

NIH GUIDE

**For Grants
and
Contracts**

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

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PLEASE NOTE: Due to summer vacation schedules, the NIH GUIDE FOR
GRANTS AND CONTRACTS will not be published on August 4, 1989. The
next issue will be August 11, 1989.

NOTICES

NIH REGIONAL CONFERENCE IN GRANTS ADMINISTRATION

P.T. 42; K.W. 1014006

National Institutes of Health

A two-day conference covering topics related to both program funding and grants administration at the National Institutes of Health is planned for October 18 - 19, 1989, at the University of Missouri-Columbia. The conference is targeted for an audience of researchers and research administrators at institutions in the midwest region which includes Colorado, Illinois, Iowa, Kansas, Missouri, Nebraska, and Oklahoma. Those interested from other states are also encouraged to attend. Investigators and staff from small and minority colleges, for-profit research organizations, hospitals, universities, and research institutes are invited. This two-day conference has a dual focus of interest to both researchers and grants administrators. Discussions of current issues that affect NIH funding and grants administration are included to give conference participants a comprehensive, up-to-date view of NIH-sponsored research.

The first day of the conference is devoted to discussions of current interest to the research programs of the various institutes that comprise the NIH. Preparation of an NIH proposal and the NIH review process are included as agenda topics. Program representatives from several NIH institutes are featured speakers. Time will be available for conference participants to meet informally with the NIH representatives and discuss topics of special interest.

The program for the second day covers topics associated with pre-award and post-award administration of NIH grants. Policy and procedural issues affecting NIH grants administration form the basis for the program. General discussions on current issues and the changes they precipitate are integrated with more specific discussions regarding special career development programs and lab safety. Mr. Geoffrey Grant, Grants Policy Officer in the Office of Extramural Research at NIH, representatives from the Division of Research Grants, and program and grants management staff of several institutes are featured speakers.

Conference schedule and fee information will be mailed out early September. For more information, contact E. Jane Rutter, conference coordinator at (314) 882-9584 or Barry Kling, Director, Continuing Education and Extension for the Health Profession at (314) 882-4105.

DATED ANNOUNCEMENTS (RFPs AND RFAs)

DISTRIBUTION OF MOUSE MODELS FOR NEURAL TUBE DEFECTS

RFP AVAILABLE: RFP-NICHD-89-25

P.T. 34; K.W. 1002002, 0755020

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) is seeking organizations to maintain and distribute two mouse models for neural tube defects to the scientific community. The mouse models have been developed under two existing contracts with NICHD. The organization needs to have the expertise and the facilities to house and maintain breeding stocks of mutant mice and the capability to distribute them to interested investigators.

This announcement is a new solicitation. The issuance of the RFP will be on August 7, 1989, and proposals will be due by 4:00 pm EDT, October 10, 1989. The Institute expects to make one award from this solicitation.

Requests for the RFP shall be directed in writing to:

Mrs. Lynn Salo
NICHD, OGC, CMS
Executive Plaza North Bldg., Rm. 515
9000 Rockville Pike
Bethesda, Maryland 20892

To receive a copy of the RFP, please supply this office with two self-addressed mailing labels. All responsible sources may submit a proposal which will be considered.

This advertisement does not commit the Government to award a contract.

NATIONAL COOPERATIVE VACCINE DEVELOPMENT GROUPS FOR THE ACQUIRED IMMUNODEFICIENCY SYNDROME

RFA: 89-AI-16

P.T. 34; K.W. 0715008, 0740075, 1002045, 0760080, 1002008, 0710030

National Institute of Allergy and Infectious Diseases

Revised Application Receipt Date: December 8, 1989

The National Institute of Allergy and Infectious Diseases has revised the application receipt date for the Request for Applications (RFA) 89-AI-16, National Cooperative Vaccine Development Groups for the Acquired Immunodeficiency Syndrome, from August 10, 1989, to December 8, 1989. The earliest award date is June 1, 1990.

