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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Room 2A14, 5333 Westbard Avenue, National Institutes of Health, Bethesda, Maryland 20014, and attach your address label to your letter. Prompt notice of your change of address will prevent your name being removed from our mailing list.

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.

Supplements, printed on yellow paper, are published by the respective awarding units concerning new projects, solicitations of sources, and requests for proposals.
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CANCER RESEARCH EMPHASIS GRANTS (CREG)

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DNA RECOMBINANT RESEARCH

Background

On May 5, 1976, the Director, National Institutes of Health, established the Office of Recombinant DNA Activities (ORDA) in the National Institute of General Medical Sciences to coordinate the administration of NIH policies and procedures pertaining to the utilization of recombinant DNA technology in research.

On June 23, 1976, the NIH issued Guidelines for Research Involving Recombinant DNA Molecules. The Guidelines govern the conduct of NIH-supported research on recombinant DNA molecules, and they establish carefully controlled conditions for the conduct of experiments involving the production of such molecules and their insertion into organisms such as bacteria. The Guidelines were published in the Federal Register, July 7, 1976, and will be updated periodically. Copies are available from the NIH Office of Recombinant DNA Activities, National Institute of General Medical Sciences, Room 4A52, Building 31, Bethesda, Maryland 20014.

These Guidelines replace the recommendations contained in the 1975 Summary Statement of the Asilomar Conference on Recombinant DNA Molecules.

Detailed procedures for the submission, review, and monitoring of projects involving recombinant DNA technology will be published in the NIH Guide for Grants and Contracts.

Application forms are also under revision to include a check block indicating whether or not DNA recombinant technology is involved. Until such time as these forms are available, applicants should specify in capital letters at the bottom of the first page of the application "THIS APPLICATION DOES/DOES NOT INVOLVE RECOMBINANT DNA." Labeling the face page of the application will assist in expediting the processing of your application.

The purpose of this communication is to inform you of interim procedures which must be undertaken if NIH-supported recombinant DNA research will be conducted in the future at your institution.

Institutional Biohazards Committee (IBC)

Your institution must establish a standing biohazards committee if research involving recombinant DNA technology supported by NIH is conducted under the sponsorship of the institution. Suggestions for the composition of such a committee are discussed under Section IV of the NIH Guidelines, which also discusses the roles and responsibilities of principal investigators and institutions. A roster of your institutional biohazards committee, with the names, addresses, occupations, and qualifications of the chairman and members of the committee must be submitted to the NIH Office of Recombinant DNA Activities (ORDA).

The composition of institutional biohazards committees is subject to review by ORDA for compliance with recommendations stated in the Guidelines.
It is the responsibility of each grantee institution to update this information at least annually.

As stipulated in the Guidelines, the ORDA will assist in the formation of an area biohazards committee when this is appropriate. Such an area committee will be necessary when additional expertise from outside a given institution is necessary for the biohazards committee to fulfill its functions.

New, Continuation, and Competing Renewal Applications

All new and competing renewal applications (Types 1 and 2) received on or after December 1, 1976, involving DNA recombinant research must be in compliance with the requirements that the application be accompanied by a Memorandum of Understanding and Agreement (MUA). If not, the application will be considered incomplete and therefore unacceptable for review. The MUA must contain:

1. An assurance that the principal investigator has become familiar with the current Guidelines issued by the NIH and agrees to abide by their provisions,

2. A description of the experiments being conducted which involve recombinant DNA molecules,

3. An assessment of the levels of physical and biological containment required by the current NIH Guidelines for these experiments,

4. A statement of the facilities and specific procedures which will be used to provide the required levels of containment,

5. Certification by an institutional official that these facilities and procedures have been reviewed by the institutional biohazards committee, and judged to be both adequate and consistent with the requirements of the NIH Guidelines,

6. Agreement that the institutional biohazards committee will monitor the facilities and procedures throughout the duration of the projects, and

7. A statement that the recombinant DNA molecules being used will not be transferred to other investigators or institutions unless their facilities and techniques have been assured to be adequate, and a new MUA is executed by them and submitted to the NIH prior to the initiation of experiments.

