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

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SPECIAL EMPHASIS RESEARCH CAREER AWARD: DIABETES MELLITUS - CARDIOVASCULAR, METABOLIC, AND ENDOCRINOLOGIC ASPECTS, NHLBI AND NIAMDD

Next two application receipt dates are October 1, 1978, and February 15, 1979. Beginning in June 1979 and annually thereafter, SERCA applications will be received on June 1. Page 31

POSTDOCTORAL FELLOWSHIPS AND INSTITUTIONAL TRAINING GRANTS IN DIABETES, ENDOCRINOLOGY, AND METABOLISM RESEARCH, NIAMDD

Application receipt dates: October 1, February 1, and June 1. Page 37
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STUDIES OF DIABETES MELLITUS AND RELATED PROBLEMS, NEI, NHLBI, NIAID, NIAMDD, NICHD, NIDR, NINCDS, AND NIA

Application receipt dates: November 1, March 1, and July 1.

CLINICAL TRIAL ACTIVITY

Comments invited by September 30, 1978, on the proposed provisions.
RESEARCH ON SWEETENERS AND DENTAL CARIES,

NATIONAL INSTITUTE OF DENTAL RESEARCH

As a part of its mission to develop effective means to prevent dental caries, the National Caries Program (NCP) of the National Institute of Dental Research desires to stimulate research on available and potential new sweeteners as possible sugar substitutes in the development of non-cariogenic foods and beverages.

Applications relating to the areas listed below are invited. The list is not in order of priority, nor is it intended to exclude other closely related research topics. For information regarding the background, rationale, and long-term objectives of this request, it is suggested that prospective applicants refer to the NCP-sponsored publication: "Sweeteners and Dental Caries," J.H. Shaw and G.G. Roussos (Eds.) a Special Supplement to Feeding, Weight, and Obesity Abstracts, Information Retrieval, Inc., Washington, D.C. (1978). A limited number of copies of this publication are available without charge from the NCP. Additional copies may be purchased from the publisher.

1. A systematic search for new, safe, noncariogenic, commercially utilisable and, preferably, noncaloric sweeteners of both natural and synthetic origin.

2. Continuation of the physicochemical characterization, sensory, stability, and safety evaluation of recently identified, potentially noncariogenic and commercially applicable sweetener candidates such as the dihydrochalcones, monellin, thaumatin, chlorosucrose sweeteners, L-sorbose, stevioside, and rebaudiosides. The proposed studies on safety evaluation should be of a preliminary nature and may include investigations into the digestion and metabolism of these sweeteners, as well as various in vitro tests for carcinogenicity such as the induction of DNA damage and repair, mutagenesis in bacteria, yeast, Drosophila melanogaster, or in mammalian somatic cell cultures, and neoplastic transformation of mammalian cells in culture.

3. Studies on the structural modification of recently identified sweetener candidates in the hope that derivatives will be found which have more desirable safety, stability, and taste quality properties.

4. Continuation of the investigations into: (a) the receptor mechanism for the recognition of sweetness, (b) the taste-structure relationships of sweet substances, and (c) the identification of the minimal structure (active site) of the monellin and thaumatin molecules responsible for the sweet-taste sensation of these immunologically closely related proteins.
5. Determination of the effects of promising new sweeteners on:
(a) the microbial and biochemical composition of human dental plaque, (b) the in vitro formation and metabolism of dental plaque in terms of various physicochemical, microbiological, and biochemical parameters, which are either known or thought to contribute significantly to dental plaque formation and activity (e.g. adsorption of salivary proteins and bacteria to hydroxyapatite, bacterial growth, acid production, and synthesis and breakdown of intracellular and extracellular polysaccharides, and bacterial aggregation), (c) plaque formation and caries development in both experimental animals and humans, and (d) various biochemical components of both experimental animal and human saliva which are thought to affect caries incidence.

General Information

This announcement identifies the scope of the Program's interest in sweeteners and caries. It leaves the choice of research objectives, identification of specific aims, development of appropriate protocols and methodology and the procedures for analysis and interpretation of data to the investigator's initiative. However, once an award is made under this program, any substantial modification of the research originally proposed must be mutually agreed upon by the investigator and the National Caries Program.

The program will be supported by research project grants (authorization 42 USC 241 42 CFR 52). Although funds have been allocated for this program in the NCP financial plans for fiscal years 1979 through 1981, award of grants resulting from this announcement is contingent upon receipt of appropriated funds. Requests should be restricted to three years of research support.

Application Procedure

Applications should be prepared on research grant application form PHS 398, available in the business or grants and contracts offices of most academic and research institutions. The first (face) page of the application and the outside of the package should be labeled "RESPONSE TO PROGRAM ANNOUNCEMENT NIDR-NCP-SWEETENERS AND CARIES."

Applications must be received on or before the regular receipt dates of November 1, March 1, or July 1.

Applications should be sent to:

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

The initial review of applications for scientific and technical merit will be by an appropriate study section of the DRG; secondary review will be by the National Advisory Dental Research Council. Applicants will be informed of the outcome of the review shortly after each Council meeting. The earliest possible funding date will be July 1, 1979.

Questions concerning this announcement and other grant-related activities of the National Caries Program should be addressed to:

Chief, Caries Grant Programs Branch
National Caries Program
National Institute of Dental Research
Room 522, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20014

Telephone: (301) 496-7884
INFORMAL PRE-AWARD APPEALS PROCESS

Recommendations 62-69 of the NIH Grants Peer Review Study Team are concerned with the establishment of a formalized grants appeals system. The Director's decision regarding this set of recommendations was that they be further studied in the light of legal, fiscal, personnel, and other implications associated with adopting the recommendations. He further directed that in the interim, immediate consideration be given to making the function and operation of the present informal appeals system widely known. The following statement is being publicized in accordance with the Director's decision.

Study Section members make judgments on grant applications based on their interpretation of what is presented in the written application and at a site visit. Reviewers and applicants do not always view proposed studies in the same light, and occasional differences of opinion are to be expected. If the principal investigator believes that there are deficiencies, errors, or misunderstandings in the review group's assessment of the application, he or she may submit a revised application for re-review. The introductory section of the revised grant application should contain: (1) documented rebuttal of the Study Section's criticism, i.e., new information or correction(s) or other changes to reply to the deficiencies pointed out in the Summary Statement and (2) an indication of the modifications in the application that reflect the areas of criticism with which the principal investigator agrees. Additional specific procedural information is listed on page 10 of the Information and Instruction for Application for Research Grant brochure enclosed in each research grant application kit.

Experience has shown that the submission of a revised application is an efficient and effective way to appeal all or part of the substantive determinations of peer reviewers. The National Institutes of Health will do everything possible to facilitate the reconsideration of such revised requests.
NURSING RESEARCH PROGRAM GRANTS

DIVISION OF NURSING

Nursing Research Program Grants (hereafter referred to as Program Grants) are awarded by the Nursing Research Branch of the Division of Nursing, Bureau of Health Manpower, Health Resources Administration, under the authority of the Public Health Service Act, Section 301c.

