# NIH Guide
## for Grants and Contracts

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES

Vol. 15, No. 5, April 25, 1986

IN THIS ISSUE:



The NIH 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.

**Have You Moved?**
If you present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

## ERRATA

## ANNOUNCEMENT

## AVAILABILITY OF REQUEST FOR COOPERATIVE AGREEMENT: RFA 86-RR-01

## ESTABLISHMENT OF A CHIMPANZEE BREEDING AND RESEARCH PROGRAM

**P.T. 34; K.W. 1002002, 0201058**

**DIVISION OF RESEARCH RESOURCES**

The above listed Cooperative Agreement Announcement #86-RR-01 published in the NIH Guide for Grants and Contracts, Vol. 15, No. 4, March 28, 1986, has an incorrect address listed in the last paragraph. The correct address for further information should read as follows:

Animal Resources Program
Division of Research Resources
Building 31 - Room 5B59
National Institutes of Health
Bethesda, Maryland 20892

Telephone: (301) 496-5175

## ERRATUM

## ANNOUNCEMENT

**THE FIRST INDEPENDENT RESEARCH SUPPORT AND TRANSITION (FIRST) AWARD (R-29)**

**P.T. 34; K.W. 0710030, 0404000, 1014002**

**NATIONAL INSTITUTES OF HEALTH**
**HEALTH RESOURCES AND SERVICES ADMINISTRATION**

VIII. PARTICIPATING BUREAUS, INSTITUTES, DIVISIONS AND CENTERS OF THE NATIONAL INSTITUTES OF HEALTH

p. 5 NATIONAL HEART, LUNG AND BLOOD INSTITUTE (NHLBI)
Phone number should read: 496-7416

p. 6 NATIONAL CANCER INSTITUTE (NCI) should read:

Mr. Hernon Fox instead of Herman Fox

p. 7 DIVISION OF RESEARCH RESOURCES (DRR) Areas of special emphasis should read:

The following are research areas appropriate to the DRR interests: (1) Research and Development in Instrumentation and Specialized Technologies for Biomedical Research. This encompasses instruments, devices, and processes to facilitate research in biomolecular and cellular structure and function. (Instrumentation includes mass spectrometry, nuclear magnetic resonance, electron spin resonance, equipment for fast kinetic research, X-ray diffraction, electron microscopy, and flow cytometry.) The application of computer science, computer engineering, and biomedical engineering to biomedical research problems is also of interest. (This includes knowledge engineering, information technology, computer graphics, image processing, computer modeling and simulation, task-dedicated computer systems, and development of implantable microsensors and transducers.); (2) Research in Laboratory Animal Sciences. (This includes the etiology, pathogenesis, and control of laboratory animal diseases, as well as the environmental requirements of laboratory animals.); and (3) Development of Biomedical Research Methods Employing Lower Organisms, Tissues/Cells in Culture, or Mathematical and Computer Simulations.

Program Contact:

Dr. James F. O'Donnell, Deputy Director
Division of Research Resources
Building 31 - Room 5B03
Bethesda, Maryland 20892

Telephone: (301) 496-6023

## NOTICE

### CHANGE IN RECEIPT DATE - REQUEST FOR COOPERATIVE AGREEMENT APPLICATIONS

**P.T. 34; K.W. 0755015, 0785210, 0715040, 0785025**

**BYPASS ANGIOPLASTY RESEARCH INVESTIGATION (BARI) CLINICAL UNITS**

The National Heart, Lung, and Blood Institute (NHLBI) has established a new receipt date for the RFA noted above, originally published in the NIH Guide for Grants and Contracts, Vol. 15, No. 4, March 28, 1986.

The new receipt date is August 15, 1986. Letters of intent are requested by June 20; the anticipated award date is March 1, 1987.

