

NIH GUIDE

**For Grants
and
Contracts**

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**U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

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NOTICES

NATIONAL WORKSHOPS ON "PROTECTION OF HUMAN SUBJECTS"

P.T. 42; K.W. 0783005

National Institutes of Health
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

I. SOUTHWEST WORKSHOP

DATES: February 4-5, 1991

WORKSHOP SITE:
Meridien Hotel
50 Third Street
San Francisco, CA 94103

SPONSOR:
University of California at San Francisco
Box 0400
San Francisco, CA 94143

REGISTRATION CONTACT:
Ms. Phyllis Colbert
Workshop Contact Person
University of California at San Francisco
Box 0400
San Francisco, CA 94143
Telephone: (415) 476-1881

TOPIC: "The Use of Human Subjects in Research: AIDS as a Model of Complexity"

II. MIDEAST WORKSHOP

DATES: March 4-5, 1991

WORKSHOP SITE:
Friday Center
Laurel Hill Parkway
Chapel Hill, NC 27599-1020

SPONSORS:
University of North Carolina at Chapel Hill
300 Bynum Hall
Chapel Hill, NC 27599-4100

Shaw University
118 E. South Street
Raleigh, NC 27611

REGISTRATION CONTACT:
Mr. Al Dawson
Director
Friday Center
Laurel Hill Parkway
C. B. 1020
Chapel Hill, NC 27599-1020
Telephone: (919) 962-1106

TOPIC: "Problems in Interpreting the Federal Code for the Protection of Human Subjects"

III. MIDWEST WORKSHOP

DATES: April 11-12, 1991

WORKSHOP SITE:
Hyde Park Hilton
4900 Lake Shore Drive
Chicago, IL 60615

SPONSORS:
University of Chicago
970 East 58th Street
Chicago, IL 60637

Chicago State University
95th Street at King Drive
Chicago, IL 60628

REGISTRATION CONTACT:
Mr. Arnold L. Aronoff
Associate Director
Faculty and Administrative Services
University Research Administration
University of Chicago
970 East 58th Street
Chicago, IL 60637
Telephone: (312) 702-8669

TOPIC: "Cultural Diversity, Ethics, and Research: A Workshop on Human Subject Protections"

NIH/FDA have planned national human subject protections workshops in other parts of the United States. For further information regarding these workshops contact:

Darlene Marie Ross
Executive Assistant for Education
Division of Human Subject Protections
Office for Protection from Research Risks
National Institutes of Health
9000 Rockville Pike
Bldg. 31, Room 5B43B
Bethesda, MD 20892
Telephone: (301) 496-8101

NEI INSTITUTIONAL TRAINING GRANTS

P.T. 44; K.W. 0720005, 1002046, 0715100

National Eye Institute

The National Eye Institute (NEI) has recently revised its supplemental instructions for Institutional National Research Service Award applications. NEI accepts these applications only once a year: January 10.

Investigators are strongly encouraged to obtain a copy of these revised instructions before submitting an application. Please contact:

Ralph J. Helmsen, Ph.D.
Research Training and Resources Officer
National Eye Institute
National Institutes of Health
Building 31, Room 6A48
Bethesda, MD 20892
Telephone: (301) 496-5983

SMALL GRANT PROGRAM FOR PILOT PROJECTS

P.T. 34; K.W. 1014006

National Eye Institute

The National Eye Institute (NEI) no longer accepts applications for the Small Grant Program for Pilot Projects. The NEI made this decision after an evaluation of the program and extensive discussions with the National Advisory Eye Council and its Vision Research Program Planning Subcommittee. The funds

that had been set aside for this program will be used to help fund additional First Independent Research Support and Transition (FIRST) Awards and Physician Scientist Awards and to help expand NEI's participation in NIH initiatives for underrepresented minorities in biomedical research. Investigators from other fields who seek support for a new vision research project are encouraged to discuss their plans with one of NEI's extramural Program Directors.

INVENTIONS: IMPORTANT NOTICE FOR RESEARCH GRANTEES AND RESEARCH CONTRACTORS

P.T. 34; K.W. 1014006, 1014002

National Institutes of Health
Alcohol, Drug Abuse, and Mental Health Administration

From the Extramural Inventions Office, Building 31, Room 5B-41, NIH, Bethesda, MD 20892: The following instructions amplify a current notice (published in the NIH Guide for Grants and Contracts, Vol. 19, No. 23, June 22, 1990), regarding grant- and contract-assisted inventions. Our careful review of incoming documents has revealed several complications.