OBJECTIVE The objective of the Program Grant is to stimulate the conduct of clusters of studies focused upon a single theme, in order to substantially enlarge the body of scientific knowledge basic to nursing practice, education, and administration. This support is also expected to aid institutions to strengthen their nursing research programs and resources, resulting in an increase in nursing research productivity within the institution. The individual studies comprising a Program Grant may investigate common questions in different populations, or explore different aspects of the single theme in varying ways, but every study in the group would have as its research goal the investigation of some dimension of the single theme selected for the Program Grant. It is this feature which distinguishes Nursing Research Program Grants from Nursing Research Project Grants. The Program Grant is particularly appropriate when there is a group of investigators with common interests within the institution. The advantages of the collaborative effort should be readily apparent from the presentation within the application.

ELIGIBILITY Nonprofit public and private institutions in the U.S. and its territories may apply for support of a Program Grant. A prospective grantee institution should:

1. be committed to basic or clinical research related to the discipline of nursing and to nursing practice;
2. have a strong potential for accomplishing this type of nursing research, as evidenced by the presence of a group of capable investigators with common interests in a research area pertinent to nursing; and
3. have the capacity for collaboration, especially with regard to the development of whatever resources are essential to the implementation of the research program.

CONDITIONS OF AWARD A Program Grant award may not exceed $100,000 in any one year in direct costs, and a minimum of three component studies must be included. Funds may be used to support the following activities:

1. salary for the support of key investigators and other personnel for the proportion of their time spent on the research program;
2. central or shared research resources, including equipment;
3. other direct research costs associated with conducting the proposed research;
4. the allocable portion of the allowable indirect costs of the institution, less applicable credits. Allowable costs are governed by Federal Regulations 45 CFR Part 74, DHEW Grants Administration Manual with PHS Supplements, and the Public Health Service Grants Policy Statement; and

5. alteration and renovation costs subject to limitations set forth in Chapter PHS 1-44 (supplementation to the DHEW Grants Administration Manual) and the Public Health Service Grants Policy Statement.

Grant funds may not be used for the following costs:

1. training and student support;
2. construction;
3. operating costs of an institutional grants and contracts office, central accounting, and similar activities; and
4. patient care costs, unless they are for purposes of the research.

ADMINISTRATION OF GRANTS Each grantee institution must appoint a program director (principal investigator) who will be responsible for the scientific direction of the research program, and for compliance with the policies and procedures of the Public Health Service. This individual must be a nurse scientist or a behavioral or biomedical scientist experienced in making discriminative scientific and administrative judgments and knowledgeable about nursing. In addition to the program director, each individual study in the Program Grant must have a project director. Public Health Service requirements relative to civil rights, patents, conduct of research involving human subjects, recombinant DNA, animal welfare, etc., apply to the Program Grant award. All publications resulting from research supported by a Program Grant must acknowledge the Division of Nursing as the source of support with a statement such as:

"This Nursing Research Program was supported by the U.S. Public Health Service under grant number (insert identity number) awarded by the Nursing Research Branch, Division of Nursing, Bureau of Health Manpower, Health Resources Administration."

The Division of Nursing is responsible for the review of applications and for the surveillance of active grants, including the evaluation of annual progress reports and the carrying out of site visits when appropriate for the assessment of the progress of the program.

The Program Grant must be administered in accordance with the policies set forth in this statement, and with respect to matters not covered herein, by applicable Federal statutes and regulations and Public Health Service policy statements.
APPLICATION PROCEDURES Application kits are available through the research offices of most institutions. Included in the application kit are the application form (PHS 398) and general instructions for preparing the application. Completed applications are submitted to the Division of Research Grants, National Institutes of Health, for assignment to the Division of Nursing for review and award. Each application for this program should have typed in under "Grant Application" (located on the upper left-hand portion of page 1 of the application): Nursing Research Program Grant. An appendix to the application should include curricula vitae for all named professional staff, consultants, and collaborators, as well as evidence of consultant consent to serve.

Early in the process of application development, applicants should contact Dr. Doris Bloch at the following address to determine programmatic eligibility:

Nursing Research Branch  
Division of Nursing, BHM, HRA  
Room 3-50, Center Building  
3700 East West Highway  
Hyattsville, Maryland 20782  
Telephone: (301) 436-6204

Following is the schedule for receipt and review of Program Grant applications:

<table>
<thead>
<tr>
<th>Receipt Date</th>
<th>Review Completed</th>
</tr>
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<tbody>
<tr>
<td>March 1</td>
<td>September/October</td>
</tr>
<tr>
<td>July 1</td>
<td>January/February</td>
</tr>
<tr>
<td>November 1</td>
<td>May</td>
</tr>
</tbody>
</table>

REVIEW OF APPLICATIONS Nursing Research Program Grant applications are subject to both a pre-review site visit and to peer review for scientific and programmatic merit. Recommendations are then forwarded to the National Advisory Council on Nurse Training for final review and recommendation to the Secretary of the Department of Health, Education, and Welfare.

CRITERIA Criteria for review of applications include, but are not limited to, the following:

A. Total Program

1. Significance of the research theme to the field of nursing.

2. Potential usefulness and capability of generalization of the research findings.

3. Evidence that the individual studies complement each other in the investigation of the research theme.

4. Feasibility of carrying out the research program within the institutional setting.

5. Qualifications of the program director (principal investigator) and other personnel whose time on the project is related to the entire program rather than to a component study.
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6. Adequacy of the available resources and environment for carrying out the research program.

7. Evidence of interdisciplinary collaboration in the development of the proposal, as well as of collaboration in carrying out the proposed research program.

B. Component Studies Each component study to be carried out as part of the research program will be reviewed on its own merit. The review committee may disapprove a component study, without necessarily disapproving the total program. The following are among the criteria applied:

1. Scientific merit of the study and its significance for research, including the degree to which it opens up or develops new fields of investigation, and the degree to which it supplements or duplicates work already done or in process.

2. The significance of the study in terms of social, historical, and health service factors.

3. Appropriateness and logic of the aims of the study.

4. Adequacy of the definition of the variables.

5. Appropriateness, adequacy, and feasibility of the suggested method and its logical relationship to the aims.

6. Adequacy of any instruments to be used, including their psychometric properties.

7. Qualifications and research experience of the project director, project staff, and consultants in terms of their ability to carry out the proposed component study.

8. Adequacy of the facilities and resources available to the investigators.


10. Adequacy of protection of human and/or animal subjects. A discussion of human subject protection issues should be included for each component study, according to directions contained in the application kit. A certification Form 596 must be submitted for each component study.
Under authority of Section 451 of the Public Health Service Act as amended (42 USC, Ch. 6A, subch. III), the National Eye Institute maintains a continuing interest into the early detection, diagnosis, treatment, and prevention of all forms of glaucoma. With the exception of low tension glaucoma, elevation of intraocular pressure (IOP) stands as a common denominator of all the different types of glaucoma thus far described clinically. The clinical sign of excessive IOP is presently the most widely recognized indication of damage to the optic nerve.

The purpose of this announcement is to emphasize the need for more laboratory and clinical research into certain aspects of the hydrodynamics of the eye affecting IOP regulation. This topic is of high priority research interest to the National Eye Institute and the following are examples of research opportunities identified by the National Advisory Eye Council in a recently published report entitled Vision Research - A National Plan.

