NIH GUIDE for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

DESCRIPTIONS OF NIH COLLABORATIVE PROGRAMS

Vol. 3, No. 21, December 26, 1974

ANNOUNCEMENT

This issue of the *NIH GUIDE FOR GRANTS AND CONTRACTS* contains revised descriptions of the collaborative programs of four institutes or divisions of the NIH: the National Heart and Lung Institute, the National Institute of Allergy and Infectious Diseases, the Cancer Control Program of the National Cancer Institute, and the National Institute of Dental Research. These announcements replace those published in the *GUIDE* on September 18, 1973 (Vol.2, No.7). Although programs of other institutes and research divisions are essentially unchanged from those described previously, they are included in this issue.

Individuals not now receiving the *GUIDE* and/or supplemental announcements and wishing to receive this material may complete the request form on page 37 of this announcement. Individuals who returned this form previously need not resubmit unless they wish to receive material other than that which they stipulated on the earlier request.

Please note that the revised form entitled, "Request for Inclusion on Mailing List," contains only two significant changes: Reorganization of the National Heart and Lung Institute has required a revision of the 1600 series, and, since the last previous publication of NIH program descriptions, reorganization has separated the
* National Institute of Mental Health (NIMH) from the NIH. Individuals interested in NIMH programs should apply directly to that agency. Those receiving specific announcements from the NHLI need to resubmit the revised form only if a new program is involved. The Guide Distribution Center will provide for number changes of existing lists (e.g., Lung Disease from 1603 on old form to 1607 on revised form).

* Grants and Contracts Management Branch, National Institute of Mental Health, 5600 Fishers Lane, Room 7C02, Rockville, Maryland 20852.

The GUIDE is published at irregular intervals to provide policy, program, 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.

NIH Biomedical Research Contracts (NIH 6000-3-60.4)

POLICY

1. *PURPOSE AND APPLICABILITY* This issuance states the policy concerning the selection and use of the contract mechanism for the support of biomedical research by the National Institutes of Health.

2. *BACKGROUND* In addition to support of research and research training through the grants mechanism, with which the biomedical research community is well acquainted, NIH accomplishes its several missions through work conducted in its own facilities and support of mission-related activities in other institutions, Federal and non-Federal. Work supported in other Federal laboratories is arranged by interagency agreements and appropriate transfer of funds. This represents only a small fraction of funds available for contracts, but is nevertheless significant in that it makes available the talents and expertise existent in other Governmental laboratories. The major part of contractual activities are conducted in universities, research foundations, and commercial and industrial organizations across the Nation.

Contracts are identified in NIH reports as "collaborative arch and development." This is because NIH seeks collaboration with other ganizations and fosters collaboration among a number of other institutions to accomplish certain research goals.

3. *BASIC CRITERIA* Contracts are used for support of research and development when one or more of the following considerations obtain:

a. the awarding Institute or Division has identified a need for certain research work to accomplish its mission and has determined that the work must be done outside its own facilities and the initiative for undertaking the activity originates primarily within the awarding unit (Institute or Division) of NIH;

b. the objective is the acquisition of a specified service or end product;

c. the collaboration of a number of institutions must be obtained, and work must be coordinated or carried on in a comparable manner by all of these so that the data collected can be combined for statistical analysis; or

d. the NIH awarding unit participates to the degree necessary to accomplish its mission in the direction and control over the manner of performance or timing of the work.

4. *COROLLARY CRITERIA* used to define the contract as the preferred instrument of support may be:

a. there is in addition a requirement for extensive participation by the staff of the awarding unit in the program design, direction, methodology, and evaluation;

b. a need to capitalize immediately on information through directed initiation or changes in particular research and developmental projects.

5. *MANDATORY USE OF CONTRACTS* When awards are made to commercial or industrial profit-making corporations, or when payment of an amount in excess of actual costs (i.e., profit or fee) is intended, the use of the contract as the instrument of support is required.

6. *SELECTION OF CONTRACTORS* It is the policy of NIH to advertise its requirements for research and development contract projects as widely as possible. Participation in such projects is sought from all segments of the biomedical scientific research community and from engineering development organizations, where the expertise for the performance of specialized work may reside. Such advertising is conducted through the medium of *COMMERCE BUSINESS DAILY*[1/] and notices in general or specialized scientific journals. It is also the policy of NIH to encourage possible contractors to submit statements of competence and interest in regard to contract programs which will be announced in general terms, henceforth, in this publication. Such statements will serve as the basis for the compilation of lists of "sources." These sources may be requested directly to submit proposals on individual projects as they are developed within a specific program.

NIH policy is to assure that awards of contracts are based on scientific and technical ability and judgment, availability of facilities, and other such factors as displayed in the contract proposal, as well as on price. Scientific review of proposals is conducted by advisory panels including non-NIH members from the scientific community. Contracts proposed for award by such bodies receive further review by a senior staff group of the awarding unit.

7. *DESCRIPTIONS OF THE LLABORATIVE PROGRAMS* of the NIH awarding units appear in this issue of the *NIH GUIDE FOR GRANTS AND CONTRACTS*. It will be the policy of NIH to assure that all new collaborative programs are announced in this manner, as well as through other media. The *GUIDE* also will provide information on the contract programs of the NIH awarding units as well as furnish information on procedural and administrative policy matters.

8. *RESCISSION* This statement supersedes *GUIDE* No. 7, Vol. 2, Sept. 18, 1973.

1/ *COMMERCE BUSINESS DAILY* available on an annual subscription rate of $40 plus an additional $30.25 for airmail service. To order, send remittance plus full mailing address to: Superintendent of Documents, Government Printing Office, Washington, D. C. 20402.

References

(1) DHEW Grants Administration Manual, Chapter 1-10, Considerations in Selecting Award Instrument--Contract or Grant.
(2) Office of Management and Budget Circular A-101, January 9, 1971.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL CANCER INSTITUTE

This issuance provides a summary of programs in treatment, in cause and prevention, and in diagnosis and cancer biology currently conducted by the National Cancer Institute (NCI). The contract mechanism is used as at least a partial means of pursuing the objectives of each of the programs described below.

CANCER TREATMENT

The objective of the Division of Cancer Treatment is the development of drugs which singly or in combination with other drugs or modalities are efficacious in producing complete remissions of clinical cancer at safe and tolerable dosages, and in extending the disease-free interval so that the patients' life expectancy approaches or equals that of the normal comparable populations. This program is implemented in laboratories and clinics in Bethesda, Baltimore, Washington, and Kampala, Uganda, by NCI scientists and at universities, commercial organizations, and other institutions under contract agreements with the NCI.

The Division of Cancer Treatment had its beginning as the Chemotherapy Program in 1955 with the establishment of the Cancer Chemotherapy National Service Center. In 1965, a thorough study of the previous 10 years' experience in drug development was undertaken and, as a result of that study, a linear array was developed and the logical steps from drug acquisition through screening to clinical trials were outlined. The program was then reorganized into three major segments along the lines of the linear array.

The first of these major segments is the Drug Research and Development area which is responsible for the input of chemical compounds and natural products for screening, drug formulation, and for drug scheduling studies. The second segment is Experimental Therapeutics where toxicology and pharmacologic disposition of drugs are studied. Those compounds that pass these first two segments successfully then undergo clinical trials in man in the Medical Oncology area of the program, either in the Clinical Center or in clinical resources under contract. In addition, the Cancer Therapy Evaluation Branch of the Division implements and monitors a comprehensive therapy clinical contract program designed to provide for clinical trials of anti-cancer drugs and studies of combined modality therapy. This unit is also responsible for the communication and filing of all information required by the Food and Drug Administration in connection with the drug development program of the Division of Cancer Treatment.

Clinically active, safe drugs eventually are cleared by the FDA and become commercially available for use by practicing physicians for the control of cancer. There are now 40 anti-tumor drugs which have either been licensed or are in clinical trial. There are currently ten types of cancer in which treatment with drugs, either singly or in combination with other drugs or with radiation or surgery may result in life expectancy approaching the normal for a comparable group in significant numbers of patients. These cancers are the more rapidly growing types but many of the drugs are effective in inducing impressive tumor regressions in the more slowly growing cancer.

