demonstration and education research project, (4) list research topics of interest in the heart, lung, and blood programs, (5) suggest special considerations about approaches in grant applications, (6) describe the peer review process and the criteria by which applications are reviewed, and (7) provide a glossary of terms.

Copies of the guidelines may be obtained from:

Director
Division of Heart and Vascular Disease
National Heart, Lung, and Blood Institute
Federal Building - Room 416
7550 Wisconsin Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-2553

Director
Division of Lung Diseases
National Heart, Lung, and Blood Institute
Westwood Building - Room 6A16
5333 Westbard Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-7208

Director
Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute
Federal Building - Room 518A
7550 Wisconsin Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-4868
Director
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building - Room 7A17
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone (301) 496-7416
ANNOUNCEMENT

HYPERTENSIVE RAT RESOURCE - DAHL MODEL

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

National Heart, Lung, and Blood Institute (NHLBI) seeks animal breeders capable of establishing a self-supporting resource for hypertensive rats.

The hypertensive rat is the Dahl model consisting of two rat strains: The S strain which develops hypertension on a high salt diet and the R strain which remains normotensive on a high salt diet. It should be noted that the S strain develops hypertension from early adulthood on. However, a life-long low salt diet prevents the development of hypertension in the S strain. The R strain remains normotensive at any age at any level of dietary salt. This model was developed in the mid-sixties and is the only genetic model of salt-induced hypertension.

The Dahl model has been used for research studies of virtually all the major blood pressure regulating mechanisms (renal, cardiac, neural, vascular, etc.). The unique value of this model is detailed in the proceedings of a symposium on the Dahl rat held in 1981(1) and in a recent review(2).

At the present time the model can be purchased in limited quantities from the Brookhaven National Laboratory in Upton, New York. This resource, supported by NHLBI funding, supplies about 600 rats per month. However, investigator interest has exceeded the current production rate. For several years, the NHLBI has provided funds, through an interagency agreement, to support this animal resource. The Institute now plans to discontinue direct support for this colony. Therefore, the Institute seeks a self-supporting resource for this model, a resource that can supply a larger number of rats to a larger number of investigators.

Initially, qualified breeders will be provided with a limited number of Dahl rats to set up and operate a pilot colony. Subsequently, a single breeder will be chosen to breed and market the Dahl rat through a formal selection procedure. A panel composed of experts in rodent colony management and users of the Dahl model will make the selection. The following guidelines describe the Dahl model further and contain the Review Criteria for selection.

GUIDELINES FOR ESTABLISHING A HYPERTENSIVE RAT RESOURCE - DAHL MODEL

Background Information

The NHLBI wishes to re-establish the Dahl rat colony, presently at the Brookhaven National Laboratory, in a self-supporting facility that can supply a greater number


of investigators than the Brookhaven resource. Brookhaven provides about 600 rats per month at $16 a rat with support from a NHLBI interagency agreement. Since most of the users are NHLBI grantees, the Institute in effect, totally supports the colony through the agreement and through the colony's major source of revenue, research grant funds.

The Brookhaven Dahl model (S and R rats) has been well used in hypertension research even though it is not yet genetically homogeneous. Brookhaven has consistently imposed high standards of quality control which have resulted in a unique model of salt-induced hypertension and a considerable amount of reliable research information. Furthermore, Brookhaven does not provide breeding pairs; this too has contributed greatly to quality control.

The hypertension research community has accepted and used the Dahl model for over a decade; it is secondary only to the spontaneously hypertensive rat (SHR) among genetic models of hypertension. The Institute projects that many more investigators would avail themselves of the model if it were accessible in greater numbers. The Institute's projection of investigator demand is further based on the following considerations:

- Many of the hypertension mechanisms are influenced by a high salt diet.
- The interplay of genetics and environment (diet, stress, drug response, etc.) in hypertension can best be studied in a rigorously controlled model.
- Salt-induced hypertension is a high priority research area.

In sum, there is a measurable demand for the Dahl model that constitutes a potential market. Through skillful colony management more animals can conceivably be made available at reasonable cost to the mutual benefit of the hypertension research community and the breeder.

Breeders who wish to establish a Dahl rat resource will be assessed by the following criteria:

1. Breeding and housing facilities.
2. Capability to supply at least 1000 rats per month.
3. Safeguards to protect the health of the animals.
4. Tagging procedures to minimize error in the identification of animals.
5. Diet and blood pressure quality control.
7. Bid price of rats (price breeder is willing to pay to Brookhaven National Laboratory for breeding stock).
8. Projected price of rats (price breeder will charge to researchers; at the present time Brookhaven's price to Dahl users is $16.00 per rat),

9. Projected date to begin supplying rats to users.

Breeders should organize their proposals accordingly. Proposals are due by December 1, 1983.

On the basis of proposal assessment by outside consultants, breeders will be selected to establish and operate a pilot colony for a period of six months (Phase I). A pilot colony will consist of 5 breeding pairs of S rats and 5 breeding pairs of R rats. The Brookhaven colony will provide the Phase I breeding pairs at no charge to the selected breeders. In effect, this will be a trial colony to test the feasibility of operation. No sales will be conducted during this period, but pricing of the rats should be attempted based on actual overhead costs. At the end of Phase I breeders will report the results of their experience. Blood pressure readings should be a part of this report.

The final selection will involve review of Phase I reports by outside consultants. A single breeder will be selected on the basis of overall performance with the pilot colony. If the degree of performance in Phase I appears to be below the level of the Brookhaven colony, the Institute is not obligated to re-establish the colony.

If the degree of performance exceeds the Brookhaven colony level, the chosen breeder will initiate a full-scale colony with breeders purchased from Brookhaven at the accepted bid price. This colony development period (Phase II) will involve phasing-in sales for the new colony and phasing-out sales for the Brookhaven colony, commensurate with supply and demand. The pace of transition will be determined by the new breeder, the Brookhaven colony and the NHLBI. The Institute and the Brookhaven colony will cooperate to expedite this transition as much as possible and maintain an uninterrupted flow of Dahl rats to the hypertension research community during Phase II. The Institute reserves the right to discontinue Phase II if the new breeder, in any way, jeopardizes the flow of Dahl rats to investigators. Once Phase II is completed (marked by the termination of sales by the Brookhaven colony) the Institute's participation ends, and the breeder can proceed as a free enterprise to market the Dahl rat.

A memorandum of understanding will be required that the new breeder will give the NHLBI at least one year's notice if they decide to discontinue marketing the Dahl rat.

**Timetable**

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
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<tbody>
<tr>
<td>December 2, 1983</td>
<td>Proposals due</td>
</tr>
<tr>
<td>February, 1984</td>
<td>Breeders selected for Phase I</td>
</tr>
<tr>
<td>April, 1984</td>
<td>Phase I initiated</td>
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<tr>
<td>November, 1984</td>
<td>Phase I reports due</td>
</tr>
<tr>
<td>December, 1984</td>
<td>Breeder selected for Phase II</td>
</tr>
<tr>
<td>January, 1985</td>
<td>Phase II initiated</td>
</tr>
</tbody>
</table>
Proposals should be sent to:

Armando Sandoval
Hypertension and Kidney Diseases Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building - Room 4C04
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1857
NOTICE OF AVAILABILITY: RFA

REQUEST FOR COOPERATIVE AGREEMENT APPLICATIONS: RFA NIADDK - 83-1

COOPERATIVE CLINICAL STUDY OF DIETARY MODIFICATION ON THE COURSE
OF PROGRESSIVE RENAL DISEASE

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY
DISEASES

Application Receipt Date: December 15, 1983

I. INTRODUCTION

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) invites applications from investigators willing to participate with the NIADDK in a Cooperative Agreement Program for a multicenter cooperative clinical study seeking to define the influence of controlled nutritional intervention on progression of chronic renal disease/renal insufficiency.

The Cooperative Agreement is similar in many respects to the traditional NIH research grant, but differs from a research grant principally in the extent and nature of the involvement of NIADDK staff. The staff of the NIADDK will be involved as an active partner in all aspects of the scientific and technical management of this study above and beyond the levels required for administration of traditional research grants.

II. BACKGROUND

Studies over the past several decades have indicated that major adaptations in residual nephrons occur following loss of renal parenchyma. Observations in animal models indicate that mechanisms which normally emerge to compensate for glomerular injury may themselves become maladaptive and propagate additional nephron loss. Some data from animal studies indicate that these maladaptation processes can be attenuated by dietary restriction of protein and/or concomitant phosphates.

In related clinical observations, dietary restriction has been suggested to exert a favorable effect on the rate of progression of several chronic renal diseases. This conclusion must be regarded as tentative and unproven because of the lack of rigorous controls in most of the reported studies and the absence of statistical analyses of the influence of covariates other than nutritional intervention on outcome. Moreover, the impact of dietary restriction on overall health, nutritional status and life quality has not been adequately addressed in these reports.