It is the present belief that IOP is maintained within physiologically normal levels largely through a steady-state balance between the rate of formation of aqueous humor and the resistance to its outflow from the anterior chamber. More research should be focused on the influence of IOP on ocular hydrodynamics particularly on making a clear distinction between the effects of IOP on the secretion of aqueous humor and those it exerts on aqueous drainage.

Spontaneous periodic variations in IOP in open-angle glaucoma are one of the most important and least understood enigmas of this disease. The interrelationships between various hormonal and neural influences which impart a circadian rhythm to IOP in normal individuals need to be elucidated and applied to the study of the variations of IOP which occur in different types of glaucoma. Understanding of this natural variation may lead to improved control of IOP in glaucoma patients. Interdisciplinary initiatives are encouraged among ocular scientists and neuroendocrinologists and neuropharmacologists who are engaged in laboratory and clinical studies of other biological circadian rhythms.

Further research is also needed to define the process of uveoscleral outflow in normal and glaucomatous individuals by which a fraction of total aqueous humor passes through the ciliary muscle to the choroid and sclera. In experimental animals, this flow is dependent on compactness of the ciliary muscle and is independent of IOP. Choroidal detachment, a complication of antiglaucoma surgery in humans, is known to interfere with aqueous humor formation and may lead to an excessive reduction of IOP. The relationship of this occurrence to the phenomenon of uvea-scleral flow requires further
investigation. Methods for stimulating aqueous formation by drugs (other than prostaglandins) should be studied for treatment of hypotony associated with such detachments.

Little is known with regard to possible alterations of the metabolic states of the tissues between the anterior chamber and Schlemm's canal in open-angle glaucoma. Clarification of the way in which these tissues respond to various drugs, hormones, and cyclic nucleotides should lead to an understanding of how cellular activity modulates aqueous outflow in both normal and in glaucomatous eyes. Such studies should be carried out in enucleated animal and human eyes and in cultures of ocular tissues obtained at surgery or postmortem.

Particular emphasis should be placed on establishing cells of human trabecular meshwork in tissue culture, especially to enable systematic investigations of the turnover of various types of glycosaminoglycans both in normal and glaucomatous tissues. It has been suggested that in vivo trabecular cells are capable of synthesizing such macromolecules which may be deposited as extracellular material in Schlemm's canal and increase resistance to aqueous outflow. Glycosaminoglycans have been postulated to play such a role in the development of glaucoma subsequent to treatment with corticosteroids.

APPLICATION RECEIPT AND REVIEW

Receipt dates for new applications are November 1, March 1, and July 1. The earliest possible award date will be approximately nine months after receipt dates. Applications received too late for one cycle of review will be held for the next.

Applicants must use the regular research grant application (form PHS 398) which is available at institutional central application control offices. The completed application should be mailed to the Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014, where it will then be assigned according to the NIH referral guidelines for research grants. All applications will be reviewed by a Division of Research Grant Study Section and the National Advisory Eye Council. All applications recommended for approval will compete for available funds with all other approved applications assigned to the NEI. Support through an NEI research project grant is subject to applicable laws, regulations, and the policies to be found in the PHS Grants Policy Statement dated October 1, 1976, DHEW Publication No. (OS) 77-50,000.

Preliminary drafts of proposals and other inquiries regarding this announcement and the Vision Research - A National Plan report may be addressed to: Glaucoma Program Director, Scientific Programs Branch, National Eye Institute, National Institutes of Health, Bethesda, Maryland 20014; telephone: (301) 496-5301.

Please identify grant applications submitted in response to this announcement by writing at the top of the face sheet of the application: "SUBMITTED IN RESPONSE TO NEI PROGRAM ANNOUNCEMENT ON HYDRODYNAMICS OF THE EYE."
Under authority of Section 451 of the Public Health Service Act as amended (42 USC Ch. 6A, subch. III), the National Eye Institute maintains a continuing interest in the role of immunological processes in the normal and abnormal function of the eye. The National Advisory Eye Council, in reports entitled Vision Research Program Planning and Vision Research – A National Plan, has indicated many important research opportunities involving immunological concepts and methods. These documents point out the need for studies involving immunological approaches to understanding, treating, and preventing ocular diseases and for additional immunologists in vision research to conduct these critical laboratory and clinical inquiries.

The unique physiologic and anatomic properties of the eye present an opportunity for comprehensive interdisciplinary studies of basic immunologic processes in normal eyes and of eye diseases having immunologic associations. New research approaches are particularly encouraged for studies of: fundamental immunologic processes of the normal eye including the roles of, and interactions among, various immunoreactive cell types, humoral factors, and immune recognition; the roles of steroid hormones, autacoids, and other biochemical compounds and enzymes in inflammatory responses; the etiology of ocular autoimmune diseases; immunogenetic correlations with susceptibility to ocular diseases, success of drug therapy, and success of corneal grafts; and effects of immuno-suppressive therapies on both normal ocular function and resistance to ocular infections. Studies in basic and clinical areas should be designed to determine how drugs and immunologic agents modulate both beneficial and harmful ocular reactions.

Problems to which immunologically oriented investigations should be directed include:

**Inflammatory Processes**

**Corneal Inflammation** The cornea which is not normally traversed by the host's vascular and lymphatic systems is surrounded by vascular tissues, and in diseased states may become vascularized and inflamed consequent to trauma, corneal transplant surgery, infections, or adhesion to adjacent tissues. Since inflammatory reactions may lead to reduced vision, an understanding of these processes is essential to both prophylaxis and therapy. The cornea may also be used in experiments to distinguish immediate from delayed type hypersensitivity, and to ascertain the potential contribution of delayed type hypersensitivity to the pathogenesis of corneal clouding due to various viral, fungal, and bacterial infectious agents (herpes simplex keratitis, trachoma, etc.)
Ocular Allergy  Allergic diseases affect the lids, conjunctiva, cornea, and uvea. Clinical use of immunosuppressive agents requires further study, since they carry an increased risk of host invasion by infectious agents, reduction of the body's defense mechanisms, and possible development of malignancies. Therapeutic measures requiring further evaluation include uses of steroid hormones, prostaglandin antagonists, antigamma globulin compounds, and emerging modes of treatment. Clinical and laboratory studies are needed to increase our understanding of the pathogenesis of allergic diseases and treatment of such conditions as vernal conjunctivitis, the lymphofollicular hyperplastic response in trachoma, and certain viral infections of the conjunctiva.

Uveitis  Inflammation of the uveal tract is observed in a variety of clinical conditions. Because of a common blood supply, there is tendency for inflammations of the uveal tract to extend to adjacent tissues and jeopardize vision. The causative mechanism(s) for this inflammatory process is generally unknown, but involves complex cellular and humoral reactions with ocular tissues. Additional investigations of uveitis will aid in: defining the roles of humoral and cell-mediated immunity and antibody-complement reactions; understanding long-term persistence of immunological memory within ocular tissues; determining possible involvement of physiologically active compounds such as kinins, prostaglandins, and histamine; assessing the roles of retinal antigens and lens antigens in induction of uveitis; correlating disease incidences with specific histocompatibility antigens. Application of modern immunological techniques should provide increased understanding of the importance of local intraocular antibody formation on recurrent uveitis following viral infections, the influence of bacterial endotoxins on uveal inflammation, and the contribution of allergic reactions to the development of lesions in ocular toxoplasmosis and histoplasmosis.

