NIH GUIDE for GRANTS and CONTRACTS

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

Vol. 9, No. 3, February 22, 1980

IN THIS ISSUE:

(over)

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

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

IN THIS ISSUE: (continued)

GENERAL CLINICAL RESEARCH CENTERS DIRECTORY REVISED

NOTICE

The 1979 revised directory of major clinical research activities and participants at the General Clinical Research Centers (GCRC) of the National Institutes of Health has been published and is available at no charge.

Titled General Clinical Research Centers, A Research Resources Directory, the booklet contains 86 pages outlining in detail facilities and investigations at all 74 Division of Research Resources-supported GCRCs throughout the country.

In addition to the current complete listing and location of the Centers, the directory identifies the names of program and associate directors, principal investigators, the specific location of the facility within the host institution, the number of beds, and the Centers' major areas of investigation. Also included are listings of special assay services or new tests available, special instruments or devices, and guides, pamphlets, or booklets from the Centers.

A geographic index is provided, indicating the General Clinical Research Centers by state, and alphabetically within each state, according to the names of the host institution.

A single free copy of the 1979 revised General Clinical Research Centers, A Research Resources Directory may be secured by writing to the:

Research Resources Information Center
1776 East Jefferson Street
Rockville, Maryland 20852

or by request from:

Office of Science and Health Reports
Division of Research Resources
National Institutes of Health
Bethesda, Maryland 20205

NIH MINORITY RESEARCH AND TRAINING PROGRAM

NOTICE

BOOKLET REVISED

The publication The National Institutes of Health Minority (Extramural) Research and Training Programs has been revised and is now available for distribution.

The 19-page brochure contains a detailed explanation of the Minority Biomedical Support Program (MBS) of NIH's Division of Research Resources, and the Minority Access to Research Careers Program (MARC) of the National Institute of General Medical Sciences.

In addition, the revised booklet includes specific information on all Institutes currently participating in the National Institutes of Health (NIH) minority program.

The MBS and MARC programs were started by NIH in 1972 in response to a presidential mandate "to help these institutions (minority) compete for students and faculty with other colleges and universities."

Both programs have steadily made progress in the development of racial and ethnic minorities as biomedical researchers.

The Division of Research Resources' MBS program currently supports 75 grants in 80 institutions, involving over 500 research projects. Within the separate MBS projects in these institutions there are approximately 2,000 individuals comprised of undergraduates, graduate students, post-doctoral participants, and faculty members.

The National Institute of General Medical Sciences' MARC activity currently supports over 200 grantees involved in their Faculty Fellowship Program, Visiting Scientist Program, and Honors Undergraduate Research Training Program.

In June 1974, the Director of the National Institutes of Health requested that all Bureaus, Institutes, and Divisions initiate and coordinate their minority support activities through the existing minority programs. Nine Institutes are now actively participating in the program efforts by extending their categorical interests through cooperative efforts with the MBS and the MARC programs.

The NIH participants are the National Institute on Aging, the National Institute of Allergy and Infectious Diseases, the National Institute of Arthritis, Metabolism, and Digestive Diseases, the National Cancer Institute, the National Institute of Child Health and Human Development, the National Institute of Dental Research, the National Eye Institute, the National Heart, Lung, and Blood Institute, and the National Institute of Neurological and Communicative Disorders and Stroke.

In addition, the National Institute of Mental Health, under the Alcohol, Drug Abuse, and Mental Health Administration, also lends cooperative support to the program.

A single free copy of The National Institutes of Health Minority (Extramural) Research and Training Programs may be secured from the Office of Science and Health Reports, Division of Research Resources; or the:

Office of Research Reports
National Institute of General Medical Sciences
National Institutes of Health
Bethesda, Maryland 20205

NIH IMPLEMENTATION PLAN FOR THE NRSA

NOTICE

STIPEND AND ALLOWANCE CHANGES

This notice includes information on NIH implementation plans for recently announced changes in NRSA stipends and allowances. Previous notices may be found in the *NIH Guide for Grants and Contracts,* Vol. 8, No. 13, October 26, 1979; and Vol. 9, No. 2, January 25, 1980.

STIPEND INCREASE

Effective July 1, 1980, stipend levels will be increased for all predoctoral and postdoctoral trainees/fellows who receive support under NIH National Research Service Award training grants and fellowships. The new increased annual stipend levels, based on full-time appointments, are as follows:

a. Predoctoral

$5,040

b. Postdoctoral

Years of Relevant Experience	Stipends
0	$13,380
1	14,040
2	14,736
3	15,468
4	16,236
5	17,040

The current three-column chart for determining postdoctoral stipend levels will no longer be applicable after July 1, 1980. For purposes of determining appropriate stipend levels for individuals already appointed under training grants or fellowships, prior years under the grant or fellowship will count as "years of relevant experience."

The stipend increases will be implemented by NIH as follows:

a. Institutional (Training) Grants

All applications requesting budget period start dates of July 1, 1980 and thereafter shall reflect the new increased stipend levels. In the case of applications for noncompeting continuation grants, funds to cover the increase in excess of the previously approved amount may be requested. All applications, competing and noncompeting, for July 1, 1980 start dates and thereafter and already received in NIH will be administratively adjusted.

Applications requesting a budget period start date before July 1, 1980 should reflect prorated stipends: the old stipend levels from the start date of the budget period to June 30, 1980; the new stipend levels from July 1, 1980 onward. Noncompeting continuation applications may include a request for the funds to cover the increase over the previously approved amount. Applications already received in NIH will be administratively adjusted.

In the case of ongoing training grant budget periods where the trainee appointment crosses July 1, 1980, the trainee shall receive the new stipend level for that part of the training on and after July 1, 1980. Grantee institutions are asked to cover the stipend increase with monies available in the grant (rebudgeted funds, stipend dollars from unfilled positions, etc.). If there is no money available in the grant, the grantee institution should consult the appropriate NIH awarding component. In any case, prior commitments to individual trainees must be honored. Revised Statement of Appointment of Trainee forms will be required on all affected trainees.

b. Fellowships

All individual fellows, competing and noncompeting, activating on July 1, 1980 or later, will receive the new increased stipend levels. Fellows whose award period crosses July 1, 1980 will receive the old stipend level through June 30, 1980 and the new stipend level thereafter. NIH will provide the additional funds to cover all stipend increases. No action is required by the fellow or applicant. NIH will revise or supplement awards where necessary.

c. Stipend Proration Table

A copy of the monthly and daily stipend rates to be used in proration cases is attached.

NONTRAINEE EXPENSES/INSTITUTIONAL ALLOWANCES

Effective for all awards (competing and noncompeting) starting July 1, 1980 and after there will be new ceilings on institutional grant nontrainee expenses and individual award institutional allowances.

a. Institutional Grants

The current policy which limits support of nontrainee expenses to 25% of the total grant award will be discontinued. Effective for all institutional (research training) grants with budget period dates starting on July 1, 1980 and thereafter, the maximum amount for nontrainee expenses will be calculated, based on the ceiling figures indicated below:

Predoctoral	up to $3,000/trainee
Postdoctoral	up to $5,000/trainee

The total requested amounts within the maximum ceiling, should be reflected in the appropriate direct cost categories included in grant application budget pages. Applications should also include appropriate justifications for the amounts requested. Trainee tuition and fees and trainee travel will continue to be trainee expenses and therefore will not be included within the $3,000/$5,000 ceiling calculation. Indirect costs may continue to be requested at 8% of total direct costs (exclusive of tuition and related fees and expenditures for equipment) or actual indirect costs, whichever is less.