This program is described in the Catalog of Federal Domestic Assistance, number 13.849, Kidney Diseases Urology and Hematology Research. Cooperative agreements will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR 74. This program is not subject to Health Systems Agency Review.
These preliminary clinical and laboratory observations form the basis for the following hypotheses to be tested in the proposed studies:

1. Restriction of dietary protein reduces the rate of progression of chronic renal disease in humans.

2. Dietary protein restriction is nutritionally safe (if effective) in patients with progressive renal failure.

This RFA is based on the premise that current methodology exists by which these limited hypotheses can be tested in human subjects.

III. STUDY OUTLINE

This clinical study is envisioned to consist of 4 sequential phases as follows:

I. Development of Protocols and Operations Manual (6-9 months)
II. Limited Pilot Studies (12-18 months)
III. Full-scale Cooperative Study (3-5 years)
IV. Data Analysis and Reporting (1 year)

Phase I will be concerned with the cooperative development of a single study protocol and Manual of Operations for Phase II by the Steering and Planning Committee, composed of the principal investigators of the participating Clinical Centers, the *Data Coordinating Center and members of the Kidney and Urology Branch of NIADDK.

The dimensions and directions of this study will be determined by the Steering and Planning Committee and, thus, are viewed as critical to the success of this initiative. In addition, an external Monitoring Committee comprised of experts selected by representatives of the Clinical Centers and Data Coordinating Center, will be appointed to review all activities of the trial, will assess progress of the study and advise the Steering and Planning Committee on how the next phase should be undertaken.

In general, the protocol is anticipated to include adults with chronic progressive renal diseases with glomerular filtration rates of less than or equal to 50% of normal at study entry. Patients with chronic glomerulonephritis should comprise the major study group, but additional groups will be considered for separate randomization including patients with chronic interstitial nephritis, hypertensive nephrosclerosis, polycystic kidney disease and hereditary nephritis. Patients with active nephrotic syndrome or malnutrition, as well as patients with diabetic nephropathy, do not appear to be suitable for inclusion in the study.

Development of the test protocol for dietary intervention may require the input of experts from the nutritional sciences, particularly for the assessment of the safety and adequacy of the prescribed dietary program, as well as approaches to documentation of compliance. It is anticipated that the low

* The Coordinating Center is being sought under a separate competition.
protein/low phosphate test diet would be derived from ordinary food processing with supplementation of essential nutrients to fulfill nutritional requirements.

It may be necessary to assess several study findings to determine efficacy and safety. However, it is anticipated that the measure of outcome would be the rate of change of renal function. It is likely that multiple variables will affect the rate of progression of chronic renal diseases. Covariates other than nutritional intervention may have a powerful effect on outcome, especially in patients with advanced renal failure and those with rapid deterioration of renal function. Thus, selection of patients with relatively early renal insufficiency, progressing at a moderate rate, would appear to be most desirable for this study. This may minimize the influence of reversible components of renal dysfunction in patients with complications of advanced uremia and reduce the size of the laboratory error in measurement of renal function tests commonly observed in late-stage renal failure.

**Phase II** will be a limited pilot study, with an initial control/observation period followed by randomization of a limited number of patients to an experimental or control diet. This phase should indicate the availability of qualifying patients; assess the appropriateness of randomization; test procedures and forms including informed consent, and other previously detailed plans to identify and document problems. If the results of Phase II demonstrate feasibility and the likelihood that a successful full-scale study can be conducted which will allow for meaningful conclusions, Phase III will be initiated.

It is not expected that sufficiently detailed plans, operations manuals, etc., can be developed initially to allow a firm NIADDK commitment for the final design of Phase III, since it is anticipated that results of the pilot phase (II) will influence the nature of Phase III.

Entrance criteria, number of patients, randomization process, dietary prescription, monitoring guidelines, and selection of measures of outcome will be critically reviewed before the initiation of the Phase III study.

A group of expert advisors, selected by the NIADDK, hereafter referred to as the Executive Advisory Group, who are independent of the trial, selected and supported by the NIADDK, will review the results of each phase of the study with special attention to patient safety, will review all actions which affect the design features of the study at the completion of each phase of the study and will make specific recommendations to the NIADDK regarding whether the proposed next phase should be undertaken.

**Phase III** will consist of the full-scale cooperative study with recruitment of adult patients with chronic progressive renal diseases who meet the entrance criteria. Following a precisely monitored initial control/observation period, during which the patients will remain on their own usual diets, status of renal function and its rate of change over time will be established and each patient will be characterized according to clinical, laboratory, dietary and nutritional/metabolic findings.

The well characterized patients will then be randomly assigned to either a control or a protein/phosphate restricted dietary regimen, who will follow the
detailed study protocol. It is anticipated that patients selected for the study will be trained intensively so that they will have a clear understanding of the objectives and dynamics of the study and the need for compliance and adherence to the specific dietary prescription.

Re-evaluation of renal function status and of clinical, biochemical, and dietary parameters, including compliance with the dietary prescription, will be assessed periodically and the standard procedures to monitor possible medical complications will be followed.

Patients will be followed longitudinally until the designated experimental period has ended or study outcome has been reached. In some cases, this will include limited follow-up into dialysis, in order to ascertain the overall safety of the dietary interventions.

Interim data analysis will be performed and reports prepared as indicated. There will be periodic reviews by the External Monitoring Committee pertaining to quality of data, safety of dietary prescriptions, evaluation of treatment effects, performance of participating Clinical Centers and the Data Coordinating Center.

Phase IV will be used by the Data Coordinating Center to complete all data analysis from the clinical trial. After final analyses, preparation of reports of the study for publication will be undertaken cooperatively by the principal investigators, the Data Coordinating Center and staff of the NIADDK.

It is anticipated that 10 Clinical Centers will participate in each phase. Each participating Clinical Center is expected to contribute a minimum of 30 patients who qualify for enrollment in the study.

Although the final experimental protocol will be developed by consensus among participants during the initial planning phase, applications submitted should be sufficiently complete to allow review of the research plan for Phases I and II. Furthermore, each applicant should provide a brief description of plans for a full scale Phase III study which would merit consideration as a model and include it as part of the application.

A Data Coordinating Center will participate with the Clinical Centers and Institute Staff during the clinical trial.

The Request for Applications (RFA) described herein is an invitation for CLINICAL CENTERS who have the scientific expertise, experience, interest, facilities and patient resources necessary TO PARTICIPATE IN ALL FOUR PHASES of this multicenter collaborative clinical study. Applications should be sufficiently complete to allow review of the research plan for the initial two phases of the study; nevertheless, each applicant is expected to provide plans for a full scale study and include it as part of the application.

It is recognized that the results of this scientific study may provide important information which in the long run may impact on costs of treating ESRD. Applicants should be aware that the National Center for Health Services Research (NCHSR) and the Health Care Financing Administration (HCFA) will be simultaneously conducting a study of the cost-effectiveness of dietary intervention in chronic renal failure. Although cost-effectiveness is not the primary aim of the
Cooperative Clinical Study of Dietary Modification on the Course of Progressive Renal Disease, applicants are encouraged to cooperate with NCHSR and HCFA in this effort. The NIADDK expects that representatives of the NCHSR and HCFA will participate with the Clinical Centers, the Data Coordinating Center and NIADDK Staff in the various committees and advisory groups described earlier in this RFA.

Although not a prerequisite for applying, potential applicants are encouraged to submit a non-binding letter of intent to apply, post-marked no later than October 15, 1983. The letter of intent does not ensure favorable review nor does it influence funding decisions but it will enable the NIADDK to plan the review, and will ensure that each potential applicant receives relevant program information prior to expending considerable effort in application preparation.

The deadline for receipt of applications by the NIH Division of Research Grants is December 15, 1983. Applications after this date will not be considered. Logistics and managerial practicality necessitate that only applicant institutions in the United States and Canada will be eligible. Additional information and copies of a more detailed RFA, which outlines the Clinical Center requirements for participation in the proposed study and the method of applying can be obtained from:

Gladys H. Hirschman, M.D.
Chronic Renal Disease Program Director
National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases
National Institutes of Health
Westwood Building - Room 621
Bethesda, Maryland 20205
Telephone: (301) 496-7571
ANNOUNCEMENT

NOTICE OF AVAILABILITY: RFA

CANCER CONTROL SCIENCE PROGRAM: PROGRAM PROJECTS

NIH-NCI-DRCCA-CCAB-83-17

NATIONAL CANCER INSTITUTE

Application Receipt Dates: January 15, 1984

Letters of Intent Receipt Dates: December 1, 1983

The Division of Resources, Centers and Community Activities (DRCCA) of the National Cancer Institute (NCI) invites Program Project (P01) grant applications from interested investigators for the support of Cancer Control Science Programs (CCSP).

The goal of this RFA is to establish Cancer Control Science Programs (CCSP) which will plan and implement focused research studies aimed at major cancer control problems. The research shall include innovative interventions with potential for reducing cancer incidence, morbidity and/or mortality, and for generalizability to larger populations.

The proposed research program should have a clearly identified theme or "program" and consist of an integrated group of projects from cancer control research phases II through V. The general areas of DRCCA's cancer control research interest are described in Cancer Control Program Guidelines which have recently been released.