Autoimmunity

Autoimmune disease may specifically account for ocular pathologies in such diseases as phacogenic uveitis (lens), sympathetic ophthalmia (uvea), Vogt-Koyanagi-Harada syndrome (uvea, retina), keratoconjunctivitis sicca (lacrimal glands), endogenous uveitis (uvea, retina), Mooren's Ulcer and cicatricial pemphigoid (cornea). What contributions autoimmune phenomena make to other ocular pathologies is not well understood. Basic and clinical investigations are required to further define the mechanisms of such diseases and to determine if immunologic reactions in these ocular pathologies are initiating events or secondary to other pathologic processes.

Immunogenetics

Genetic correlates of ocular disorders are still poorly defined. The roles of histocompatibility antigens should be better defined in graft rejection and as indicators of susceptibility to ocular or systemic diseases having ocular complications (ankylosing spondylitis, acute iridocyclitis, Hodgkin's disease, chronic hepatitis, Still's disease, and Reiter's disease).

The Eye as a Model

The readily accessible cornea offers an excellent experimental system for studying the basic immunologic mechanisms involved in graft acceptance or rejection including: donor-recipient histocompatibility relationships, effects of
immunosuppressive agents and anti-inflammatory drugs, tissue reactions with cellular and humoral antibodies, prophylactic immunological treatments, roles of hormones and autacoids in the immune response, how enzymes may be induced or activated during inflammation, and how specific inhibitors may be used in therapy. Knowledge derived from studies with the cornea should have general applicability to other ocular inflammatory conditions.

APPLICATION RECEIPT AND REVIEW

Receipt dates for new research grant applications are November 1, March 1, and July 1. The earliest possible award dates will be approximately nine months after receipt dates. Applications received too late for one cycle of review will be held for the next.

Applicants must use the regular research grant application (form PHS 398) which is available at institutional central application control offices. The completed application should be mailed to the Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014, where it will be assigned according to the NIH referral guidelines for research grants. All applications will be reviewed by a Division of Research Grant Study Section and the National Advisory Eye Council. All applications recommended for approval will compete for available funds with all other approved applications assigned to the NEI. Support through an NEI research project grant is subject to applicable laws, regulations, and the policies to be found in the PHS Grants Policy Statement dated October 1, 1976, DHEW Publication No. (OS) 77-50,000.

Preliminary drafts of proposals and other inquiries regarding this announcement and the reports Vision Research Program Planning and Vision Research - A National Plan may be addressed to: Scientific Programs Branch, National Eye Institute, National Institutes of Health, Bethesda, Maryland 20014; telephone: (301) 496-5301.

Please identify grant applications submitted in response to this announcement by writing at the top of the face sheet of the application: "SUBMITTED IN RESPONSE TO NEI PROGRAM ANNOUNCEMENT ON IMMUNOLOGICAL ASPECTS OF OCULAR DISEASE."
RESEARCH GRANT APPLICATIONS SOUGHT BY

THE NATIONAL EYE INSTITUTE

ON

SECONDARY GLAUCOMAS

Under authority of Section 451 of the Public Health Service Act as amended (42 USC, ch. 6A, subch. III) the National Eye Institute maintains a continuing interest into the prevention, early detection, diagnosis, and treatment of all forms of glaucoma. Glaucoma constitutes a group of disorders characterized by symptoms including increased intraocular pressure, alterations in the optic nervehead, and abnormalities in the visual field. Twelve percent of all blindness in the United States is attributable to these diseases. The recent report of the National Eye Council, Vision Research - A National Plan, emphasized the need for more research into the heterogenous group of disorders referred to as the secondary glaucomas. These glaucomas may be complications of other conditions including inflammatory diseases, tumors, vascular diseases, diabetes, or may accompany other ocular diseases. Thus, secondary glaucomas may follow: (a) uveitis, (b) exfoliation syndrome, (c) hemolytic or erythroclastic glaucoma, (d) leakage of lens antigens, (e) neovascularization of uveal tissues, (f) pigment dispersion syndrome, (g) epithelial invasion of the anterior chamber, and (h) retinal detachment.

Secondary glaucomas are difficult to manage clinically and produce a disproportionately high percentage of blindness relative to their prevalence. Ophthalmologists presently must rely upon therapies which are only partially satisfactory, using either drugs or surgery to reduce aqueous formation or improve aqueous humor drainage. Research into the specific pathogenesis of each of the secondary glaucomas should lead to new approaches to their prevention, early detection, and treatment. Brief descriptions of the secondary glaucomas and some suggested research approaches are listed below:

(a) Glaucomas Secondary to Uveitis The etiology of uveitis is still poorly understood, and the processes by which intraocular pressure is raised following uveitis are largely unknown. One possible mechanism may involve prostaglandins, which experimentally produce ocular inflammatory responses similar to those observed in uveitis. How prostaglandins or other products of inflammatory reactions of biochemical, immunological, or cellular nature relate to the etiology of glaucoma remains to be determined.

(b) Glaucoma Following Exfoliation Syndrome The fine gray material observed on the lens, iris, and in the filtration angle is distinctive to this condition. The composition of exfoliation material, its origin and possible precursors in serum or tissues are unknown and require investigation.
Hemolytic or Erythroclastic Glaucoma  Hemorrhage into the anterior or posterior chambers as a result of eye injury or some disorder of the retinal blood vessels may produce glaucoma by obstruction of the aqueous outflow system by aged red blood cells or ghosts. The effects of erythrocytes, ghost cells or their fragments, and accompanying macrophages on aqueous outflow are not well defined.

Glaucoma Secondary to Release of Lens Antigens  Products derived from lysis of lens or autoimmune responses to lens antigens (phacoanaphylactic glaucoma) may cause this disease. If not recognized early and treated definitively, these secondary glaucomas may lead to loss of vision and necessitate enucleation. Experimental studies defining the roles of individual lens proteins as antigens and the nature of the inflammatory responses to them are essential to an understanding of lens-induced glaucoma. Improved non-invasive methods for diagnosis of this condition must be developed.

Neuvascular Glaucoma  This disease occurs as a complication of many conditions having retinal ischemia as a factor. Present treatments involving drugs or surgery are often unsatisfactory once this disease is full blown, and therapy is primarily for prevention of pain. Research is clearly needed on the pathogenesis of neovascular glaucoma especially into defining the events initiated by retinal ischemia. Fundamental studies should also be directed toward identification of postulated vasculogenic factors. Controlled clinical trials should be undertaken to determine the value of panretinal photocoagulation of the peripheral fundus in preventing neovascularization of the iris and subsequent invasion of the aqueous humor drainage.

Pigment Dispersion Syndrome  Pigment derived from the iris may be deposited on the back of the cornea and in the anterior chamber angle in myopic young adults. However, not all persons with pigment dispersion syndrome develop glaucoma. Further description of the natural history of this condition is needed and improved methods for prophylaxis and treatment require development.

Glaucoma Following Invasion of the Anterior Chamber of Corneal or Conjunctival Epithelium  This condition which may arise as a result of a laceration to the eye or intraocular surgery may result in loss of the eye. Factors which influence intraocular growth of epithelium and the mechanisms producing the associated glaucoma are poorly understood. Useful experimental approaches might employ cell culture techniques as well as in vivo studies. Development of an appropriate animal model would aid this research.