All institutional training grants with budget periods starting before and crossing July 1, 1980 will be governed by the 25% nontrainee costs ceiling policy for that entire budget period.

It should be stressed that either method for calulating the non-trainee expenses represents a ceiling only and the final award is dependent on the usual administrative review process.

All applications requesting budget period start dates of July 1, 1980 and thereafter shall be governed by the new nontrainee expense ceiling. Conversion to the new ceiling may result in a different dollar level than previously recommended or requested. Applications already received in NIH will be administratively adjusted where appropriate. Only when deemed necessary, will revised budgets be requested.

b. Individual Awards

Sponsoring institutions may continue to request an allowance for each research fellowship starting (activating) on or after July 1, 1980 to help defray such expenses as tuition and fees, appropriate health insurance, supplies, equipment, travel to scientific meetings, and related items. The allowance may not exceed $5,000 per year for each postdoctoral fellow sponsored by a non-Federal institution. The allowance may not exceed $2,000 per year for each postdoctoral fellow where the sponsoring organization is a Federal institution. Applications already submitted to NIH or awards already issued, will be administratively adjusted by NIH.

Fellowship awards starting (activating) before and crossing July 1, 1980 will be governed by the old postdoctoral institutional allowance ceilings (up to $3,000 for non-Federal sponsoring institutions and up to $1,000 for Federal sponsoring institutions) for that entire award year. There will be no proration of institutional allowances.

NRSA Stipends--Annual--Monthly--Daily

Current Levels			Revised Levels		
Year	Month	Day	Year	Month	Day
3,900	325.00	10.83	5,040	420.00	14.00
10,000	833.33	27.78	13,380	1,115.00	37.17
10,400	866.67	28.89	14,040	1,170.00	39.00
10,800	900.00	30.00	14,736	1,228.00	40.93
11,200	933.33	31.11	15,468	1,289.00	42.97
11,500	958.33	31.94	16,236	1,353.00	45.10
11,600	966.67	32.22	17,040	1,420.00	47.33
11,900	991.67	33.06			
12,200	1,016.67	33.89			
12,300	1,025.00	34.16			
12,600	1,050.00	35.00			
12,800	1,066.67	35.56			
13,000	1,083.33	36.11			
13,200	1,100.00	36.67			
13,600	1,133.33	37.78			
14,000	1,166.67	38.89			

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NIGMS-PBME-80-01

ANNOUNCEMENT

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

TITLE: *AN EVALUATION OF A $^{13}CO_2/^{12}CO_2$ INFRARED HETERODYNE RATIOMETER IN BIOMEDICAL STUDIES*

Application receipt date, May 15, 1980

I. BACKGROUND INFORMATION

The Physiology and Biomedical Engineering Program of the National Institute of General Medical Sciences, has as one of its missions the support of development of new instruments and devices which will improve the knowledge base of che biomedical sciences. Support is also provided for the application of engineering knowledge to the solution of significant physiological and biomedical problems, including those involving intermediary products of metabolism in the human organism. The recent availability of a large and relatively inexpensive supply of highly enriched stable carbon isotope (^{13}C) through project ICON (USAEC-ERDA) has stimulated interest in the use of this isotope for biological studies and has led to an awareness of the need for adequate instrumentation for its measurement.

Elemental carbon has several isotopes ranging from mass 9 through mass 14. Of these, ^{12}C and ^{13}C are stable. (^{12}C has a natural abundance of 98.89% and ^{13}C a natural abundance of 1.11%.) Both of radioactive species (^{11}C, which is a positron emitter with a half life of 20 minutes, and ^{14}C, a beta emitter with a half life of over 5,000 years) have been used for many years as tracers in animal studies of intermediary metabolism; however, both exposed the body to radiation hazard, making them relatively undesirable for use in human studies. An attractive alternative for use in metabolic studies is ^{13}C. In these studies the $^{13}C/^{12}C$ ratios are artificially increased over the natural abundance ratio by the administration of compounds that have been enriched with respect to ^{13}C. When this is done, the expired CO_2, as well as intermediary metabolites, can be isolated, and their enrichment with ^{13}C measured. The measurements require sensitive instruments capable of detecting small changes in the $^{13}C/^{12}C$ ratio.

This program is described in the Catalog of Federal Domestic Assistance number 13.821. Awards will be made under the authority of the Public Health Service Act, Section 301 (Public Law 78-410, as amended; 42 USC 241). Grants will be administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74.

Under contract to the NIGMS, an industrial organization has developed a unique infrared heterodyne ratiometer (IHR) which is designed to accurately measure the $^{13}CO_2/^{12}CO_2$ ratio in carbon dioxide derived from human material and to detect changes in the ratio with a sensitivity of $1:10^4$. In the case of non-gaseous carbon compounds, these must first be converted to CO_2 before they can be measured by the IHR instrument.

The intent of this request for applications (RFA) is to identify a single scientifically meritorious proposal that would require and incorporate this instrument as a key element in the research to be performed.

II. DESCRIPTION OF INSTRUMENT

The $^{13}CO_2/^{12}CO_2$ infrared heterodyne ratiometer is a non-dispersive infrared gas analyzer. Carbon dioxide is detected by its property of absorbing infrared radiation at characteristic discrete wavelengths. Other gases, or other isotopic species of the same gas, will have absorption at a different set of wavelengths, and although the bands may overlap, the overlap of individual lines is small (line widths are typically 10 times smaller than the line spacing).

The instrument fits on a conventional electronics equipment rack 3 feet square by 6 feet high. Electrical requirements are for 110 volts 60 cycle current. The instrument is water cooled at the rate of 1 gallon per minute. It is supplied with a Hewlett Packard programmable desk calculator (model 9825) which directs the operation of the system and performs the data reduction. A batch processing system has been developed which will accommodate up to 20 sample bags to be analyzed over the period of 1 hour without the need for operator attention. Sample size is usually 1 liter @ 1% CO_2 concentration. Since experience has shown that nearly all synthetic materials are significantly permeable to CO_2, samples should be collected in nylon bags made to specifications. These are inexpensive.

III. GENERAL DESCRIPTION OF THE RESEARCH APPLICATIONS SOUGHT

A research grant application which proposes to use $^{13}CO_2/^{12}CO_2$ infrared ratiometer should be a well-developed scientific investigation of a significant biomedical research problem. In addition, the application should discuss the appropriateness and advantages of using this technique as compared to more conventional approaches and should give detailed procedures regarding the use of the instrument for the research problem. If human subjects will be involved, a consideration of the biological effects of ^{13}C on human subjects, as well as the usual protocols, should be included. Since a determination of the usefulness of the IHR is one aspect of this research proposal, it is expected that the successful grantee would, in addition to normal reporting requirements, keep NIGMS informed of progress and problems relating to the IHR instrument, and make particular effort to publish in scientific journals the results of the research using the IHR instrument.