Applicants are strongly encouraged to submit a letter of intent and consult with NCI program staff before submitting an application because of the need for a clear understanding of cancer control research issues and the P01 guidelines, and to facilitate planning for the review of applications.

Non-profit and for-profit institutions within the United States are eligible to apply for project periods of up to five years. It is anticipated that a maximum of five awards will be made as a result of this RFA. This RFA is the successor to the "Cancer Control Science Program" announcement previously published in the NIH Guide for Grants and Contracts (Vol. 11, No. 4, March 26, 1982, page 28) and cancelled (NIH Guide, Vol. 12 No. 4, April 22, 1983, page 3).

This program is described in the Catalog of Federal Domestic Assistance No. 13.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 403 (Public Law 78-410, as amended; 42 USC 284) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
Copies of the complete RFA, the 1983 Cancer Control Program Guidelines, and the 1983 NCI Program Project Guidelines may be obtained from:

Carlos E. Caban, Ph.D.
Program Director
Cancer Control Applications Branch, DRCCA
National Cancer Institute
National Institutes of Health
Blair Building - Room 1A01
Bethesda, Maryland 20205

Telephone: 301/427-8735
ANNOUNCEMENT

NOTICE OF AVAILABILITY: RFA

CANCER CONTROL RESEARCH UNITS NIH-NCI-DRCCA-CCAB-83-18

NATIONAL CANCER INSTITUTE

Application Receipt Dates: January 15, 1984

Letters of Intent Receipt Dates: December 1, 1983

The Division of Resources, Centers and Community Activities (DRCCA) of the National Cancer Institute (NCI) invites grant applications from interested investigators for the support of Cancer Control Research Unit (CCRU).

The goal of this RFA is to establish Cancer Control Research Units which will plan and implement focused research studies aimed at major cancer control problems. The research will address cancer control interventions with potential for reducing cancer incidence, morbidity and/or mortality, and for generalizability to larger populations. The CCRU will be a long term resource for research and training for the Cancer Control Program of NCI.

The proposed CCRU should have one or more clearly identified "themes" or "programs", each consisting of an integrated group of projects from cancer control research phases II and V. The general areas of DRCCA's cancer control research interest are described in Cancer Control Program Guidelines which have recently been released.

The required components of a CCRU will include:

- A rationale for the CCRU in terms of the cancer control themes and problems which will be investigated;
- A CCRU Director with research and administrative experience;
- A multidisciplinary cancer control research team of qualified investigators, and an underlying research base;
- At least three high quality research projects which are approved with the CCRU application, of which two must be defined population studies;
- Organizational, administrative and institutional procedures, commitments and support.

This program is described in the Catalog of Federal Domestic Assistance No. 13.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 403 (Public Law 78-410, as amended; 42 USC 284) and administered under PHS Grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
Optional components of a CCRU are:

- Limited developmental or research projects, including applied epidemiology studies;
- Shared resource cores which are integral to two or more projects.

The CCRU will be encouraged to establish cancer control research training programs, including field involvement and applications. At this time, however, there will be no funds specifically earmarked for training within the CCRU grant, and potential applicants are encouraged to seek peer-reviewed support through the NCI training grant mechanisms. After the CCRU grants are awarded and underway, spinoffs such as training programs may develop.

Applicants are strongly encouraged to submit a letter of intent and consult with NCI program staff before submitting an application because of the need for a clear understanding of cancer control research issues and the P30 guidelines, and to facilitate planning for the review of applications.

Non-profit and for-profit institutions within the United States are eligible to apply for project periods of up to five years. It is anticipated that a maximum of five awards will be made as a result of this RFA. This RFA is the successor to the RFA entitled "Cancer Control Research Units for Defined Population Studies" which was previously announced in the NIH Guide for Grants and Contracts (Vol. 11, No. 2, January 29, 1982, page 15-18).

Copies of the complete RFA, the 1983 Cancer Control Program Guidelines, and the 1983 NCI Program Project Guidelines may be obtained from:

Carlos E. Caban, Ph.D.
Program Director
Cancer Control Applications Branch, DRCCA
National Cancer Institute
National Institutes of Health
Blair Building - Room 1A01
9000 Rockville Pike
Bethesda, Maryland 20205

Telephone: (301) 427-8735
REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCBD-DB-83-15

APPLICATION OF RECOMBINANT DNA TECHNOLOGY TO DIAGNOSIS OF CANCER

NATIONAL CANCER INSTITUTE

Application Receipt Date: February 15, 1984

The Division of Cancer Biology and Diagnosis (DCBD) of the National Cancer Institute (NCI) is inviting grant applications from interested investigators to search for new applications of recent advances in recombinant DNA technology for the diagnosis of patients with cancer. The development of molecular approaches to the identification of malignant and premalignant cells may improve the accuracy of cancer diagnosis, result in detection of the disease, and lead to improved methods for classification of tumors.

This type of solicitation (the RFA) is issued to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Support for such awards is through the customary NIH grant-in-aid and is governed by the policies applicable to such grants. All applications in response to the RFA will be reviewed by an appropriate peer review group of NIH.

The present RFA announcement is for a single competition with a specified deadline of March 1, 1984, 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. RESEARCH GOALS AND SCOPE
III. MECHANISMS OF SUPPORT
IV. REVIEW PROCEDURES AND CRITERIA
V. METHOD OF APPLYING
VI. INQUIRIES

I. BACKGROUND INFORMATION

The DCBD has a major responsibility in the Diagnosis Branch for research in improving the diagnosis of cancer. Because of the current state of the art in molecular genetics and recombinant DNA technology and because relatively little attention has been placed on clinical diagnosis using this technology, it is timely to

This program is described in the Catalog of Federal Domestic Assistance 13,394, Cancer Detection and Diagnosis Research. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended: 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems review.
stimulate research in this area for its application in cancer diagnosis. In this RFA, the Program is expressing interest in grant applications which would result in novel approaches to diagnosis of cancer exploiting cellular changes at the molecular level.

II. RESEARCH GOALS AND SCOPE

The techniques of molecular genetics, especially restriction endonuclease analyses of DNA, nucleic acid hybridization after electrophoretic separation of nucleic acid fragments, and in situ hybridization with DNA probes (e.g. oncogenes) are widely employed in basic cancer biology research. The purpose of this RFA is to encourage the submission of research applications that use this technology as sensitive tools for diagnosing cancer and/or determining the predisposition to cancer. Recent basic scientific studies have shown that non-random chromosome mutations, translocations, deletions, and amplifications are associated with specific kinds of malignancies, often accompanied by the increased or altered expression of oncogenes. The possibility exists that specific genetic changes may be identified in malignant cells of cancer patients which are not present in cells from suitable control patients. Ideally, suitable collaborations can be developed between basic scientists who have experience with the technology and clinicians who have access to patients. In this way the NCI hopes to stimulate proposals that rigorously test the value of state-of-the-art molecular genetic techniques and recombinant DNA technology to cancer detection and diagnosis.

III. MECHANISMS OF SUPPORT

The support mechanism for this program will be the traditional NIH grant-in-aid. Applicants will plan and execute their own programs. Approximately $600,000 will be set aside to fund applications which are submitted in response to the RFA. These applications will not compete for funding within the general pool of dollars available for other investigator-initiated research proposals. However, all applications received will be evaluated by the rigorous standards of Study Section review. Only applications of sufficiently high scientific merit will be funded. The expected starting date is December 1, 1984. Although this program is provided for in the financial plans of the NCI, the award of grants pursuant to this RFA is contingent upon availability of funds appropriated for Fiscal Year 1985.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and the NCI staff for responsiveness to this announcement. If the application is judged unresponsive, the applicant will be given an option to withdraw the application or to submit it for consideration in the traditional grant program of NIH.

Applications judged responsive will be reviewed initially for scientific merit by an NIH peer review group. The recommendation of the peer review group will be considered by National Cancer Advisory Board.
B. Review Criteria

The factors considered in the scientific merit evaluation of each application will be the same as those used in traditional NIH research grant application evaluations including:

1. The assessment of the importance of the proposed research problem.

2. The scientific merit of the proposed approach. Technical merit includes adequacy and novelty of methodological approach and research design.

3. The expertise and qualifications of Principal Investigator and proposed staff.

4. Documentation of the adequacy of the facilities and resources.

5. The appropriateness of the requested budget relative to the work proposed.

V. METHOD OF APPLYING

A. Application Format

Applications should be submitted on form PHS 398, available from the business office of most institutions or from the Division of Research Grants (DRG). The conventional presentation for grant applications should be utilized and the points identified under the Review Criteria must be fulfilled. The number and title of this RFA should be typed in Section 2 on the front page of the application form.