Requests for copies of this RFA should be addressed to:

Dr. Charles G. Hollingsworth
Cardiac Diseases Branch, DHVD, NHLBI
Federal Building - Room 3C06
7550 Wisconsin Avenue
Bethesda, Maryland 20892

Telephone: (301) 496-1081

## NOTICE

### CANCER EDUCATION GRANT (R25)

**P.T. 34; K.W. 0785140, 0715035**

**NATIONAL CANCER INSTITUTE**

The National Cancer Institute is restructuring the Cancer Education Grant (R25). No more applications for this grant will be accepted until further notice. Any such applications received for the June 1, 1986 receipt date or later will be returned.

# NOTICE

## NIADDK KIDNEY AND UROLOGICAL RESEARCH CENTERS

**P.T. 04; K.W. 0785220, 0785070, 0715085**

**NATIONAL INSTITUTE OF ARTHRITIS DIABETES, AND DIGESTIVE AND KIDNEY DISEASES**

The Division of Kidney, Urologic and Hematologic Diseases (DKUHD) of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) announces that RFA 86-AM-01 for Kidney and Urological Research Centers, with a prospective reply date of March 15, 1986, and later extended to July 15, 1986, which appeared in the October 11, 1986 issue of the NIH Guide for Grants and Contracts (Vol. 14, No. 11), has been withdrawn.

The DKUHD intends to reannounce the RFA for Kidney and Urological Research Centers.

Inquiries may be addressed to:

M.J. Scherbenske, Ph.D.
Assistant to the Division Director
for Administration
Renal Physiology/Pathophysiology
Program Director
DKUHD/NIADDK
Westwood Building - Room 621
Bethesda, Maryland 20892

Telephone: (301) 496-7458

## NOTICE

**ALL RECIPIENTS OF NIH GUIDE FOR GRANTS AND CONTRACTS AND GUIDE SUPPLEMENTS**

**P.T. 04, 22, 34, 44; K.W. 1014002**

**NATIONAL INSTITUTES OF HEALTH**

The Notice of September 13, 1985, which NIH sent to all recipients of the NIH Guide and Guide Supplements, announced a change in how these announcements will be printed and distributed. The separate printing and distribution system of the past will be replaced by a single one published weekly, containing all information related to grants, cooperative agreements and contracts. NIH hopes to implement this new procedure in early summer.

It is expected that the new schedule will facilitate negotiation of a printing contract that will prevent recurrence of late mailing such as occurred late in 1985 with the Guide and early in 1986 with the Guide Supplements. The recent problem related to Guide Supplements occurred during the peak period (December through March) when contracting staff were initiating their annual procurements. That peak period has now passed. During 1985, NIH processed only four Guide Supplement announcements during April and May.

Because serious delays in receipt of these timed announcements render them worthless, **NIH will publish no more separate Guide Supplements** but, when possible, will include them in the regular Guide until June when all Supplements will appear in the weekly Guide issues.

NIH regrets the inconvenience these delays have caused. The Commerce Business Daily continues to carry all material which appears in Guide Supplements.

## NOTICE

## NIH REGIONAL WORKSHOP - HUMANE CARE AND USE OF LABORATORY ANIMALS BY AWARDEE INSTITUTIONS

**P.T. 42; K.W. 1014003**

**NATIONAL INSTITUTES OF HEALTH**

The National Institutes of Health (NIH), Office for Protection from Research Risks, (OPRR) is continuing to sponsor a series of workshops on implementing the revised "Public Health Service Policy on the Humane Care and Use of Laboratory Animals by Awardee Institutions" and the NIH Guide for the Care and Use of Laboratory Animals. The workshops are open to institutional administrators, and others who share in responsibility for sound management of humane animal research. The current schedule includes:

| Date - 1986 | Place | Contact |
|---|---|---|
| May 8 | Atlanta, GA | Dr. M. S. Silberman<br>Emory University<br>Robert Woodruff Health<br>Sciences Ctr.<br>P.O. Drawer KK<br>Atlanta, GA. 30322<br>(404) 321-0111 Ext. 4389 or 4389 |
| June 10-11 | Chicago, IL | University of Illinois at Chicago<br>Sue Korienek or Bettie Cleveland<br>Conferences and Institutes<br>912 South Wood St.<br>Chicago, IL 60612<br>(312) 996-8025 |