Secondary Glaucoma Associated with Retinal Detachment  is a rare phenomenon; elucidation of the pathogenesis of this condition should reveal fundamental information about glaucoma as well as retinal detachment. A cooperative multiclinical study of this syndrome should provide sufficient cases both to define clinical features and to develop improved approaches to treatment.
Solutions to the above problems involve cross-disciplinary efforts among clinical researchers and pharmacologists, biochemists, immunologists, and cell biologists.

**APPLICATION RECEIPT AND REVIEW**

The receipt dates for new applications are November 1, March 1, and July 1. The earliest possible award date will be approximately nine months after receipt dates. Applications received too late for one cycle of review will be held for the next.

Applicants must use the regular research grant application (form PHS 398) which is available at institutional central application control offices. The completed application should be mailed to the Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014, where it will then be assigned according to the NIH referral guidelines for research grants. All applications will be reviewed by a Division of Research Grant Study Section and the National Advisory Eye Council. All applications recommended for approval will compete for available funds with all other approved applications assigned to the NEI. Support through an NEI research project grant is subject to applicable laws, regulations, and the policies to be found in the PHS Grants Policy Statement dated October 1, 1976, DHEW Publication No. (OS) 77-50,000.

Preliminary drafts of proposals and other inquiries regarding this announcement or the Vision Research - A National Plan report may be addressed to: Glaucoma Program, Scientific Programs Branch, National Eye Institute, National Institutes of Health, Bethesda, Maryland 20014; telephone: (301) 496-5301.

Please identify grant applications submitted in response to this announcement by writing at the top of the face sheet of the application, "SUBMITTED IN RESPONSE TO NEI PROGRAM ANNOUNCEMENT ON SECONDARY GLAUCOMAS."
BIOMEDICAL RESEARCH DEVELOPMENT
GRANT PROGRAM

The Division of Research Resources, National Institutes of Health, announces that the next deadline for receipt of applications for the institutionally oriented Biomedical Research Development Grant (BRDG) Program is October 1, 1978. BRDG applications are reviewed once each year.

The objective of the BRDG Program is to strengthen or expand biomedical and/or health-related behavioral research in institutions that have an explicit need for an enhanced research environment to improve the training of manpower for clinical professions or health-related research or both. The production of health manpower per se is not an objective.

Applicants therefore should demonstrate conclusively the need for developing, strengthening, or expanding their institutional health-related research environment to improve their health manpower training. Applicants are expected to demonstrate a commitment to sustain biomedical and/or health-related behavioral research capability upon termination of an award. They must show also a strong potential for scientific merit of the research to be developed. Documentation must be provided that will permit evaluation of applications with regard to each of these objectives and requirements.

The BRDG Program is a subprogram of the Biomedical Research Support Grant (BRSG) Program. Up to 10 percent of the funds available annually for the BRSG Program will be allocated for the BRDG Program. The program is highly competitive, and no more than 12 to 15 new awards are made each year. Applications may request up to three years of support, with average funding of no more than $100,000 per year.

Eligibility is limited to nonprofit institutions in the United States and its territories which, during the latest 12-month period ending September 30, have received less than $200,000 (direct and indirect costs) in Public Health Service (PHS) research grants. Each individual campus of a multi-campus university is considered as a separate "institution." Each health professional school is considered an "institution", even though it may be a component of a university. Institutions that receive other PHS research development grant support are not eligible for BRDG awards.

Eligible institutions may obtain application forms with special instructions, BRDG Program General Policy and Information Statement, advice on the preparation of applications, and information about eligibility or other matters from:

Biomedical Research Development Grant Program
Division of Research Resources
Room 5B23, Building 31
National Institutes of Health
Bethesda, Maryland 20014

Telephone: (301) 496-6743
GUIDELINES FOR NATIONAL EYE INSTITUTE
CORE GRANTS
FOR
VISION RESEARCH CENTERS (REVISED)

The purpose of this announcement is two-fold: first, to indicate the availability of the revised Guidelines for National Eye Institute Core Grants for Vision Research Centers; and second, to encourage prospective applicants for new, competing renewal, and competing supplemental core grants to contact National Eye Institute Scientific Programs Branch staff well in advance of application submission. Unsolicited core grant applications are not encouraged. For additional information on the revised Guidelines and the opportunities for discussion with NEI staff, please contact:

Chief, Scientific Programs Branch
National Eye Institute
National Institutes of Health
Room 6A49, Building 31
Bethesda, Maryland 20014

Telephone: (301) 496-5303
NEW INVESTIGATOR RESEARCH AWARDS IN DIABETES
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM,
AND DIGESTIVE DISEASES

The Diabetes Program of the National Institute of Arthritis, Metabolism, and Digestive Diseases announces initiation of a new award which will provide support for the initial independent research efforts of new investigators who are developing research interests and capabilities related to diabetes mellitus and its sequelae.

Eligibility Requirements

Applicants for the New Investigator Research Awards (NIRA) in Diabetes grant must (1) have been awarded a doctoral degree (or the equivalent) by the time of the award, (2) have had at least two years of prior full time research experience by the time of the award, (3) not have been named as the primary recipient of a federally-supported research grant or contract award except for a fellowship or traineeship, (4) meet certain U.S. citizenship or residency requirements at the time of application, (5) prepare and submit (through his/her institution) a grant application proposing a suitable project which is relevant to research problems in diabetes and related areas, and (6) submit with this application the names of three persons who are present or past supervisors or preceptors and who will forward letters attesting to the applicant's ability to undertake the project.

Provisions of the Award

Applicants may request support for a period of up to three years in an amount not to exceed $90,000 direct costs, of which no more than $35,000 may be requested for any 12-month period. The NIRA in Diabetes grant is not renewable and, because of its special nature, applicants are advised that proposed budgets will be reviewed carefully to ensure that they are consistent with the objectives of the award. In this regard, support may be requested for personnel, equipment, supplies, travel to scientific meetings, patient expenses, publications, and other expenses as justified in terms of the proposed research. In addition, indirect costs will be provided in accordance with established DHEW policies for regular research grants. It is anticipated that each NIRA will have a duration of three years and that the experience obtained by the investigator during this period will, in a majority of cases, help provide the basis for successful competition in the regular research programs of the Institute. The NIAMDD intends, after termination of each award, to follow the progress of each NIRA recipient for a period of six years in order to help evaluate the effectiveness of the program in fulfilling its objectives.
Implementation

NIRA applications will be received in accordance with the regular NIH cycle for new research grant applications as follows:

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<tr>
<th>APPLICATION RECEIPT</th>
<th>INITIAL REVIEW</th>
<th>COUNCIL REVIEW</th>
<th>EARLIEST START DATE</th>
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<tr>
<td>Nov. 1</td>
<td>Feb./March*</td>
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* of the year following application receipt.