B. Application Procedure

The present RFA announcement is open to all interested investigators. Applications must be received no later than February 15, 1984. Applications received after this date will be returned. The original and six copies of the application should be sent or delivered to:

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

A brief covering letter should accompany the application indicating that it is in response to this RFA. A copy of the covering letter should be sent to:

Bill Bunnag, Ph.D.
Chief, Pathology/Cytology Section
Diagnosis Branch
Division of Cancer Biology and Diagnosis
National Cancer Institute
Westwood Building - Room 10A15
Bethesda, Maryland 20205
VI. INQUIRIES

Inquiries concerning this announcement should be directed to Dr. Bill Bunnag at the above address (Phone 301-496-7147).
ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NICHD-CPR-DBSB-83-2

THE CAUSES AND CONSEQUENCES OF CHANGES IN FAMILY AND HOUSEHOLD STRUCTURE

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Application Receipt Date: December 15, 1983

I. PURPOSE

The Demographic and Behavioral Sciences Branch (DBSB) of the Center for Population Research (CPR) of the National Institute of Child Health and Human Development (NICHD) invites grant applications for a single competition for the support of research on the Causes and Consequences of Changes in Family and Household Structure. The major purpose of this special grant program is to stimulate the investigation of the individual and societal level causes and/or consequences of changes in family and household structure. The researcher may propose the analyses of existing data, gathering new data or some combination of the two. The research may focus on causes and/or consequences due to compositional or structural changes in the family and/or household.

II. ADMINISTRATIVE BACKGROUND

The Demographic and Behavioral Sciences Branch of CPR, NICHD supports research on causes and consequences of population change. A prominent component of the program is directed toward understanding demographic change measured from the perspective of the family and related household structures. The Branch is attempting to target research on the causes RFA.

The family and household are commonly used units of population analysis. Until recently the two concepts were regarded as virtually synonymous. Recent research has indicated that not only are these concepts no longer synonymous but that each is undergoing rather rapid transformations that imply rather dramatic compositional shifts in the population of household and family units. Moreover, there appear to be parallel developments under way in most developed countries.

This program is described in the Catalog of Federal Domestic Assistance No. 13.864, Population Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42USC 241) and administered under PHS Grant Policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74.
Recent research has concentrated primarily on the analyses of existing, large micro data sets. This body of research has elucidated the magnitude and trend of the component forces associated with the transformation of the family and household. These projects have documented the accelerating rates of divorce, later ages of marriages, rising rates of remarriage, the rise of nontraditional households and households containing single-parent families and the increasing propensity to live alone. The transformation of the family and household implies that the component individuals are exposed to an ever-increasing variety of living conditions. The time has come to probe more deeply into the causes and consequences of these changes.

It is the intent of this RFA to allow investigators a relatively unconstrained opportunity to explore the consequences associated with changes in the family and household. The recent advances in understanding the demographic dimensions of these changes now make it possible to propose research addressing questions of causality and consequences and this one-time solicitation is intended to target resources for an accelerated yet orderly exploration of the many unanswered questions associated with these changes. Examples of appropriate studies are: investigation of the socioeconomic correlates of marriage, divorce, and/or household formation; investigations of the effects of living in a single-parent household on the individuals involved or on society (e.g., rising demand for child care service), and investigation of the influence of female labor force participation on family structure, living arrangements and division of labor within the family.

III. OBJECTIVES

This special grant program is intended to encourage scientists to propose and investigate questions involving causes and consequences associated with changes in family and/or household structures. Investigators are encouraged to propose whatever research designs are appropriate to accomplish the research goals of this announcement. Investigations may focus on individual level analysis, societal level analysis or some combination of the two. Investigation may focus on the family or household or some combination of the two. Designs may be longitudinal or cross-sectional. Of the many interesting questions that are possible to explore in response to this solicitation, several rise to prominence because of their scientific importance. They are as follows:

A. Is the American society developing a new structure of family and household units, or in the alternative, do the observed patterns of structural changes in the family and household imply a return to those characteristics of a pre-Depression era? Recent research evidence on this question is quite mixed. On one hand, marriage patterns are reverting to those existing before the Great Depression, but on the other hand, rising rates of divorce and the increasing incidence of single-parent households and other nontraditional households imply that we may be entering a new demographic age. An understanding of why these changes have occurred should enable us to determine which characterization of the population is correct and could enable us to predict the societal and individual level of consequences implied by these patterns.

B. Recent research indicates that a growing proportion of children (perhaps a majority of children) will be exposed to significant intervals during which they are living in a household that does not contain both natural parents and all of their siblings. What do these changes imply for the children in question and for society as a whole?
C. Recent research indicates that households may be relying less on the family as a support network and relying more on goods and services purchased on the open market (e.g., child care) as a substitute for family support or, perhaps, on other forms of social support network as a substitute for family support. Is this observation correct and, if so, why is it occurring and what does it imply for the individuals involved?

Investigators are encouraged to propose research on any combination of the above mentioned questions or other questions that relate to the causes and consequences of changes in family and household structure.

IV. SCOPE

Investigators are invited to propose projects that focus on one or more research questions relevant to the objectives of this RFA. However, because these questions are germane to the American population and other developed societies, research predicated on the analyses of data gathered in a less developed country is inappropriate. Investigators proposing the collection of new data should document that the information does not already exist in a public access data resource.

V. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual research-project grant. Although funds for this program are included in the financial plans for Fiscal Year 1984, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that approximately five grants will be awarded under this program. This specific amount will, however, depend on the merit and scope of the applications received and the availability of funds.

Upon initiation of the program, the DBSB will sponsor annual workshops in Bethesda, Maryland to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for a two-day meeting each year to be held in Bethesda, Maryland. Applicants should also include a statement in their application indicating their willingness to participate in such a workshop. The award period for this grant activity must not exceed five years. At the end of the initial award period renewal applications may be submitted for further competitive review through the regular grants program of the National Institutes of Health. It is anticipated that support will begin on July 1, 1984.

In the event that an investigator proposes a topic that pertains to an area traditionally supported by the National Institute on Aging or the National Institute of Mental Health (NIH), the application will be assigned according to existing referral guidelines with appropriate secondary assignment. Principal investigators on projects submitted in response to this announcement will be included in the annual workshop regardless of funding source.

The current policies and requirements that govern the research grant programs of the NIH will prevail.
VI. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications responding to the RFA will be reviewed for scientific and technical merit by an initial review group which will be convened by the Division of Research Grants (DRG), of the NIH solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged nonresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grants programs of the NIH.

Applications that have relevance to some aspect of the National Institute on Aging or the National Institute of Mental Health will be given a dual assignment to both NICHD and NIA or NIMH.

If a proposal in response to the RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of the scientific merit of each application will be those used in the review of traditional research-project grant applications, including the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator; the adequacy of the research design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An additional criterion will be the importance of the proposed research to the objectives of this RFA.

VII. METHOD OF APPLYING

A. Format for Application

Submit the application on form PHS 398, the application form for the traditional research-project grant. This form is available in an applicant institution's office of sponsored research, or business office, or from the Division of Research Grants (DRG) of the NIH. Use the conventional format for a research-project grant application (please observe page limitations) and ensure that the points identified in the section on review procedure and criteria are fulfilled. To identify these applications as being in response to the RFA check "yes" on item 2 of page 1 of the application and enter the title: "The Causes and Consequences of Changes in Family and Household Structure" and the RFA number NIH-NICHD-CPR-DBSB-83-02.

B. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:
Applications must be received by December 15, 1983. An application received after this date will be considered ineligible, but, after discussion with the applicant, it may be considered as a regular research-project grant application.

**Timetable**

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
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<tbody>
<tr>
<td>Application receipt date</td>
<td>December 15, 1983</td>
</tr>
<tr>
<td>Review by the National Institute of Child Health and Human Development Advisory Council</td>
<td>May 1984</td>
</tr>
<tr>
<td>Anticipated award date</td>
<td>July 1, 1984</td>
</tr>
</tbody>
</table>

**C. Inquiries**

Inquiries regarding this announcement may be directed to the program administrator:

V. Jeffery Evans, Ph.D., J.D.
Demographic and Behavioral Sciences Branch
Center for Population Research, NICHD
National Institutes of Health
Landow Building - Room 7C25
Bethesda, Maryland 20205

Telephone: (301) 496-1174
ANNOUNCEMENT

REQUEST FOR GRANT APPLICATIONS: RFA

RFA-NIH-NICHD-CPR-DBSB-83-3

CONSEQUENCES OF PREGNANCY LOSSES FOR ADOLESCENTS

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Application Receipt Date: December 5, 1984

I. BACKGROUND INFORMATION

The Demographic and Behavioral Sciences Branch (DBSB), Center for Population Research (CPR), National Institute of Child Health and Human Development (NICHD), supports research on the antecedents and consequences of adolescent pregnancy, contraception, and childbearing. This RFA invites scientists to submit grant applications for the support of research on an important aspect of adolescent fertility, the consequences which pregnancy losses have for adolescents, their partners, and their families.

Adolescents experience about 600,000 pregnancy losses per year, of which approximately 500,000 are induced abortions, and about 100,000 are miscarriages. Considerable research has been done on the consequences of abortion for women who are beyond adolescence. However, there is a paucity of research on the psychological, social, health, and other consequences of abortions for adolescents, and there is practically no research on the consequences of miscarriages for adolescents. In-depth research on these problems is needed because important differences between adolescents and adults may contribute significantly to differential consequences of pregnancy losses. For example, adults and adolescents differ in biological, psychological, social, and educational maturity. Also there are differences in such factors as life-style and degree of independence, as well as in relationships with parents, other family members, sexual partners, peers, friends, and service providers.