Additional workshops will be announced later. For further information regarding education programs contact:

Roberta H. Garfinkle
Education Program Coordinator
Office for Protection from Research Risks
National Institutes of Health
Building 31 - Room 4B09
9000 Rockville Pike
Bethesda, Maryland 20892

## ANNOUNCEMENT

## RESEARCH CENTERS IN MINORITY INSTITUTIONS AWARD

**P.T. 04, 34, FF; K.W. 0710030**

**DIVISION OF RESEARCH RESOURCES**

Application Receipt Date: June 16, 1986

The National Institutes of Health (NIH) is pleased to re-announce the Research Centers in Minority Institutions (RCMI) Award. Its purpose is "to establish research centers in those predominantly minority institutions which offer doctoral degrees in the health professions or the sciences related to health...."(Report of the House/Senate Conferees on the Fiscal Year 1985 Appropriation for the Office of the Director, NIH).

The RCMI Program is managed by the Office of the Director, Division of Research Resources (DRR). The program is designed to provide grants of up to $1,000,000 per year, for five years, to help eligible institutions enrich their research environments via selected improvements in their human and physical resources. For example, the funds awarded could be used for the salaries of key research and research-support personnel, instrumentation, and alteration and renovation of facilities. Such expenditures would complement ongoing and planned research activities (e.g., projects funded by Minority Biomedical Research Support grants, Minority Access to Research Career awards, traditional NIH and ADAMHA research projects, and individual and institutional research fellowships).

To be eligible to compete for an RCMI award, an institution must have more than 50 percent minority enrollment and offer doctoral degrees in the health professions or the sciences related to health. This program is open only to institutions within the United States and its territories.

Eligible institutions who need additional information (e.g. program guidelines) should contact:

Dr. Sidney A. McNairy, Jr.
Director, RCMI Program
Division of Research Resources
Building 31 - Room 5B19
National Institutes of Health
Bethesda, Maryland 20892

Telephone: (301) 496-6341

## ANNOUNCEMENT

**AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA**

**86-AG-03**

**EXPLORATORY STUDIES GRANT IN MINORITY AGING**

**P.T. 34; K.W. 0710010, 0785165, 0710030, 0414000, 0404000, 0730000**

**NATIONAL INSTITUTE ON AGING**

Application Receipt Date: September 30, 1986

I. BACKGROUND

There has been tremendous progress in improving the health of the American population in general, but progress in improving the health and longevity of segments of the population, especially ethnic minorities has been less dramatic. The disparity in health status between minority populations and whites has implications for aging of minorities. However, there is a lack of scientific expertise focused on minority aging and an absence of broad interdisciplinary programs of research to provide this knowledge. Programs of research composed of multiple projects rather than discrete, single projects are required in order to provide a unified approach to aging, taking into consideration the interactive influences of biological, medical, behavioral and social factors on aging. These programs of research should provide basic information about aging of minorities which will ultimately be useful in decreasing the gap in health status and in longevity between minority and majority populations.

II. RESEARCH GOALS AND SCOPE

The objective of exploratory studies grants in minority aging is to provide support for planning for research, and for preliminary studies leading to the development of high quality research on aging of ethnic minority groups. The planning activities may consist of the specification of goals and objectives of research, development and expansion of specialized resources and facilities, and the convening of workshops or meetings of consultants to obtain advice relating to the expansion or development of programs of research on aging. Planning activities and preliminary research should be aimed at development of large-scale research on issues related to aging of minority populations, including basic biological processes of aging, disease processes and chronic disabilities which accompany aging, psychological and social factors in aging and health care strategies among aging populations.

III. MECHANISMS OF SUPPORT

The administrative and funding mechanism to be used to support the studies carried out under this RFA will be the exploratory grant which supports planning for new programs, expansion or modification of existing resources and feasibility studies aimed at the development of programs of research on problems of special

significance to NIH. The regulations (Code of Federal Regulations, Title 42, Part 52 and Title 45, Part 74) and policies that govern the research grant programs of the Public Health Service will prevail. This RFA is a one time invitation. These awards will be made in amounts up to $50,000 in direct costs for up to 12 months. The start date for projects will be July 1, 1987. Applications will be reviewed as a single competition by an initial review group convened by the National Institute on Aging Scientific Review Office.