Questions concerning this revised due date and requests for copies of the full RFA document may be directed to:

Dr. Wayne Koff
AIDS Program, NIAID
Vaccine Research and Development Branch
6003 Executive Bldg., Room 234P
Rockville, Maryland 20892
Telephone: (301) 496-8200

NATIONAL COOPERATIVE DRUG DISCOVERY GROUPS FOR THE TREATMENT OF ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

RFA AVAILABLE: 89-AI-19

P.T. 34; K.W. 0715008, 0740020, 0710100, 1003006, 1003002, 1002045, 0710070

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: October 2, 1989

Application Receipt Date: December 8, 1989

The National Institute of Allergy and Infectious Diseases (NIAID) announces availability of a Request for Application (RFA) for funding of the National Cooperative Drug Discovery Groups for the Treatment of Acquired Immune Deficiency Syndrome (NCDDG/AIDS). It is the purpose of this RFA (copies available upon request) to invite applications aimed at the discovery of more effective, selective, and diverse new agents which can be used for the treatment of AIDS. Applications which include a research project or a core component from the private sector (e.g., pharmaceutical, chemical, or biotechnological companies) are encouraged. Research on the use of either the humoral or the cellular arm of the immune system, on the structure and biophysical properties of cellular or viral proteins, the biochemistry of viral-host interactions, drug targeting, ribozymes, drug metabolism, potentially efficacious natural products or certain synthetic chemical approaches may be judged responsive to this RFA. Applications should not include the following research areas which have already been integrated into other NIH initiatives: synthesis or development of analogues of known anti-HIV nucleosides, lipophilic carriers of nucleosides, prodrugs of existing nucleosides, testing in animal retroviral models other than those that utilize HIV, research on the opportunistic infections associated with AIDS, evaluation of recombinant human cytokines, development of glycosylation inhibitors, development of soluble CD4 or CD4 conjugates, and large scale random screening in cell culture-based systems. Specifically excluded from the Group's activities are activities related to clinical evaluation of the drug. (A program for large-scale screening of compounds for activity against HIV is operated by the National Cancer Institute.) For those that propose screening in cell culture-based systems, screening of natural products, biologics and/or synthetic compounds can not exceed 25 percent of the total effort of the Group. A separate Request for Applications (RFA) for the National Cooperative Drug Discovery Groups for the Treatment of Opportunistic Infections Associated with AIDS was issued on June 30, 1989, in the NIH Guide for Grants and Contracts (Vol. 18, No. 22).

Each NCDDG/AIDS will be assembled by the Principal Investigator to form a multidisciplinary consortium representing the various skills needed to successfully design, synthesize, and evaluate, at the preclinical level, treatment entities and strategies for the treatment of AIDS. Inasmuch as it is unlikely that all of the outstanding talents required to exploit fundamental leads from various scientific disciplines will be found in a single institution, each Group is envisioned as being multi-institutional as well. Thus, each NCDDG/AIDS will be assembled by the Principal Investigator and will consist of a number of research projects representing the scientific disciplines required to attain the Group's goal and objectives. The various research projects, including that of the Principal Investigator, may be mobilized from academia, research institutions, and/or industry. It is expected that the rationale for design of potential treatments, the synthesis of specific agents, and the preclinical models for evaluation will originate within the Group and be based on leads from their own and others' fundamental research.

Awards will be made as Cooperative Agreements. The Cooperative Agreement funding mechanism differs from the traditional research grant in that the Government component (NIAID) awarding the Cooperative Agreement anticipates substantial involvement during performance. The nature of NIAID staff participation is described in the RFA. However, the applying Group must define its objectives in accord with its own interests and perceptions of approaches to anti-AIDS treatment.

The proposed applicant institution will be responsible for the Group's application. Awards will be made to the applicant institution on behalf of the Group as a whole and not to individual research projects within the Group. The applicant institution will provide a Central Operations Office for the Group. The applicant institution will be responsible for the performance of the entire Group and will be accountable for the funds awarded. The participation of the Government through the NIAID extramural staff is aimed at facilitating a concerted effort by the Group by making available to the Group biological materials for testing, appropriate existing data bases, and appropriate ancillary testing and other resources available under existing contracts. The interaction of academic and non-profit research institutions with commercial organizations and Government is expected to favor efficient invention of anti-AIDS treatment and will facilitate their subsequent development to clinical trial.