The strategy for the future includes studies attempting to explain the differences between rapidly growing and slowly growing tumors, and perfection of animal models for slowly growing tumors; the continuation of a broad screening operation involving chemicals and natural products obtained through developments in university

laboratories, industry, and other institutions in this country and abroad as well as those selected on the basis of biochemical or biological rationales; in vitro biochemical screens as well as the use of slowly and rapidly growing animal tumor models to select the best drugs, schedules, and combinations; increased toxicologic and pharmacologic studies in animals and man; and the organization of clinical trials to study each new agent in representative rapidly and slowly growing tumors. Clinical trials of drug combinations and combinations of drugs with other modalities including surgery, radiotherapy, and immunotherapy are also sponsored. Finally, there are extensive basic and clinical studies of the biology of cancer, and of the supportive care of patients, particularly those at high risk to infection as a consequence of cytotoxic therapy. This includes studies of granulocyte transfusions, bone marrow transplants, and laminar flow protected environments. For further information write Associate Director for Program, DCT, National Cancer Institute, Bethesda, Md. 20014.

CANCER CONTROL

The Division of Cancer Control and Rehabilitation (DCCR) has the principal Federal responsibility for assuring the rapid and effective application of cancer research findings in the prevention, detection, diagnosis and treatment of cancer and for the rehabilitation and continuing care of cancer patients. It is the ultimate DCCR goal to reduce the incidence, morbidity and mortality from cancer through a five-pronged effort.

1. Identification of new methods, knowledge, and techniques that may be applicable to control activities. These activities will involve close monitoring of the progress of research efforts and potential results; surveys to identify proven, practical knowledge and techniques; and data collection efforts to compile available information directly applicable to control activities.
2. Field testing of potential control knowledge and techniques in limited community field trials to determine their potential for widespread community usage. This effort provides an orderly transition from Phase III clinical research trials to community usage.
3. Evaluation of potentially useful control knowledge and techniques to determine their effectiveness, practicality, acceptability, impact on the disease, and economic or cost-benefits prior to embarking on costly wide-scale community demonstration and promotion efforts.
4. Demonstration of effective, practical, control knowledge and techniques in large-scale community environments that are widespread geographically and demographically to provide the public and health professionals with first-hand knowledge of the utility and effectiveness of the demonstrated knowledge and techniques; and to provide the basis for continued community support of the efforts.
5. Promotion of demonstrated effective, practical knowledge and techniques to assure their rapid widespread utilization in all areas in the nation.

DCCR will not support laboratory or clinical research to develop new procedures or techniques, except for research in rehabilitation. DCCR has full responsibility for development and implementation of research in rehabilitation and will support research projects in this area. DCCR will also support work to improve the application and distribution of existing procedures and techniques recommended for general use. Such refinement research will compete for DCCR resources on the same basis as other projects.

DCCR is concerned with the entire scope of the cancer problem, from the prevention of the disease to the rehabilitation and continuing care of the cancer patient during and after treatment. Program thrusts, therefore, are in three major intervention areas: (1) Prevention; (2) Detection, Diagnosis and Pretreatment Evaluation; and (3) Treatment, Rehabilitation and Continuing Care.

Prevention activities will include identifying methods and techniques to inform, educate, and persuade the American public to fully utilize available cancer prevention services.

Activities in Detection, Diagnosis, and Pretreatment Evaluation will be concentrated on promoting more effective communication among physicians, health professionals, and the public regarding the detection, diagnosis, and pretreatment evaluation of cancer patients, with particular emphasis on improvements to this end through the use of existing community resources and mechanisms. Identifying new methods and techniques and disseminating information on them to both health professionals and the public where appropriate is also being stressed.

Treatment, rehabilitation, and continuing care activities will undertake to promote more effective communications among physicians, health professionals, and the public regarding the treatment and rehabilitation of cancer patients. Particular emphasis will be placed on the use of community resources and mechanisms. Additional emphasis will be placed on the identification of new methods and techniques to be demonstrated to both health professionals and the public where appropriate. It will also be necessary to develop and demonstrate a broad spectrum of rehabilitative and continuing care activities. In addition to the traditional approach, such activities will include counseling to the patient and his or her family to maintain family competence assuring adequate self-care, personal care, and vocational functions.

DCCR supports these program activities with both grants and contracts. Identification, and field testing, with the accompanying evaluation, are envisaged to be the first steps in translating and transmitting research results to the medical providers and cancer patients or potential patients, and DCCR support for these activities will be on an individual project basis by the most appropriate support mechanism. The second steps, demonstration and promotion, with the accompanying evaluation are to be accomplished in a contract-supported community-based cancer control program.

The grant-supported portion of the DCCR program encompasses all three intervention areas. It is intended (1) to provide new concepts for a more effective utilization of existing procedures and/or techniques and (2) to provide information on refinement of established procedures and/or techniques for a more vigorous prosecution of Cancer Control.

Grant applicants should submit PHS Grant Application form NIH 398 to the Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

Applicants should type "CANCER CONTROL" in the top margin of the application's face page. Applications must be received by February 1, 1975; June 1, 1975; and November 1, 1975, in order to be reviewed at the succeeding NCI Advisory Board Meeting (i.e., June, November, and March respectively).

DCCR contracts are advertised in the Commerce Business Daily and other publications. All noncompetitive contracts require special justification and DCCR should be queried before fully developed unsolicited proposals are submitted.

Any inquiries concerning either DCCR grants or contracts should be directed to the Director, Division of Cancer Control and Rehabilitation, National Cancer Institute, Bethesda, Maryland 20014 (telephone: 301 427-7996).

CANCER BIOLOGY AND DIAGNOSIS

The Division of Cancer Biology and Diagnosis carries out intramural research in three general aspects of the cancer problem: Cancer Biology, Tumor Immunology, and Clinical Research. Cancer Biology includes the efforts of the National Cancer Institute's Laboratories of Biology, Biochemistry, Molecular Biology, Physiology, Pathophysiology and Theoretical Biology. Tumor Immunology includes the Laboratory of Cell Biology and the Immunology Branch, and Clinical Research includes the work of the Surgery, Radiation, Metabolism and Dermatology Branches and the Laboratory of Pathology.

The Division of Cancer Biology and Diagnosis also plans and manages collaborative contract research programs in three areas, Tumor Immunology, Cancer Diagnosis and Breast Cancer. The Tumor Immunology contract research program is divided into three general areas, tumor immunobiology, cancer immunodiagnosis, and the immunotherapy of cancer. The contract program in Cancer Diagnosis has two goals, the development of screening tests for the early detection of cancer, and the improvements of methods for the localization of cancer once detected. Present efforts include work on hormonal and other biochemical screening tests, as well as immunological tests; the application of cytologic methods in cancer screening; and the development of automated methods for reading cytologic specimens. In the future it is hoped to develop improved radiologic methods for cancer diagnosis, and improved instruments for localization of the disease. The Division of Cancer Biology and Diagnosis manages the contract program of the Institute's Breast Cancer Task Force. This broadly conceived approach to cancer of this organ site is divided into four subprograms in the epidemiology, experimental biology, diagnosis, and treatment of the disease.

For further information write to Associate Director for Program Planning, DCBD, National Cancer Institute, Bethesda, Maryland 20014.

CANCER CAUSE AND PREVENTION

General The Division of Cancer Cause and Prevention is responsible for planning and executing a broad research program on etiology and prevention of cancers. Experimental and epidemiologic research is conducted on potential and actual viral, chemical, and radiologic carcinogenic agents and on their combinations. Evaluations of carcinogenic hazards and studies on mechanism of cancer induction are included. Biometric and epidemiologic investigation of cancers are conducted in populations, and extensive demographic data are continually compiled. The various areas of research complement each other, with data from one area providing input for another area in the planning, conduct and evaluation of research programs. Laboratory findings provide leads that must be evaluated in human populations; observed associations of cancer with other factors determined in epidemiologic studies require further clarification in experimental investigations.

