

# NIH GUIDE

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The NIH Guide announces scientific  
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**NOTICES**

**NATIONAL WORKSHOPS ON THE PROTECTION OF HUMAN SUBJECTS**

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are sponsoring a series of workshops on the responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

**WEST COAST WORKSHOP**

**DATES:** January 23 and 24, 1992 (REVISED DATES)

**WORKSHOP SITE:** Los Angeles, CA

**SPONSORS:** University of Southern California  
Los Angeles, CA 90089-4014

California State University - Los Angeles  
5151 State University Drive  
Los Angeles, CA 90032-8202

**REGISTRATION CONTACT:**

Ms. Lily Patterson  
Assistant to the Director  
Research and Sponsored Programs  
California State University - Los Angeles  
5151 State University Drive  
Los Angeles, CA 90032-8202  
Telephone: (213) 343-3820

**TOPIC: Whose Research is it Anyway? A Workshop on the Protection of Human Subjects in Research**

For further information regarding these workshops and future NIH/FDA National Protection of Human Subjects Workshops, please contact:

Ms. Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
9000 Rockville Pike  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

**NOTICES OF AVAILABILITY (RFPs AND RFAs)**

**CLOSED LOOP CONTROL OF FUNCTIONAL NEUROMUSCULAR STIMULATION**

RFP AVAILABLE: NIH-NINDS-92-01

P.T. 34; K.W. 0745047, 0740050, 0706040, 0715140

National Institute of Neurological Disorders and Stroke

The Neural Prosthesis Program of the National Institute of Neurological Disorders and Stroke (NINDS), NIH, is developing neural prostheses based on functional neuromuscular stimulation (FNS) for the restoration of quadriplegic individuals. The principal goal of the proposed project is to enhance the utility of FNS systems for hand grasp. Specific tasks include: developing and evaluating closed-loop FNS systems for hand grasp utilizing external force and position integrating FNS wrist stabilization, FNS elbow control and surgical procedures such as tendon transfer and arthrodesis with an FNS hand grasp system; developing a biomechanical model of the hand for use in evaluating advanced FNS systems; and investigating new techniques for programming of FNS systems and for selection of electrode sites. A research team with experience in neural prostheses, spinal cord rehabilitation, hand surgery, control theory, biomechanics and physiology will be required to successfully conduct this research. It is anticipated that one award will be made for a period of three years in August 1992.

This is not a Request for Proposals (RFP). To receive a copy of the RFP, submit a written request to the following address, and supply this office with two self-addressed mailing labels. All responsible sources shall be considered by the agency. The RFP will be issued on or about November 15, 1991, with proposals due on January 14, 1992.

Contracting Officer  
Contracts Management Branch, DEA  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 901  
7550 Wisconsin Avenue  
Bethesda, MD 20892  
Attention: RFP No. NIH-NINDS-92-01

**DEVELOPMENT AND TESTING OF NEW SPERMICIDES**

RFP AVAILABLE: NICHD-BAA-92-6

P.T. 34; K.W. 0750020, 0715182

National Institute of Child Health and Human Development

The Contraceptive Development Branch of the Center for Population Research, National Institute of Child Health and Human Development (NICHD), has a requirement to develop new spermicidal products that will incorporate either new spermicidal drugs or new formulations of existing drugs. The products must be developed as single dose units. The desired characteristics of the final product should include: (1) high contraceptive effectiveness, together with the ability to protect the user against STDs; (2) employ vehicles for rapid

spermicide delivery; (3) can protect vaginal and cervical epithelia from irritation; and (4) are long-acting after a single application. Both preclinical and clinical studies with new products will be considered. It is anticipated that three contract awards will be made for a maximum period of four years each, depending upon the nature and complexity of the proposed research.

This announcement is not a Request for Proposals (RFP). The RFP will be issued on or about November 15, 1991. Proposals will be due approximately four months thereafter. Copies of the RFP may be obtained by sending written requests with a self-addressed label to:

Paul J. Duska, Contracting Officer  
Contracts Management Branch, OGC  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 610  
9000 Rockville Pike  
Bethesda, MD 20892  
FAX: (301) 402-0915

#### GMP FORMULATION OF PEPTIDE T

##### SOURCES SOUGHT

P.T. 34; K.W. 0740021, 0755010

National Institute of Mental Health

The National Institute of Mental Health (NIMH) is currently involved in the clinical testing of Peptide T. The NIMH is seeking a contractor capable of formulating and producing dosage forms, carrying out quality control and stability tests, packaging, labeling, storage and shipment of products, and preparing documentation. The data prepared must be adequate to support chemistry requirements of Investigational New Drug or New Drug Applications submitted by NIMH or NIMH-supported investigators to the Food & Drug Administration. The dosage form to be produced includes intranasal formulations and will involve compounding, sterilizing, and safety testing bulk pyrogen-free aqueous solutions according to standardized pharmaceutical formulations and USP methods and the FDA Good Manufacturing Procedures (GMP). The NIMH will provide bulk drug substances, assay methodology, and reference standards. The contractor must provide washed and sterilized containers (capable of administering metered doses of intranasal solution) to be filled with 20 ml of sterilized peptide solution, cap, label, and package according to specifications provided by the Government, and refrigerate. The contractor shall be responsible for sterility and bioburden testing, HPLC analysis, storage, and shipping of the final product. The work requires that the contractor's facility be maintained in accordance with FDA prescribed Current Good Manufacturing and Laboratory Practices. It is anticipated that the NIMH may solicit proposals at a later date for preparation of approximately 10,000 vials.