II. RESEARCH GOALS AND SCOPE

This RFA invites researchers to concentrate on the effects of abortions and miscarriages on adolescents. While this research will be more concerned with females than males, studies of these effects on male partners are also encouraged. Investigators interested in the consequences of the abortions and
miscarriages of adolescents for their families could pursue this line of inquiry. A thorough analysis of the literature and identification of data sets relevant to a proposed project are required. It should then be possible for the investigator to decide if available data sets are adequate to meet the objectives of the project, or if the collection of new data is necessary. Standardized measuring instruments should be used to collect new data if it is possible to do so. The research may be multidisciplinary or may be conducted within a single discipline. Comparative, cross-cultural, transnational or historical approaches may be utilized.

The identification of appropriate comparison groups for adolescents who obtain abortions or have miscarriages is a major problem of the research design, which requires special consideration and innovative approaches. The research design should include a conceptual model of the interrelationships among the consequences of pregnancy losses for adolescents, and the factors affecting such consequences. Careful selection of variables and samples within a well-defined conceptual framework should contribute to the development of efficient and cost-effective designs.

In developing the research project, consideration should be given to the possibility that the study, especially the results, might affect adolescents' understanding of the consequences of pregnancy losses. Increased understanding should provide adolescents with better bases for making decisions about engaging in sexual relations, using contraception, and resolving unintended pregnancies. Such knowledge and understanding should also be of value to parents, counselors, physicians, teachers, and others who make important contributions to adolescent decision-making.

In general, there are two major groups of questions to be answered.

Consequences

What are the psychological, social, health, familial, educational, economic, and other consequences of pregnancy losses for adolescents? How may these consequences be identified and measured? In what ways do these consequences change over time? How do these consequences interrelate and what effect do these interrelationships have on the adolescents?

Contributing factors

How do various relevant factors interact to contribute to the psychological, social, health and other consequences of pregnancy losses for adolescents, including subsequent sexual and fertility regulating behavior? Factors which may be considered include, but are not limited to, age, race, ethnicity, educational status, knowledge, level of development and maturity (biological, psychological, social), psychological characteristics (relevant motivations, attitudes, decision-making, etc.), personal/social relationships (with parents, partners, peers, etc.), service providers (physicians, clinic staffs, etc.), religion, socioeconomic status, pregnancy and abortion history, techniques of abortions, use of fertility regulating methods, length of time following abortions and/or miscarriages, and life events following abortions and/or miscarriages (living with parents, marriage, dropping out of school, obtaining employment, etc.).
III. MECHANISM OF SUPPORT

The support mechanisms for this program will be the individual research project grant and the New Investigator Research Award. Although this solicitation is included in the plans for Fiscal Year 1984, the support of grants to be awarded as a result of this RFA is contingent upon the receipt of funds for this purpose.

It is anticipated that up to five grants will be awarded, depending on the overall merit of the applications and available funds. It is probable that there will be a range of costs among the grants which are awarded.

Applicants will furnish estimates of the time which will be required to conduct the proposed research.

The current policies and requirements that govern the research grant programs of NIH will prevail.

IV. REVIEW PROCEDURES AND CRITERIA

Applications submitted in response to this RFA will be reviewed for scientific merit by an initial review group (IRG) established and administered by the Division of Research Grants (DRG) of the NIH. Applications judged by the DRG and NICHD as nonresponsive to this RFA will be assigned to the most appropriate regular grant program in the Public Health Service. If such an assignment is not possible, the application will be returned to the applicant. If an application submitted in response to this RFA is the same as one already submitted to the NIH, the applicant will be asked to withdraw the pending application before the new one is accepted.

The factors to be used in evaluating the scientific merit of each application will be similar to those used in judging individual research project grant applications, including originality of the proposed research and feasibility of approach; quality of theoretical-conceptual framework; adequacy of research design; appropriateness of data analysis techniques; suitability of facilities; training, experience, and research competence of investigators; and soundness of proposed budget.

V. METHOD OF APPLYING

Applicants are asked to submit a letter of intent to the Demographic and Behavioral Sciences Branch, NICHD (see address below) at least one month prior to formal submission of an application. Include name of principal investigator, institutional address, title of application, and abstract of proposed research. Indicate that the application is in response to this RFA. When preparing the formal application, use Form 398 (Revised 5/82) for the individual research projects and the New Investigator Research Awards. If your institution does not have this application booklet, copies may be obtained from:

Office of Grant Inquiries
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205
Telephone: (301) 496-7441
In order to identify the application as being in response to this RFA check "yes" on item 2, page 1, of the application form and enter the title "Consequences of Pregnancy Losses for Adolescents" and the RFA number. A cover letter repeating that this application is in response to the RFA of the NICHD Demographic and Behavioral Sciences Branch will expedite the routing of the application.

Send or deliver the completed application and six (6) signed, complete copies of it to:

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

Applications must be received by December 5, 1984. An application which is not received by this date will be considered ineligible and returned.

VI. TIMETABLE

Preliminary letter
Application receipt date
Initial review date
Review by National Institute
of Child Health and Human
Development Advisory Council
Anticipated award date

November 1, 1983
December 5, 1983
February/March 1984
June 1984
July 1, 1984

Inquiries regarding this announcement may be directed to:

Sidney H. Newman, Ph.D.
Behavioral Scientist Administrator
Demographic and Behavioral Sciences Branch
National Institute of Child Health
and Human Development
Landow Building - Room 7C25
7910 Woodmont Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1174
ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NICHD-CPR-RS-83-3

HUMAN MALE INFERTILITY

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Application Receipt Date: February 15, 1984

I. BACKGROUND

The Reproductive Sciences Branch (RSB) of the Center for Population Research (CPR) of the National Institute of Child Health and Human Development (NICHD) is inviting research grant applications for investigations in selected topics in human infertility. By issuing this Request for Applications (RFA), CPR is indicating its wish to encourage investigator interest in a specific research area important to its mission and currently not supported at appropriate levels.

RSB supports research dealing with the biomedical basis of reproduction and its application to patient care. Reproductive Medicine, one of the four programs of the RSB, concerns investigation into the clinical implications of that information and includes human infertility. Infertility is defined as the inability of couples to reproduce as they wish.

The study of human infertility has been designated an area of high priority for research support by NICHD. Increasing numbers of couples are presenting to physicians with complaint of infertility, and the diagnosis and management of such problems has become a significant concern. New research methodologies have expanded investigative opportunities in this area. A vigorous research effort is essential to continued progress.

This program is described in the Catalog of Federal Domestic Assistance No. 13.864, Population Research. Awards will be made under the authority of the Public Health Service Act, Title X, Section 1004 (Public Law 91-572, as amended; 42 USC 241) and Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
This RFA will be restricted to studies in the biologic basis for infertility in men and the evaluation and management of such problems. It is meant as an accompaniment to an earlier announcement (NIH-NICHD-CPR-83-3) pertaining to similar interests in the female. Excluded is research in malignant conditions, infectious diseases, and the aging process supported by other Institutes of the NIH.

II. RESEARCH GOALS AND SCOPE

Human infertility is a function of the reproductive capacity of both male and female partners, but the development of a sound base of scientific information concerning the function of the male reproductive system has lagged behind that of the female. In recent years, new lines of investigation have evolved in the reproductive sciences and support in broadening and extending these investigational efforts appears strongly desirable. Several areas of particular interest are specified in this RFA but are not meant to constitute an inclusive list of topics appropriate for research in the male component of human infertility.

A. Normal Male Reproduction

There is urgent need for controlled observations of normal functions in human male reproduction. Included among such topics are spermatogenesis, sperm transport, epididymal function, semen emission and ejaculation, capacitation and acrosomal change in human spermatozoa. Short term variability of testicular function and semen composition has long been recognized and documented, but the mechanisms underlying such variability are important and remain uncertain. Though variability of gonadotropin secretion is far less prominent in males than females, the roles of central nervous system opioids and other factors in the regulation of gonadotropin synthesis and episodic secretion deserve further investigation. The nature of exchange functions in fluid transfer through seminiferous tubules, rete testis and epididymis remains largely unexplored in the human. Confirmation of the purported maintenance of constancy of androgen concentrations in such fluid noted in animals, despite variable ambient concentrations in serum, warrants further investigation in man. Continued research in the energetics of human sperm motility, quantitative appraisal of sperm function, and the possible relationship of spermatozoal rheology and metabolic rates to fertilizability seems desirable. Further evaluation of in vitro systems to evaluate sperm-oocyte penetrability is of interest. Identification of the role of estrogen in the regulation of spermatogenesis and as a function of advancing age constitute important studies. The testis is nearly unique with respect to the heterogeneity of cell type and function, as well as to the various degrees of cell proliferation and degeneration which have been noted in its structure at any time. The application of new techniques, such as monoclonal antibody affinity or differential centrifugation to defining rigorously the coherent cell sets which comprise the normal testis, and changes in those sets with time, is of considerable interest.