ACKNOWLEDGEMENT OF GOVERNMENT SUPPORT: 37 CFR 401.14 (f)(4) requires the grantee/contractor to protect the government's interest in the invention by including within the specifications of any United States patent application and any patent issuing thereon covering the subject invention, the following statement, "This invention was made with government support under (identify the grant or contract) awarded by (identify the Federal agency). The government has certain rights in the invention." Clearly, this statement is required in continuation and divisional patent applications as well.

Copies of patent applications that fail to acknowledge Government support continue to be submitted to the Invention Reports Office. Failure of applicants to include this clause in the initial submission of the patent application requires this Office to contact grantees and request them to file application amendments at additional costs to them.

PAPERWORK REDUCTION: The vast majority of patent applications proceed to orderly conclusions without Agency intervention. Consequently, for most cases, this Office does not need substantial portions of the appreciable volume of paperwork submitted by grantee organizations in accordance with the requirements of 37 CFR 401. While reserving the Government's right to receive complete documentation upon request, we propose the following alternate procedure.

PATENT APPLICATIONS: Before submitting copies of patent applications to the Inventions Reports Office, please remove the detailed specifications, background, and all drawings and their description. What will serve instead as an acceptable alternate are the introductory page with the statement acknowledging the Government's support plus the summary, abstract, and all claims.

MAILING and REQUESTS FOR ACKNOWLEDGEMENT OF RECEIPT: For the most part, documents may be posted via ordinary surface mail. If the grantee institution wishes a written response acknowledging receipt of the package, a stamped, self-addressed return envelope should be furnished.

INVENTION UTILIZATION REPORTS: Grantees are reminded of their obligation under 35 USC 202 (c)(5), to file periodic (currently biennial) reports on the utilization of each invention with the funding Agency (NIH). These reports shall contain information regarding the status of development, data of first sale or use, and gross royalties received by the grantee. Information in these utilization reports is treated as privileged and confidential and not subject to disclosure under the Freedom of Information Act.

SAMPLE (SIMPLIFIED) LICENSE FORM for use by an Institutional official or any individual inventor receiving title by waiver from the Federal Agency:

LICENSE TO THE UNITED STATES GOVERNMENT

This instrument confers to the United States Government, as represented by the Department of Health and Human Services, a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced on its behalf throughout the world the following subject invention:

Invention Title :
Inventor(s) :
Patent Application
Serial No. :
Filing Date :
Title :
Country, if other than the
United States :

This license will extend to all divisions or continuations of the patent application and all patents or re-issues which may be granted thereon.

This subject invention was made with government support from Grant/Contract No. _____ awarded by the National Institutes of Health.

Principal rights to this subject invention have been left with the Licensor: _____ subject to the provisions of Title 35 USC 200-212, 37 CFR 401, and 45 CFR 8.

Signed: _____ Date: _____

Typed Name: Title:

Seal

NOTICES OF AVAILABILITY (RFPs AND RFAs)

SPECIALIZED RESEARCH CENTER PROGRAMS OR CENTER CORE GRANTS TO SUPPORT RESEARCH IN REPRODUCTION - REVISION

RFA: HD-91-01

P.T. 04; K.W. 0710110, 0710115, 0413002, 1002042

National Institute of Child Health and Human Development

Application Receipt Date: May 6, 1991

The Reproductive Sciences Branch (RSB), Center for Population Research (CPR), National Institute of Child Health and Human Development (NICHD), recently announced (NIH Guide, Vol. 19, No. 30, page 4, August 17, 1990) the availability of a Request for Applications (RFA) for Specialized Research Programs (P50s) or Center Core Grants (P30s) to support research in reproduction. This announcement is hereby revised to include clarifications of policy guidelines relevant to applications to be submitted for this competition. These clarifications are as follows:

The application should be prepared in a manner consistent with the general guidelines presented in the publications entitled either P50 SPECIALIZED RESEARCH CENTER GRANT GUIDELINES or P30 CENTER CORE GRANT GUIDELINES which are available from the NICHD office listed below. The current policies and requirements that govern the research grant programs of NIH will prevail (Code of Federal Regulations, Title 42, Part 52 and Title 45, Part 75). Applications prepared for this competition should not propose multi-institutional consortiums.