The Division of Cancer Cause and Prevention is divided into three program areas, each headed by an Associate Director. The Viral Oncology area is concerned with determining the significance of viruses in the induction of cancers in man and with developing means for preventing these cancers with virological, immunological, and other techniques. The Carcinogenesis area is concerned with determining the significance of chemical agents in the induction of cancer in man and with developing means of preventing these cancers. The Field Studies and Statistics area is concerned with continued monitoring of populations for cancer incidence, prevalence, and mortality; identification of groups with different risks of cancers and determination of associated internal and external environmental and genetic factors; conduct of observational research in situations where society or nature has provided experiments on cancer, such as studies on occupational groups, migrant populations, groups with other diseases, etc.; studies on diagnosis and therapy, including design and evaluation of therapeutic trials, end results of the therapies, diagnostic and detection studies, etc.; and collaboration in a variety of investigations requiring epidemiologic, demographic, statistical and mathematical expertise.

The program is conducted through in-house research and through research contracts for a nationwide effort of the integrated programs in the three areas. The Division of Cancer Cause and Prevention staff are responsible for planning, coordination, evaluation of the contract-supported efforts as well as for the conduct of in-house investigations, with major scientific and review input from the scientific community at large. These efforts are coordinated with investigations conducted by NCI grantees.

Viral Oncology The Viral Oncology program is responsible for the Institute's research into the role of viruses in the causation of cancer in man and animals, intended ultimately to prevent and control neoplastic diseases of viral etiology. The three branches within the Office of the Associate Director for Viral Oncology are responsible for the planning and supervision of broad programs of basic, developmental, and applied research directed toward these objectives, as well as for the management of similarly directed special programs of national scope under the direct operations activities of the NCI.

The many disciplines and skills needed to study problems of viral causation of cancer are located in three branches and are available for deployment in varying combinations for collaboration in problem-solving approaches to disease entities at the program and project levels. This type of collaborative utilization of research capabilities and disciplines has served to unify research efforts and to reduce unnecessary duplication to a minimum.

The mission-oriented research of the Virus Cancer Program started in 1964 with a special Congressional appropriation of $10 million. Launching of the Program was predicated upon the underlying belief that at least one virus is causally related to human leukemia and lymphoma and persists in the diseased individual. Management of this Program was under the Leukemia and Lymphoma Branch. Increased evidence of a relationship of viruses to the etiology of solid tumors led to additional funding and the launching of a Solid Tumor Virus Program in 1967, under the management of the Viral Carcinogenesis Branch. The growth of both programs and their many common interfaces led to their merger in 1968 into the Special Virus Cancer Program, which now embraces viral etiological research on cancers of all types. The program now employs a research convergence technique to provide coordination of objectives, personnel, resources, and information under the general direction of the Office of the Associate Director for Viral Oncology.

All organizational units under the Office of the Associate Director for Viral Oncology, as well as members of other organizational units in the Division of Cancer Cause and Prevention, participate in the program. The resources of the Institute are strongly complemented by the numerous academic and industrial research groups collaborating in this effort. This integration has made possible the sharing of information resulting from the examination and treatment of large numbers of leukemic patients without which it would be difficult or impossible to conduct significant research programs directed to the etiology, prevention, and control of this disease. It has also made possible concurrent studies on the leukemia sarcoma complex in animals, particularly those common to the human environment. Such studies are expected to yield answers to the possible interrelationships of these diseases and to provide models for the study of the counterpart human studies.

Carcinogenesis The Carcinogenesis area is responsible for planning, implementing, and managing the coordinated research program of the NCI on carcinogenesis by chemical and physical factors and on cancer prevention.

Intramural research and a contract-supported collaborative program, directed by the scientific staff, encompass an integrated effort for the identification of population groups at different risks to cancers, the selection of chemical agents for bioassay with emphasis on suspected environmental carcinogenic hazards, the development and

selection of biological models for carcinogenesis bioassays and studies, the identification of carcinogenic activity to selected chemicals by bioassay, and the identification of processes required for the carcinogenic action of selected agents as target points for prevention or inhibitory measures. Processes studied include the penetration of chemicals into the organism and their molecular logistics, metabolic pathways and enzymatic mechanisms of activation, interaction with cell constituents, neoplastic transformation, growth regulation of transformed cells, and immunological control.

The newly established Lung Cancer Branch conducts investigations to identify carcinogenic agents and biological factors involved in the development of lung cancer and attempts to determine means by which these factors may be inhibited or prevented. It develops, designs, and standardizes biological and chemical assay systems for testing the carcinogenic and/or synergistic effects of chemical and physical agents involved in lung cancer causation.

Field Studies and Statistics The Field Studies and Statistics area has three major functions: (a) research into the etiology of cancer in free-living populations, largely but certainly not exclusively human; (b) consultation and support in mathematics, statistics (including experiment design and analysis) and system analysis in problems of cancer research; (c) development of the basic data of cancer incidence, prevalence, and mortality in the United States sufficiently precise to permit administrators and research workers to measure their successes (and failures) in preventing, diagnosing, or treating cancer. The two Branches (Biometry and Epidemiology) within the Office of the Associate Director for Field Studies and Statistics supplement and support each other in these activities.

Objectives for 1973 The major objectives in the Virus Cancer Program are: (a) the determination of cancer-causing activity in animals by viruses already isolated from human cancers; (b) relating this activity, and other characteristics of the candidate viruses, to cancer in man; (c) the determination of the entire sequence of molecular events, including specific enzymatic activities (e.g., polymerases) in viral replication and tumor induction; and (d) relating this information to the control of cancer in man.

The Carcinogenesis area will give high priority to the identification of chemical-viral interaction mechanisms, the role of various chemicals and dusts in the induction of lung cancer, short term in vitro carcinogenesis bioassay, and the establishment of data collection and retrieval systems to improve efficiency in coordinating information generated by the program and disseminating it to the scientific community.

In Field Studies and Statistics, epidemiology studies will be made in human populations of the role of viruses and chemicals in cancer initiation. In 1973, the activities of the Third National Cancer Survey will shift from analysis of the initial data to the setting up of a permanent data collection and analysis system.

For further information write to Associate Director for Program, DCCP, National Cancer Institute, Bethesda, Maryland 20014

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL EYE INSTITUTE

In 1971 and 1972, the National Eye Institute (NEI) initiated a program for targeted research and development in glaucoma. In 1973, the NEI continued this effort and initiated similar undertakings in the study of retinal disease. For 1973, the NEI is planning to establish a targeted research program for the development and clinical application of new knowledge related to corneal disorders.

Opacification, painful injuries, and irregularities in curvature impair or destroy the optical properties of the cornea. Corneal disorders cause approximately 3% to 4% of the blindness in the United States.

Although many corneal disorders are congenital, degenerative, or due to nutritional deficiencies, one of the most common causes of opacification and subsequent visual loss or blindness to an individual is the scarring that follows injuries resulting from infections, lacerations, heat burns, and chemical burns. In addition to the impairment of an individual's visual capacity, concern is expressed for the considerable industrial and economic loss resulting from numerous small injuries or external diseases involving the cornea which render individual workers nonproductive for extended periods of time (without rendering them legally blind), deprive society of their earning power, and force these individuals to become dependent on others.

General areas of interest to the NEI are: immunology and immunopathologic mechanisms of corneal diseases, infectious diseases involving the cornea, opacification and edema, and tear film.

This announcement is not a request for proposals and does not commit the government to award any contracts. Proposals may be solicited on a competitive basis through published announcements by the NEI. Further information is not available until the solicitation is published. However, specific areas of investigation to be pursued are being identified, and the NEI will make every effort to keep all interested parties informed of developments concerning this program through announcements in the Commerce Business Daily, NIH Guide for Grants and Contracts (Supplement), and by direct mail.

For further information write Dr. Thomas C. O'Brien, Scientific Programs Branch, National Eye Institute, Bethesda, Maryland 20014.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL HEART AND LUNG INSTITUTE

DIVISION OF HEART AND VASCULAR DISEASES
ETIOLOGY OF ARTERIOSCLEROSIS AND HYPERTENSION

A major component of the program of the Division of Heart and Vascular Diseases is concerned with basic, animal and clinical research in the etiology and pathogenesis of arteriosclerosis and of hypertension. Most of the work being supported in this area is supported by research grants, but a number of problem areas have been identified for which collaborative research supported by contract may be more appropriate. One such area is the establishment of resource centers in which models of chronic atherosclerosis and hypertension in non-human primates can be developed and studied. It is expected that activities in this area will be initiated in FY 1975.