IV. MECHANISM OF SUPPORT

This announcement is open to all interested investigators for a single competition, with a deadline for receipt of applications of May 15, 1980. The award will use the customary grant-in-aid mechanism which will be governed by the policies in common use for regular research grants. The responsibility for planning, directing, and executing the proposed research project will be solely that of the applicant.

The total project period of this proposal must not exceed 5 years. Starting dates as early as December 1, 1980, may be requested.

Support of the single grant pursuant to this request for applications will be drawn from Physiology and Biomedical Engineering Program allocations. The award of the individual grant will be influenced by the amount of funds available to the program, by the overall merit of the proposal, and by its relevance to the program goals. The NIGMS is under no obligation to make an award as a result of this RFA.

Any renewal proposal involving research begun under an award resulting from this RFA will be processed through the regular investigator-initiated research grant mechanism.

V. REVIEW PROCEDURES AND CRITERIA

A. Review Method

Each application submitted in response to the RFA will be reviewed by an appropriate DRG review panel. All applications will be evaluated on a competitive basis.

B. Review Criteria

Applications must be responsive to this RFA; that is, they must be relevant to the goals of this program announcement and guidelines. Applications judged by the Institute not to be responsive will be returned to the applicant.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of the proposed research, including design, approach and methodology.

2. Rationale for using this instrument as opposed to other methods of analysis.

3. Research experience and competence of the staff to conduct the proposed investigations.

4. Adequacy of existing and proposed facilities and resources.

5. Adequacy of time (effort) to be devoted to the project by the principal investigator and staff.

6. Appropriateness and justification of budget.

Expenses incurred in moving the IHR instrument from its present site in Berkeley, California, to the site of research will be borne by the National Institute of General Medical Sciences, and should be included in the proposed budget.

A two-day training session to acquaint the recipient with details of operation and maintenance of the IHR instrument will be provided by the manufacturer at Berkeley, California, and travel funds for this session should be included in the proposed budget.

Disposition of the instrument after completion of the initial research project will be made according to Public Health Service policy regarding equipment acquired through research grant funds.

VI. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a one-page letter of intent, which should include a very short synopsis of proposed areas of research and identification of any other participating institutions. This letter should be received no later than April 1, 1980, at the following address:

Dr. Sue Badman
Chief, Instrumentation Section
Physiology and Biomedical Engineering Program
National Institute of General Medical Sciences
5333 Westbard Avenue
Bethesda, Maryland 20205

The Institute requests such letters only to provide an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any proposal subsequently submitted nor is it a necessary requirement for application.

B. Format for Application

Applications must be submitted on form PHS 398, the application form for the traditional research grant. The conventional presentation in format and detail for regular research grant applications should be utilized, with care taken to fulfill the points identified under "Review Criteria."

C. Deadline for Submission

Applications must be received by May 15, 1980. Applications received after this date will be returned.

D. Application Procedure

The original and six (6) copies of the completed application should be sent or delivered to:

Application Receipt
Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

Label the outside of the mailing package and the top of the face page "RESPONSE TO RFA, NIH-NIGMS-PBME-80-01"

E. Inquiries

Inquiries may be directed to Dr. Badman at the address shown under Item A of Section VI. Telephone: (301) 496-7294

VII. REFERENCES

"The Development of a $^{13}CO_2/^{12}CO_2$ Ratio Analyzer Using a Nondispersive Infrared Heterodyne Technique."
Edward A. McClatchie, Ph.D., Andros, Inc.

DHEW Publication No. (NIH) 75-762, "Selected Approaches to Gas Chromotography-Mass Spectrometry in Laboratory Medicine."
Pages 132-144. Editors: Melville, R. and Dobson, V.

SPECIAL EMPHASIS RESEARCH CAREER AWARD: DIABETES MELLITUS IN THE ELDERLY

ANNOUNCEMENT

MOLECULAR AND BIOCHEMICAL AGING PROGRAM,
NATIONAL INSTITUTE ON AGING

AND

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM,
AND DIGESTIVE DISEASES

Application receipt date, June 1, 1980

Diabetes mellitus is a major health problem afflicting the elderly. It is highly prevalent in persons aged fifty and above, and may range in severity from a mild glucose intolerance, which can be regulated through proper dietary control, to an extreme insulin dependent disease.

Although the high incidence of diabetes in the elderly has been observed for several years, its underlying cause is still unknown. This Special Emphasis Research Career Award (SERCA) is therefore intended to:

- encourage qualified individuals to develop research interests in problems related to diabetes and aging.
- provide support for these individuals to allow them to pursue a multidisciplinary program of research in various basic and clinical research disciplines relevant to diabetes and aging.
- create a pool of highly qualified investigators with experience and expertise in the area of diabetes and aging for a future role in research, teaching, and clinical care.

This SERCA is designed to foster an interdisciplinary approach to the metabolic and endocrinologic aspects of diabetes in the elderly by encouraging qualified individuals to acquire in-depth experience and skills in the basic and clinical scientific disciplines that bear upon this area. This non-renewable award provides support for a five-year period of full-time research and related activities. The latter may include further development of research skills, participation in workshops, symposia, and professional meetings, as well as involvement in patient care to the extent required to maintain clinical skills and strengthen research skills. A minimum of 75% of an awardee's time must be spent in the actual conduct of research.

Provisions of the Award

The SERCA grant is made to the awardee's parent institution and provides up to $30,000 per year for full time salary support plus fringe benefits. A maximum of $8,000 per year during the first three years and up to $20,000 per year during the remaining two years may be provided for research costs including technical assistance, limited equipment, supplies, consultant costs, travel, publication and other costs.

Eligibility Requirements

Candidates for the SERCA Award must hold an M.D. or equivalent professional degree (e.g., D.D.S., D.O., D.V.M., etc.) and by the beginning date of the award have a minimum of three years post-M.D. experience including two years of clinical training, or the equivalent. M.D./Ph.D. applicants should possess some experience in endocrinology, physiology biochemistry, pharmacology, or other relevant areas of interest, such as epidemiology. Candidates must be citizens or non-citizen nationals of the United States or its possessions or territories or must have been lawfully admitted to the U.S. for permanent residence at the time of application and meet certain other eligibility requirements specified in the SERCA Program Guidelines.

Prospective applicants should request and review the SERCA Guidelines which detail eligibility requirements and application procedures. In addition, prior to preparing an application, individuals should discuss their potential eligibility as well as their areas of research interest with the Program Director listed below. Requests for copies of the SERCA Guidelines as well as questions related to eligibility, etc., should be directed to:

Dr. Richard Irwin
Health Scientist Administrator for Diabetes
Molecular and Biochemical Aging Program
Biomedical Research and Clinical Medicine Program
National Institute on Aging
Room 5C-23A, Building 31
National Institutes of Health
Bethesda, Maryland 20205

There will be a one-time receipt date of June 1, 1980 for the first round of applications; thereafter there will be a single, annual receipt date of October 1, beginning October 1, 1980.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

ANNOUNCEMENT

NIH-NIAID-80-3

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

TITLE: *ASTHMA AND ALLERGIC DISEASE CENTERS*

Application receipt date, October 15, 1980

BACKGROUND INFORMATION

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for grants to be initiated during FY 1981 for participation in the ongoing Asthma and Allergic Disease Centers (AADC) program.