Applications will be reviewed by the appropriate subcommittee of the NIAID AIDS Research Review Committee. NIAID has set aside \$2.3 million for the initial year's funding. The amount spent will be dependent on the continuing availability of funds for this purpose and the quality and diversity of applications recommended for approval.

This RFA is available from:

Ms. Nancy R. Brown
Developmental Therapeutics Branch
Division of Acquired Immunodeficiency Syndrome
National Institute of Allergy and Infectious Diseases
6003 Executive Boulevard, Room 243P
Bethesda, Maryland 20892
Telephone Number: (301) 496-0637

ONGOING PROGRAM ANNOUNCEMENTS

TECHNOLOGY DEVELOPMENT, MAPPING, AND DNA SEQUENCING IN SUPPORT OF THE HUMAN GENOME PROGRAM

P.T. 34; K.W. 1215018, 0755045, 1002058, 1004017, 1003012, 1002008, 0710030

Office of Human Genome Research

This Program Announcement restates the interest of the National Institutes of Health (NIH) in receiving research grant applications for studies related to the Human Genome Initiative. The present announcement supersedes the previous NIH-wide Program Announcement (November 4, 1988) on mapping and determining the DNA sequence of the genomes of the human or of model organisms. The objective is to stimulate creative, innovative research that will substantially improve the rapidity, efficiency and accuracy with which mapping and DNA sequence data can be obtained, analyzed, and distributed.

BACKGROUND INFORMATION

The NIH is currently engaged, along with several other federal, private, and international organizations, in a research program known as the Human Genome Initiative. This program is designed to characterize the human genome and the genomes of selected model organisms. It has several interrelated goals: the construction of high resolution genetic linkage maps; the development of a variety of physical maps; the determination of the complete nucleotide sequence of the DNA of selected organisms; the development of the capability for collecting, storing, distributing, and analyzing the data and materials produced; and the development of appropriate new technologies necessary to achieve these objectives. The information that will be obtained within the genome project will be a resource for studies of gene structure and function and will promote research into the genetic aspects of human disease. In this way, the Human Genome Initiative will serve as an underlying source of information for, and stimulus to, a wide range of studies from the most basic to targeted and clinical programs across the spectrum of NIH interests and responsibilities.

In the past two years, several announcements/solicitations for grant applications related to the Human Genome Initiative have been published in the NIH Guide for Grants and Contracts. These include two broad Program Announcements and several Requests for Applications. This Program Announcement consolidates the prior announcements/solicitations in one document and emphasizes the continuing, ongoing interest on the part of the NIH in receiving grant applications for support of research projects that address the goals of the genome program with a wide range of research activities. One area in which research activities are encouraged is the development of improved technology for physical mapping, for the determination of DNA sequences, and for the management of the information that accrues. A separate, but equally important, area includes research projects that seek to increase the information available about specific genomic regions through the expansion of genetic maps, the construction of physical maps, or pilot projects for large-scale DNA sequence determination.

Creative, novel approaches in all these areas will be essential to the success of the genome project. To this end, the NIH encourages interdisciplinary programs that draw from fields such as information science, chemistry, physics, and engineering, in addition to the biological sciences.

Progress will be accelerated by cooperation and interaction among investigators. Therefore, it is expected that all materials and information derived from this work will be made available to the scientific community in a timely manner, in accord with Public Health Service policy. Within the genome program, awardees will be expected to share information and to work closely with other laboratories involved in related projects.

RESEARCH SCOPE

This Program Announcement is intended to emphasize the ongoing commitment of the NIH to the specific goals of the genome project and to the development of methodological tools and resources which would support this effort, including the storage and retrieval of materials and data. Applications responsive to this announcement will include a broad spectrum of research approaches to genetic and physical mapping, DNA sequencing, data handling and new methods of data interpretation. Development of new and imaginative technologies needed to support the genome project are especially encouraged. The topics described below are not intended to limit the types of applications that are acceptable in response to this announcement, but rather to illustrate the range of work that will be needed to attain the goals of the genome project.