For Additional Information

Individuals interested in obtaining additional information regarding the NIRA may obtain a copy of the guidelines and an application kit from:

Manpower Development Program Director  
Diabetes, Endocrine, and Metabolic Diseases  
NIAMDD-EP  
Room 626, Westwood Building  
Bethesda, Maryland 20016

Telephone: (301) 496-7348
SPECIAL EMPHASIS RESEARCH CAREER AWARD:
DIABETES MELLITUS - CARDIOVASCULAR, METABOLIC,
AND ENDOCRINOLOGIC ASPECTS
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
AND
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM,
AND DIGESTIVE DISEASES

This award is intended to:

- encourage qualified individuals in the early stages of their postgraduate medical and scientific careers to develop research interests and skills in the metabolic, endocrinologic, and cardiovascular aspects of diabetes mellitus;

- provide support for individuals to pursue a program of research in various fundamental and clinical research disciplines related to diabetes mellitus and its sequelae, at one or more domestic institutions which offer superior opportunities in these areas; and

- create a pool of highly qualified investigators with experience and skills in the cardiovascular, metabolic, and endocrinologic aspects of diabetes mellitus for future roles in related areas of research.

The Special Emphasis Research Career Award (SERCA) provides the opportunity for an individual with developing research interests to acquire experience and skill in the broad fundamental and clinical scientific disciplines essential for a multidisciplinary approach to the study of the metabolic, endocrinologic, and cardiovascular aspects of diabetes mellitus. In contrast to existing NIH awards which encourage the development of skills in a single discipline within a single laboratory, this award emphasizes in-depth experience in several fundamental and clinical scientific disciplines which are not necessarily dependent upon a single laboratory or institution.

Provisions of the Award

This nonrenewable award provides support for a five-year period of full time research and related activities. The latter may include research development activities as well as involvement in patient care to the extent that it will strengthen research skills. The SERCA grant made to the awardee's parent institution provides up to $30,000 per year for full time salary support plus fringe benefits. A maximum of $8,000 per year during the first three years...
and of up to $20,000 per year during the last two years will be provided for necessary research costs including technical assistance, equipment, supplies, consultant costs, domestic travel, patient care costs, publication, and other costs.

While working closely with an advisor, the awardee is expected to develop capabilities in fundamental, applied, and/or clinical research in each of three areas, namely the cardiovascular, metabolic, and endocrinologic aspects of diabetes. This should include exposure to multiple disciplines, such as physiology, biochemistry, biophysics, pharmacology, nutrition, and epidemiology. Investigators are encouraged to pursue these activities in several laboratories, and if appropriate, at more than one institution. In addition, an applicant must propose a research project of his/her own design which focuses on the cardiovascular, endocrinologic, and metabolic aspects of diabetes and which is of such scope that within three years, evidence of independent investigative capability will be presented. At the completion of this five-year award, the individual should be in a position to compete in regular NIH research grant and award programs.

Eligibility Requirements

In brief, candidates for the SERCA Award must (1) hold an M.D. or equivalent professional degree (e.g. D.D.S., D.O., D.V.M., etc.); (2) have a minimum of three years post-M.D. experience, including one year of clinical training in the sub-specialties of either cardiovascular disease or endocrinology-metabolism, or two years post-M.D./Ph.D. experience or equivalent. M.D./Ph.D. applicants should possess significant experience in metabolic, endocrine, or related areas, cardiovascular physiology, biochemistry, pharmacology, or other relevant areas of interest, such as epidemiology; (3) be citizens or noncitizen nationals of the United States or its possessions or territories or must have been lawfully admitted to the U.S. for permanent residence at the time of application; (4) meet certain other eligibility requirements specified in the SERCA Program Guidelines (see "For Additional Information").

Deadline for Receipt of Applications

The next two receipt dates for SERCA applications will be:

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<th>APPLICATION RECEIPT</th>
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<tr>
<td>October 1, 1978</td>
<td>Jan./Feb. 1979</td>
<td>July 1, 1979</td>
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<td>February 15, 1979</td>
<td>May 1979</td>
<td>July 1, 1979</td>
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Beginning in June 1979 and annually thereafter, SERCA applications will be received according to the following schedule:

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*of the year following application receipt.
For Additional Information

Prospective applicants are encouraged to review the new SERCA guidelines (dated July 1, 1978) which detail eligibility requirements and application procedures. In addition, prior to preparing an application, individuals are strongly encouraged to discuss their potential eligibility as well as their areas of research interest with the Program Director listed below. Requests for copies of the SERCA Guidelines as well as questions related to eligibility, etc., should be directed to:

Manpower Development Program Director
Diabetes, Endocrine, and Metabolic Diseases
National Institute of Arthritis, Metabolism, and Digestive Diseases
Room 626, Westwood Building
Bethesda, Maryland 20016

Telephone: (301) 496-7348
POSTDOCTORAL FELLOWSHIPS
AND
INSTITUTIONAL TRAINING GRANTS
IN
DIABETES, ENDOCRINOLOGY, AND METABOLISM RESEARCH
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

The Diabetes, Endocrinology, and Metabolic Diseases Program of the National Institute of Arthritis, Metabolism, and Digestive Diseases announces the continued availability of National Research Service Awards for both individual postdoctoral fellowships and institutional training grants. The purpose of these awards is to further develop the national manpower capability for biomedical research in diabetes mellitus, endocrinology, and metabolism. Emphasis is on the development of research manpower in diabetes and related areas, but development of research manpower in endocrinology and metabolism is also sought. Multidisciplinary programs providing opportunities for combined exposure to and experience in diabetes, endocrinology, and metabolism research are particularly encouraged. The Institute anticipates making new awards for both individual postdoctoral fellowships as well as institutional training grants subject to the receipt of meritorious applications and the availability of funds.

Postdoctoral Fellowships

Awards are made for specified training proposals from individual applicants in the area of diabetes, endocrinology and/or metabolism, selected as a result of national competition. Applicants must (1) be citizens or noncitizen nationals of the United States, or have been lawfully admitted to the U.S. for permanent residence and have in their possession an Alien Registration Receipt Card (I-151) at time of application; (2) have received a Ph.D., M.D., or equivalent degree.

Prior to formal submission, an applicant must arrange for an appointment to an appropriate institution and acceptance by a sponsor who will supervise his or her training and research experience. The institutional setting may be a domestic or foreign nonprofit private or public institution including the NIH and ADAMHA. The application must document the availability of staff and facilities to provide a suitable environment for performing high quality work. The major emphasis of the application should be the research training experience and broadening of scientific competence in areas related to diabetes mellitus, endocrinology and/or metabolism.
The award, which may be for a period of up to 3 years, provides a stipend of $10,000 to $14,000 per year depending on the extent of prior relevant postdoctoral experience. Stipend supplementation from non-federal funds is permitted. The award also provides up to $3,000 per year to a non-federal sponsoring institution to help defray trainee expenses such as tuition and fees (including appropriate medical insurance), research supplies, equipment, travel to scientific meetings, and related items.

Applications for individual postdoctoral fellowships will be evaluated on the basis of past academic and research records, the research training proposal, the sponsor's general qualifications, the training environment, the applicant's research goals, reference reports, and other relevant information. Applications will be evaluated first by an Initial Review Group and subsequently by the National Arthritis, Metabolism, and Digestive Diseases Advisory Council as outlined below under "Application Procedures and Additional Information."