B. Reproductive Disturbances

Long term studies of the natural history of disturbances in normal male reproductive functions are important with respect to decisions in medical intervention and, later, to the evaluation of treatment. Such studies are conspicuously lacking in the management of infertility in the human male, and seem highly desirable. The consequences in the adult male of prior
delayed onset of puberty or development of teenage varicocele are examples. The long term impact of varicocele, genitourinary tract infection, and systemic illness are suitable topics for investigation as well. The impact of ionizing radiation, chemotherapy, infectious and autoimmune disease, and some antimicrobials are of interest. Observations of possible male-mediated effects of certain environmental toxins, pharmaceuticals and controlled substances on embryogenesis and fetal development add emphasis to the need to explore the effects of such agents in disordered reproduction. Though hyperprolactinemia is rare in males and appears to affect reproduction primarily through associated changes in gonadotrophin deficiency, the possible effects of excessive prolactin on spermatogenesis and steroidogenesis deserve further investigation.

C. Treatment of Male Infertility

Rigorously controlled clinical trials in male infertility, employing appropriate scientific methodology with internal controls, standard disease classification and defined therapeutic protocols are highly desirable. The rationale for employment of gonadotropins, androgens, LHRH, antiestrogens, clomiphene citrate, and glucocorticoids in idiopathic oligospermic infertility would be challenged by this approach. Similarly, surgery for cryptorchidism and varicocele ligation have been incompletely evaluated in this sense.

D. Reproductive Failure in Couples

The fertility of a couple is a combined function of the capacity of both the male and female partners to reproduce. When either exhibits an absolute barrier to reproduction as through ductal obstruction or gonadal dysgenesis, estimate of their combined fertility is evident. Construction of quantitative estimates of a couple's combined fertility based on mathematical treatment of probability estimates of fertility of both members of the couple are essential to rational patient counselling, therapeutic decision-making and evaluation of treatment.

Clinical investigation of an infertile couple involves the application of investigative and management protocols which are generally uniform and could be widely employed among a number of practitioners. Either detailed evaluation of large treatment populations, or pooling and interchanging experience among treatment groups, would seem to be desirable in view of the wide-spread need for such protocols. Such efforts might provide important quantitative probabilistic estimates of fertility.

III. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional grant-in-aid (R01). The receipt date for this single-competition announcement is February 15, 1984. The earliest requested start date for grants would be December 1, 1984. Applications will be reviewed in competition with each other, and it is anticipated that 10-12 grants will be awarded under this program.
IV. REVIEW PROCEDURES AND CRITERIA

A. Procedures

Research grant applications should be submitted on Form PHS 398, and labelled in item 2 of the face page "In Response to RFA-NIH-NICHD-CPR-RS-83-3." This form is available in most institutional business offices or from the Division of Research Grants (DRG), NIH. Applications will be reviewed by NIH staff for responsiveness to the RFA. Applicants judged to have submitted a non-responsive application will be contacted and given an opportunity to withdraw the application, or to have it assigned for review in the same manner as unsolicited grant applications. A proposal submitted in response to this RFA identical to a research grant application already submitted to NIH for review, is not acceptable for this RFA.

Applications submitted in response to this RFA will be reviewed for technical merit by an initial review group convened by the DRG solely to review these applications. The National Advisory Child Health and Human Development Council will review the applications in October 1984.

B. Review Criteria

Criteria for evaluation by the initial review group will, except for consonance with the goals of the RFA, be the same as for other research grant proposals. They are as follows:

1. scientific merit--the significance of proposed questions, research design, methodology, data analysis and interpretation;
2. research experience and competence of the applicant(s);
3. adequacy of time and effort dedicated to the project by investigators and staff;
4. adequacy of collaborative relationships, if applicable;
5. adequacy of existing and proposed facilities and resources; and
6. costs in relation to scope of the project.

V. METHOD OF APPLYING

Applications should be submitted on Form PHS 398. The conventional mode of preparation should be employed. The original and four (4) copies should be received by the Division of Research Grants no later than February 15, 1984. Applications should be directed to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205
In addition to those mailed to the Division of Research Grants, two (2) copies of the application should be sent to:

Thomas Kirschbaum, M.D.
Reproductive Sciences Branch
Center for Population Research
National Institute of Child Health
and Human Development
Landow Building - Room 7C33
National Institutes of Health
Bethesda, Maryland 20205

Questions relating to this announcement may be directed to Dr. Kirschbaum or by phone (301/496-6515).
ANNOUNCEMENT

USE OF GROWTH FACTORS, MATURATION FACTORS AND ANTI-GROWTH FACTORS IN ANIMAL TUMOR MODELS

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: November 1, March 1, July 1

The National Cancer Institute's (NCI) Division of Cancer Treatment (DCT) desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the therapeutic effects of growth factors, maturation factors, and monoclonal antibody to growth factors on the growth and metastasis of cancer in animal tumor models. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: November 1, March 1, July 1.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the Program Announcement.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building - Room 240  
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long  
Program Director for Pre-Clinical Trials, BRB, BRMP  
Building 426 - Room 1  
Frederick Cancer Research Facility  
Frederick, Maryland 21701  

Telephone: (301) 695-1098

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.
ANNOUNCEMENT

DEVELOPMENT OF GENETICALLY ENGINEERED CELL PRODUCTS

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: November 1, March 1, July 1

The National Cancer Institute's (NCI) Division of Cancer Treatment (DCT) desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the development of genetically engineered cell products for therapeutic application as biological response modifiers. This announcement will support diverse approaches into the use of genetic engineering to transpose genes coding for biological response modifiers such as interferons, lymphokines, growth factors and other gene products into microbial organisms for a large scale production, isolation, purification and characterization of these factors for therapeutic application as biological response modifiers. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: November 1, March 1, July 1.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the program announcement.

This program is described in the catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS Grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building - Room 240  
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long  
Program Director for Pre-Clinical Trials, BRB, BRMP  
Building 426 - Room 1  
Frederick Cancer Research Facility  
Frederick, Maryland 21701  

Telephone: (301) 695-1098

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.
ANNOUNCEMENT

USE OF TUMOR ASSOCIATED ANTIGENS AS IMMUNOGENS

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: November 1, March 1, July 1

The National Cancer Institute's (NCI), Division of Cancer Treatment (DCT), desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the development of methods of immunization that evoke effective in vivo anti-tumor immunity using purified tumor associated antigens as immunogens. Isolation of tumor associated antigens is now possible using monoclonal antibodies. However, there is considerable uncertainty how best to administer purified antigens in vivo to evoke effective anti-tumor immunity. Certain antigens may facilitate and others may inhibit tumor growth and metastases. The proposed studies should investigate this issue in both normal and tumor bearing animals using purified antigens as therapeutic agents. Preference will be given to non-viral tumor associated antigens on recently derived spontaneous or chemically induced fully syngeneic tumors although consideration will be given to viral coded tumor antigens and even normal cell surface alloantigens as model antigens. The use of various immunization schedules and adjuvants in therapy models with detailed monitoring of the host cellular and immune responses will be required. These studies must be directed toward optimizing the therapeutic effects of these antigens in vivo as demonstrated by protection studies against subsequent tumor growth. Proposals to investigate monoclonal antibody purified tumor associated antigens as therapeutic reagents in man may also be submitted. As in the animal models, homogenous preparations of high purity are preferred for these investigations. End points may be assessed by in vivo assays or by in vivo therapeutic effects. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: November 1, March 1, July 1.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the program announcement.

Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

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For further information, investigators are encouraged to contact:

Dr. Cedric W. Long  
Program Director for Pre-Clinical Trials, BRB, BRMP  
Building 426 - Room 1  
Frederick Cancer Research Facility  
Frederick, Maryland 21701

Telephone: (301) 695-1098

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.
DEVELOPMENT OF CELL LINES PRODUCING LYMPHOKINES AND CYTOKINES

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: November 1, March 1, July 1

The National Cancer Institute's (NCI), Division of Cancer Treatment (DCT), desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the development of cell lines producing lymphokines and cytokines with therapeutic effects as biological response modifiers. This announcement will encourage research in the development of such cell lines and the development of methods to isolate, purify and characterize the therapeutic potential of the various products of these cell lines in appropriate test systems. These products may have a potential long-term usefulness in the treatment of cancer and/or in the alteration of biological responses in the course of cancer. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accord with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are November 1, March 1, July 1.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts office at most academic and research institutions or from the Division of Research Grants (DRG), NIH.