The Allergy and Clinical Immunology Branch of the Immunology, Allergic, and Immunologic Diseases program of NIAID sponsors fundamental and clinical research grants and contracts and the procurement and application of research resource and reference reagents concerned with asthma, allergic and immunologic diseases and with relevant mechanisms of hypersensitivity and inflammation. This request for applications is intended to encourage the development of proposals from clinical investigative groups meeting the criteria and requirements for an AADC and to coordinate the submission of new and renewal applications providing equitable opportunity for both to compete for funds currently available for this programmatic activity.

Since its inception in 1971, the AADC program has progressively expanded with the gradual addition of new Centers on an open application basis. In accordance with established policy announced in the *NIH Guide for Grants and Contracts*, Vol. 7, No. 8, p. 1, June 9, 1978, proposals for AADCs are received only periodically and at designated times. Applications for both renewal of existing AADCs and creation of new Center programs will be expected to compete for funds available through the periodically announced awards.

The AADC program currently consists of 16 centers. Each year several are scheduled to terminate and may compete for renewal. During FY 1981, NIAID expects to make 3 AADC new or competing renewal awards.

This program is described in the Catalog of Federal Domestic Assistance number 13.855. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74.

NIAID's fundamental objective in continuing the AADC program remains unchanged: acceleration of the application of emerging knowledge on the immune system and from relevant biomedical sciences to clinical investigations concerned with asthma, allergic diseases, and hypersensitivity disorders. Especially sought as the requisite factors within a participating institution are quality research in (a) basic science(s) and clinical investigation supported by adequate clinical facilities, staff expertise in diagnosis and management of asthmatic and allergic patients, and access to (an) appropriate patient population(s) within a suitable academic/ investigative setting designed to favor multidisciplinary interaction.

RESEARCH GOALS AND SCOPE

1. There should be indication by the sponsoring university or medical institution of willingness and preparedness to commit resources to insure development, operation, support, and function of the proposed Center in devoting its efforts to an identified study on asthma and/or allergic disease as a fundamental prerequisite.

2. The applicant's achievements in basic science research should have reached that stage of development where experimental leads are sufficiently encouraging to warrant transition from promising laboratory findings to corresponding investigations at the clinical level with the ultimate goal of developing new and improved methods for diagnosis, prevention, and treatment of asthma and/or the other allergic diseases.

3. A prospective Center should be in a position to present evidence of experience, orientation, laboratory and clinical facilities, scientific and professional staff, support personnel and the expertise to design proposals, execute protocols representing a multifaceted long-term approach, and bring diverse institutional strengths to bear upon the study of major problems in asthma, other (of the) allergic disease(s) and/or pathophysiologic mechanisms underlying these disorders.

4. Suitable subjects for study within the provision of this program may include those relevant to:

   a. asthma and its multifactorial aspects;

   b. atopic diseases (e.g., allergic rhinitis, urticaria, atopic dermatitis);

   c. identification, isolation, and characterization of etiologic agents of allergy (e.g., drugs, chemicals, foods, airborne allergens);

   d. pathologic expressions, pathophysiologic mechanisms, and genetic factors of allergic disease and allergic inflammation;

e. immune mechanisms and agents of immediate hypersensitivity and of related hypersensitivity manifestations of antigen-antibody reactions or cell mediated immunity (e.g. hypersensitivity, pneumonitis, allergic dermatitis, vasculitis, allergic gastro-enteritis, drug reactions) and the development of corresponding improved diagnostic materials and methods;

f. immunopharmacology, immunotherapy, and the development of specific pharmacologic agents designed for prevention and treatment of asthma and the other allergic diseases.

5. Study of animal models will be considered acceptable as a partial segment or adjunct to a Center's program only if this line of research is applicable to the character of the primary investigation of asthma or the human allergic disease central to the proposal.

6. Designation of a Center Director should be based upon accomplishment and experience as a senior scientist and ability to assume both leadership of the investigative group and responsibility for scientific, professional, and administrative functions.

7. More than one delineated avenue of research may be pursued within a Center with provision for unified operation and coordination of component projects and collaborative investigators.

8. A Center should not rely upon its ability to conduct research activity solely within the confines of a single discipline, but rather should have established the associations to involve participation by workers in the pertinent biomedical fields and medical specialities allied to asthma, allergy, and clinical immunology (e.g. immunobiology, biochemistry, microbiology, biostatistics, bioinstrumentation and computer science; and the clinical subspecialities, e.g. dermatology, rheumatology, infectious diseases, pulmonary medicine, hematology, otorhinolaryngology).

9. The Center Director will be expected to communicate freely with the NIAID and other designated Centers for effective exchange of new information, to interact with scientists working in other Centers on related investigative problems, and to present progress reports and share experimental data with other Centers through exchanges and attendance at NIAID sponsored meetings of study groups and AADC workshops.

MECHANISM OF SUPPORT

In fiscal year 1981, the NIAID plans to award at least three Asthma and Allergic Disease Center Awards. Each grant will have a duration of not more than five years. Funding beyond the first year of the grant will be contingent upon satisfactory progress during the preceding year.

The receipt date for applications will be October 15, 1980. They will undergo initial review in February-March and subsequent review by the National Advisory Allergy and Infectious Disease Council in May 1981. September 1, 1981 will be the earliest starting date for successful applicants.

Grant funds may be utilized to support the research activities of scientific and professional personnel, administration, consultation services, central support services, equipment, supplies, travel, and publication costs. Support for research-related costs of patient involvement and medical care may be authorized. Since the program cannot provide funds for new construction, adequate physical facilities must be available for the primary needs of the Center. However, moderate alterations or renovations to enhance clinical facilities may be allowed if they are necessary to meet objectives of the Center's program.

Only those institutions that can demonstrate expertise in both basic and clinical areas and can direct their resources toward a multifaceted attack on asthma or the other allergic diseases can be supported under the provisions of the AADC program.

REVIEW PROCEDURES AND CRITERIA

For preliminary screening by NIAID staff, a "letter of intent" must first be prepared by the prospective program director.

Letters of intent should cover the following points:

1. a brief description of the intended project;

2. a description of available laboratory facilities;

3. a brief description of ongoing basic immunologic and clinical research relating to asthma, allergy, or hypersensitivity with especial reference to any studies of the immediate type;

4. a brief description or reference to published research works by the investigators on asthma, allergy, or hypersensitivities especially pointing out those that may relate to the immediate type and identification of existing projects and sources of support;

5. a description of all clinic facilities available for use by the proposed Center;

6. specific information on the institution's present patient load and projections for patient involvement in clinical investigation;

7. the academic positions and major research interests of the program director and his professional staff who will be involved in the work of the Asthma and Allergic Disease Center;

8. collaborative possibilities with other area laboratories and investigators and delineation of the roles and manner of anticipated participation and interaction of the principal investigators, consultants, and collaborators.