IV. INQUIRIES

A copy of the complete RFA describing the research objectives and scope, review criteria and method of applying can be obtained by contacting:

Associate Director
Biomedical Research and Clinical Medicine
National Institute on Aging
Building 31 - Room 5C11
National Institutes of Health
Bethesda, Maryland 20892

Telehpone: (301) 496-4996

Associate Director
Behavioral Sciences Research
National Institute on Aging
Building 31 - Room 4C32
National Institutes of Health
Bethesda, Maryland 20892

Telephone: (301) 496-3136

## ANNOUNCEMENT

## RESEARCH GRANTS ON ALCOHOL AND IMMUNOLOGY INCLUDING ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

**P.T. 34; K.W. 0710070, 0715120, 0404003**

**NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM**

### I. BACKGROUND INFORMATION

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) makes grant awards for basic andapplied alcohol research projects. NIAAA has a longstanding interest in the relations between alcohol consumption and immunologic disorders and it now wants to increase the level of activity in this research area. Further, the emergence of Acquired Immunodeficiency Syndrome (AIDS) as a significant public health concern has served to re-emphasize NIAAA's commitment to research on the effects of alcohol consumption on immunologic functioning and, specifically, the role of alcohol as a potential co-factor in AIDS. Virtually no information is available regading the use/abuse of alcohol by AIDS patients or how alcohol may affect the course and/or treatment of the disease process. This special announcement is intended to encourage the submission of applications from investigators to compete for funds for the study of the relationship of alcohol consumption to immunologic disorders and infectious diseases.

### II. AREAS OF INTEREST

The Institute wishes to expand its support for research on all aspect of the relation between alcohol and infectious disease. Investigators in all relevant fields are encouraged to apply including those in epidemiology, immunology, bacteriology, virology, pathology, and other relevant clinical and basic scientific disciplines. The following are some broadly defined areas related to alcohol, immunology, and infectious diseases which are of interest and in need of further investigation:

- o Epidemiologic studies of the incidence and prevalence of the various types of immune deficiencies and infectious diseases among alcohol abusers and alcoholics.

- o Basic and applied research related to the effects of alcohol use/abuse on increasing risk for infection, including laboratory studies of immune function and studies of resistance to bacterial/viral challenge.

- o Relation between the rate and persistence of alcohol consumption and the degree of immunosuppression. Studies of mechanisms by which alcohol suppresses immune function.

- o Studies on the role of alcohol use/abuse in modifying the course and treatment of bacterial or viral disease after infection. The relationship of alcohol liver disease to the incidence of infection.

- The effects of alcohol on existing immune function in immunodeficiency disease states.

- The role of nutritional deficiency which may interact along with the consumption of alcohol in the suppression of immune function.

More specific areas of interest related to AIDS are listed below:

- Epidemiologic studies of drinking practices of AIDS and AIDS-related complex (ARC) patients, of persons testing positive for HTLV-III antibody, and of persons in high risk groups for infection.

- Incidence and prevalence studies of HTLV-III positive, ARC and AIDS among alcoholics and alcohol abusers, especially those who are not inavenous drug abers.

- The role of alcohol consumption in increasing risk taking behavior (e.g., disinhibition) which may enhance the probability of HTLV-III infection by exposure, for example, to other high risk sexual or durg abuse behaviors.

- Studies using animal models to determine the potential role of alcohol as a co-factor for HTLV-III infection and/or the development of AIDS.

- Mechanisms of alcohol effects on cell mediated immunity and the relationship to acquisition of HTLV-III and related viruses.

- Studies of the differential immunosuppressive effects of acute intoxication as opposed to the chronic consumption of alcohol.