For further information write Dr. Gardner McMillan, Associate Director for Etiology of Arteriosclerosis and Hypertension, Division of Heart and Vascular Diseases, NHLI, Bethesda, Maryland 20014.

DIVISION OF HEART AND VASCULAR DISEASES
ISCHEMIC HEART DISEASE

Program objectives are the planning and support of research leading to a reduction of death and disability from acute myocardial infarction, chronic ischemic heart disease, and sudden cardiac death. The program consists of regular research and program project grants directed at problems of ischemic heart disease as well as Institute-initiated and solicited research in defined areas of high interest. The areas of solicited research include the Myocardial Infarction Research Units (to be replaced by the Ischemic Heart Disease Specialized Centers of Research), sudden cardiac death, quantifying infarct size, protecting ischemic myocardium, lethal arrhythmias, and a national collaborative trial of coronary artery surgery. Workshops and symposia related to these projects have been held or are planned and one program of induced myocardial infarction in animal models has been completed.

The nine Myocardial Infarction Research Units begun in 1967 and 1968 are multidisciplinary research programs directed primarily at the problem of acute myocardial infarction. Each unit includes clinical studies, pathology, data management and a number of laboratory projects in basic science areas. These units, which will be phased out in the current year, will be replaced by grant-supported Ischemic Heart Disease Specialized Centers of Research which will represent a similar type of multidisciplinary programs focused more broadly on the problems of ischemic heart disease.

The projects on sudden cardiac death include a review of multiphasic screening examinations and a collaborative study of the clinical histories and pathologic examinations of sudden cardiac death victims. Other projects involve emergency rescue operations with monitoring of patients during the acute event and long-term follow up of resuscitated patients. Research on re-entrant arrhythmias, bundle branch block, and patients with impending infarction are also included.

Protection of ischemic myocardium is the goal of a number of projects studying biochemical changes in ischemic myocardial cells and interventions which might prevent these alterations. Parallel clinical studies are testing some of these interventions in patients with acute myocardial infarction. Projects designed to quantify infarct size are focused primarily on ultrasonic and radioisotope imaging techniques.

The lethal arrhythmia projects are primarily centered on studies of ischemic tissue in electrophysiology and biochemistry laboratories. Additional projects include research on arrhythmias in surgical, coronary care, and post coronary care unit patients.

The National Coronary Artery Surgery Trial is designed as a seven-year study to test the effects of coronary artery surgery in randomized subgroups of patients with angina pectoris; a registry is also included. Eleven participating institutions and a coordinating center are presently involved in this study which is in the early phases of data collection.

For further information write Dr. Alan L. Pinkerson, Chief, Clinical Cardiac Diseases Branch, Division of Heart and Vascular Diseases, National Heart and Lung Institute, Bethesda, Maryland 20014.

DIVISION OF HEART AND VASCULAR DISEASES
LIPID METABOLISM

The Lipid Metabolism Branch is responsible for planning, developing, and directing a collaborative program of research into the structure, metabolism, and functions of lipids and lipoproteins as they relate to atherosclerosis, and coordinating a national research program designed to increase knowledge related to the diagnosis and management of lipid disorders, especially those associated with premature vascular disease.

The Lipid Metabolism Branch implements its program goals in part through (1) a network of twelve Lipid Research Clinics and (2) a Patient Registry and Coordinating Center, a Lipid Standardization Laboratory, a Central Exercise Laboratory, and a Central Clinical Chemistry Laboratory.

The objective of the Lipid Research Clinics' Program includes:

1. Evaluation of current techniques for the diagnosis of hyperlipoproteinemia and the development of better ones. Standardization of methodology techniques and definitions dealing with hyperlipoproteinemia and its diagnosis.

2. Improvement of detection, diagnosis, and medical care for hyperlipidemic patients by providing guidance and assistance to physicians on the management of these patients and by the testing and development of improved therapy (both dietary and drug) for specific disorders.

3. Determination of the prevalence of hyperlipoproteinemia and its natural history.

4. Design and implementation of an intervention study to test the lipid hypothesis in high-risk patients, i.e., will lowering blood lipids reduce cardiovascular mortality and morbidity in patients with specific types of hyperlipoproteinemia? Will it delay the development and/or progression of cardiovascular disease?

In the future the Branch hopes to support, through the contract route, additional areas of study in lipid metabolism including the development of animal models of the human dyslipoproteinemias and study of the determinants of cholesterol absorption.

For further information write Dr. Basil Rifkind, Chief, Lipid Metabolism Branch, Division of Heart and Vascular Diseases, National Heart and Lung Institute, Bethesda, Maryland 20014.

DIVISION OF HEART AND VASCULAR DISEASES
CARDIOVASCULAR DEVICES

The goals of the program are the reduction of death and disability from cardiovascular diseases through the development of therapeutic and diagnostic devices, instrumentation, and related components.

The major current effort is in the development of circulatory assist and cardiac replacement devices. This involves not only the development and assessment of pumps, energy conversion, storage, and transmission systems, control systems, and materials, but also the necessary physiological assessment and evaluation of reliability.

Diagnostic devices of particular interest are likely to be in the area of the detection and quantification of arteriosclerotic lesions. There is an existing program in flow and pressure measurement and cardiovascular imaging devices.

For further information write Peter Frommer, M.D., Associate Director for Cardiology, Division of Heart and Vascular Diseases, National Heart and Lung Institute, Bethesda, Maryland 20014.

DIVISION OF HEART AND VASCULAR DISEASES
CLINICAL APPLICATIONS AND PREVENTION

Primary research interests and activities in this area are directed toward the conduct of epidemiological studies, clinical trials, biometrics research, and research into the prevention of heart and vascular diseases.

Preventive Cardiology Branch The research conducted and supported in this branch is directed toward studies of preventive measures to reduce morbidity and mortality from atherosclerosis, hypertension, and stroke. Examples of these prevention studies are the Hypertension Detection and Follow-up Program in 14 communities, to determine the extent to which mortality from hypertension can be reduced in the general population; and the Multiple Risk Factor Intervention Trial (MRFIT) in 20 centers is a primary prevention trial to determine the extent to which coronary heart disease mortality can be reduced by reduction of serum cholesterol, elevated blood pressure, and cigarette smoking in men who have above average risk of developing coronary disease because of these factors.

Clinical Trials Branch Cooperative clinical trials supported by contracts are the primary responsibility of this branch. The aspirin-myocardial infarction clinical trial involving 30 clinical centers will be initiated in 1975. The centers have been selected and will be enrolling about 3500 patients with proven myocardial infarction into this 3-year secondary prevention trial. Medical and biometrics staff of the Branch maintain direct liaison with the involved investigators throughout the duration of these trials.

Epidemiology Branch Conducts epidemiological studies of the heart and vascular diseases in populations within the United States and in cooperation with medical investigators in other countries. The Framingham Heart Disease Epidemiology Study and other prospective studies in Puerto Rico, Japan, Honolulu, Israel, and Yugoslvaia are examples of such investigations conducted with direct funds, contract funds, and P.L. 480 counterpart currencies. Genetic studies among twins are also in progress in this Branch.

For further information write Dr. William J. Zukel, Associate Director for Clinical Applications and Prevention, Division of Heart and Vascular Diseases, National Heart and Lung Institute, Bethesda, Maryland 20014.

DIVISION OF BLOOD DISEASES AND RESOURCES

The Division of Blood Diseases and Resources (DBDR) supports contract research in blood banking sciences, thrombosis, hemorrhagic diseases, biomaterials and sickle cell disease and related red cell disorders. In addition, the clinical evaluation of promising drugs and biologics is occasionally undertaken by the Division as a direct operation.