Applications for grants involving clinical studies should include members of minority groups and women in the study populations. Otherwise, a clear rationale for their exclusion must be provided in the application.

The cost of a center will be a material consideration in the selection of applications for funding. New Specialized Research Center Grant (P50) applications should not request more than \$600,000 in direct costs for the first year. New Center Core Grant (P30) applications should not request more than \$500,000 in direct costs for the first year. Renewal applications from existing P30 or P50 Centers should not request initial year direct costs exceeding 120 percent of the Council recommended direct costs for the final year of the preceding project period. Unless prior written approval of the NICHD has been obtained, applications with requests exceeding these guidelines will be administratively withdrawn by the NICHD and returned to the applicant.

For further information please contact:

Michael E. McClure, Ph.D.
Chief, Reproductive Sciences Branch
Center for Population Research
National Institute of Child Health and Human Development
National Institutes of Health
Executive Plaza North, Suite 603
Bethesda, MD 20892
Telephone: (301) 496-6515

RESEARCH ON NEURONAL CEROID LIPOFUSCINOSES (BATTEN DISEASE)

RFA: NS-91-01

P.T. 34; K.W. 0715138, 1003002, 1002019, 0765033

National Institute of Neurological Disorders and Stroke

Letter of Intent Receipt Date: February 1, 1991

Application Receipt Date: March 15, 1991

PURPOSE

The neuronal ceroid lipofuscinoses (NCL) are a group of neurodegenerative diseases of children and adults. Despite various lines of scientific inquiry, the cause(s) of NCL remain unknown, with no biochemical, genetic, or single pathognomonic feature unambiguously identified to aid in understanding and treating this heterogeneous group of disorders. This Request for Applications (RFA) is intended to expand and sustain the NINDS Batten disease research endeavor through the R01 grant mechanism.

RESEARCH GOALS AND SCOPE

Research proposals may include but are not limited to the following areas:

o Biochemical Studies

Biochemical studies should use state-of-the-art techniques to identify and quantify the structural and mechanistic biochemical defects underlying NCL. Studies employing either human or animal tissues may be pursued, but careful attention in protocol designs must be given to identifying and explaining discrepancies among new and existing data that may arise from differences in the source, handling and preparation of tissue samples, or variability in clinical diagnostic criteria.

o Genetic Studies

Genetic studies should focus on elucidating the hereditary basis of NCL and explaining the heterogeneity of NCL with respect to age of onset and clinical manifestations. Studies applying techniques of molecular biology should focus on identifying genetic defects associated with particular loci and the consequences of any defects with respect to the production, processing, and function of relevant proteins within cells.

o Pathology and Diagnosis

These studies should contribute to more precise diagnosis and understanding of the pathology of NCL and facilitate biochemical and genetic projects.

MECHANISM OF SUPPORT

This is a one-time request that NINDS will support through the regular research grant (R01) mechanism. Up to \$2 million are available in support of this program. Awards will be contingent upon scientific merit and may be made for a period of one to five years. Funding for projects beyond the initial award will be subject to competitive renewal.

APPLICATION REQUIREMENTS AND PROCEDURES

The application deadline is March 15, 1991. NINDS invites applications from those knowledgeable about NCL and also encourages applications from highly qualified experts in basic and clinical neuroscience who may apply the expertise, techniques, and insights of their specialized areas to new studies directly relevant to NCL. In all cases, however, applications must be related clearly to NCL and address one or more specific research aims. Applications not meeting these criteria will be considered unresponsive and returned.

Investigators should carefully consider the appropriate length of time for their study, and proposals for periods less than five years and smaller budgets will be accepted without prejudice. Prospective applicants are encouraged to communicate with the staff contact who may provide guidance on the relevance of proposed concepts to the goals of the RFA. A non-binding letter of intent that includes a descriptive title, the name of the Principal Investigator and other Key Investigators, and any other participating institutions is requested to be submitted directly to the staff contact by February 1, 1991.