However, research directed toward analysis of the biological function of specific genes or gene systems, or the application of genetic information to the understanding, diagnosis, prevention, or treatment of specific genetic disorders is not within the scope of the genome program. Such work is currently supported by a number of other programs at the NIH. Information about these programs can be obtained from individual Institutes. Potential applicants are encouraged to contact one of the representatives listed below to discuss the proposed research project and for additional information.

Technology Development

The objective is to stimulate creative, innovative research that will lead to substantial improvements in the speed, efficiency and accuracy with which mapping and DNA sequence data can be obtained, analyzed, and distributed. Such improvements can be achieved through automation of existing methodology, development of new approaches, or both. Multi-disciplinary approaches to the

attainment of these goals are encouraged. Examples of the problems for which improved technological solutions and/or automation are needed are:

- o generating, purifying, and cloning large DNA fragments;
- o constructing physical maps, including long-range restriction maps and overlapping sets (contigs) of DNA fragments that are derived from specific chromosomal regions and are connected into more extensive physical arrays;
- o determining relationships between genetic and physical maps;
- o locating specific genes on genetic and physical maps and within regions of sequenced DNA;
- o determining DNA sequence, including assembling overlapping DNA sequences into longer arrays;
- o storing, analyzing, and distributing the data obtained in each of these activities; and
- o storing and distributing the materials generated by all of these activities.

Applicants are advised to take several general considerations into account when designing new projects.

- o Methodological improvements have played an important role in advancing biological research, never more so than in the past twenty years. In general, when technology development has been successful, it has been driven by the desire to solve specific scientific problems. Therefore, it is reasonable to expect that, within the context of the genome program also, the most successful new technologies will come from those endeavors in which the attempt to develop better technology occurs in the context of a specific research problem related to genomic analysis. Applicants are encouraged to clearly define the biological problem for which the technological solution is being devised. Applicants whose expertise is primarily non-biological and who are interested in addressing problems of genome analysis with new, non-biological tools are especially encouraged to interact closely with biologists.
- o It has been suggested that to significantly increase the rate at which mapping and sequence data can be acquired, efforts should be directed toward improving by three- to five-fold the scale and/or efficiency with which particular steps in mapping, sequence determination, or data analysis can be accomplished. Such an incremental increase can serve as a useful benchmark in designing a research program.
- o Achievement of such a significant improvement in analytical capability may require entirely new approaches. Methods that have been useful for addressing particular needs in the past, such as determining the sequence of a few kilobases of DNA, may not be adequate for addressing comparable problems on a much larger scale. The NIH recognizes that novel approaches may involve a considerable degree of risk and encourages submission of high-risk, high pay-off projects in response to this announcement.

Mapping and DNA Sequencing

The objective is to increase our knowledge of the genetic and physical maps and the DNA sequence of selected organisms, leading up to the complete maps of the human genome and the complete human DNA sequence. Research projects in the following areas are encouraged:

- o expanding the genetic map of the human, or of those model organisms for which such information would serve to promote the objectives of the overall genome program;
- o constructing physical maps of the chromosomes of the human and of model organisms, including projects for large-scale physical mapping; and
- o pilot projects for large-scale DNA sequence determination, involving the DNA of model organisms or regions of the human genome.

The primary goal of research projects proposed under this section will be the generation of a substantial amount of new mapping and/or sequence information. The project may utilize current technology or propose new or improved technology. If current technology is used, it should be used at or near its limits in order to explore its capabilities.

Because of the extensive amount of information already available about the genetics and molecular biology of *E. coli*, *S. cerevisiae*, *D. melanogaster*, *C. elegans*, and *M. musculus*, the genome program is particularly interested in promoting study of these models. However, research projects that involve other models are also expected to make important contributions to the Human Genome Initiative by means of both development of new technology and improved understanding of genome structure through comparative studies. Thus, no model organism is excluded from the genome program a priori. However, applicants proposing to study models other than those named above must provide a rationale, in terms of the goals of the overall genome program, for the use of such another model.