## III. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional investigator-initiated research project grant. The project period during which the research will be conducted should adequately reflect the time required to accomplish the stated goals and be consistent with the policy for grant support. Support will be provided for up to five years (renewable for subsequent periods) subject to the availability of funds and progress achieved.

Research grant applications may be submitted by nonprofit organizations and institutions, state or local governments and their agencies, for profit organizations, and eligible agencies of the Federal Government.

## IV. REVIEW PROCEDURES

Applications in response to this solicitation will be reviewed for scientific and technical merit by an appropriate peer review group. A secondary review for policy and program relevance will be made by the National Advisory Council on Alcohol Abuse and Alcoholism.

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

February 1
June 1

October 1

## V. METHOD OF APPLYING

Potential applicants should obtain a copy of the special announcement by contacting the National Clearinghouse for Alcohol Information, Reference Department, Box 2345, Rockville, Maryland 20852 (telephone 301-468-2600). Applications must be submitted on form PHS 398 (revised 5/82), which is available in the business or grants and contracts office at most academic and research institutions or from the National Clearinghouse for Alcohol Information. State and local government agencies should use form PHS 5161 (revised 3/79).

The signed original and six copies (two copies is using form PHS 5161) of the application should be sent to:

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

## VI. STAFF CONTACT

More detailed information about application procedures can be obtained from:

Dr. Helen M. Chao
Chief, Biomedical Research Branch
or
Dr. Ernestine Vanderveen
Chief, Clinical and Psychosocial Research Branch
Division of Extramural Research, NIAAA
5600 Fishers Lane
Room 14C-17
Rockville, Maryland 20857

Telephone: (301) 443-4223

## ANNOUNCEMENT

## BREAST CANCER IN DIETHYLSTILBESTROL TREATED MOTHERS AND IN DES-EXPOSED OFFSPRING

**P.T. 34; K.W. 0715035, 0785140, 0760025, 0785055, 0785165, 0775025**

**NATIONAL CANCER INSTITUTE**

Application Receipt Dates: February 1, June 1, October 1

The Division of Cancer Prevention and Control (DCPC) of the National Cancer Institute (NCI), through the Organ Systems Program (Breast Cancer), seeks applications for studies on breast cancer in DES-treated mothers and in DES-exposed daughters. The objectives are evaluate whether there is an increased incidence of breast cancer among women with prior exposure to DES, to characterize the types of breast cancer and of "benign" or premalignant breast lesions that develop in these women, and to compare women exposed to DES who develop breast cancer with women so exposed who do not, to explore possible interacting risk factors. It is anticipated that information on breast cancer associated with DES exposure should lead to a better understanding of breast cancer pathogenesis in relation to estrogens. It is also important to understand possible interaction of DES exposure with other, perhaps avoidable risk factors for breast cancer. The cohort of DES-exposed individuals is large. For their possible benefit, it is of concern to assemble as accurate a picture and as much potentially useful information as possible.

I. BACKGROUND

Diethylstilbestrol (DES, a synthetic, non-steroidal estrogen first produced in 1938) was reported in the 1940's to reduce fetal loss and prevent some of the complications of pregnancy. In the 1940's and 1950's, there was frequent prescription of DES and other exogenous estrogens for these purposes; it has been estimated that there may have been up to 4 to 6 million people in the U.S. thus exposed to DES (mothers during pregnancy plus offspring in utero)(1). Two controlled, randomized trials in the 1950's, one in England and another in the United States, failed to show a therapeutic value of DES for prevention of miscarriage or other pregnancy hazards; this did much to curb the administration of sex hormones to pregnant women, but the practice continued on a smaller scale through the 1960's.

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This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

In 1970, unusual occurrence of a rare clear-cell adenocarcinoma in young women was linked to exposure in utero to DES, and various subsequent studies have associated certain cancers and other health risks in the offspring with their DES exposure in utero. In 1978, a U.S. government task force evaluated the evidence related to the health risks of DES-treated mothers and offspring exposed in utero, and recommended careful followup of all exposed individuals (1). This included attention to possible breast cancer risk for DES-treated mothers, based on the evidence then at hand and on a review of the general biological relationship between estrogens and various cancers.