The Blood Resources Program supports research in blood banking systems management aimed at improving the operations of blood banking nationwide. Other work supports improved methods of blood fractionation development of new fractionation products, improved storage of blood and blood products, improved utilization of blood components, and elimination of the hazards of blood transfusion, with special emphasis on the problem of post-transfusion hepatitis. This program includes development of blood substitutes and research in transplantation biology.

The program in thrombosis has supported development and application of agents that dissolve formed blood clots. Currently, trials have been initiated to test the efficacy of heparin and platelet inhibiting agents to prevent venous thrombosis in high risk groups. Other work involves preparation of highly purified reagents used in coagulation research and studying the relationship between diet, platelet function and thrombosis.

The program in hemophilia has supported pilot epidemiologic studies of the hemophiliac population and continues to evaluate the availability of treatment facilities and their impact on the national blood resource. Other work supports standardization and improvement of clotting factor preparation necessary for treatment of hemophilia, assessment of the usefulness of highly purified animal clotting factors, development of methodology for identifying the hemophilia carrier, and exploration and evaluation of methods to develop a nationwide system with comprehensive care potential in hemophilia. Studies are envisioned to assess the value of prophylactic and self-treatment with Factor VIII to explore and evaluate genetic counseling techniques in hemophilia.

The Biomaterials Program supports basic and applied investigations to study the interaction between blood components and synthetic materials as well as naturally occurring macromolecules. The major aim is to understand better what factors are involved in blood compatibility. This is a necessary requirement for the development of improved blood compatible materials for implantable cardiovascular assist devices, artificial organs, catheters, cannulas, as well as non-implantable extracorporeal assist devices such as blood oxygenators. The major areas currently supported by the Biomaterials Program include the following: (1) investigations of natural macromolecules of the blood vessel wall; (2) preparation of synthetic macromolecules; (3) microfiber/scaffolded structures involving tissue culture techniques; (4) studying the long-term mechanical properties of polymers in the physiological environment; (5) investigating the biological and physicochemical properties of biomaterials; (6) biological evaluation and testing of candidate materials and (7) conducting systematic clinical trials with suitable biomaterials made into appropriate devices.

The Sickle Cell Program in cooperation with the Center for Disease Control supports a proficiency testing program to evaluate laboratory testing procedures for hemoglobinopathies, a basic and advanced laboratory training course for identification of abnormal hemoglobin and a reference bank of abnormal hemoglobins. Other areas of support include investigation of agents to alter the sickling process and treat the painful "sickle crisis," new techniques for improving the diagnosis of hemoglobinopathies in utero, in cord blood and in screening clinics, continuing education programs for professional and lay populations and clinical trials to evaluate methods of managing the iron overload problem in Cooley's anemia.

For further information write Dr. Ernest R. Simon, Director, Division of Blood Diseases and Resources, National Heart and Lung Institute, Bethesda, Maryland 20014.

DIVISION OF LUNG DISEASES

The Division of Lung Diseases implements its mandate through four major program activities: Research and Development Program, Manpower Program, Research and Demonstration Centers Program, and Prevention and Control Program, utilizing for each type of activity the support mechanisms most appropriate for achieving its objectives.

The contract mechanism is used to complement and supplement research on problems inadequately represented in investigator-initiated research projects and goal-oriented centers.

The Research and Development Program is addressed to studying the structure and function of the lung, pediatric pulmonary diseases, chronic bronchitis and emphysema, fibrotic and immunologic pulmonary diseases, pulmonary vascular diseases and respiratory distress syndromes, as well as the development of techniques and devices for pulmonary diagnosis and respiratory assistance, monitoring and control.

Contract Research activity within this program is administered through three of the Division's four Branches: The Pathophysiology Branch, Etiology Branch and Special Programs and Resources Branch.

The Pathophysiology Branch fosters a program of basic and applied, clinical and nonclinical research on the lung and respiratory system in normal and diseased states. Contract-supported programs include the development of physical and chemical methods of separating, culturing and identifying individual lung cells; characterization of lung structural components and the metabolic changes involved in their development and destruction; and studies of the pathophysiology of respiratory disorders.

The Etiology Branch fosters a program concerned with causal factors of respiratory diseases and the factors affecting their natural history. Representative contract activities include delineation of the role of heterozygosity of alpha-1-antitrypsin in the etiology and pathogenesis of respiratory diseases; determination of the prevalence of chronic respiratory diseases in selected populations; and definition of "host factors" as determinants of susceptibility to chronic respiratory disease.

The Special Programs and Resources Branch, through its Bioengineering Program, stimulates investigations that require both engineering and medical expertise, thus bringing sophisticated technology to bear on problems of diagnosis and treatment. Presently, the Branch sponsors a contract program which includes a clinical trial to determine the efficacy of the clinical application of membrane oxygenators to patients with acute respiratory failure, and also contracts to develop and evaluate blood gas sensors for the continuous monitoring of adults and neonates.

The Prevention and Control Program is designed to demonstrate the applicability, in community settings, of diagnostic, therapeutic or prevention procedures, activities or techniques which have been tested in a research environment; and to educate community physicians, allied health personnel and the general public with regard to pulmonary diseases. Contract research within this program is administered by the Centers and Control Programs Branch.

The Centers and Control Programs Branch directs activities which facilitate or implement the transfer of knowledge into clinical practice through education, demonstration and control programs. Present contracts support education programs for the recognition and early treatment of acute respiratory insufficiency and respiratory failure.

The Manpower Program, administered by the Special Programs and Resources Branch, and the Research and Demonstration Centers Program, administered by the Centers and Control Programs Branch have at present no activities supported through the contract mechanism.

For further information write Dr. Jay Moskowitz, Associate Director for Program Planning and Evaluation, Division of Lung Diseases, National Heart and Lung Institute, Bethesda, Maryland 20014.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

OBJECTIVES

Collaborative Research activities of the National Institute of Allergy and Infectious Diseases are designed to translate into human health benefits newer scientific information and technology acquired through research in the fields of immunology and infectious diseases. To achieve this end the program provides and evaluates a variety of essential research resources and develops associated research methodology and related information. Activities include: the production, distribution, and evaluation of reagents in immunology and microbiology; development and testing of vaccines and antiviral substances to combat selected infectious diseases; and support of research in carefully defined areas of transplantation immunology. These are projects through which specific needs of medical research and delivery of health services can be met. Information on program is published in the *NIH GUIDE FOR GRANTS AND CONTRACTS* and made available through announcements in scientific journals. Progress reports and scientific results are published in journals and/or deposited in the National Technical Information Service.

Collaborative programs are designed, through use of contracts, to be flexible and responsive to research needs and promising scientific opportunities. When an activity reaches an appropriate stage of development, efforts are made for other Federal agencies or the private sector to assume responsibility for delivery and utilization. New programs are initiated in response to public health needs and related opportunities resulting from research breakthroughs.

PROGRAM AREAS

Within Collaborative Research are four operating branches--Infectious Diseases, Research Resources, Transplantation and Immunology and Geographic Medicine--each designed to carry out a facet of a broad mission of meeting vital health research needs. The programs of these four branches are described below:

Infectious Disease Branch The Institute's Infectious Disease Branch functions in particularly close concert with intramural scientists of the NIAID and the Bureau of Biologics, FDA. It also benefits from the experience of advisory groups and collaboration with university and drug industry scientists. Within this framework, the branch promotes targeted research leading to the development and evaluation of promising prophylactic and therapeutic agents for the control of selected infectious diseases. A vaccine development program was initiated in 1962 to conduct collaborative vaccine studies, especially against acute respiratory infections. A rubella (German measles) vaccine program, undertaken in 1965 aided in the final evaluation of vaccines under consideration for licensure. Vaccines were licensed in 1969.

Current interests include development and evaluation of vaccines against pneumococcal pneumonia, meningococcal and Hemophilus influenzae meningitis, influenza, respiratory syncytial virus and parainfluenza virus infections, mycoplasmal and streptococcal infections. Another Infectious Disease Branch program is designed to bring interferon and other promising antiviral substances into clinical application. A recently initiated program in hepatitis sponsors developmental studies on hepatitis B antigens and antibodies, experimental infections in animal models, epidemiologic surveillance in high-risk groups and clinical evaluation of

hyperimmune hepatitis B antibody gamma globulin for the prevention of infection following parenteral inoculation of possible infectious material. A small effort on venereal disease research has been initiated, consisting of attempts to grow Treponema pallidum in vitro. The Infectious Disease Branch is also initiating efforts toward resolving problems with nosocomial infections.