Applications should be submitted on Form PHS 398 (revised 10/88). To identify response to this RFA, check the "yes" box in Item Number 2 on the face page of the application and type: "In response to NS-91-01 Research On Neuronal Ceroid Lipofuscinoses (Batten Disease)" on line two. The RFA label available in the application form PHS 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review.

Investigators should be aware that NIH requires applicants to give added attention, where feasible and appropriate, to the inclusion of minorities and women in study populations. Gender and minority population differences should be noted and analyzed wherever possible. If minorities and/or women are not included in a given study, a clear reason for their absence must be provided. Merely including an arbitrary number of minority group and women participants in a given study is insufficient to guarantee generalization of results.

Minority institutions are encouraged to apply, and other institutions are encouraged to establish collaborative arrangements with minority institutions.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator included with the application is requested.

REVIEW PROCEDURES

Applications will be reviewed by NIH staff for responsiveness to the RFA. Responsive applications will be evaluated for scientific/technical merit by a Special Review Committee convened by the Scientific Review Branch of NINDS solely for this purpose. A second-level review will be made by the National Advisory Neurological Disorders and Stroke Council.

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

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

Two copies of the application also must be sent to:

Chief, Scientific Review Branch
National Institute of Neurological Disorders and Stroke
Federal Building, Room 9C10A
7550 Wisconsin Avenue
Bethesda, MD 20892

STAFF CONTACT

For further information, potential applicants may contact:

Karen J. Skinner, Ph.D
Federal Building, Room 8C-04
National Institute of Neurological Disorders and Stroke
Bethesda, MD 20892
Telephone: (301) 496-5821

This program is described in the Catalog of Federal Domestic Assistance No. 93.853, Clinical Research Related to Neurological Disorders, and 93.854, Biological Basis Research in the Neurosciences. Grants will be awarded under the authority of the Public Health Service Act, Title IV, 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 services agency review of the intergovernmental review requirements of Executive Order 1372.

EXPLORATORY GRANTS TO DEVELOP NATIONAL MULTI-PURPOSE RESEARCH AND TRAINING CENTERS

RFA AVAILABLE: DC-91-02

P.T. 34; K.W. 0715050, 0715055, 0720005

National Institute on Deafness and Other Communication Disorders

Letters of Intent will be due (optional): February 22, 1991
Application Receipt Date: March 15, 1991

PURPOSE

The National Institute on Deafness and Other Communication Disorders (NIDCD) requests Exploratory Grant applications (P20) from institutions wishing to develop a National Multi-Purpose Research and Training Center (RTC) for the multi-disciplinary study of communication sciences and disorders.

BACKGROUND

In December 1989, NIDCD issued a Request for Applications (RFA) (NIH Guide to Grants and Contracts, Volume 18, Number 45), announcing its intent to designate and support a limited number of National Multi-purpose Research and Training Centers (RTC) for the multi-disciplinary study of communication sciences and disorders. The goal of the RTC was the support of basic and clinical research; research training; continuing education for health professionals; and dissemination of information to the general public, in one or more of the program areas of the Institute (hearing, balance, smell, taste, voice, speech, and language).

The purpose of the Exploratory Grant is to plan or strengthen the essential components of the RTC (noted above) and to enable an institution subsequently to compete for such a center. It is expected that particular components for an RTC may already be in place for some Institutions.

The Exploratory Grant program for this RFA provides funding for the developmental phase of (1) planning and administration of one or more of the components of an RTC and/or (2) small-scale studies used to develop or test procedures to be employed in the RTC or to support a particular research direction. Up to five awards are possible if meritorious grant applications and funds are available.

The review criteria for Exploratory and RTC Grants include the adequacy of plans for the inclusion of underrepresented minorities, women, and individuals with disabilities as research subjects in the basic and clinical research components of the Exploratory Grant. For research projects not including any of these groups a clear rationale must be provided. (See NIH Guide, Vol. 19, No. 31, August 24, 1990, and Vol. 19, No. 35, September 28, 1990 for additional information).

MECHANISM OF SUPPORT, NUMBER OF YEARS, AND BUDGET

This RFA will be funded through the Exploratory Grant (P20) mechanism. Exploratory Grants may provide up to two years of support. Direct costs may not exceed \$100,000 per year. The Exploratory Grants are not renewable and supplements to these Grants are not allowed.