All noncompeting continuation applications (Type 5) involving DNA recombinant research projects must be accompanied by an MUA (including certification by the IBC). Each Type 5 application received for subsequent budget periods must contain an updated certification statement from the IBC that the proposed facilities and staff have been reviewed again by the IBC within 30 days prior to submission of the application and continued to be in compliance with NIH Guidelines.
Applications that have recently been approved by council will have MUA's requested, if necessary. It is suggested that documentation be supplied as soon as possible so that funding will not be delayed.

This notice generally applies to contracts also. Detailed information concerning contracts will be published in the Guide at a later date.

Additional information is available from the Office of Recombinant DNA Activities, National Institute of General Medical Sciences, National Institutes of Health, Room 4A52, Building 31, Bethesda, Maryland 20014, (301) 496-2323.
SPECIALIZED CENTERS OF RESEARCH IN UROLITHIASIS
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM,
AND DIGESTIVE DISEASES

ANNOUNCEMENT

The National Institute of Arthritis, Metabolism, and Digestive Diseases announces a national competition to establish a limited number of Specialized Centers of Research focused on urolithiasis. Copies of the Guidelines for this program are now available.

The objective, in the establishment of Specialized Centers of Research in Urolithiasis, is to bring together the resources of a number of scientific and medical disciplines with a combined basic and clinical research focus upon this important disorder. The goal of this initiative is to elucidate the underlying mechanisms of urolithiasis, with an eye toward eventual development of improved therapies for patients with urolithiasis and rational means for prevention of urolithiasis. This goal is to be pursued at each Specialized Center of Research in Urolithiasis through a carefully composed program of research studies on the etiology, pathogenesis, detection, and treatment of this disease.

A Specialized Center of Research in Urolithiasis is characterized by a strong, well-defined program of collaboration among a multidisciplinary group of investigators. The disciplines represented might include: nephrology, urology, physiology, physical chemistry, biochemistry, microbiology, genetics, pathology, epidemiology, etc. Thus, a Specialized Center for Research in Urolithiasis has a unique organization which bridges the departments and schools of the sponsoring institution or institutions.

Specialized Centers of Research in Urolithiasis are funded by a grant-in-aid. This Center award differs from other research grants-in-aid in its emphasis on a central research theme, the requirement for interdisciplinary collaboration, and the degree of coordination by the National Institute of Arthritis, Metabolism, and Digestive Diseases.

Copies of the Guidelines and further information are available from:

Kidney and Urologic Diseases Program
National Institute of Arthritis, Metabolism, and Digestive Diseases
National Institutes of Health
Bethesda, Maryland 20014

Telephone: (301) 496-7133

Letters of intent to apply for a Specialized Center of Research in Urolithiasis must be received by December 15, 1976. This letter will allow Institute staff to begin discussions with applicants regarding the research theme of the proposed Center as well as administrative and financial details. Applications will be reviewed and evaluated by a committee of appropriate scientific peers and then by the National Advisory Arthritis, Metabolism, and Digestive Diseases Council.
The National Institute of Arthritis, Metabolism, and Digestive Diseases is planning to initiate this program in fiscal year 1977. The award of grants pursuant to this request, however, is contingent upon the appropriation and apportionment of funds for this purpose. Applications must be received at the National Institutes of Health by February 1, 1977. Successful applicants will be notified after mid-August 1977, but prior to October 1, 1977.
The Arthritis, Bone, and Skin Diseases Program of the National Institute of Arthritis, Metabolism, and Digestive Diseases intends to make a limited number of NIAMDD Clinical Investigator Awards based upon the anticipated appropriation and apportionment of funds for fiscal year 1977. These awards will provide an opportunity for promising clinically trained individuals with demonstrated aptitude in research, to develop into independent biomedical investigators in the fields of:

- Arthritis Research
- Orthopedics Research
- Dermatology Research

The NIAMDD Clinical Investigator Award is designed to provide intensive, guided, research experience for individuals with clinical background and training, rather than to foster the further development of research skills of individuals already having shown significant research achievement. Thus, candidates are restricted to those holding health professional degrees in the clinical sciences (M.D., D.O., D.V.M., or equivalent) with four to seven years of total professional postdoctoral clinical and research experience by the projected start of the award. It is expected that candidates will have a minimum of two years of clinical experience and two years of research training. In exceptional circumstances, individuals with less than four or more than seven years of such experience may apply, but must justify those special circumstances. Holders of the Ph.D. or comparable research degree, either with or without accompanying health professional degree, are not eligible. Candidates should have broad training, have demonstrated individual competence in clinical activities, and show research potential in the chosen area of interest. Candidates responding to this announcement will be expected to provide evidence of a serious intent for an academic career related to arthritis, orthopedics, or dermatology.

Awards will enable successful candidates to concentrate on a well-defined research problem related to the fields of arthritis, orthopedics, or dermatology, with a sponsor (or sponsors) competent to provide guidance in the chosen problem. Awards will be for up to three years and will provide annual support for the salary of the awardee (up to $25,000) and for research supplies, equipment, and travel (up to $10,000). Awardees will spend a minimum of 75% of time in research and must hold a full-time staff appointment at the sponsoring institution.

Applications will receive initial merit review by an NIH peer review panel and subsequently by the National Advisory Arthritis, Metabolism, and Digestive Diseases Council. Applications in response to this announcement
are to be received by February 1, 1977. It is anticipated that successful applications will be funded prior to September 30, 1977. Additional information and application materials can be obtained from:

Office of the Associate Director for Extramural Program Activities
National Institute of Arthritis, Metabolism, and Digestive Diseases
Bethesda, Maryland 20014
MULTIPURPOSE ARTHRITIS CENTERS
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

ANNOUNCEMENT

The National Institute of Arthritis, Metabolism, and Digestive Diseases announces its intent to establish a number of Multipurpose Arthritis Centers under authority of Part D of Title IV of the Public Health Service Act as amended by the National Arthritis Act of 1974 (P.L. 93-640) (42 USC 289c-6). Copies of the Guidelines are now available.

A Multipurpose Arthritis Center is defined as a resource which consists of the facilities of a single institution or a consortium of cooperating institutions through which a group of formally cooperating health personnel can be brought together to demonstrate and foster the prompt and effective application of available knowledge and the development of urgently needed new knowledge. Each Center will have or will develop a program in three major fields: education, research, and community-related activities.

Each Center, in accord with the National Arthritis Act of 1974, shall conduct:

A. Basic and clinical research into the cause, diagnosis, early detection, prevention, control, and treatment of arthritis and complications resulting from arthritis;

B. Training programs for physicians and other health and allied professionals in current methods of diagnosis, screening and early detection, prevention, control, and treatment of arthritis;

C. Information and continuing education programs for physicians and other allied health professionals who provide care for patients with arthritis; and

D. Programs for the dissemination of information to the general public.

The National Institute of Arthritis, Metabolism, and Digestive Diseases plans to make new awards for Centers during fiscal year 1977, contingent upon the appropriation and apportionment of funds for this purpose. In addition, it is anticipated that, following appropriate peer review of all applications submitted, the Institute will be able to make a number of awards with consideration given to geographic distribution.

Applications for Multipurpose Arthritis Center grants must be submitted, in accord with the required format, prior to February 1, 1977. Potential applicants are requested to submit letters of intent, prior to December 15, 1976; and are invited to consult with staff of the National Institute of Arthritis, Metabolism, and Digestive Diseases prior to the submission of an application, to determine if the proposed program meets the criteria of a Center. Copies of the Guidelines, application materials, and further information may be obtained from:

Office of the Associate Director
for Extramural Program Activities
National Institute of Arthritis,
Metabolism, and Digestive Diseases
Bethesda, Maryland 20014
STUDIES OF DIABETES MELLITUS AND RELATED PROBLEMS
REQUEST FOR RESEARCH GRANT APPLICATIONS
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

ANNOUNCEMENT

The National Institute of Arthritis, Metabolism, and Digestive Diseases of the National Institutes of Health invites applications for research grants in the general area of diabetes mellitus and related problems.