Research Resources Branch The Research Resources Branch was established in 1962 and conducts a collaborative program for the support of research by stimulating the production, testing and distribution of a wide range of reagents. These reagents for health research purposes include viral and mycoplasma seed cultures and their corresponding antisera, allergens and interferons. All reagents are characterized by appropriate microbiological, immunological and biochemical methods and provide the recipients with well-characterized reference materials. Reagents for most of the important viruses and mycoplasmas involved in infections of the respiratory and gastrointestinal tracts are available for distribution. Reagents are also available for selected arthropod-borne viruses and for the antigens of hepatitis B. The reagents related to allergic diseases have recently received greater emphasis, and this expanded program is working toward the acquisition of reagents for ragweed, ryegrass and ascarid allergens. The program also provides support for research requiring high-technology biophysical separation, purification and concentration procedures. These facilities and procedures are needed in the preparation of antigen subunits used for newer, more sophisticated reagents for research in virology.

Transplantation and Immunology Branch The program of the Transplantation and Immunology Branch was started in 1964 to encourage research and provide resources designed to solve the immunological problem of graft rejection in organ transplantation.

From the beginning, the Transplantation and Immunology Committee, made up of experts in the field, has helped to identify objectives to be pursued through contracts with a variety of laboratories. The Branch's program now includes developing and providing well characterized and standardized reagents useful in tissue typing; providing technical advice and information on reagents, techniques and transplants through workshops and publications; investigating biological immunosuppressive agents which help to retard graft rejection; and developing methods for recognition of early graft rejection.

Programs to acquire information relating directly to clinical studies are in progress. These are focused on the evaluation of tissue matching as an appropriate predictor of graft survival, and a program to collect and analyze information on the efficacy of anti-thymocyte globulin in abrogating renal graft rejection. These investigations are designed to establish a better understanding of the graft rejection process. In turn, this information is ultimately to be applied in the circumvention of the graft rejection process. A program is also underway to evaluate, in the animal model, new techniques for the regulation of immune responsiveness.

Geographic Medicine Branch The Geographic Medicine Branch was created in 1968 to manage several programs transferred to the NIAID from the former Office of International Research. This Branch currently supports contracts and grants under the United States-Japan Cooperative Medical Science Program within the following selected areas: cholera, leprosy, the parasitic diseases schistosomiasis and filariasis, immunology and pathogenesis of tuberculosis, and the viral diseases rabies, dengue, dengue hemorrhagic fever and other selected areas of arbovirus research. Each of the foregoing scientific areas of interest are further delimited

to afford a very specific program focus. In addition, under direct cognizance of the National Institute of Arthritis, Metabolic and Digestive Diseases, the Branch supports research on selected aspects of malnutrition, including the relationship between malnutrition and infection. Finally, under the sponsorship of the National Institute of Environmental Health Sciences, research is conducted on methods to evaluate environmental mutagenesis and carcinogenesis.

Another activity managed by the Geographic Medicine Branch is the International Centers for Medical Research (ICMR) Program. This Program has no NIAID contract support, but rather it is funded through four research project grants.

For further information write Associate Director for Collaborative Research, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20014.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM AND DIGESTIVE DISEASES

The Artificial Kidney-Chronic Uremia Program was established by the National Institute of Arthritis, Metabolism and Digestive Diseases in the fall of 1965 with funds earmarked by Congress for a target-oriented, planned program of research and development in chronic uremia, dialysis, and the artificial kidney. The goals of this program are achieved through contracts placed with universities, non-profit research laboratories, and industrial concerns. Currently about 70 contracts are in effect for carefully selected research and development program elements. Research contract proposals to the Artificial Kidney-Chronic Uremia Program are reviewed for scientific merit and program relevance by two levels of peer review in a manner similar to the double peer review which characterizes NIH's extramural research grant operation.

Research and development in the program includes studies in the pathophysiology of uremia, blood access and clotting mechanisms, dialyzers and dialysate delivery systems, therapy and its evaluation, and membranes and other materials. Studies in pathophysiology are directed toward minimizing some of the complications of dialysis patients as well as developing a better understanding of the mechanisms of the disease in order to design improved therapy.

Toward these goals, studies are underway in biochemistry and metabolism, anemia, bone disease, neurological and psychological disorders of uremia, gastrointestinal pathophysiology and hyperlipidemia of uremia.

High program priorities are in studies of therapy and its evaluation particularly with the view of quantitating dialysis therapy and various measurements of patient well-being especially in the known parameters of complications of dialysis. Blood access problems continue to be of moderately high priority.

At present, about 8,500 patients in the United States are being maintained by chronic dialysis. Estimates are that 10,000 new patients each year will be suitable candidates for artificial kidney therapy or for renal transplants when they reach a stage where their own kidneys no longer can support them. The NIAMDD Artificial Kidney-Chronic Uremia Program is one of the major efforts to create the technology to enable these persons to attain a higher level of rehabilitation at lower cost.

At present, opportunities for new contracts are limited; when they are feasible again they will be announced in the *GUIDE*.

For further information write Dr. Robert J. Wineman, Associate Chief, Artificial Kidney Program, National Institute of Arthritis, Metabolism, and Digestive Diseases, Bethesda, Maryland 20014.

Collaborative (Contract) Activities in Population Research, National Institute of Child Health and Human Development

OBJECTIVES

The Institute uses the contract mechanism when the initiative for carrying out a research project, including design, direction, and methodology, originates primarily within the National Institute of Child Health and Human Development (NICHD) or when the research requires extensive participation by staff in its development. Contracts are used (1) to stimulate research in gap areas; (2) to develop resources, methodology, instrumentation, or specific products; (3) to provide services to investigators; (4) when staff can function as both stimulator for collaborative efforts and coordinator of research among a number of investigators; (5) to provide for innovative, creative, pioneering projects which may be of general value to the scientific community; (6) to give coherence to a relatively unstructured field; (7) to support organizational activities such as conferences which are program or mission oriented and provide for information exchange or the development of methods.

PROGRAM AREAS

The Center for Population Research, NICHD, currently has contracts in the following areas:

Contraceptive Development

1. Development of new potential contraceptive drugs including the synthesis and biological evaluation of novel steroids, unique prostaglandin analogs, novel analogs of luteinizing hormone releasing factor (LRF), and other miscellaneous non-steroids to determine the extent and nature of their possible antifertility activity.

2. Development of systems and/or materials for uninterrupted administration of antifertility drugs aimed at improving the safety and efficacy of presently available drugs; and evaluation of biological evidence concerning slow and constant release of contraceptive drugs.

3. Development of methods for permanent and reversible sterilization in females and reversible sterilization in males. Design of devices that are safe and effective, easily implantable, and acceptable to various population groups; testing and evaluation of these devices.

4. Studies of how sperm mature and acquire the capacity to fertilize ova; functions of the male duct system and accessory glands; factors affecting the transport of sperm to the site of fertilization; the survival and movement of sperm in the female tract; study of enzymes of sperm.

5. Development of techniques for observing the normal function of segments of the oviduct in ovum pick-up and transport, and studies of the effect of hormones and physical factors on the oviduct.

6. Studies of hormones involved in reproduction and of methods for measuring them; the role of hormones in the initiation and maintenance of pregnancy; regulation of the function of the corpus luteum; and studies to elucidate the control of ovulation.

7. Studies of the ovum, including maturation and ovulation; the biochemistry and physiology of egg membranes and their possible alteration for contraceptive purposes; biochemical function of the fertilized egg before implantation; and the dynamics of decidualization and implantation.

Evaluation of Existing Contraceptive Methods

1. Clinical and laboratory studies of selected subjects (particularly long-term oral contraceptive users) which will elucidate elements of excess risk, estimates of extent of risk, unique properties of presently available drugs, and interaction between steroid drugs and commonly used prescription drugs.