INQUIRIES

Applicants must obtain the following materials before beginning their applications: complete RFA for the Exploratory Grant; December 1989 RFA for National Multi-purpose Research and Training Centers; Application Guidelines: RTC; and PHS 398 Application Form (rev. 10/88). Applications should be developed in close cooperation with NIDCD Program Administrators below who will provide guidance to applicants on technical and substantive aspects of this RFA.

Maureen Hannley, Ph.D., (Hearing) or
Daniel Sklare, Ph.D., (Balance) or
Judith A. Cooper, Ph.D., (Voice, Speech, and Language) or
Jack Pearl, Ph.D., (Smell and Taste)

Division of Communication Sciences and Disorders
National Institute on Deafness and Other Communication Disorders
National Institutes of Health
Executive Plaza South, Suite 750
6120 Executive Boulevard
Rockville, MD 20852
Telephone: (301) 496-1804
Fax: (301) 402-0104

ONGOING PROGRAM ANNOUNCEMENTS

SMALL GRANT PROGRAM

PA: PA-91-11

P.T. 34; K.W. 0715050, 0715055, 0410001

National Institute on Deafness and Other Communication Disorders

This announcement for the National Institute on Deafness and Other Communication Disorders (NIDCD) Small Grant Program supersedes the one issued in February 1990. This current Small Grant Program provides support for pilot research to determine the feasibility of a subsequent research project. The research must be focused on areas within the mission of NIDCD, that is, hearing, balance/vestibular, smell, taste, voice, speech, or language.

ELIGIBILITY

In contrast to the previous announcement, the current Small Grant Program is designed solely to support basic and clinical scientists with limited research experience. Current or previous recipients of NIH research awards (R01 or R29) are ineligible for this Small Grant Program. Participation in the program by investigators at minority institutions is encouraged.

TERMS AND CONDITIONS OF THE AWARD

Small grant funds may not be used to support thesis or dissertation research.

Applicants may request up to \$25,000 (direct costs) per year. The grant may not exceed two years and is not renewable. Following completion of the Small Grant support, investigators are encouraged to seek support for research through an Individual Research Project Grant (R01) or a First Independent Research Support and Transition Award (R29).

APPLICATION SUBMISSION AND REVIEW PROCEDURES

Only one Small Grant application may be submitted by an individual or investigative team per receipt date. Applicants may not submit R01 or R29 applications with the same scientific content concurrently with the submission of a Small Grant application.

The submission, review and award schedule for the Small Grant Program is:

Receipt Dates for 1991	Institute Committee Review	Council Review	Earliest Funding
January 7	Feb-March	May	July
May 6	June	Sept-Oct	Dec
September 16	Oct-Nov	Jan-Feb	April

A review committee of the NIDCD will evaluate each Small Grant application with respect to these criteria:

- o significance and scientific merit of the proposed project with respect to the existing body of scientific knowledge;
- o scientific merit of the concept and underlying hypotheses;
- o investigator's potential for carrying out the research, as demonstrated by publication record and/or previous research/clinical experience or training relative to the goals and methods of the proposed study;
- o adequacy of the investigator's time commitment to the project;

- o potential of the proposed studies to lead to more extensive research;
- o adequacy of the facilities, supporting personnel, and existing equipment for carrying out the proposed studies; and
- o justifications of budget requests.

All applications will subsequently be reviewed by the National Deafness and Other Communication Disorders Advisory Council. The award of grants is contingent on receipt of proposals of high scientific merit; responsiveness to this announcement, including the eligibility of investigators; relevance to the program; and the availability of appropriated funds.

GRANT APPLICATION

Use the standard research grant application form, PHS 398 (rev. 10/88). Application kits are available from the business offices or the offices of sponsored research of most institutions, the Division of Research Grants, National Institutes of Health (301-496-7441), and NIDCD Division staff listed below.

Face page. Item 2. Type "Small Grant Program NIDCD, PA-91-11". Check the "YES" box.

Section 2. Do not exceed five pages. Applications that exceed the page limitation or NIH requirements for type size and margins will be returned to the investigator. Include the following sections: specific aims and significance, progress report/preliminary studies and methods. Provide introduction only for revised applications.