Since 1978, additional reports relevant to this particular issue have been published. The two that have attracted most attention are recent observational followup studies on fairly large cohorts of women (2, 3); both of these reported an overall excess risk of breast cancer of 40% or greater associated with DES treatment during pregnancy. In the largest cohort (2), the relative risk increased with interval after exposure, and rose from 1.6 in years 20-29 after exposure to 2.5 for those followed 30 years or more. The results of these investigators also suggested that prior spontaneous abortion, the major indicator for DES use, probably did not confound the association noted between DES treatment and subsequent breast cancer. This is important since hormonal patterns or other factors involved in complications of pregnancy have themselves been cited as possible risk factors for breast cancer.

Based on these latest studies, the Department of Health and Human Services reconvened a DES Task Force in January 1985, to review the investigations published since the 1978 Task Force Report and to update the conclusions and recommendations. The report of the 1985 Task Force was released in July 1985 (4). This report states that "there is now greater cause for concern about breast cancer risk among DES mothers than there was in 1978," although "a causal relationship has not been established." The Task Force recommended that research continue the followup studies that have been reported and also initiate other investigations of this issue to follow up other individuals, paying particular attention to the specific research recommendations made in the Task Force Report. The biological rationale for increased risk of breast cancer from DES exposure exists for daughters exposed in utero as well as for mothers. These offspring are only now reaching likely ages for breast cancer appearance, and an examination of their risk is likewise important. DES-treated mothers and in daughters exposed in utero.

1. DES Task Force Summary Report, 1978. NIH Publ 83-1688, US DHHS, Washington, D.C., 1983.
2. Greenberg ER, Barnes AB, Resseguie L, Barrett JA, Burnside S, Lanza LL, Neff RK, Stevens M, Young RH, and Colton T. Breast Cancer in Mothers Given Diethylstilbestrol in Pregnancy. New Eng J Med 311: 1393-1396, 1984.
3. Hadjimichael OC, Meigs JW, Falcier FW, Thompson WD, and Flannery JT. Cancer Risk Among Women Exposed to Exogenous Estrogens During Pregnancy. JNCI 73: 831-834, 1984.
4. Report of the 1985 DES Task Force. US DHHS, PHS, NIH, NCI, 1985.

II. RESEARCH GOALS

The request is for followup and study of women who were treated with DES during pregnancy, and equivalent followup and study of daughters exposed in utero. The questions to be addressed are (1) is there an increased incidence of breast cancer in DES-exposed individuals relative to appropriate comparison groups; (2) if so, can the increase in incidence be clearly associated with DES exposure (as distinguished, for example, from association with difficulties in maintaining pregnancy that precipitated the use of DES); (3) in relation to breast cancer development, is DES exposure interactive with, or potentiated by, any other of the known risk factors for breast cancer, e.g., other exposure to exogenous estrogens, or family history of breast cancer; (4) what are the pathologic types, receptor status, and other characteristics of breast cancers developing in DES-exposed persons; and (5) is there an increased incidence of benign or premalignant breast lesions in DES-exposed individuals, and what are the histopathologic and other characteristics of any such benign or premalignant lesions, especially in women who susequently developed breast cancer.

It is important to explore in considerable detail the questions of DES and breast cancer, as the 1985 DES Task Force has recommended. Long-term followup is also clearly of value. Aspects that have been identified as being of particular interest include the following:

A. Possible documentation of dosage, timing, and duration of DES treatment, and any comparison of doses.

B. Reason(s) for DES treatment, and any information on hormonal characteristics of exposed and comparison women, and of DES-exposed women who developed breast cancer compared with those who did not.

C. Any data on alternative hormone treatment or other hormone exposures.

D. Incidence of, and information on, breast cancers developing in DES-treated mothers and DES-exposed daughters: age of onset, pathologic type, receptor status, prior benign or premalignant breast lesions and details of such lesions, etc.