I. PROGRAM SPECIFICATIONS

A. Program Objectives

Diabetes mellitus is a major public health problem in the United States today. Because of the serious and widespread health problems associated with diabetes the National Commission on Diabetes recommended in 1975, and the Congress approved for fiscal year 1977, an expanded national research effort on this disease. That plan recommended an increased effort in basic and clinical research into the cause, cure, and prevention of diabetes mellitus and related endocrinologic and metabolic disorders. The National Institute of Arthritis, Metabolism, and Digestive Diseases currently supports a variety of basic and clinical research studies related to diabetes and associated problems. A number of significant and valuable advances in our knowledge have resulted from these research activities. Nevertheless, it is clear that there is both need and opportunity for additional basic and applied research in the area of diabetes mellitus.

B. Research Scope

The emphasis of this solicitation is upon research in diabetes and in 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 a diabetes-related endocrine or metabolic disorder; and
3. Projects which are not directly concerned with diabetes but which could reasonably be expected to contribute to the diagnosis, treatment, cure, or prevention 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 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. Studies of the nature, epidemiology, etiology, pathogenesis, treatment, and "complications" of diabetes mellitus. Such studies may be approached from any discipline appropriate to basic research, clinical investigation, or epidemiology.

2. Basic and clinical studies of the mechanism of hormone action as it relates to diabetes. Studies of insulin, insulin cofactors, glucagon and other hormones such as somatostatin, somatomedin, growth hormone and catecholamines, to name but a few, may be included, but only as they relate to diabetes as defined on page 1. Investigation of the integrated action of these hormones in the regulation of metabolic processes is appropriate.

3. 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.

4. 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.

5. Research into the development of new or improved techniques for establishing the diagnosis of diabetes, including the development of satisfactory and reliable markers of the disease.

6. Studies of normal and abnormal metabolic regulation as they relate to diabetes mellitus.

7. Assessment of the role of viruses in the etiology of diabetes, their mechanism of action, and the host-parasite relationship determining their diabetogenic action.

8. Research into the role of genetic factors in diabetes mellitus including the identification of specific genetic markers which would identify individuals who have predisposing genes for diabetes. Such studies could consider the genetic character of juvenile and late-onset diabetes mellitus.

9. Studies of the epidemiology of diabetes mellitus including its prevalence and incidence in the population as a whole, as well as in discrete populations well characterized as to factors known to be associated with the disease such as sex, age, nutritional patterns, body weight, physical activity, and others.

10. Research into the relationship between nutrition and diabetes, including the relationship between diabetes and obesity. Such studies may focus on nutrition in early life as well as in the adult. Research into the regulation of appetite and feeding behavior within the context of diabetes would be appropriate.
11. Research approaches to transplantation of the pancreas or pancreatic islets. (Development of artificial devices to monitor blood glucose and administer insulin appropriately will be supported by a contract program, but expression of interest may be submitted.)

12. Research into the nature, etiology, pathogenesis, and management of the microvascular, macrovascular, and neurologic "complications" of the chronic diabetic syndrome. Such studies may assess the efficacy of control of blood glucose on the development of these chronic, life threatening disorders in the diabetic.


14. Studies developing or utilizing spontaneous or induced models of diabetes in experimental animals, directed toward elucidating the pathogenesis of this disorder and its "complications."

The areas of interest cited above are for illustrative purposes only; other subjects with a clearly demonstrable relation to diabetes can be conceived. All of these subjects may be approached from any discipline appropriate to fundamental research, clinical investigation, or epidemiology.

C. Mechanism of Support

The mechanism of support for this program will be the grant-in-aid. The only difference between this and the usual type of National Institutes of Health research grant is in its specified goal orientation. While it is expected that each successful applicant will plan, direct, and execute his own research program, any departure from diabetes and related endocrine and metabolic disease as the principal focus of the program must be mutually agreed upon by the participant and the National Institute of Arthritis, Metabolism, and Digestive Diseases. 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.