Applicants are required to include, where feasible and appropriate, minorities and women as well as men in the study populations for all clinical research efforts and to analyze, where appropriate, differences between these populations. If women and minorities are not to be included, a clear rationale for their exclusion must be provided.

Section 3. Appendix materials are not allowed.

Use the mailing label in the application kit to mail the original and four copies of the application to the Division of Research Grants. To expedite the review, send one copy of the application to:

Dr. Earleen Elkins, Chief, Scientific Review Branch
 National Institute on Deafness and Other Communication Disorders
 National Institutes of Health
 Executive Plaza South, Rm. 750
 6120 Executive Plaza Blvd.
 Rockville, MD 20852
 Telephone: (301) 496-8683

Investigators are encouraged to call (301-496-5061) or write (at the Institute address noted above) Institute staff responsible for the investigator's particular area of scientific interest:

Dr. Judith Cooper (voice, speech, language) or
 Dr. Maureen Hannley (hearing) or
 Dr. Jack Pearl (chemical senses) or
 Dr. Daniel Sklare (balance/vestibular)

This program is described in the Catalog of Federal Domestic Assistance No. 93.173, Research Related to Deafness and Communication Disorders. Awards will be made under the authority of the Public Health Service Act, 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. The program is not subject to Executive Order 12372.

CLINICAL STUDIES TO PREVENT INSULIN-DEPENDENT DIABETES MELLITUS BY IMMUNOMODULATION

PA: PA-91-12

P.T. 34; K.W. 0715075, 0710070, 0745040, 0715015, 0785035, 0785050

National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Allergy and Infectious Diseases
National Institute of Child Health and Human Development

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute of Allergy and Infectious Diseases (NIAID), and the National Institute of Child Health and Human Development (NICHD) are seeking applications for clinical studies designed to test the hypothesis that immunomodulation will prevent insulin-dependent diabetes mellitus (IDDM) in high-risk populations.

BACKGROUND

Over the past 10 years, significant progress has been made in defining the autoimmune etiology and pathophysiology of IDDM. Several clinical trials of general immunosuppressive agents in patients with newly diagnosed IDDM have induced a temporary clinical remission of this disease. These observations have led to the hypothesis that immunomodulatory interventions may be effective in the prevention of this disease in individuals who are asymptomatic but who are in an earlier period of the autoimmune process.

A workshop on Clinical Trials of Immunosuppression for Prevention of IDDM was held on April 19-20, 1990, in Bethesda, Maryland. This workshop was sponsored by the NIDDK, NIAID and NICHD. It was the charge of this group to assess the status of scientific and medical knowledge necessary to initiate a clinical trial of immunomodulatory intervention for the prevention of IDDM. Participants for the meeting were drawn from the diabetes and immunology research communities and were chosen to provide a broad range of insight and judgment in these areas. Several major issues were extensively discussed, and consensus was reached in some areas while others remained open for continued examination, evaluation, and debate. There was general consensus based on the published literature and discussion on the following important issues:

1. IDDM in humans is an autoimmune disease and, as such, should be amenable to immunotherapeutic intervention;
2. There are measurable parameters that can identify a group of individuals at high risk for the development of IDDM; and
3. Further clinical studies in high-risk individuals to explore the ability of immunomodulation to alter the natural history of IDDM are timely and warranted.

A summary of this workshop is available from the NIDDK staff listed at the end of this announcement.

RESEARCH GOALS AND SCOPE

The goal of this Program Announcement is to stimulate clinical research that will evaluate the effectiveness of immunomodulatory therapies for the prevention of IDDM in high-risk populations. The research scope of this program will encompass a range of basic and clinical research disciplines, such as immunology, endocrinology, genetics, biochemistry, pharmacology, physiology and pediatrics. Some examples of relevant research areas to be addressed by these clinical studies include:

- o Identification and characterization of markers that have value in predicting remission or progression in pre-IDDM individuals on long-term immunotherapy;
- o Using presently available markers, determine the natural history of high-risk individuals; and
- o Evaluation of the effect of immunomodulatory interventions in high-risk individuals including efficacy in prevention of progression of the autoimmune process and parameters such as dosage, duration, and deleterious side effects.