MECHANISMS OF SUPPORT

Support for this program will be through research grants, including project grants (R01), program project grants (P01), FIRST awards (R29), resources related research projects and biotechnology resource grants (R24, P41), Research Career Development Awards (K04), conference grants (R13) and Small Business Innovation Research (SBIR) grants (R43, R44). Because not all institutes support all of the above mechanisms, potential applicants are encouraged to contact the representatives listed below for additional information. Policies that govern research grant programs of the NIH apply to this program. Consortium arrangements and collaborative projects among scientists with skills in biological sciences, chemistry, physics, information science, and engineering are encouraged.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures. They will first be reviewed for scientific and technical merit by a special study section in the Division of Research Grants organized for this purpose. Following the initial review, the applications will be considered by the appropriate National Advisory Board or Council. Review criteria that will be used to assess the scientific merit of an application are the following:

- o Scientific merit;
- o Potential value of the research for furthering the goals of the genome project;
- o Feasibility of the research and adequacy of the experimental design;
- o Significance and originality of the research and methodological approaches, as they relate to the genome project;
- o Training, experience, research competence, and dedication of the investigator(s);
- o Adequacy of available facilities;
- o Provisions for the protection of human subjects, the humane care of animals, and biosafety conditions;
- o Appropriateness of the requested budget for the work proposed.

Because the significance of the proposed research project to the goals of the Human Genome Initiative is a criterion for review, consultants must consider this aspect in the evaluation of an application submitted in response to this Program Announcement. Applicants are, therefore, encouraged to consult with one of the staff listed below before submission, to discuss the relevance of a proposed application to the genome program.

METHOD OF APPLYING

Applications should be submitted on Form PHS 398 (rev. 10/88). Application kits are available in most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, Westwood Building, Room 449, National Institutes of Health, Bethesda, Maryland 20892; telephone (301) 496-7441.

Applications will be accepted in accordance with the usual NIH receipt dates that apply for the various mechanisms listed under MECHANISMS OF SUPPORT. It is essential that applicants type "Technology Development, Mapping, and DNA Sequence Determination in Support of the Human Genome Initiative" in item 2 on the face page of the application form. The original and six copies of the application should be submitted to the following office:

Application Receipt Office
 Division of Research Grants
 Westwood Building, Room 240
 National Institutes of Health
 Bethesda, Maryland 20892**
 Telephone: (301) 496-7273

The conventional presentation for grant applications should be utilized.

Funding decisions will be based on recommendations of the initial review group and of the National Advisory Council regarding scientific merit and program relevance, as well as on the availability of funds.

INQUIRES

It is strongly recommended, but not required, that potential applicants contact the Office of Human Genome Research (OHGR) or the staff member at the appropriate NIH institute to discuss research objectives.

BID	CONTACT	BUILDING	ROOM	TELEPHONE
OHGR	Bettie Graham, Ph.D.	Shannon	201	496-0844
NIDDK	Robert Katz, Ph.D.	Westwood	607	496-7997
NCI	Cheryl Marks, Ph.D.	Executive	630	496-7028
		Plaza South		
FIC	Lynn Amende, Ph.D.	38A	613	496-6688
DRR	Charles Coulter, Ph.D.	Westwood	8A11	496-5411
NIA	Huber R. Warner, Ph.D.	31	5B39	496-6402
NICHD	Delbert Dayton, M.D.	Executive	5C19	496-5541
		Plaza North		
NINDS	N.C. Myriantopoulos, Ph.D.	Federal	8C04	496-5821
NLM	Arthur Broering, Ph.D.	38A	8C16	496-4621
NIDR	John Townsley, Ph.D.	Westwood	506	496-7807
NIGMS	Irene Eckstrand, Ph.D.	Westwood	920	496-7137
NIAMS	Steven Hausman, Ph.D.	Westwood	403	496-7495
NHLBI	Carol Letendre, Ph.D.	Federal	506	496-6402
NIAID	William Duncan, Ph.D.	Westwood	754	496-5598
NEI	Jack McLaughlin, Ph.D.	31	6A08	496-9110

Mailing address for the above offices: Bethesda, Maryland 20892
 All Bethesda telephone numbers are in area code 301.

**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