This program is included and provided for in the financial plans of the National Institute of Arthritis, Metabolism, and Digestive Diseases for fiscal year 1977. However, 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. Review for Program Responsiveness

It is anticipated that the vast majority of applications in response to this request will be assigned to the National Institute of Arthritis, Metabolism, and Digestive Diseases. In the event, however, that a particular application fits more appropriately
within the scope and responsibility of another Institute, arrange-
ments will be made for assignment to that Institute. Thus normal
programmatic considerations will not be obviated.

B. Review Procedures

Proposals in response to this solicitation will be reviewed on a
nation-wide basis in competition with each other, and in accord
with the usual National Institutes of Health peer review procedures.
They 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 Arthritis,
Metabolism, and Digestive Diseases Advisory Council. Successful
applicants will be notified after mid-August 1977, but prior to
October 1, 1977. The review criteria customarily employed by the
National Institutes of Health for regular research grant applica-
tions will prevail.

III. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants should submit a brief, one-page letter
stating their intent to submit an application, and describing the
general area of research to be proposed. The letter of intent
should be submitted not later than January 1, 1977, to:

Diabetes Program Director
Extramural Programs
National Institute of Arthritis,
Metabolism, and Digestive Diseases
National Institutes of Health
Bethesda, Maryland 20014

The Institute requests such letters only to provide an indication
of the number and the scope of applications which will require
consideration. A letter of intent is not binding, and it will
not enter into the review of any proposal subsequently submitted.

B. Format for Applications

Applications should be submitted on form NIH 398, which is the
regular application form for the traditional research grant, and
which is available in the business or grants and contracts office
at most academic and research institutions. The conventional
presentation in format and detail for regular grant applications
should be utilized. The words "PROPOSAL IN RESPONSE TO RFA:
DIABETES, 11/76" must be typed in bold letters across the top of
the face page of the application.
C. Application Procedure

Applications must be received by March 1, 1977. 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

It is important that a brief covering letter accompany the application indicating that it is in response to this program announcement. A copy of the covering letter should be sent to:

Diabetes Program Director
Extramural Programs
National Institute of Arthritis, Metabolism, and Digestive Diseases
National Institutes of Health
Bethesda, Maryland 20014

to indicate that the application has been submitted.
SPECIAL DENTAL RESEARCH AWARD ANNOUNCEMENT

This announcement is a revision of, and thus supersedes, the announcement contained on page 19, Vol. 5, No. 2, NIH Guide for Grants and Contracts.

The National Institute of Dental Research (NIDR) makes Special Dental Research Awards (SDRA) to provide funds for young scientists to conduct independent investigations during the early stages of their careers. Recently trained scientists are encouraged to seek grant funds through this award and make their contributions in the expanding field of oral health research. Investigators with no more than four years of research experience beyond completion of research training may apply for an SDRA grant.

NEW PROVISIONS Applicants may continue to request up to $10,000 for supplies, technical support, travel, publications, etc., per year for three years. Additional funds may also be requested to pay up to 50% of the principal investigator's salary (commensurate with percent of effort). The total direct costs, however, may not exceed $25,000 per year. Such funds cannot be used to support thesis research, nor to supplement projects already funded by the Public Health Service or other Federal agencies. All other policies pertaining to NIH grant-supported research projects apply to the SDRA program.

APPLICATION PROCEDURES Applicants should use the regular research grant application (NIH 398) and write "Special Dental Research Award" on the top of the face page. Applications are available at institutional central application control offices (see Vol. 2, No. 8, October 26, 1973). The deadlines for submission of applications are July 1, November 1, and March 1.

When the SDRA grant period terminates, the investigator may apply for a renewal of the grant for an additional period, but the grant will no longer be considered a special award. Instead, renewal applications will be considered as competing continuations of regular research grants without the financial restrictions of the special grant.