E. Similar information on benign breast lesions: incidence in DES-treated mothers and DES-exposed daughters, age of onset, histologic type, treatment, etc.

F. For breast cancer cases and comparison women, epidemiologic information on other risk factors related to breast cancer.

G. Information on other cancers developing in DES-exposed mothers or offspring and time relationship of these to breast cancer and/or premalignant breast lesions.

Collaborative investigations should be feasible and are to be encouraged, to use comparable methodology, to increase sample sizes, and/or to achieve standardized pathology review. Observational followup studies on women known to have been exposed to DES have already been shown to be appropriate, feasible, and fruitful. A case-control study design might also be feasible, perhaps among women in the age group of daughters exposed in utero, especially if such studies focussed on are

as or groups known to have experienced a particularly high frequency of DES exposure during the years of peak usage of this compound for pregnant women.

III. MECHANISM OF SUPPORT

Support for this program will be through the traditional research grant. Policies that govern research grant programs of the NIH will prevail. Non-profit and for-profit institutions may apply. All applications submitted in response to this Announcement will be classified as new grants (type 1).

IV. APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual Public Health Service peer review procedures for research grants (Study Section). Review criteria include the significance and originality of the research goals and approaches; feasibility of the research and adequacy of the experimental design; training, experience, research competence, and dedication of the investigator(s); adequacy of available facilites; provision for the protection of human subjects; and appropriateness of the requested budget relative to the work proposed.

Following Study Section review, the application will be evaluated for program relevance by the Organ Systems Program, DCPC, NCI. Funding decisions will be based on Initial review group and National Cancer Advisory Board recommendations, program relevance, and availablity of appropriate funds. Applications should be submitted on form PHS-398, available in the business or grants office at most academic or research institutions, or from the Division of Research Grants, NIH. Applications will be accepted in accordance with the dates for new applications on an indefinite basis:

February 1 June 1 October 1

The phrase **"RESPONSE TO NCI PROGRAM ANNOUNCEMENT: BREAST CANCER IN THE DES-EXPOSED"** should be typed on line 2 of the face page of the application. The original and six copies should be sent or delivered to:

Grant Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20892-4500

For further information contact:

Dr. Elizabeth P. Anderson
Breast Cancer, Organ Systems Section, CCB
DCPC, National Cancer Institute
National Institutes of Health
Blair Building - Room 717
Bethesda, Maryland 20892-4200
Telephone: (301) 427-8818

It would be appreciated if a brief letter of intent could be sent, simultaneously with the grant application submission, to the Program Director named above.

## ANNOUNCEMENT

## REQUEST FOR COOPERATIVE AGREEMENT APPLICATIONS: RFA 86-AI-09

## ENHANCEMENT/POTENTIATION OF VACCINE ANTIGENS

**P.T. 34; K.W. 0740075, 0710060, 0715125, 1710015**

**NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES**

Application Receipt Date: July 15, 1986

I. BACKGROUND

The Development and Applications Branch (DAB) of the Microbiology and Infectious Diseases Program (MIDP) of the National Institutes of Allergy and Infectious Diseases (NIAID) invites applications for Cooperative Agreements to support research and development projects for the use of microencapsulation as a technique for enhancing immune responses to isolated viral and/or bacterial antigens. The Accelerated Vaccine Initiative of the NIAID encompasses efforts to develop vaccines (live attenuated, inactivated, subunit, rDNA-derived polypeptides, synthesized polypeptides) for selected human pathogens. Included in this effort are influenza, respiratory syncytial, parainfluenza, herpes simplex, hepatitis A and B viruses, Hemophilus influenzae type b, Bordetella pertussis, Neisseria gonorrhoeae, Streptococcus pneumoniae, and Plasmodium falciparum. In many cases, attempts are being made to identify specific antigens, antibodies to which are correlated with immunity.