2. In vitro and in vivo (human and animal) studies of the absorption, metabolism, and excretion of steroid contraceptive drugs.

3. Studies to clarify further the effects of oral contraceptives on blood pressure, including extent and magnitude of risk, characteristics of high-risk subpopulations; unique properties of certain contraceptive formulations; physiological mechanism of production of increased blood pressure; and desirable methods of treatment.

4. Human studies which will lead to a more precise estimation of the minimal dose of a drug which will provide acceptable contraceptive effect and/or minimal biochemical or toxic effects; evaluation of potentially toxic effects may be done in animal models.

5. Studies of the effects of oral contraceptives on dietary nutrients.

6. Studies to ascertain whether vasectomy is a relatively innocuous surgical procedure or whether it may be associated with acute adverse effects and/or significant long-term medical complications.

Social Science Research Related to Population

1. Studies of the interrelations between social change and population size, structure, and distribution with particular emphasis upon the social, economic, and other determinants and consequences of population change.

2. Analyses of trends in fertility as affected by age at marriage, divorce, abortion, and related variables; studies of the interrelations of fertility and other socioeconomic variables, such as income, education, religion, and residence; and the relationship between trends in fertility and broad socioeconomic changes such as level of economic activity, women's participation in the labor force, etc.

3. Studies of interrelations between family structure, sexual behavior, and fertility, illegitimacy and abortion; motivations and decisions which determine a couple's number and spacing of children; attitudes toward methods of fertility control and use-effectiveness of various methods among various subgroups of the population; and alternatives to child-bearing which couples perceive and how these perceptions affect fertility.

4. Social, economic, and psychological consequences for both parents and children of various childbearing patterns, size of family, etc.

5. Evaluation of policies aimed at regulating population and of policies which indirectly affect population growth or distribution. Past and present policies--including family allowances, direct incentives and family planning programs--are evaluated for their impact on population.

For further information write: Director, CPR, National Institute of Child Health and Human Development, Bethesda, Maryland 20014.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL INSTITUTE OF DENTAL RESEARCH

NATIONAL CARIES PROGRAM

Much of the collaborative (contract) research in the National Institute of Dental Research relates to the National Caries Program. The development of means to reduce further the universal disease of tooth decay was identified by the Administration as a special initiative area of biomedical research. Substantially increased funds were made available for that purpose in the beginning of fiscal year 1971, with $3,500,000 allocated to collaborative research.

Primary emphasis is placed on projects that encompass the application of existing knowledge and will either prove or disprove the findings of earlier laboratory and animal studies when applied to man; projects that seek new preventive modalities that are feasible, effective, and less demanding of the time of scarce professional manpower; and projects that assess new, promising variations of current approaches. Most of the collaborative research in the caries area will be targeted to the acceleration of the development of preventive methods for decreasing the incidence of caries and making this disease almost completely preventable.

Three factors, all of which interact, are implicated in caries: (1) susceptibility of teeth to the demineralizing action of acids, (2) the presence of caries-inducing bacteria, and (3) a diet which favors the colonization and destructive activity of cariogenic organisms. Because of the complex nature of caries, it is unlikely that any one approach will completely solve the problem of its control and prevention. Efforts are therefore directed to depressing the effects of all factors to a minimum and utilizing a combination of techniques instead of concentrating on one.

The collaborative (contract) research mechanism is also used by the extramural categorical programs of the National Institute of Dental Research listed below. Their major emphasis, however, is grant-supported research.

The PERIODONTAL AND SOFT TISSUE DISEASES PROGRAM supports research relating to the etiology, pathogenesis, diagnosis, treatment, and prevention of periodontal disease, oral-facial ulcerative disorders, oral neoplastic and salivary gland disease and tumors, and disorders of the dental pulp.

The CRANIOFACIAL ANOMALIES PROGRAM supports studies of the etiology and treatment of such conditions as cleft lip and palate, malocclusion, temporomandibular joint disturbances, neuromuscular disorders, and acquired disfigurements. It also sponsors studies of the physiology of mastication, deglutition, speech, and oral sensation and perception.

The RESTORATIVE MATERIALS PROGRAM seeks to develop and test dental restorative materials, adhesive tooth sealants, maxillofacial prostheses, artificial tooth implants, and diagnostic and treatment devices.

The MINERALIZATION, SALIVARY SECRETIONS, AND NUTRITION PROGRAM encompasses studies of mineralization, calcification, and connective tissue matrices as they relate to dental and craniofacial structures. Other major concerns are the structure and function of salivary glands, the biochemistry of saliva, and the relationship of nutrition to craniofacial development and to oral disease.

The PAIN CONTROL AND BEHAVIORAL STUDIES PROGRAM is concerned with the pain, fear, and anxiety associated with dental treatment and with trigeminal neuralgia and other conditions. Oral-facial sensory responses and the behavioral aspects of dental conditions and their treatment, including subjective factors in pain response also are of major interest.

Each proposal is reviewed for technical merit by an ad hoc initial review group composed mainly of nongovernmental scientists, and then for policy compliance and funding priority by the NIDR Contracts Review Staff.

All "Sources Sought" or "RFP Available" announcements appear in the Commerce Business Daily and the NIH Guide for Grants and Contracts Supplement.

For further information write Associate Director for Collaborative Research, National Institute of Dental Research, Bethesda, Maryland 20014.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

The mission of the National Institute of Environmental Health Sciences is directed to definition and explanation of toxicologic mechanisms and effects induced by environmental stressors as related to human health. The NIEHS collaborative research program is limited to support of research efforts intrinsic to the mission of the Institute. Collaborative projects, including both research contracts and interagency agreements, are activities which by virtue of required expertise or logistics lie beyond the scope of the NIEHS intramural program and require NIEHS initiative and participation.

Contract proposals are solicited on a competitive basis, through published announcements and direct contract with research groups of recognized competency. Proposals are subject to competitive evaluation by an ad hoc technical committee and final evaluation by the NIEHS Contract Review Committee.

The current and projected scope of the NIEHS collaborative research program includes efforts in areas of heavy metals toxicity, chemical mutagenesis, biological effects of microwaves and noise, and environmental factors associated with defects of reproduction and development. Future contract research needs, in the aforementioned or other areas, will be published through the usual mechanisms.

For further information write to Special Assistant for Program Planning and Development, NIEHS, P.O. Box 12233, Research Triangle Park, North Carolina 27709.

Collaborative (Contract) Activities of the National Institute of General Medical Sciences

The Institute awards contracts for research and development in three principal areas. This notice is being published for informational purposes, since no active solicitation for sources or proposals is planned at present.

Automation of the Clinical Laboratory Research, development, and evaluation of rapid, reliable automated systems and instruments, for potential application in all aspects of clinical laboratory sciences, including clinical chemistry, toxicology, hematology, microbiology, virology, blood banking, etc. Subject areas of interest include sample collection and labelling techniques, new or improved analytical methods, data handling and reduction techniques for compact computers, miniaturized and portable test systems for emergency use, all intended to increase reliability, throughput, and clinical significance.

Pharmacology/Toxicology Research, development, and evaluation in all aspects of therapeutic drug use, including synthesis, testing, assays in body fluids, and surveillance for effectiveness, side effects, and drug interactions. The principal aim is to promote safer and more effective use of drugs. Related problems include dose-response patterns, kinetics of uptake, distribution, and elimination, metabolic transformations of administered drugs, and quantitative analytical methods and instruments for identification and assay.

Genetics and Genetic Chemistry Research, development, and production in areas where technological constraints impede progress in genetics research. Representative problem areas include isolation, synthesis, separations, purification, and production procedures for material and synthetic genetic materials such as nucleic acids, related enzymes, tissue culture cells, genetically determined animals, etc.

For further information write Special Assistant to the Director, National Institute of General Medical Sciences, Bethesda, Maryland 20014.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

PURPOSE OF RESEARCH CONTRACT ACTIVITIES

The National Institute of Neurological Diseases and Stroke (NINDS) identifies specific research areas within its sphere of interest which are not receiving the necessary investigative attention required for the development of knowledge leading to the prevention or cure of disease and disabilities of major and general concern to the public. It is not always possible for the Institute using its own resources exclusively to mount a complete research program to promote knowledge in the required areas. In such situations, NINDS relies upon negotiated research contracts to support such required research.