AREAS OF INTEREST Special Dental Research Awards support meritorious basic or clinical research projects directed toward the improvement of oral and dental health. The Institute encourages investigations on Periodontal Disease, Dental Caries, and Oral Soft Tissue Diseases, including herpes simplex, aphthous ulcers, oral tumors, and other lesions. For example, the recent findings that specific bacteria may cause certain forms of periodontal disease need confirmation in other population groups; and comprehensive immunology studies should be done on both animals and humans to elucidate the host response pattern to each of the suspected pathogens. Since dental caries requires bacterial fermentation of foodstuffs on a susceptible tooth, caries research focuses on combating the bacteria, modifying the diet, and increasing the resistance of the tooth. Especially
in order are projects on anticaries vaccine development and on the efficacy of antimicrobial agents. There is also a need for proposals related to Oral-facial Growth and Development, Malocclusion, Craniofacial Anomalies, and Acquired Disfigurement. Such projects may be basic in nature, employing laboratory approaches, or may consist of applied research involving animals or humans. In the field of Orofacial Pain, there is a need for studies of sensory responses, fear and anxiety, and painful conditions such as trigeminal neuralgia. Projects on the Social and Behavioral aspects of oral diseases are also invited. Two other important areas of inquiry are the function of Specific Constituents of Salivary Secretions and the relationship of Nutrition to oral health and disease. Of immediate importance to the NIDR is the improvement of Dental Filling Materials, Adhesive Sealants, Maxillofacial Prosthetic Materials, and the development of effective Tooth Implants.
TITLE - PATHOPHYSIOLOGICAL MECHANISMS INVOLVED IN THE FORMATION OF INFRARED PATTERNS EMITTED BY NORMAL SUBJECTS AND PATIENTS WITH BENIGN AND MALIGNANT DISEASES

SCIENTIFIC PROGRAM REQUIREMENT The National Cancer Institute (NCI) is accepting applications for support of research projects to study the basis for the patterns of infrared emission from the human body surface. Factors affecting variations of those patterns in normal subjects require elucidation along with the identification of the nature of changing influences upon those patterns in benign and malignant diseases. Specifically, the study could profitably concentrate on the infrared emission patterns from the human female breast because detection of breast abnormalities is the most common application of thermographic examination.

SIGNIFICANCE TO NCI PROGRAM GOALS Thermography is receiving considerable attention at the present time as a possible means to detect early cancer, particularly breast cancer. It is the third method, in addition to X-ray mammography and physical examination, used for breast cancer screening. The results of present efforts to evaluate the effectiveness of thermography as a screening mode for breast cancer vary widely. Currently, the interpretation of thermograms appears to be extremely difficult to standardize. Therefore it is generally agreed that basic knowledge must be improved about the underlying pathophysiological mechanisms responsible for the infrared emission patterns. Conceivably such information could lead to improved cancer detection by thermography and allow that mode to assume a more important role in the detection protocols.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years.

3. SUBMISSION Use the standard research grant application form NIH 398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCBD-003 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014. If your institution cannot supply you with form NIH 398, it may be requested from the Division of Research Grants.
4. **RECEIPT DATE** Applications received on or before June 1, 1977, will be processed for study section review in October 1977 and for the National Cancer Advisory Board review in January 1978.

**REVIEW**

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. Irvin C. Plough, (301) 496-3251, Division of Cancer Biology and Diagnosis, National Cancer Institute.
TITLE - EFFECTS OF NEW ANTICANCER DRUGS ON THE CELL CYCLE

SCIENTIFIC PROGRAM REQUIREMENT The National Cancer Institute (NCI) is accepting applications for support of research projects on the cell biology of new anticancer drugs. The objective of this research is to characterize the cell cycle effects of new anticancer drugs used singly and in combination therapies and to provide information which may allow the optimal clinical use of the drugs or its analogs. The approach and methods are to be specified by the applicant. Examples of the kinds of information that may be valuable are the cycle and phase sensitivity of cells to their cytotoxic activity, time and concentration dependence on their cytotoxic activity, and cycle progression effects in cell culture and in vivo. The new drugs to be studied are to be selected from among those in Phase I clinical trials or those currently being developed for clinical trials by the Division of Cancer Treatment (DCT). This information will be made available, upon request, from the DCT. It is expected that new drugs selected from development by DCT, during the grant period, may also be the subject of study. The applicant may specify the drugs to be studied but is not obliged to do so. The DCT will provide the grantee with supplies of drugs requested whenever possible. Progress reports will be submitted to the Program Director every six months describing interim results of studies on each drug.