Letters of intent are due no later than July 15, 1980, and upon receipt will be screened by NIAID staff to determine the eligibility and suitability of the projected proposals for the Asthma and Allergic Diseases Centers program.

Inquiries and letters should be directed and addressed to:

Robert Goldstein, M.D., Ph.D.
Chief, Allergy and Clincal Immunology Diseases Program
National Institute of Allergy and Infectious Diseases
Room 755, Westwood Building
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-7104

CONSEQUENCES OF LACK OF RESPONSIVENESS TO THE RFA OR LATE SUBMISSION

Based upon the letter of intent, potential applicants will be promptly advised whether or not their proposal is found to be within the research goals and scope of the program as defined in this RFA. Applicants will then have an opportunity to correct deficiencies or weaknesses and to restructure their submissions accordingly. Formal applications that are not responsive to the RFA or are not received by October 15, 1980, will not be accepted for review and will be returned to the applicant.

METHOD OF APPLYING

Before preparing an application, the prospective applicant should request from NIAID program staff a copy of the NIAID Information Brochure on Program Projects which contains details on the requirements for multi-disciplinary grant applications.

Use the standard research grant application form PHS 398, available from most institutional business offices or the Division of Research Grants, NIH. In addition to following accompanying format instructions for the development of a Center application, include expanded material listed above under the eight points for the "letter of intent." For purposes of identification and processing, the words "ASTHMA AND ALLERGIC DISEASE CENTER" should be typed on the face page of the application and a brief covering letter should be attached indicating submission is in response to this NIAID announcement.

Forward to:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

Please forward a copy (not the original) of the cover letter and the application face page to: (1) the NIAID Program Director (Dr. Robert Goldstein, see address above) in order to alert NIAID to the submission of the proposal, and (2) the Chief, Program and Project Review Branch, NIAID, Room 703, Westwood Building, National Institutes of Health, Bethesda, Maryland 20205.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

ANNOUNCEMENT

FDA-BRH-DBE-80-1

BUREAU OF RADIOLOGICAL HEALTH,

FOOD AND DRUG ADMINISTRATION

TITLE: *DELAYED EFFECTS OF ULTRASOUND EXPOSURE*

Application receipt date, May 7, 1980

The Division of Biological Effects (DBE) of the Bureau of Radiological Health (BRH), Food and Drug Administration (FDA), conducts a nation-wide program of animal experimentation and epidemiological research on the biological effects of exposure to electro-magnetic radiation. The Division, through workshops, symposia, research and literature review, studies and evaluates experimental, epidemiological, and clinical research to assess the health effects resulting from radiation exposure.

This RFA will use the customary grant-in-aid mechanism which will be governed by the policies for regular research grants. The responsibility for planning, directing, and executing the proposed research project will be solely that of the applicant.

The present RFA announcement is open to all interested investigators for a single competition with a specified deadline for receipt of applications. It is anticipated that all applications in response to the RFA will be reviewed at the same time by a single review panel. Grants will be made under the legislative authorization in Section 356(b)(2) of the Public Health Service Act and will be administered according to policies applicable to research project grants. This program is outlined in 13.103 of the Catalog of Federal Domestic Assistance.

Potential applicants are requested to send, by April 1, 1980, a letter of intent to submit an application. The original and six (6) copies of the application are to be sent to the Division of Research Grants by May 7, 1980. A brief covering letter should be enclosed indicating that the application is being submitted in response to the RFA, FDA-BRH-DBE-80-1: DELAYED EFFECTS OF ULTRASOUND EXPOSURE. Applications should be prepared in accordance with the aims and requirements described in the following sections:

I. BACKGROUND INFORMATION
II. GOALS AND SCOPE
III. MECHANISM OF SUPPORT
IV. REVIEW PROCEDURES AND CRITERIA
V. METHOD OF APPLYING
VI. SELECTED BIBLIOGRAPHY

I. BACKGROUND INFORMATION

At present, the diagnostic use of ultrasound is generally accepted as safe. This acceptance is based on animal experiments which show an apparent threshold below which acute effects observed at high levels of exposure do not occur. Acceptance of safety is reinforced by the absence of reports of acute adverse effects in humans. However, the potential for acute adverse effects from ultrasound has not been systematically explored and the potential for delayed effects has been virtually ignored.

Human studies to date report no short-term effects of ultrasound exposure on the fetus in utero. Although no increase in infant abnormalities were observed, the studies were not designed to detect anomalies. Anatomic abnormalities obvious at neonatal examination would be expected to result from insult during the period of major organogenesis in the embryo, but the majority of exposures in these studies occurred well after organogenesis. In addition, the studies provide no basis for inferences about the possibility of delayed effects.

We are currently aware of two epidemiological studies ongoing to determine possible delayed effects of ultrasound on children exposed in utero. One is utilizing medical records and detailed followup examinations of children exposed to ultrasound in utero during the period 1968-1972. This study will attempt to detect detriment to the general health, physical and intellectual development, and neurological function. The second is primarily based on medical records, with possible followup on a sample from the study group. This study will examine morbidity and mortality data and physical development parameters (height, weight, etc.)

Animal studies are performed to detect possible adverse effects and to indicate the social and ethical boundaries that limit human exposure. Many of the early animal studies utilized intensities orders of magnitude above diagnostic levels, and observed gross effects such as mortality, tissue necrosis and paralysis.

Recently, there have been reports of more subtle biological effects in animals exposed to levels of ultrasound representative of current diagnostic applications. In fact, some of the studies involve the use of a clinical device as the exposure source. These effects include functional and behavioral alterations and fetal anomalies in experimental animals, and growth and metabolism changes in cultured cells. There is also a report of increased movement of human fetuses during exposure to a doppler fetal detector. It is unclear how the available bioeffects data translate into risk to patients exposed to ultrasound. However, the possibility of altered functional development in a child, even minor aberrations, would be of concern to a pregnant mother undergoing an ultrasonic examination.

Much of the current bioeffect information is controversial. Often the ultrasound dosimetry is inadequate, most of the studies do not mimic the conditions of the clinical situation, and almost none of the studies has been independently verified to date.

Other problems associated with the current data base include the lack of dose-effect data, the lack of threshold data, and the lack of data on long-term effects. In addition, much of the data is from exposure to continuous wave ultrasound. The biological impact of short pulses of high intensities of ultrasound, such as used in pulse-echo ultrasound imaging, is little understood. These pulses may have a temporal peak intensity 1000 times greater than the average intensity.

II. GOALS AND SCOPE

The objective of the proposed studies is to encourage experimental research on the possible deleterious effects of ultrasound exposure. Experimental studies of biological effects of ultrasound exposure have, to date, concentrated on prompt responses. Thus, many questions pertinent to risk assessment are still unexplained. Since relatively little is known about possible responses to ultrasound exposure that are not immediately manifested, the scope of this RFA is general to accommodate a variety of proposals that would be potentially responsive. However, the program is oriented toward defining potential risks which may be associated with medical usage of ultrasound. Therefore, primary interest is in the range of ultrasonic frequencies, intensities and delivery formats typical of current diagnostic techniques. Also, since the study of ultrasound induced bioeffects is a very complex area involving both biological and physical implications, interdisciplinary collaborations are strongly encouraged.