In space #2 on the first page of this form, indicate the title of the program announcement.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building - Room 240  
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long  
Program Director for Pre-Clinical Trials, BRB, BRMP  
Building 426 - Room 1  
Frederick Cancer Research Facility  
Frederick, Maryland 21701

Telephone: (301) 695-1098

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.
ANNOUNCEMENT

DETERMINATION OF THE THERAPEUTIC USEFULNESS OF PURIFIED CYTOKINES AND ANTI-CYTOKINE MONOCLONAL ANTIBODIES IN CANCER MODELS

BIOLOGICAL RESPONSE MODIFIERS PROGRAM

NATIONAL CANCER INSTITUTE

Application Receipt Dates: November 1, March 1, July 1

The National Cancer Institute (NCI), Division of Cancer Treatment (DCT) desires to expand its support of research on cytokines (lymphokines, monokines, growth factors, etc.) and in determining the potential for using these factors in the treatment of cancer. The Biological Response Modifiers Program is seeking applications for research grants concerned with the modes of action of purified cytokines in ways that will be relevant to determination of therapeutic potential through the augmentation or regulation of certain components of the immune response or through direct effects on certain types of malignant cells or on supportive tissue of tumors. Methods of regulating or manipulating the specific cytokine levels through utilization of purified cytokines and/or utilization of anti-cytokine monoclonal antibodies are of interest. Work with in vivo animal models would be particularly relevant. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to the biological response modifier research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

I. DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: November 1, March 1, July 1.

This program is described in the catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
II. METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the Program Announcement.

Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this Program Announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Gary B. Thurman
Program Director for Molecular Immunology,
BRB, BRMP
Building 426 - Room 1
NCI-Frederick Cancer Research Facility
Frederick, Maryland 21701

Telephone: (301) 695-1098

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifier research, a copy of the covering letter should be sent under separate cover to Dr. Thurman.
ANNOUNCEMENT

AGING AND VISUAL PERCEPTION

THE NATIONAL INSTITUTE ON AGING

I. INTRODUCTION

The National Institute on Aging (NIA) invites qualified researchers to submit grant applications for research projects designed to examine the nature of age-related differences and changes in visual perception, as these relate to the effective functioning of older people in everyday life.

Laboratory research has demonstrated age-related declines in such visual functions as acuity, dark/light adaptation, contrast sensitivity, or color perception. But further studies are sought on visual perception—that is, on how visual signals and information are interpreted and responded to in later life. Most importantly, visual perception should be scrutinized in the light of older people's experiences and expectations and within the contexts of their everyday lives at work, in the household, and in the community. Such research will contribute new behavioral and aging perspectives to visual science, and it will provide a knowledge base for developing devices and environmental designs to compensate for visual deterioration and for helping impaired individuals to use their residual vision.

This announcement of NIA's special initiative on visual perception supplements, but does not replace NIA's broad announcement on HEALTH AND EFFECTIVE FUNCTIONING IN THE MIDDLE AND LATER YEARS. (See NIH GUIDE FOR GRANTS AND CONTRACTS, VOL. 12, NO. 6, JUNE 17, 1983, pp. 10-15; see also pp. 5-9.) This initiative is coordinated with related programs in the National Eye Institute. (See Vision Research--A National Plan: 1983-1987, Volume 2, Part 6, Report of the Panel on Visual Impairment and Its Rehabilitation. DHHS Publication No. (NIH) 82-2476, 1983.)

II. BACKGROUND

An agenda for research on aging and visual perception has been set out for the NIA with the cooperation of the Committee on Vision of the National Research Council. Full details, recommended as background reading in preparing applications, appear in: Robert Sekuler, Donald Kline, and Key Dismukes (eds.), Aging and Human Visual Function. New York: Alan R. Liss, Inc., 1982. This volume describes issues, needs, and opportunities in aging research on vision. It makes clear that, while some people experience severe deterioration in vision with age, most people must adjust to some reduction in visual function as they grow older. Changes in vision with aging substantially alter the quality of individuals'

This program is described in the Catalog of Federal Domestic Assistance No. 13.866, Aging Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
lives. It is estimated that at least a million elderly people in the United States—and the number is rising rapidly—cannot see well enough to read ordinary newspaper print without optical aids such as magnifiers. Not only reading, but also occupational involvement, performance of everyday skills such as walking or driving, social participation, psychological well-being, even survival, are dependent upon a complex chain of visual processes, beginning with the eye and extending to perceptual and cognitive processes in the brain. All of these processes are subject to change with aging.

However, individuals differ widely in nature and degree of age-related decline in visual perception, a fact which leads to the search for complex explanatory factors that are not only genetic or neurophysiological, but also include personal differences in life experiences or cognitive styles, as well as social and cultural differences in expectations and opportunities for performance. Such explanations can be useful in maintaining productivity, effective functioning, and independence through the middle and later years of life.

III. SPECIFIC OBJECTIVES

The NIH seeks research grant applications for the study of selected aspects of the relationship in older people between visual perception and effective functioning in real-life contexts, as this relationship may be mediated by cognitive processes and by compensatory and rehabilitative aids. The following are offered as illustrations of appropriate topics, though applications need not be limited to these issues. In assigning applications to NIA or other Institutes, accepted referral guidelines will be followed.

Visual Perception and Functioning in Real-Life Context

Whether a particular visual impairment interferes with functioning depends in part on the reciprocal relation between the social context and the experience, motivation, and coping skills of the older person. Research is needed to identify those characteristics of the social and physical environment and of individuals that lead to optimum functioning. For example:

- What environmental conditions, such as reduction of glare, use of color contrast, or spatial arrangements in the household or the workplace allow for optimal visual performance?
- What are the effects of visual deterioration on performance of complex tasks? How much of the variance in complex task performance among individuals can be accounted for by differences in measurable visual function?
- To what degree do social conditions of stress (as from rapid pacing) and information overload affect age changes in visual performance?
- What visual skills are important to the performance of tasks in the home, work, and community environments of the aging individual?
- How does the experience of visual decline (including its occurrence in association with other sensory, social, and economic loss) affect an older person's sense of well-being and of personal control?
How do social supports aid the functioning of the visually impaired, or enhance compensatory learning?

How is a visually impaired person's performance in a particular setting affected by early life experiences with that setting? How does education, income, or sex relate to coping with visual handicaps?

Visual Perception and Cognitive Processes

In explaining the differences among similarly impaired individuals performing real-world visual tasks, motivational differences and cognitive factors, such as perceptual learning and special cognitive strategies may play important roles. Research is needed that clarifies how sensory data are transformed into perceptual experience, and that specifies cognitive strategies used to cope effectively with the consequences of declining vision.

What changes occur with age in the interplay between visual functions and higher level perceptual processes?

To what degree do aging individuals use alternative perceptual and cognitive strategies to perform given tasks adequately, even though there has been some deterioration of visual functions?

To what degree does the aging individual's experience and acquired knowledge affect the processing of visual information?

What changes occur with age in the systems that operate upon sensory information: sorting, timing, interpreting, and organizing it?

To what extent does the older person actively control attention, selection, organization, and retrieval of visual information?

How is visual perception in older people affected by conditions of overload in the level and array of sensory input? Of task demands?

Compensatory and Rehabilitative Aids

Although various aids have been devised to offset age deficits in visual function and visual perception, further research is needed to provide the knowledge base for optimum compensation and rehabilitation. For example:

To what extent can older individuals compensate for particular declines in perceptual function, and can the compensatory skills be taught?

How are age-related differences in visual perception affected by such interventions as job redesign or training?

How can older persons be taught to utilize optical aids, such as special lenses or complex electronic equipment?

Can older persons develop special techniques to match and reinforce visual information with input from other sensory and motor channels?
IV. REVIEW CRITERIA

Applications compete on the basis of scientific merit with all applications before the NIA. The review criteria are the traditional considerations underlying scientific merit. Research applications need not be limited to any particular methodology of data collection or analysis. Designs may include demographic studies, cohort and longitudinal designs, multivariate analyses, or controlled experiments. Research should be done in representative real-life settings or under conditions that allow generalization to real-life settings or tasks. Multidisciplinary teams of researchers may be required, composed of visual scientists (including ophthalmologists or optometrists) in collaboration, e.g., with psychologists concerned with broad perceptual or cognitive processes, or with social scientists concerned with the match between performance and specific aspects of everyday settings as at work or in the household.

V. APPLICATION PROCEDURES

Researchers considering submitting an application in response to this announcement are strongly encouraged to discuss their project and the range of grant mechanisms available with NIA staff in advance of formal submission. This can be done either through a telephone conversation or through a brief written letter of intent describing the proposed project and identifying the principal investigator and, when known, other key participants.

Applicants should use the regular research project and program project grant application form (PHS 398), available at the applicant's institutional Application Control Office or from the Office of Grants Inquiries, Division of Research Grants, (DRG), NIH, (Tel.: 301-496-7441). In order to expedite the application form's routing within NIH, please (I) check the box on the application form's face sheet indicating that your proposal is in response to this announcement and print (next to the checked box) NIA AGING AND VISUAL PERCEPTION and (2) enclose a cover letter repeating that your application is in response to this announcement.

Mail the cover letter and the completed application (with 6 copies) to:

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

Receipt dates for Research Project Grant and New Investigator Award applications are: November 1, March 1, and July 1; for others, including Postdoctoral Fellow and Program Project applications: October 1, February 1 and June 1.