These recommendations are not necessarily all inclusive and any new ideas with credible hypotheses that would appropriately fall within the scope of this announcement may be the basis for an application.

APPLICATION AND REVIEW PROCEDURES

The mechanism for support for this program will be the individual research grant (R01). The application may include subcontracts or consortia with multiple institutions. Applicants should use the standard research grant application (PHS 398, revised October 1988). If application kits are not available at the institution's business office or central application control office, an individual copy may be requested by writing to the National Institutes of Health, Division of Research Grants, 5333 Westbard Avenue, Room 449, Bethesda, MD, 20892.

The clinical studies anticipated as a result of this announcement will likely require the screening of large numbers of individuals. It is anticipated that this may necessitate the coordinated efforts of several clinical centers. Because of the complexity of reviewing multi-center clinical studies, responders to this announcement are advised to submit their applications by June 1, 1991.

Applications in response to this solicitation will be reviewed in accordance with the usual NIH 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). Secondary reviews will be by appropriate national advisory councils. Applications recommended for approval will compete for available funds with all other approved applications assigned to the Institutes. However, because the Institutes and their Advisory Councils have identified this research area to be of particular program interest, applications responsive to this announcement will be brought to the special attention of the Councils.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center of Research Resources may wish to identify the Center as a resource for conducting the proposed research. In such a case, a letter of agreement from the GCRC Program Director should be included in the application material.

Applicants are reminded that applications and awards for extramural support for clinical research studies involving human subjects should include women and minorities unless a compelling justification is made for their exclusion. For further information, consult the statements of NIH policy on the inclusion of minorities and women in study populations that appeared in the NIH Guide for Grants and Contracts. The issue dated August 24, 1990, (Vol. 19, No. 31, pp. 18-19) announced the policy on women; the policy on minorities appeared in the issue dated September 28, 1990, (Vol. 19, No. 35, pp. 1-2).

In order to identify the application as a response to this Program Announcement, check "yes" on Item 2 of the application face page with the title "Clinical Studies to Prevent IDDM by Immunomodulation, PA-91-12." The original and six copies of the application should be mailed to:

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

Potential applicants are encouraged to discuss their plans with appropriate NIH program staff listed below.

Dr. Joan T. Harmon
Executive Director, Diabetes Research Program
NIH, NIDDK, DDEM, DPB
Westwood Building, Room 622
Bethesda, MD 20892
Telephone: (301) 496-7731

Dr. Howard B. Dickler
Acting Deputy Director
Division of Allergy, Immunology and Transplantation
NIH, NIAID
Westwood Building, Room 755
Bethesda, MD 20892
Telephone: (301) 496-7104

Dr. Gilman D. Grave
Chief, Endocrinology, Nutrition and Growth Branch
NIH, NICHD, CRMC
Executive Plaza North - Room 637
Bethesda, MD 20892
Telephone: (301) 496-5593

This program is described in the Catalog of Federal Domestic Assistance No. 93.847, Diabetes, Endocrinology and Metabolism Research.

THE IMMUNOLOGY OF INSULIN-DEPENDENT DIABETES MELLITUS

PA: PA-91-13

P.T. 34; K.W. 0715075, 0755030, 0765035, 0710070, 1002004, 1002008, 1002019

National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Allergy and Infectious Diseases
National Institute of Child Health and Human Development

This announcement is intended to encourage submission of research proposals to develop our knowledge and understanding of the etiology and pathophysiology of insulin-dependent diabetes mellitus (IDDM). It is anticipated that new insights into identification and monitoring of individuals at risk for this disease, as well as novel interventions effective in the prevention of this disease, will be forthcoming.

BACKGROUND

Understanding of IDDM has been greatly improved by the elucidation of the role that the immune system plays in the pathophysiology of the development of this disease. Parameters such as islet cell autoantibody (ICA) titers, competitive insulin autoantibody (CIAA) titers, and reductions in the first phase plasma insulin response to intravenous glucose (IVGTT) can be employed to select individuals at high risk for the development of IDDM. However, the relationship of these parameters to the natural history or to the etiology of this disease remains unclear, and the parameters presently identify only a minority of the individuals who will eventually develop IDDM.