The factors to be addressed in developing studies should include, but not necessarily be limited to:

1. reproducible endpoints indicative of adverse effects;

2. means by which damage is ascribed (i.e., is it accumulative, repairable, linear or otherwise with repeated exposures);

3. consideration of effects as function of peak or average intensity in pulsed exposures; and

4. development of possible chronic disease states.

III. MECHANISM OF SUPPORT

The support for this program will be the traditional grant-in-aid. Applicants, who are expected to plan and execute their own research programs, are requested to furnish an outline of the phases into which the program can be logically divided, their own estimates of the time required to achieve specific objectives of the proposed work, and a schedule for completion of the work.

The total project period of this proposal must not exceed three years, and single-year applications are encouraged. Starting dates as early as September 15, 1980, or later, may be requested.

Support of grants pursuant to this request for applications is contingent upon ultimate receipt of appropriated funds for this purpose. The award of grants will be influenced by the amount of funds available to the Bureau, by the overall merit of proposals, and by their critical relevance to the program goal. Total funding of this program is not anticipated to exceed $100,000 this year including indirect costs.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

The applications will be evaluated on a competitive basis. The initial scientific merit review will be arranged by the Division of Research Grants, NIH.

B. Review Criteria

Applications must be responsive to this RFA; that is they must be relevant to the goals of this program announcement and guidelines. Applications judged by FDA not to be responsive will be returned to the applicant.

The factors considered in evaluating each application will be:

1. Scientific merit of the research design, approach and methodology;

2. Methods of analyses;

3. Adequacy of existing and proposed facilities and resources;

4. Research experience and competence of the staff to conduct the proposed investigations;

5. Adequacy of time (effort) to be devoted to the project by the investigators and the technical staff;

6. Evidence of institutional commitment to the program;

7. Duration of proposed program; and

8. Cost reasonableness of the program.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief one-page letter of intent, which should include a very short synopsis of proposed research plan. This letter should be received no later than April 1, 1980, at the following address:

Dr. DeWitt G. Hazzard (HFX-14)
Acting Director
Extramural Research Staff, OMS
Bureau of Radiological Health, FDA
5600 Fishers Lane
Rockville, Maryland 20857

The Bureau requests such letters only to provide an indication of the number of scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any proposal subsequently submitted, nor is it a necessary requirement for application.

B. Format for Application

Applications must be submitted on form PHS 398, the application form for the traditional research grant. Application kits are available at most institutional business offices or from the Division of Research Grants, NIH. The conventional presentation in format and detail for regular research grant applications should be utilized, with care taken to fulfill the points identified under Review Criteria.

C. Deadline for Submission

Applications must be received by May 7, 1980. Applications received after this date will be returned.

D. Application Procedure

The original and six (6) copies of the completed application should be delivered to:

Application Receipt
Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

Label the outside of the mailing package and the top of the face page "RESPONSE TO RFA, FDA-BRH-DBE-80-1."

A brief covering letter must accompany the application indicating that it is submitted in response to the RFA: DELAYED EFFECTS OF ULTRASOUND EXPOSURE. A carbon copy of this covering letter and a single copy of the application should be sent to Dr. DeWitt G. Hazzard (address above).

E. Inquiries

Inquiries may be addressed to:

Dr. Mel E. Stratmeyer (HFX-120)
Division of Biological Effects, EXSB
Bureau of Radiological Health, FDA
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-3466

VI. SELECTED BIBLIOGRAPHY

1. David, H., J.B. Weaver and J.F. Pearson, "Doppler Ultrasound and Fetal Activity," British Medical Journal, 2:62-64, 1975.

2. Liebeskind, D., R. Bases, F. Elequin, S. Neubort, R. Leifer, R. Goldbert and M. Koenigsberg, "Diagnostic Ultrasound: Effects on DNA and Growth Patterns of Animal Cells," Radiology, 131:177-184, 1979.

3. Scheidt, P.C. and F.E. Lundin, "Investigations for Effects of Intrauterine Ultrasound in Humans," Symposium on Biological Effects and Characterizations of Ultrasound Sources, June 2 and 3, 1977, pp. 19-26, HEW Publication (FDA) 78-8044.

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REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

ANNOUNCEMENT

FDA-BRH-DTMA-80-2

BUREAU OF RADIOLOGICAL HEALTH,

FOOD AND DRUG ADMINISTRATION

TITLE: *APPLICATION OF NEW TECHNOLOGY IN DIAGNOSTIC RADIOLOGY*

Application receipt date, May 7, 1980

The Division of Training and Medical Applications (DTMA) of the Bureau of Radiological Health (BRH), Food and Drug Administration (FDA), conducts a nationwide program to reduce unnecessary exposure from the use of radiation in the healing arts with special emphasis on studies and evaluation of conditions of exposure to medical diagnostic radiation. The Division identifies trends in medical radiation practices and procedures which cause unnecessary patient exposure and plans, develops, and implements action programs that encourage improvement in radiological practices to ensure that radiation exposure to patients is the minimum consistent with the highest standards of medical care. This request for applications (RFA) is intended to foster clinical studies that will lead to improved radiological practices.

This RFA will use the customary grant-in-aid mechanism which will be governed by the policies for regular research grants. The responsibility for planning, directing, and executing the proposed research project will be solely that of the applicant.

The present RFA announcement is open to all interested investigators for a single competition with a specified deadline for receipt of applications. It is anticipated that all applications in response to the RFA will be reviewed at the same time by a single review panel. Grants will be made under the legislative authorization in Section 356(b)(2) of the Public Health Service Act and will be administered according to the policies applicable to research project grants. This program is outlined in 13.103 of the Catalog of Federal Domestic Assistance.

Potential applicants are requested to send by April 1, 1980, a letter of intent to submit an application. The original and six (6) copies of the application are to be sent to the Division of Research Grants by May 7, 1980. A brief cover letter should be enclosed indicating that the application is being submitted in response to the RFA, FDA-BRH-DTMA-80-2: APPLICATION OF NEW TECHNOLOGY IN DIAGNOSTIC RADIOLOGY. Applications should be prepared in accordance with the aims and requirements described in the following sections.

I. BACKGROUND INFORMATION

The Bureau of Radiological Health is interested in encouraging studies to evaluate the use of certain dose reducing new technologies in diagnostic radiology facilities (1). In addition to demonstrating the practical utilization of the new technologies in a clinical environment, the Bureau wishes to identify problems associated with the implementation and the routine use of these technologies and to develop approaches to solve these problems. The information developed will be used to encourage and assist the adoption of those technologies found beneficial.

Recent technological developments in diagnostic radiology, such as the introduction of x-ray intensifying screens containing more efficient phosphors, although demonstrating a potential for the reduction of patient radiation dose, have received limited evaluation in terms of their total impact on the clinical diagnostic radiology facility (2-10).