SIGNIFICANCE TO NCI PROGRAM GOALS As promising new anticancer drugs are discovered and developed for clinical trials a knowledge of their cell cycle properties is important. The application of this information to its optimal use in clinical trials is the goal of this research. The information resulting from this research could be of value for the design of clinical protocols and as a guide to the design of investigations in clinical pharmacology.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the application pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key personnel. The application should also state the duration of time for which the support is requested.

3. SUBMISSION Use the standard research grant application form NIH 398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCT-6 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014. If your institution cannot supply you with form NIH 398, it may be requested from the Division of Research Grants.
4. **RECEIPT DATE** Applications received on or before June 1, 1977, will be processed for study section review in October 1977 and for the National Cancer Advisory Board review in January 1978.

**REVIEW**

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information, potential applicants may contact Dr. Saul Schepartz, (301) 496-6404, Division of Cancer Treatment, National Cancer Institute.
TITLE - RESEARCH TEAMS FOR ANTITUMOR DRUG DEVELOPMENT

SCIENTIFIC PROGRAM REQUIREMENT The National Cancer Institute (NCI) is accepting applications for support of research projects that represent a coordinated multidisciplinary approach to the development of antitumor drugs. The work would be conducted by an accomplished team of established scientific investigators. Preference will be given to the development of novel drugs and/or drug-analog series differing in structure from existing clinically useful cancer chemotherapeutic agents. The purpose of these studies is to develop new and potentially more effective antitumor agents by the application of novel conceptual approaches not currently under investigation in ongoing NCI-supported collaborative research programs.

Proposals from groups with multidisciplinary capabilities are desired. These groups should consist of at least two experienced research scientists in synthetic medicinal chemistry, a supporting investigator in pharmacology with expertise in biological testing and screening techniques for antitumor activity, and an additional investigator with experience in mode of action studies, e.g. molecular pharmacologist, biochemist, etc.

The choice and development of screening systems (in vivo, in vitro, biochemical, etc.) employed for initial evaluation of antitumor activity is optional and is left to the discretion of the individual investigator. In the event that promising agents are developed under this project, the Division of Cancer Treatment (DCT) is prepared to enter into a mutually agreeable arrangement to assist in the further development of these agents for clinical trial. This includes large-scale antitumor testing in currently used NCI screening systems, large-scale preparation of bulk drug, clinical formulation and large animal toxicological evaluation as a necessary prelude to the preparation of an Investigational New Drug Application (INDA) and subsequent clinical trial.

A semi-annual report summarizing the research progress on this project will be transmitted to the DCT Program Director for this announcement.

SIGNIFICANCE TO NCI PROGRAM GOALS This project is highly relevant to the program objectives of the DCT. The emphasis is directed toward the solicitation of novel conceptual approaches in the rational design, synthesis, and development of compounds not previously assessed for antitumor activity. It is hoped that the use of this multidisciplinary team approach should help to achieve a highly effective and efficient mechanism for the more rapid introduction into the clinic of agents representing new structures and classes as well as broader spectra of antitumor activities.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose a program project. Applicants may elaborate on the purposes, objectives, rationale and significance stated in this announcement and must complete portions of the application pertaining
to rationale and descriptions of specific projects including procedural details, the investigators' related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years.

3. **SUBMISSION** Use the standard research grant application form NIH 398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCT-4 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014. If your institution cannot supply you with form NIH 398, it may be requested from the Division of Research Grants.

4. **RECEIPT DATE** Applications received on or before June 1, 1977, will be processed for study section review in October 1977 and the National Cancer Advisory Board Review in January 1978.