**Institutional Training Grants**

Domestic nonprofit private or non-federal public institutions may apply for institutional grants to support training programs in diabetes, endocrinology and/or metabolism. Both predoctoral and postdoctoral trainees may be supported if either or both levels of training are justified in and approved on the basis of the application. The applicant institution must have, or be able to develop, the staff and facilities required for the proposed programs. The training program director at the institution will be responsible for the selection and appointment of trainees and for the overall direction of the program.

The proposed program must encompass supervised biomedical research training in diabetes mellitus, endocrinology and/or metabolism. In addition, a proposed predoctoral program must offer opportunity for research training leading toward a research degree and a proposed postdoctoral program must offer opportunity for individuals to broaden their scientific backgrounds. These awards are not made to support study leading to the M.D., D.O., D.D.S., or similar professional degrees nor are they made to support nonresearch clinical training.

Awards for institutional training grants may be made for project periods of up to 5 years. However, no individual appointed for training in the institutional award may receive more than 3 years of NRSA support in the aggregate. Institutional awards provide predoctoral stipends of $3,900 per year and postdoctoral stipends of $10,000 to $14,000 per year depending upon the extent of prior relevant postdoctoral experience. Stipend supplementation from non-federal funds is permitted. In addition, the institution may request funds for tuition, fees (including appropriate medical insurance), travel for trainees, actual indirect costs or 8% allowable direct costs (whichever is less) and up to 25% of the total award for costs deemed essential to carry out the training program such as salaries, equipment, research supplies, staff travel, etc.
Institutional training grant applications will be evaluated by an NIAMDD Special Review Committee as well as by the Institute's National Advisory Council. The application will be evaluated on the basis of records and qualifications of participating faculty, the proposed research training objectives and program design, previous training record of the program and its ability to attract high caliber students, institutional commitment, facilities and environment, and the relationship of the proposed program goals to the need for research training in diabetes mellitus and related areas, endocrinology and/or metabolism.

Application Procedures and Additional Information

Applications for individual postdoctoral fellowships as well as for institutional training grants will be received and reviewed in accordance with the following schedule:

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*of the year following application receipt.

Application materials, as well as additional information regarding both individual postdoctoral fellowships and institutional training grants may be obtained from:

Manpower Development Program Director
DEMD
NIAMDD
Room 626, Westwood Building
Bethesda, Maryland 20016

Telephone: (301) 496-7348
STUDIES OF DIABETES MELLITUS AND RELATED PROBLEMS

NATIONAL EYE INSTITUTE
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
NATIONAL INSTITUTE OF DENTAL RESEARCH
NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE
NATIONAL INSTITUTE ON AGING

The above-named Institutes of the National Institutes of Health invite applications for research grants in the general area of diabetes mellitus and related problems. Investigators working in other areas of research are particularly encouraged to develop diabetes-related projects either independently or, where appropriate, in collaboration with individuals currently engaged in diabetes research.

I. PROGRAM SPECIFICATIONS

A. Program Objectives

Diabetes mellitus is a major public health problem in the United States today. In recognition of this, the National Commission on Diabetes recommended an expanded national research effort in basic and clinical research into the cause, cure, and prevention of diabetes mellitus and related endocrinologic and metabolic disorders. It is anticipated that additional funds will be appropriated for the support of these activities.

B. Research Scope

The emphasis of this solicitation is upon research in both diabetes and diabetes-related activities. Activities identified as being related to diabetes generally fall into one of the following categories:

1. projects directly concerned with diabetes;
2. projects directly concerned with diabetes-related endocrine, metabolic, or vascular disorders;
3. projects directly concerned with the prevention, etiology, natural history, or treatment of disorders caused by diabetes, within specific organ systems; and
4. projects which are not directly concerned with diabetes but which could reasonably be expected to contribute new knowledge relative to the prevention, diagnosis, or cure of diabetes or a diabetes-associated disorder.
These projects may have their relationship to diabetes anywhere along the research spectrum, i.e., research on etiology, pathogenesis, epidemiology, diagnosis, and/or treatment of the disease.

Some areas of research interest are listed below. They are not listed in any order of priority. Moreover, these are examples only; other areas of research may occur to the applicant which are related to diabetes and which would be appropriate to the scope described above:

1. **AGING** Research on the effects of age on the etiology, epidemiology, and pathogenesis of diabetes. Studies that examine the inter-relationship of the physiological change with age and diabetes on the mechanism of hormone release and action; the effects on body composition, nutrition, and physical activity; standards for diagnosis; and the special problems of complications and treatment of diabetes in the geriatric population are also appropriate.

2. **ANIMAL MODELS** Studies which develop or utilize spontaneous or induced models of juvenile onset diabetes as well as maturity onset diabetes, obesity, and insulin resistance in experimental animals and which are directed toward elucidating the pathogenesis of this disorder or of its "complications."

3. **DENTAL COMPLICATIONS** Studies on the dental complications of the chronic diabetic syndrome, especially on the increased susceptibility of diabetics to periodontal disease. Such studies may focus on alterations in white cell functions (chemotaxis and phagocytosis), in the oral flora, in the immune response, or in collagen metabolism. Studies on the incidence of cleft palate in offspring of diabetic mothers, and research to develop artificial sugar substitutes for dietary control of tooth decay and diabetes are also appropriate.

4. **DIAGNOSIS** Research into the development of new or improved techniques for establishing the diagnosis of diabetes and of specific complications of diabetes (e.g. proliferative retinopathy), including the development of satisfactory and reliable genetic, enzymatic, biochemical, or other markers of the disease or its complications.

5. **EPIDEMIOLOGY** Studies of the epidemiology of diabetes including its prevalence and incidence in the population as a whole, as well as in discrete populations well characterized as to factors associated with the disease such as sex, age, nutritional patterns, body weight, physical activity, exposure to viruses, and other factors. Studies of prevalence and incidence of specific complications of diabetes within well-defined populations, including identifications of risk factors for such complications.

6. **ETIOLOGY, NATURAL HISTORY, PATHOGENESIS, TREATMENT** Studies of the nature, epidemiology, etiology, pathogenesis, treatment, and "complications" of diabetes mellitus. Studies of the complications of treatment of diabetes, such as exaggerated immune
responsiveness to insulin and infections in immuno compromised or otherwise normal diabetes, are also appropriate. Such studies may be approached from any discipline appropriate to basic research, clinical investigation, or to epidemiology.

7. GENETIC FACTORS Research into the role of genetic factors in diabetes mellitus, including identification of specific genetic markers which characterize individuals who have predisposing genes for diabetes, and definition of the mechanisms by which the genes associated with these loci express themselves. Such studies could consider the genetic character of juvenile-onset diabetes mellitus, maturity-onset diabetes mellitus, and maturity-onset diabetes mellitus of youth.

8. GLUCOSE HOMEOSTATIS Studies of factors that influence glucose tolerance and related hormone secretion and action, including age, body weight, nutrition, and physical activity, to name but a few. Clinical, metabolic, nutritional, and epidemiologic studies all offer appropriate approaches.

9. HORMONE SYNTHESIS AND SECRETION Basic and clinical studies of normal and abnormal mechanisms of biosynthesis and secretion of insulin, glucagon, and other hormones as they relate to diabetes mellitus.