The recent introduction of carbon fiber reinforced plastics, which have low x-ray attentuation properties, has led to their use in cassette and film changer fronts and x-ray table tops. Physical measurements indicating a potential for reduced patient radiation exposures have been reported (11) but there are no reported studies documenting this is the clinical situation nor identifying the problems, if any, associated with the implementation or use of carbon fiber technology in diagnostic radiology.

Examples of other new technologies with the potential for reduced patient radiation doses, in addition to the potential for improved image quality, are the use of special filters to obtain optimal x-ray beam quality for a specific examination and image receptor system (12, 13), and the use of scatter reduction devices (14-16).

This RFA is intended to encourage more detailed evaluation of the implementation and use of these technologies in the clinical diagnostic radiology facility. It intends to do this by awarding a number of modest grants, depending upon the availability of funds, aimed at evaluating some of these technologies and identifying any user problems associated with the implementation of these technologies.

II. OBJECTIVES AND SCOPE

The objective of these studies is to encourage research that will measure and evaluate the impact of new technological devices or procedures in clinical diagnostic radiology.

The new technologies in diagnostic radiology under consideration are those devices and/or techniques that show potential for patient radiation dose reduction while providing image quality adequate for the goals of the examination being performed. These technologies should be those which have reached a developmental point so as to be presently available to the radiologic community, but ones which have not been sufficiently evaluated in the scientific literature as of this time. The primary technologies of interest are the newer film-screen systems and the carbon fiber materials, though consideration will be given to any other new technologies that might be submitted for support.

The research should identify user problems associated with the implementation and/or the routine use of these new technologies. These studies should be directed at documenting the benefits, if any, of the new technology and identifying user problems that need special attention. They should be controlled, quantitative evaluations of the technology under consideration in specific applications.

III. MECHANISM OF SUPPORT

The support for this program will be the traditional grant-in-aid which is intended to partially defray the cost of equipment, materials, and personnel. This form of assistance is intended to encourage the initial implementation of one of the new technologies and to support more critical evaluation and documentation of its impact than otherwise might occur. As such, the grant-in-aid is not intended to totally defray the costs of the implementation of a new technology or the operation of the facility.

Applicants, who are expected to plan and execute their own research programs, are requested to furnish an outline of the phases into which the program can be logically divided, their own estimates of the time required to achieve specific objectives of the proposed work, and a schedule for completion of the work. It is anticipated that this proposal need not exceed one year, however, meritorious applications of longer duration will not be rejected. A starting date as early as September 15, 1980, or later may be requested. Support of grants pursuant to this request for applications is contingent upon ultimate receipt of appropriate funds for this purpose. The number of grants awarded will be influenced by the amount of funds available to the Bureau, by the overall merit of proposals, and by their critical relevance to the program goal. Total funding of this program is not anticipated to exceed $90,000, including indirect costs, for this year.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Procedures

The applications will be evaluated on a competitive basis. The initial scientific review will be arranged by the Division of Research Grants, NIH.

B. Review Criteria

Applications must be responsive to this RFA; that is, they must be relevant to the objectives of this program announcement and guidelines. Applications judged by FDA not to be responsive will be returned to the applicant. The factors considered in evaluation of each application will be the following:

1. The technology to be evaluated must have sufficient merit in terms of anticipated patient radiation dose reduction and image quality;

2. Methods of measuring the impact of this technolgy (patient exposure, diagnostic yield, examination repeat rates, image quality, etc.);

3. Methods of identifying user problems in implementing this technology;

4. Adequacy of existing and proposed facilities and resources;

5. Adequacy of quality assurance program;

6. Research experience and competence of the staff to conduct the proposed investigations;

7. Availability of appropriate patient populations;

8. Evidence of commitment to the program by the applicant;

9. Cost reasonableness of the program (we do not propose to totally defray all costs of establishing or operating a facility; only to assist in introducing and evaluating new technologies).

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief one-page letter of intent, which should include a very short synopsis of proposed areas of research and identification of any other participating institutions. This letter should be received no later than April 1, 1980, at the following address:

Dr. DeWitt Hazzard (HFX-14)
Acting Director
Extramural Research Staff, OMS
Bureau of Radiological Health, FDA
5600 Fishers Lane
Rockville, Maryland 20857

The Bureau requests such letters only to provide an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any proposal subsequently submitted, nor is it a necessary requirement for application.

B. Format for Application

Applications must be submitted on form PHS 398, the application form for the traditional research grant. Application kits are available at most institutional business offices, or from the Division of Research Grants, NIH. The conventional presentation in format and detail for regular research grant applications should be utilized, with care taken to fulfill the points identified under Review Criteria.

C. Deadline for Submission

Applications must be received by May 7, 1980. Applications received after this date will be returned.

D. Application Procedure

The original and six (6) copies of the completed application should be sent or delivered to:

Application Receipt
Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

Label the outside of the mailing package and the top of the face page "RESPONSE TO RFA, FDA-BHR-DTMA-80-2."

A brief cover letter must accompany the application indicating that it is submitted in response to the RFA: APPLICATION OF NEW TECHNOLOGY IN DIAGNOSTIC RADIOLOGY. A copy of this cover letter with a single copy of the application should be sent to Dr. DeWitt Hazzard at the address shown under item A.

E. Inquiries

Inquiries may be directed to:

Mr. Orhan H. Suleiman (HFX-70)
Bureau of Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-2436

VI. REFERENCES

1. Wagner, RF, Jennings, RJ: The bottom line in radiologic dose reduction. Proceedings of the Society of Photo-optical Instrumentation Engineers 206:60-66, 1979.

2. Buchanan, RA, Finkelstein, SI, Wichersheim, KA: X-ray exposure reduction using rare-earth oxysulfide intensifying screens. Radiology 105:185-190, October 1972.

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11. Phillips, R, Gross, R, Shuping, R: A new approach to dose reduction in diagnostic radiology. (Scientific Exhibit #201 at the Radiological Society of North America annual meeting 1979.) Information available from the authors at the Bureau of Radiological Health, Rockville, MD 20857.

12. Villagran, JE, Hobbs, BB, Taylor, KW: Reduction of patient exposure by use of heavy elements as radiation filters in diagnostic radiology. Radiology 127:249-254, April 1978.

13. Jennings, RJ, Fewell, TR: Filters-photon energy control and patient exposure. In Reduced Dose Mammography, Edited by W.W. Logan and E.P. Muntz (Masson, N.Y., 1979)

14. Barnes, GT, Cleare, HM, Brezovich, IA: Reduction of scatter in diagnostic radiology by means of a scanning multiple slit assembly. Radiology 120:691-694, 1976.

15. Sorenson, JA, Nelson, JA, Niklasen, LT, Jacobsen, SC: Rotating disc device for slit radiography of the chest. Radiology 134:227-231, January 1980.

16. Wagner, RF, Barnes, GT, Askins, BS: The effect of reduced scatter on radiographic information content and patient exposure: a quantitative demonstration. Medical Physics Volume 1, 1980. (To be published.)