The use of the research contract as a mechanism for research support implies a significant role for the supporting Institute (NINDS) in the framing of project goals and the parameters within which work will be carried out, in the monitoring of research underway, and often in the dissemination or further utilization of the research results. Contract-supported research is undertaken only when such research can and will be carefully monitored by a Project Officer or Project Officers from the full-time scientific staff of the Institute.

ONGOING PROGRAMS

Currently, NINDS supports approximately 100 research contracts in a broad variety of scientific areas. Research is supported at a number of institutions, including academic institutions, hospitals, not-for-profit research organizations, and commercial research and development organizations. Contractors are widely distributed geographically. Current contract-supported programs include the following general program areas:

The Collaborative Perinatal Project A comprehensive analysis is being made of data collected on 50,000 pregnancies and the resultant neurological and mental development of the offspring. Contractors capable of developing and applying sophisticated analytic techniques to highly specialized and complex clinical phenomena will be offered opportunities to participate in this closely coordinated data analysis effort. Twenty specific areas for major and minor data analysis efforts have been identified.

Infectious Diseases A varied research program on infectious diseases of the nervous system, particularly related to early life and development, is being conducted.

Epilepsy and Convulsive Disorders A program of investigation of promising anticonvulsant compounds is being supported, as are highly focused studies into methodology for the improvement of the diagnosis, therapy, and rehabilitation of epileptics.

Head Injury and Stroke NINDS has initiated a carefully directed research effort designed to elucidate the processes of brain damage due to trauma or circulatory infarction.

Epidemiologic Studies Measures of the incidence and prevalence of neurologic and sensory diseases, require a variety of surveys depending on the methodology employed. Surveys involving prospective or retrospective approaches include demographic as well as genetic and environmental components. Research contracts support activities which are a direct extension of in-house studies, or independent studies of direct interest to the Institute.

Communicative Disorders NINDS has initiated programs of applied research on improved methods of detecting and diagnosing hearing loss in infants and children; on developing, refining and testing new speech analytic techniques and hearing aid systems; and on the specific etiology of hearing loss.

Biomedical Engineering and Instrumentation NINDS recognizes the need for overall coordination in the development of needed neurologically useful diagnostic and therapeutic instrumentation through all the stages of developmental research, prototype development, and clinical evaluation. The in-house efforts of NINDS laboratories and clinics are supplemented by directed research projects supported by contract in laboratories of other institutions where the necessary expertise and facilities are available.

Neural Prostheses NINDS has embarked on a multidisciplinary study of basic physiology and biophysics of neural transmission, and of applied engineering problems involved in developing and utilizing artificial mechanisms to replace sensory and neuromuscular activity. Contracts for various phases of such development are being awarded.

Supporting Services In order to conduct a broad variety and scope of complex research activities in various laboratories and clinics, NINDS must from time-to-time seek supporting research and services outside of the NIH. Such supporting research and services are varied in nature and complexity but include such activities as long-time holding of research animals; production and delivery of specific biological reagents, cell cultures and antigens; provision of data processing and information storage and retrieval services; and, the provision of specialized professional and technical services.

For further information write Associate Director, C&FR, National Institute of Neurological Diseases and Stroke, Bethesda, Maryland 20014.

COLLABORATIVE (CONTRACT) ACTIVITIES OF THE DIVISION OF RESEARCH RESOURCES

Biotechnology Resources Program The Biotechnology Resources Branch (BRB) uses the contract mechanism to fund activities that enhance the effectiveness of its grant supported programs, facilitate program planning and evaluation, or further develop technological advancements of potential benefit to BRB's clientele. For example, the need for and importance of a national high voltage electron microscopy program was established through a contract awarded to the United States Steel Corporation to provide time on their one million volt electron microscope to biomedical research scientists. Also, a contract to the University of Iowa enabled the BRB to improve on the design of a low-cost computer graphics terminal developed in one of its grant-supported resources. As a result of this contract, prototype units were constructed and evaluated.

For further information write to Dr. W. R. Baker, Jr., Asst. Chief, Biotechnology Branch, Division of Research Resources, Bethesda, MD 20014.

Chemical/Biological Information-Handling (CBIH) Program The CBIH Program is concerned with providing biomedical scientists with the research support capabilities they most need to pursue their investigations effectively. The focus specifically is on (a) designing and developing computer-based information-handling tools important to studies of chemical/biological interactions (a line of inquiry relevant to almost every major medical area); (b) making these tools available to the national scientific community in an easy-to-use and highly reliable form; and (c) collaborating with the users of these tools in order not only to refine and extend them but also to develop deeper insights into the investigative process itself. Particular emphasis is placed on questions of where and how computer technology and information science can catalyze the emergence of predictive capabilities regarding the interactions of chemical substances and living systems.

For further information write to Dr. W. F. Raub, Chief, Biotechnology Branch, Division of Research Resources, Bethesda, MD 20014.

Animal Resources Program (ARB) The overall objective of the ARB is to support resource projects that provide or enable biomedical scientists to effectively use animals in human health related research. Special attention is given to those animal resource activities that are broadly supportive of the missions of the various NIH components. The Branch objectives are accomplished through a Primate Research Centers Program, a Laboratory Animal Science Program, and Research Contracts. The ARB has used the research contract mechanisms as an adjunct to its resource grant programs to support specific, essential services or to initiate activity in vital resource areas that have not responded or are not eligible to respond to the grant mechanism.

For further information write to Dr. Charles McPherson, Chief, Animal Resources Branch, Division of Research Resources, Bethesda, MD 20014.

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- 1406 ☐ Tumor Immunology
- 1407 ☐ Cancer Detection and Diagnosis
- 1408 ☐ Breast Cancer

1500 ☐ National Eye Institute (All Programs)

1600 ☐ National Heart and Lung Institute (All Programs)
- 1601 ☐ Arteriosclerosis and Hypertension
- 1602 ☐ Cardiology including Ischemic Heart Disease
- 1603 ☐ Lipid Metabolism
- 1604 ☐ Cardiovascular Devices
- 1605 ☐ Clinical Applications and Prevention
- 1606 ☐ Blood Diseases and Resources
- 1607 ☐ Lung Diseases

1700 ☐ National Institute of Allergy and Infectious Diseases (All Programs)
- 1701 ☐ Viral Diseases
- 1702 ☐ Bacterial Diseases
- 1703 ☐ Parasitic Diseases
- 1704 ☐ Research Resources
- 1705 ☐ Transplantation and Immunology

1800 ☐ National Institute of Arthritis, Metabolism and Digestive Diseases (All Programs)

1900 ☐ National Institute of Child Health and Human Development (All Programs)
- 1901 ☐ Contraceptive Development
- 1902 ☐ Evaluation of Existing Contraceptive Methods
- 1903 ☐ Social Science Research Related to Population

2000 ☐ National Institute of Dental Research (All Programs)

2100 ☐ National Institute of Environmental Health Sciences (All Programs)
- 2101 ☐ Environmental Physical Factors
- 2102 ☐ Mutagenesis
- 2103 ☐ Pharmacology and Toxicology
- 2104 ☐ Reproduction and Development

2200 ☐ National Institute of General Medical Sciences (All Programs)
- 2201 ☐ Automation of the Clinical Laboratory
- 2202 ☐ Pharmacology/Toxicology
- 2203 ☐ Genetics and Genetic Chemistry

2300 ☐ National Institute of Neurological Diseases and Stroke (All Programs)
- 2301 ☐ Collaborative Perinatal Project
- 2302 ☐ Infectious Diseases
- 2303 ☐ Epilepsy and Convulsive Disorders
- 2304 ☐ Head Injury and Stroke
- 2305 ☐ Epidemiologic Studies
- 2306 ☐ Communicative Disorders
- 2307 ☐ Biomedical Engineering and Instrumentation
- 2308 ☐ Neural Prosthesis
- 2309 ☐ Supporting Services

2400 ☐ Division of Research Resources (All Programs

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