10. IMMUNOLOGY, VIRUSES Assessment of the role of viruses in the etiology of diabetes, including investigation of their mechanism(s) of action and the host-parasite relationship determining their diabetogenic action, including further work on animal models of viral etiology. Assessment of the role of the immune response in the etiology of both juvenile-onset and adult-onset diabetes mellitus is appropriate. Studies of immunologic aspects in pathogenesis or complications of treatment such as autoimmune processes, Ir gene control of anti-insulin antibodies, mechanisms of insulin resistance, tolerance, and allergic reactivity are also appropriate.

11. INFANTS OF DIABETIC MOTHERS Developmental studies of intermediary metabolism and the control of hormonal synthesis, release and interaction in infants of diabetic, gestational diabetic, and nondiabetic women.

12. MECHANISM OF HORMONE ACTION Basic and clinical studies of the mechanism of hormone action as it relates to diabetes. Studies of insulin, insulin co-factors, insulin receptors, glucagon, and other hormones such as somatostatin, somatomedin, growth hormones and factors, and catecholamines may be included, but only as they relate to diabetes as defined on page 1. Investigation of the integrated reaction of these hormones and the regulation of metabolic processes is appropriate. Studies involving production of defined or single component insulin by such means as biochemical fractionation or recombinant DNA are also appropriate.
13. METABOLIC REGULATION Studies of normal and abnormal metabolic regulation as they relate to diabetes mellitus.

14. NEUROLOGICAL COMPLICATIONS Studies including physiological, biochemical, morphologic, and morphometric analysis of nerves from diabetics. Information of the type and distribution of lesions in the various forms of human diabetic neuropathy is needed and expected to offer insight into possible metabolic, vascular, or immunologic injuries. Data on vascular permeability, endoneurial pressure, axoplasmic flow and myelin composition may be obtained in experimental animals (genetic, surgical, alloxan, and streptozotocin diabetes) and correlated with physiologic and biochemical findings. Morphologic, biochemical, and physiological investigations of the structure and functions of peripheral nerves in organ cultures subjected to conditions similar to those occurring in diabetics are also appropriate. These may be expected to help define the roles of insulin, glucose, sorbitol, and myoinositol on myelination, Schwann, and nerve cell metabolism.

15. NUTRITION, OBESITY Research into the relationship between nutrition and diabetes, including the relationship between diabetes and obesity and insulin resistance. Such studies may focus on nutrition in early life as well as in the adult. Studies of feeding patterns in infancy and childhood are sought as well as research on the development of appetite, tastes, and dietary habits as antecedents to the development of obesity, insulin resistance, and diabetes mellitus. In addition, research into the central and peripheral regulation of appetite and feeding behavior within the context of diabetes, obesity, and insulin resistance is also appropriate.

16. OCULAR COMPLICATIONS The ease of observation of pathologic events in the retinal vasculature and elsewhere in the eye make the visual system a particularly appropriate model for studies of diabetic retinopathy and other manifestations of the microangiopathy that frequently accompanies diabetes. Research related to the role of metabolic agents in the etiology and management of diabetic cataract is also appropriate.

17. PREGNANCY AND DIABETES Research into the effects of pregnancy and parity on glucose tolerance and the development of gestational diabetes. Studies on all types of diabetes in pregnancy, including functional definition of optimal diabetic control throughout pregnancy are appropriate. Studies of the pathophysiologic mechanisms which contribute to abnormalities of the infants of diabetic mothers such as congenital malformations, stillbirths, neonatal deaths, and perinatal complications are also appropriate.

18. PSYCHO-SOCIAL ASPECTS Studies of the emotional and psycho-social factors associated with diabetes and its complications which may influence the course of the disease, and identification of approaches aimed at modifying the impact of these factors on the diabetic patient, the family unit, and the community.
19. RENAL COMPLICATIONS  Research relating to diabetic nephropathy.

20. TRANSPLANTATION, ARTIFICIAL DEVICES  Research approaches to transplantation of the pancreas or pancreatic islets (including special requirements and techniques for tissue matching, development, and monitoring of islet antibody) and development of "closed-loop" devices which both monitor plasma glucose and administer insulin appropriately.

21. VASCULAR COMPLICATIONS  Studies of the nature, epidemiology, etiology, pathogenesis or complications of atherosclerosis as they may relate to or be affected by diabetes or glucose intolerance in men and/or women. Studies of normal and abnormal cardiac phenomena as affected by or induced by diabetes or glucose intolerance in humans or in models of the diabetic state in experimental animals. Studies of macro- and microvascular disease in diabetes that may contribute to a better understanding of the epidemiology, etiology, and pathogenesis of peripheral vascular disease, gangrene of the lower limb and cerebrovascular disease among diabetics. Studies of the interactions in some individuals of carbohydrate intolerance, hypertriglyceridemia, adiposity, hypertension, and vascular disease. Studies utilizing spontaneous or induced models of diabetes in animals directed toward elucidating micro- or macrovascular circulatory disease or its complications. Studies relating to the rheology and coagulation of platelets in the diabetic state. Studies relevant to diabetes and infant respiratory distress syndrome are also appropriate.

C. Mechanism of Support

The mechanism of support for this program will be the grant-in-aid. The regulations (Code of Federal Regulations, Title 42, Part 52 and, as applicable to the state and local governments, Title 45, Part 74) and policies which govern the research grant programs of the National Institutes of Health will prevail. The award of grants pursuant to this request for grant applications is contingent upon ultimate receipt of appropriated funds for this purpose.

II. METHOD AND CRITERIA OF REVIEW

A. Assignment of Applications

Applications will be received by the NIH Division of Research Grants, referred to an appropriate study section for scientific review, and assigned to individual Institutes for possible funding. These decisions will be governed by normal programmatic considerations as specified in the DRG Referral Guidelines.

B. Review Procedures

Applications in response to this solicitation will be reviewed on a nationwide basis in competition with other research grant applications, and in accord with the usual National Institutes
of Health peer review procedures. Applications will first be reviewed for scientific and technical merit by a review group composed mostly of non-federal scientific consultants (study section), and then by the National Advisory Council of the appropriate Institute(s). The review criteria customarily employed by the National Institutes of Health for regular research grant applications will prevail.

C. Deadline

Applications will be accepted in accordance with the usual NIH receipt dates for new applications as follows:

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III. METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the business or grants and contracts office at most academic and research institutions. The phrase "PREPARED IN RESPONSE TO NIH DIABETES PROGRAM ANNOUNCEMENT" should be typed across the top of the first page of the application.

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

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

For further information, investigators are encouraged to contact one or more of the following individuals:

National Eye Institute

Chief, Scientific Program Branch  
NEI Extramural and Collaborative Programs  
Room 6A49, Building 31  
Bethesda, Maryland 20014

Telephone: (301) 496-5303
National Heart, Lung, and Blood Institute

Associate Director
Etiology of Arteriosclerosis and Hypertension Program
Division of Heart and Vascular Diseases
NHLBI
Room 516, Federal Building
Bethesda, Maryland 20014

Telephone: (301) 496-1613

National Institute of Allergy and Infectious Diseases

Chief
Office of Program Planning
NIAID
Room 7A17, Building 31
Bethesda, Maryland 20014

Telephone: (301) 496-2321

National Institute of Arthritis, Metabolism, and Digestive Diseases

Diabetes Program Director
Cellular and Molecular Studies
NIAMDD Extramural Programs
Room 628, Westwood Building
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