**REVIEW**

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information, potential applicants may contact Dr. Saul Schepartz, (301) 496-6404, Division of Cancer Treatment, National Cancer Institute.
TITLE - STUDIES OF POPULATIONS AT LOW RISK FOR CANCER

SCIENTIFIC PROGRAM REQUIREMENT The National Cancer Institute (NCI) is accepting grant applications for support of epidemiologic research projects on human populations with low cancer risks. The purpose of this announcement is to encourage investigators to conduct descriptive and analytic studies of groups of people with cancer incidence and mortality rates significantly below expected rates. Such groups or populations may be located anywhere in the world. Studies should be directed toward a clear identification of the population at risk, an accurate estimate of the risk, and a search for factors which will explain this low risk. The risk may be related to a single cancer site or to multiple types of cancer. Current information indicates that several factors may be related to low risk, such as age, sex, race, genetics, religious practices, diet, nutritional status, socioeconomic status, country of birth, place of residence, occupation and behavioral habits. Analytic studies should include tests for the presence or absence of known risk factors associated with specific types of cancer.

SIGNIFICANCE TO NCI PROGRAM GOALS In our efforts to identify the causes of cancer and prevent the disease, it may be possible to learn as much about cancer etiology by studying factors leading to low risks as by studying high-risk factors. The resulting sets of information should be complimentary and reinforce each other in testing etiologic hypotheses. It is also possible that new etiologic factors may be identified in these studies. The accurate measurement of unusually low cancer incidence and mortality rates in certain defined populations will add to our knowledge of the basic cancer problem and will allow improved estimates of risks attributable to host and environmental factors. Recognition of the true magnitude of attributable risks may lead to measures for cancer prevention and control.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed five years.

3. SUBMISSION Use the standard research grant application form NIH 398. In both the covering letter and at top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-31 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014. If your institution cannot supply you with form NIH 398, it may be requested from the Division of Research Grants.
4. **RECEIPT DATE** Applications received on or before June 1, 1977, will be processed for study section review in October 1977 and for the National Cancer Advisory Board review in January 1978.

**REVIEW**

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. James L. Murray, (301) 496-3116, Room C505, Landow Building, Division of Cancer Cause and Prevention, National Cancer Institute, Bethesda, Maryland 20014.
TITLE: MECHANISM OF ACTION OF NEW ANTICANCER DRUGS

SCIENTIFIC PROGRAM REQUIREMENT The National Cancer Institute (NCI) is accepting applications for support of research projects on the mechanism of action of new anticancer drugs. The objective of this research is to characterize the biochemical activities of new anticancer drugs and to provide information which may allow the optimal clinical use of the drug or its analogs. The approach and methods are to be specified by the applicant. The new drugs to be studied are to be selected from among those in Phase I clinical trials or those currently being developed for clinical trials by the Division of Cancer Treatment (DCT). This information will be made available, upon request, from the DCT. It is expected that new drugs selected for development by DCT, during the grant period, may also be the subject of study. The applicant may specify the drugs to be studied but is not obliged to do so. The DCT will provide the grantees with supplies of drugs requested whenever possible. Progress reports will be submitted to the Program Director every six months describing interim results of studies on each drug. It is anticipated that several grants will be awarded.

SIGNIFICANCE TO NCI PROGRAM GOALS As promising new anticancer drugs are discovered and developed for clinical trials a knowledge of their membrane transport processes, biochemical transformation (leading to activation or inactivation), receptor site interactions, and effects on the molecular biology of the cell is important. The application of this information to their optimal use in clinical trials is the goal of this research. The information resulting from this research could be of value for the design of clinical protocols, and as a guide to the design of investigations in clinical pharmacology.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the application pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years.

3. SUBMISSION Use the standard research grant application form NIH 398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by
its title and number DCT-5 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014. If your institution cannot supply you with form NIH 398, it may be requested from the Division of Research Grants.

4. **RECEIPT DATE** Applications received on or before June 1, 1977, will be processed for study section review in October 1977 and for the National Cancer Advisory Board review in January 1978.

**REVIEW**

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information, potential applicants may contact Dr. Saul Schepartz, (301) 496-6404, Division of Cancer Treatment, National Cancer Institute.