At the recent workshop on the Clinical Trials of Immunosuppression for Prevention of IDDM (April 19-20, 1990, Bethesda, Maryland), general consensus was reached on several important issues. First, IDDM is an autoimmune disease. Second, there are several parameters that can identify a group of individuals at high risk for the development of IDDM. As a result of this consensus, clinical studies to explore the ability of immunomodulation to alter the natural history of IDDM are considered timely and warranted. A companion Program Announcement designed to be complementary to the present one is to alert the scientific community of our interest in considering the support of such clinical studies at the present time.

A number of other issues that require further research efforts were discussed at the workshop. This Program Announcement specifically seeks to address these issues. A summary of this workshop is available from the NIDDK staff member listed at the end of this announcement.

RESEARCH GOALS AND SCOPE

The goal of this Program Announcement is to stimulate basic and clinical research that will elucidate the etiology and pathophysiology of IDDM.

The research scope of this program will encompass a wide range of basic and clinical research disciplines, such as biochemistry, immunology, cellular biology, endocrinology, genetics, molecular biology, pharmacology and physiology. The areas of research recommended include:

- o Development of methods to ascertain beta cell mass in normal, high-risk, and diseased individuals;
- o Determination of the natural history of IDDM with respect to the presently available selection parameters;
- o Identification of new parameters that will allow early detection of susceptible individuals, expansion of screening protocols to the general population, or that will correlate with the disease process;

- o Identification of the initiating event that triggers the autoimmune process in this disease;
- o Establishment of new immunomodulatory interventions tailored specifically to IDDM; and
- o Utilization of appropriate animal models to ascertain the efficacy of potential interventions.

These recommendations are not necessarily all inclusive and any new ideas with credible hypotheses that would appropriately fall within the scope of this announcement may be the basis for an application.

APPLICATION AND REVIEW PROCEDURES

The mechanisms of support for this program will include the individual research project grant (R01), the First Independent Research Support and Transition (FIRST) Award (R29), the National Research Service Award (F32 and F33), and career awards such as the Research Career Development Award (K04), Clinical Investigator Award (K08) and Physician Scientist Awards (K11). The award of grants pursuant to this announcement is contingent upon both the receipt of proposals of high scientific merit that are responsive to this announcement and the availability of appropriated funds.

Applications will be received by the NIH Division of Research Grants (DRG), referred to an appropriate Study Section for scientific merit review, and assigned to individual Institutes for possible funding. Referral decisions will be governed by normal programmatic considerations as specified in the Referral Guidelines of the Public Health Service.

Applications in response to this solicitation will be reviewed on a nation-wide basis in competition with other applications and in accordance with the usual NIH 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 NIH will prevail.

Applicants are reminded that applications and awards for extramural support for clinical research studies involving human subjects should include women and minorities, unless a compelling justification is made for their exclusion. For further information, consult the statements of NIH policy on the inclusion of minorities and women in study populations that appeared in the NIH Guide for Grants and Contracts. The issue dated August 24, 1990, (Vol. 19, No. 31, pp. 18-19) announced the policy on women; the policy on minorities appeared in the issue dated September 28, 1990, (Vol. 19, No. 35, pp. 1-2).

Applications should be submitted on PHS Form 398 (revised October 1988), which is available in the business or grants and contracts office at most academic and research institutions. On the face page of PHS Form 398, under item 2, indicate that the application was prepared in response to the program announcement entitled "The Immunology of IDDM, PA-91-13." The original and six copies of the application should be sent or delivered to:

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

Applications will be accepted in accordance with the usual NIH receipt dates for applications.

For further information, investigators may contact one or more of the following individuals:

Dr. Joan T. Harmon
 Executive Director, Diabetes Research Program
 NIH, NIDDK, DDEM, DPB
 Westwood Building, Room 622
 Bethesda, MD 20892
 Telephone: (301) 496-7731

Dr. Howard B. Dickler
Acting Deputy Director
Division of Allergy, Immunology and Transplantation
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Telephone: (301) 496-5593

This program is described in the Catalog of Federal Domestic Assistance No. 93.847, Diabetes, Endocrinology and Metabolism Research.

**THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:

5333 Westbard Avenue
Bethesda, Maryland 20816