Address requests for additional information, research prospectuses, and/or letters of intent to:

National Institute on Aging  
Behavioral Sciences Research  
Attention: "Visual Perception"  
Building 31C - Room 4C32  
Bethesda, Maryland 20205  

Telephone: (301) 496-3136
ANNOUNCEMENT

GENETICS, MOLECULAR AND CELLULAR BIOLOGY PROGRAMS

MOLECULAR AND CELLULAR BIOLOGY BRANCH

BIOMEDICAL RESEARCH AND CLINICAL MEDICINE PROGRAM

NATIONAL INSTITUTE ON AGING

Application Receipt dates: November 1, March 1, July 1

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

The Molecular and Cellular Biology Branch (MCBB) is one of the three branches which comprise the Biomedical Research and Clinical Medicine Program (BRCM) of the NIA. MCBB contains four substantive categories: three of these are research oriented and one is concerned with research resources and services. MCBB administers grant-supported research and research training on fundamental molecular and genetic research on the biology and mechanisms of aging (1) at the cellular level, (2) on invertebrate organisms and plants, and (3) through theory elaborated by abstract modeling. In support of these three research areas, MCBB supports development of characterized biologic resources, and training and services related to the use of these biologics.

Grant-supported research is sought emphasizing the use of mammalian and human models. The content of these program areas is described below.

Molecular Biology

Studies on the mechanisms of aging at the molecular level using state-of-art approaches such as a recombinant DNA technology and Monoclonal antibodies for microanalysis. Molecules of particular interest are those which have been postulated to participate in aging processes, i.e., DNA.

Genetics and Cellular Aging

Herein are supported studies on the mechanisms of cellular aging, utilizing the technologies of cell culture, somatic-cell genetics, cell and tissue transplantation, chimeric and genetic-mosaic biology.

Genetics and Comparative Aging

Herein are supported studies on mechanisms of senescence and longevity in plants, prokaryotes, invertebrates and mammals. All applicable research strategies are encouraged; however, genetic approaches are especially emphasized.
Genetic and Cellular Resources

Fundamental to gerontology research is the availability of high quality and well-characterized biologics. This component of MCBB is responsible for biologics supply, characterization, and related services in the fields of cell culture, invertebrates, plants, and prokaryotes. These services are in support of both Extramural Research and research ongoing within the NIA Intramural Research Program. Research currently supported by grants includes research on cell lineage and population characteristics of human diploid cells in culture, the establishment, isolation, and characterization of new cell model systems and the training of postdoctoral scientists in the technologies of tissue-specific cell line development. Resources supported by contract include the NIA Cell Line Repository which supports acquisition, characterized, and distribution of cell lines of special utility to NIA grantees, prospective grantees, and other gerontologists.

Support by NIA for genetic, molecular and cellular aging research includes, but is not limited to, the specific areas designated above. Applications in other basic aging areas found meritorious by NIH's Peer Review groups and the NIA's National Advisory Council on Aging will be considered for support by NIA. Applications not responsive to this announcement will be assigned to awarding units following programmatic guidelines used by the Referral Branch, DRG.

Applications responding to this announcement should use form PHS 398, the standard application form for research project grants, and follow the procedure described therein. If the Institution's Business Office or Central Application Control Office does not have this form, a copy may be requested by writing to the following:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 449
Bethesda, Maryland 20205

Telephone: (301) 496-7441

Forward the completed application to the above-mentioned address. Receipt dates for applications are November 1, March 1, and July 1.

For further information, direct inquiries to:

Richard L. Sprott, Ph.D.
Chief
Molecular and Cellular Biology Branch
Biomedical Research and Clinical Medicine
National Institute on Aging
National Institutes of Health
Building 31 - Room 5C15
Bethesda, Maryland 20205

or to
DeWitt G. Hazzard, Ph.D.
Head
Cellular Biology Program
Biomedical Research and Clinical Medicine
National Institute on Aging
National Institutes of Health
Building 31 - Room 5C15
Bethesda, Maryland 20205

Telephone: (301) 496-6402
ANNOUNCEMENT

RESEARCH GRANTS RELATED TO BASIC MECHANISMS IN THE PHAKOMATOSES

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

The Developmental Neurology Branch, Convulsive, Developmental, and Neuromuscular Disorders Program, National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) encourages the submission of traditional research project grant applications (R01) related to the etiology, developmental embryology, pathogenesis, genetics and prevention of the phakomatoses.

I. BACKGROUND

The phakomatoses (Von Recklinghausen neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, Von Hippel-Lindau disease, the various lentiginoses and other neurocutaneous syndromes) are a group of hereditary developmental disorders which involve the ectodermal, mesodermal and endodermal germinal layers. Collectively, the phakomatoses affect one in about 2,500 births. Von Recklinghausen disease, the most common phakomatosis, has a birth incidence of one in 3,000. Most phakomatoses are inherited in autosomal dominant fashion, but irregularities in transmission and the high proportion of sporadic cases make genetic counseling and proper management of patients and their families difficult. These disorders manifest a constellation of systemic dysgenetic features including neoplasms which may undergo malignant transformation. Although in general the phakomatosis syndromes are clinically distinct, combined and transitional forms occur, and symptoms from different syndromes may coexist in many combinations in a patient or a family.

Tuberous sclerosis exemplifies the devastating effects that these disorders have on affected individuals and their families. Destructive lesions in the central and peripheral nervous systems usually appear in childhood and include tumors, angiomatous changes, calcifications and other processes. These lesions result in nervous system degeneration, mental retardation, ataxia, seizures, psychiatric disorders, blindness and deafness. The etiology is unknown and there is no effective therapy. Studies are, therefore, needed that go beyond the clinical delineation of these syndromes and the description of abnormal structure, to provide knowledge about basic mechanisms involved in the phakomatoses.

This program is described in the Catalogue of Federal Domestic Assistance No. 13.854, Fundamental Neurosciences. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.
II. RESEARCH GOALS AND SCOPE

The goals of this research program are to obtain information about basic mechanisms in the production of the phakomatoses, the developmental pathways through which these mechanisms operate, and the biochemical defects which result in the great variety of abnormalities seen in these disorders; and to develop measures for the prevention, early diagnosis and treatment of the phakomatoses.

The research scope of this program encompasses the developmental, genetic and biochemical aspects of the phakomatoses, and a variety of experimental approaches and methods. Some examples are given below, but applications are not limited to them, and proposals with new ideas and initiatives would be welcome.

A. Subjects

These may include experimental animals and human subjects. Animal mutants in particular could greatly facilitate research and provide direct and crucial information about the etiology, developmental embryology, pathogenesis, and genetics of the phakomatoses.

B. Developmental embryology

Developmental studies in humans are usually not practical because most phakomatosis phenotypes appear in childhood or adolescence. Efforts in this area should be directed towards the discovery of animal models exactly comparable to the human phakomatoses. Such models should make possible detection of early biochemical changes, characterization of the chemical pathology, and investigation of the developmental pathways by which a single gene mutation causes multiple tumor formation and the constellation of multisystemic dysgenetic features of these protean diseases.

C. Biochemistry

Studies in this area should extend the modest beginnings that have been made in biochemistry of the phakomatoses as well as explore new possibilities. For example, in Von Recklinghausen disease some abnormalities of hormone metabolism have been identified, but it is not clear if these abnormalities are causal or associated defects. In tuberous sclerosis an increase in hydroxyproline content has been found in kidney, pancreas, heart and lung tumors that might reflect a disturbance in collagen metabolism. Biochemical studies should be pursued at the cellular and molecular level with the currently available precise and highly sensitive techniques of immunochemistry and membrane microchemistry, tissue culture and the high-resolving power methods of rapid flow microfluorimetry and two-dimensional electrophoresis.

D. Genetics

The classical genetic studies of the phakomatoses have left many important questions unanswered. Further genetic studies, using modern, precise and sophisticated methods, are needed to determine if the various clinical types within a particular syndrome, such as the peripheral and central types of
Von Recklinghausen neurofibromatosis, are due to genetic heterogeneity; to assess the nature and significance of the sporadic cases; to identify the chromosomal and spatial relationship of the loci for the various phakomatoses; and to derive precise figures for genetic counseling.

E. **Early detection**

Identification of a biochemical marker should make possible early detection of the phakomatoses and thus lead to treatment, and management of sporadic cases. Assessment of the efficacy of CAT and PET scanning procedures for early detection and recognition of formes frustes would be highly desirable.

III. **MECHANISM OF SUPPORT**

Support for this program will be through the traditional research grant-in-aid. Successful applicants will direct and carry out the individual research projects.

IV. **APPLICATION AND REVIEW PROCEDURES**

Applications should be prepared on Form PHS 398 according to instructions contained in the application kit. Application kits are available from most institutional business offices, or may be obtained from the Division of Research Grants (DRG), at the address given below. Check "Yes" in item 2 on the face sheet of the application and type "Grants related to basic mechanisms in the phakomatoses" in the space provided.

The original and six copies of the application should be mailed to the following address:

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

Deadline dates for the receipt of individual research grant (R01) applications are November 1, March 1, and July 1.

An information copy of the application should be sent to the address below. Also, for further information applicants may contact:

Dr. Ntinos C. Myrianthopoulos  
National Institute of Neurological and Communicative Disorders and Stroke  
Federal Building - Room 8C-16A  
Bethesda, Maryland 20205

Telephone: (301) 496-5821