ANNOUNCEMENT

CANCER CLINICAL TREATMENT RESEARCH

NATIONAL CANCER INSTITUTE

The National Cancer Institute's Division of Cancer Treatment desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the clinical treatment of cancer. Appropriate studies include the elucidation of the effects of various treatments and related tissue responses, toxicology and the importance of host factors in disease occurence, rate of progression and curability. Improved experimental design, data management, statistical analysis, as well as specific experimental developments in supportive care methods and moldalities are integral aspects of this program. Applications dealing with innovative approaches in surgical oncology are of particular interest. In making this program announcement, it is not the intent of the National Cancer Institute to make or imply any delimitation related to cancer clinical treatment research, but rather to stimulate investigator-initiated research in clinical treatment.

Applications in response to this announcement 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. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the National Institutes of Health for regular research grant applications will prevail.

Deadline

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

July 1 November 1 March 1

Method of Applying

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

This program is described in the Catalog of Federal Domestic Assistance number 13.395. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74.

Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement.

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

Application Receipt Office
Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. William DeWys
Program Director for Clinical
Treatment Grants
Room 8C17, Landow Building
Bethesda, Maryland 20205

Telephone: (301) 496-4844

In order to alert the Division of Cancer Treatment to the submission of proposals with primary thrust directed to clinical treatment research, a copy of the covering letter should be sent under separate cover to Dr. DeWys.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

ANNOUNCEMENT

NIH-NCI-DCBD-BCPCB-80-1

NATIONAL CANCER INSTITUTE

TITLE: *STUDIES OF IMMUNOCOMPETENT CELLS INFILTRATING HUMAN BREAST CANCER*

Application receipt date, June 1, 1980

The Division of Cancer Biology and Diagnosis of the National Cancer Institute invites grant applications from interested investigators for studies of the immunologic activity of cells invading breast cancer tissue. The objectives will be to isolate and characterize the infiltrating lymphoreticular cells from human mammary tumor tissue and to correlate the numbers and functional capacities of these cells with the prognosis of the breast cancer patient.

This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated basic and clinical research projects in areas of special importance to the National Cancer Program. The research stimulated by this RFA is supported through the customary NIH grant-in-aid and follows the policies for regular research grants. However, the RFA solicitation represents a single competition, with a specified deadline for receipt of applications. All applications in response to the RFA will be reviewed by the same initial review group of NIH.

The present RFA announcement is for a single competition with a specified deadline of June 1, 1980 for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. BACKGROUND INFORMATION
II. OBJECTIVE AND SCOPE
III. MECHANISM OF SUPPORT
IV. REVIEW PROCEDURES AND CRITERIA
V. METHOD OF APPLYING
VI. INQUIRIES

This program is described in the Catalog of Federal Domestic Assistance number 13.393. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74.

I. BACKGROUND INFORMATION

A. Division of Cancer Biology and Diagnosis (DCBD)

DCBD through the Breast Cancer Program Coordinating Branch sponsors both fundamental and clinical research grants and contracts in a continuing search for biologic markers of breast cancer. In the past few years, it has been shown that the reaction of lymphoid cells and histiocytes to human mammary carcinoma, as determined by immunologic examination of draining lymp nodes and inflammatory cells which infiltrate the tumor, may be important prognostic indicators. This request for applications is intended to encourage submission of investigator-initiated research grant proposals designed to identify immune mechanisms which are relevant to prognosis of the breast cancer patients.

B. Statement of the Problem

Recently, methods for determining the enzyme content and surface markers on tumor infiltrating cells have been used to characterize these cells. Some investigators find T-lymphocytes predominant in most tumors with a lymphocytic infiltration. Studies of acid phosphatase, non-specific esterase and receptors for the Fc portion of the immunoglobulin molecule indicate that many cells of the monocyte/macrophage series may be present. Natural killer cells have also been isolated from tumors. Earlier studies had identified plasma cells and demonstrated local immuno-globulin production.

Methods for separation and functional characterization of the cells invading tumors have been worked out in experimental animal systems. Some work with isolation and morphological characterization of these cells has been accomplished in human tumors, including mammary carcinoma. This project should be designed to develop methods for isolation and functional characterization of inflammatory cells (especially macrophages and lymphoid cells) invading human breast tumors. Correlation of such analyses to pathological and clinical findings should lead to better understanding of the prognostic significance of intratumor inflammatory cells.

II. OBJECTIVES AND SCOPE

A. Objectives

The overall objective of this proposed study is to identify immune mechanisms of tumor destruction which are relevant to the prognosis of human breast cancer. To achieve this, the morphologic and functional characteristics of cells found in primary and metastatic lesions must be known and the relationship of the numbers and functional capacities of these cells to histologic type of the tumor and prognosis of the patient determined.

B. Scope

The proposals should address themselves to the identification and description of the patient population which will be studied; methods of cell isolation and characterization; methods to be used in relating the results to diagnosis and/or prognosis, including criteria for pathological classification; methods of collecting and maintaining clinical data and methods of statistical analysis appropriate for the expected sample size.

However, support is not limited to the above subjects. Investigators are encouraged to devise innovative approaches to the understanding of the immunological activity of cells invading breast cancer tissue.

III. MECHANISM OF SUPPORT

The support for this program will be the traditional National Institutes of Health grant-in-aid. Applicants are expected to plan and execute their own research protocol. It is anticipated that this project need not exceed three years. At least two projects will be funded totalling an approximate direct cost of $200,000 for the first year, $214,000 for the second year and $230,000 for the third year. Project start dates early in 1981 are anticipated. Although this program is provided for in the financial plans for fiscal year 1981, award of grants pursuant to this request for application is contingent upon availability of funds for this purpose.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

Upon receipt, applications will be reviewed by Division of Research Grants (DRG) and NCI staff for their responsiveness to the specific objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to submit it for consideration with all other unsolicited grant applications received by NIH for that review cycle. For those applications judged responsive, DRG will arrange for the scientific merit review by appropriate peer review group.

B. Review Criteria

In addition to the usual elements of scientific merit, the factors considered in evaluating each application will be:

1. Availability of clinical collaboration for obtaining appropriate materials and numbers of patients.

2. Experience with techniques of cell separation.

3. Experience with characterization of cells.

4. Demonstration of sound arrangements for collaboration of pathologist to correlate functional tests with pathological classification.

5. Plan for data management and statistical analysis.

6. Availability of appropriate personnel and facilities.

V. METHOD OF APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398, the application form for the traditional research grant. Application kits are available in most institutional business offices, or from the Division of Research Grants, NIH. The conventional presentation in format and detail for regular research grant applications should be followed and the points identified under the "Review Criteria" must be fulfilled. The words "PROPOSAL IN RESPONSE TO RFA: STUDIES OF IMMUNOCOMPETENT CELLS INFILTRATING HUMAN BREAST CANCER" must be typed in bold letters across the top of the face page of the application.

B. Application Procedure

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications must be received by close of business, June 1, 1980. Applications received after this date will be returned. The DRG will also not accept any application in response to this announcement that is the same as one concurrently being considered by any other NIH awarding unit.

VI. INQUIRIES

Inquiries may be directed to:

Dr. Bernice T. Radovich
Breast Cancer Program Coordinating Branch
Division of Cancer Biology and Diagnosis
National Cancer Institute
Room 4B-04, Landow Building
Bethesda, Maryland 20205

Telephone: (301) 496-6774

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