Past research efforts have indicated that many highly purified bacterial and viral components exhibit reduced antigenicity in animal models or humans. Attempts have been made over the years to develop adjuvants suitable for administration to humans, but alum still remains the utilized adjuvant primarily because of its demonstrated safety in administration to millions of humans (i.e., pertussis and hepatitis B vaccines). There is a need to investigate other immune enhancement methodologies, particularly now that molecular biology is making available small, highly purified antigenic components of infectious disease organisms.

One technique that may facilitate utilization for isolated vaccine antigens is microencapsulation. Microencapsulation has the potential advantage of controlled

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This program is described in the Catalog of Federal Domestic Assistance No. 13.856, Microbiology and Infectious Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301(c), (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. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

and/or targeted release of antigen. Several microencapsulated biologic products (i.e., hormones, antibiotics) are currently undergoing clinical studies. There are nevertheless, numerous questions that need to be addressed before the feasibility of this procedure for vaccine delivery can be assessed.

II. RESEARCH GOALS AND SCOPE

The purpose of this RFA is to stimulate studies aimed at the feasibility of immune potentiation of viral/bacterial antigens by microencapsulation. It is intended to encourage studies on methods for microencapsulation of isolated antigens, evaluation of encapsulated antigens as immunogens in appropriate animal models, evaluation of timed release of antigens, and determination of appropriateness of immune response for protection against infectious challenge. Investigators will choose the antigen(s) they wish to use for these studies in consultation with and assistance from NIAID staff.

III. MECHANISM OF SUPPORT

Award(s) will be made as Cooperative Agreements. These are assistance relationships with substantial involvement with NIAID staff. At present, NIAID anticipates making one award as a result of this request. Up to $150,000 direct costs will be allocated to fund the initial year's award for meritorious applications. Award(s) will be made for project periods of 3 years. All policies and requirements which govern the grant programs of the PHS apply.

IV. All inquiries and requests for the full text of this RFA should be directed to:

Dr. Franklin Tyeryar, Chief
Development and Applications Branch
Microbiology and Infectious Diseases Program
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building - Room 750
Bethesda, Maryland 20892

Telephone: (301) 496-7051

## NOTICE

## ALZHEIMER DISEASE PATIENT REGISTRY (ADPR) - CLARIFICATION OF ELIGIBILITY

**P.T. 34, 36; K.W. 0715180, 0745020, 0785055, 0755015, 0411005, 0710030, 0414000, 0745055**

**NATIONAL INSTITUTE ON AGING**

Application Receipt Date: May 28, 1986

The March 25 edition of the Guide included a notice of availability of a request for applications (RFA) 86-AG-01, Alzheimer Disease Patient Registry. Inadvertently omitted from the "Background" section was a statement on applicant eligibility describing the full scope of Public Health Service (PHS) research interest on Alzheimer's disease. Please substitute the following paragraph and note that eligible applicants are not restricted to those currently funded by the National Institute on Aging (NIA).

> The overall goal of this solicitation is to foster the development of a model for an Alzheimer Disease Patient Registry (ADPR) which eventually will serve as a national resource for clinical and epidemiological studies related to dementias of old age. In addition to collecting epidemiological data about the incidence of Alzheimer disease (AD), the resources of the registry may be used for training purposes. The Public Health Service, through the National Institute on Aging (NIA), National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), National Institute of Mental Health (NIMH), and National Institute of Allergy and Infectious Diseases (NIAID) supports a broad spectrum of basic and clinical research related to AD and other dementias of old age. A substantial portion of the NIA support for AD is provided through the program project mechanism and the ten Alzheimer Disease Research Centers (ADRC). The Centers, as well as many program projects, have three common resources: a) clinical expertise and technical means for diagnosis, b) biostatistical knowledge and computer facilities for gathering, storing and analyzing clinical information, and c) neuropathology expertise for postmortem confirmation of diagnosis. This request for applications (RFA) is intended to encourage the development of projects which would build upon existing clinical data resources (e.g., ADRC, or other currently funded projects) and expand these to include information for epidemiological studies. It should be emphasized that applicants are not restricted to those currently receiving NIA grant support. All proposals from qualified investigators will be considered.

For additional information or a copy of the complete RFA, please contact the NIA program director:

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