Interested parties may submit a capability statement that describes the GMP facilities, technical expertise to provide the above services, and expected timeframe for completion of services. Interested parties are requested to respond within 21 days of the date of this announcement to:

LouEllen M. Rice  
Contracting Officer  
Contracts Management Branch  
National Institute of Mental Health  
5600 Fishers Lane, Room 7C-18  
Rockville, MD 20857

#### BASIC RESEARCH ON GROWTH REGULATION IN BENIGN PROSTATIC HYPERPLASIA

RFA AVAILABLE: DK-92-13

P.T. 34; K.W. 0715105, 0760020, 0765015, 1002004, 1002008

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: November 30, 1991  
Application Receipt Date: February 18, 1992

##### PURPOSE

The Division of Kidney, Urologic and Hematologic Diseases (DKUHD) of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) announces the availability of a Request for Applications (RFA) from new and experienced investigators for research that will utilize state-of-the-art cellular, molecular, and genetic techniques to elucidate the features of prostate growth regulation that are unique to the development of benign prostatic hyperplasia (BPH). The purpose of this RFA is to gain new insights into the factors that initiate and regulate benign hyperplastic growth in normal prostatic tissues. The utilization of transgenic animal models and cell and tissue cultures that display the features of human BPH is encouraged in this RFA.

## BACKGROUND

BPH is a major cause of morbidity in the adult male. The diagnosis and treatment of this disorder contributes significantly to health care expenditures worldwide. The spontaneous initiation of the benign hyperplastic growth of the mature prostate gland is a clinical event that is unique to primates and a few other animals. Although it has been amply demonstrated that normal and abnormal prostate growth is dependant on the presence of androgens, the factors that initiate and regulate the benign hyperplastic growth of the mature prostate have not been adequately elucidated.

## RESEARCH GOALS AND SCOPE

The overall goal of this request is to increase the knowledge of the initiation and regulation of the growth of the prostate gland as it applies to the development of BPH.

The purpose of this RFA is to fund investigators who use techniques and models to go beyond the normal endocrine regulatory mechanisms already demonstrated for prostate growth and look at the role of such factors as peptide growth factors, interleukins, oncogenes, collagen synthesis, calmodulin, extracellular matrix, apoptosis, and inflammatory mediators, in the initiation and regulation of benign hyperplastic prostate growth. Applications are not limited to the aforementioned factors but must develop innovative approaches using proven findings from other spontaneous hyperplastic disorders such as keloids, adrenal hyperplasia, tissue regeneration, and mesangial cell hyperplasia.

A major goal of this initiative is to foster extensive collaboration between the various disciplines of the basic sciences including biochemistry, cellular biology, embryology, endocrinology, molecular genetics, immunology, pharmacology and physiology and research disciplines in the clinical sciences such as dermatology, nephrology, and endocrinology, in developing new models for investigating the basic science aspects of this significant clinical problem.

It is not the intent of this initiative to fund projects that will elucidate solely the structure of steroid hormone receptors in the prostate cell or further characterize only the role of the sex hormones in prostate growth. APPLICATIONS THAT UTILIZE MALIGNANT CELL LINES OR CANCER TUMOR MODELS TO REPRESENT NORMAL OR BENIGN HYPERPLASTIC GROWTH WILL NOT BE FUNDED BY THIS RFA.

Applications are strongly encouraged that investigate the interaction of the known promoters and regulators of prostate growth, such as androgens, with other factors intrinsic and extrinsic to the prostate gland, such as growth factors and interleukins.

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit, public and private organizations, such as universities, colleges, hospitals, laboratories, and eligible agencies of the Federal Government. Applications from minority individuals and from women are especially encouraged.

## MECHANISM OF SUPPORT

Support for this program will be through the traditional investigator-initiated research grant (R01). The regulations and policies that govern the research programs of the National Institutes of Health will prevail. Support will be provided for up to five years.

## FUNDS AVAILABLE

For FY 1992, \$1.25 million in total costs per year will be committed to fund applications submitted in response to this RFA. It is anticipated that five to seven awards will be made. Applicants must limit the budget requests to no more than \$160,000 in direct costs for the first year.

## APPLICATION PROCEDURES

Applications must be submitted using Form PHS 398 (rev. 10/88), available in the business or grants offices of most academic or research institutions and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, 5333 Westbard Avenue, Bethesda, MD 20892, telephone 301/496-7441.

Applications must be received by close of business on February 18, 1992.

Detailed instructions on application submission are described in the RFA.

## REVIEW PROCEDURES

Applications that are not responsive to the research goals and scope of this RFA will be returned to the investigator. Acceptable applications received in response to this RFA will first be reviewed for scientific and technical merit by an Initial Review Group convened by the Review Branch, Division of Extramural Program Activities, NIDDK. A secondary review for policy and program relevance to the NIDDK mission will be made by the National Diabetes and Digestive and Kidney Diseases Advisory Council.

## INQUIRIES

It is **IMPERATIVE** that the RFA be obtained by all prospective applicants prior to developing an application. Requests for the RFA and any other inquiries regarding it may be addressed to:

Leroy M. Nyberg, Jr., Ph.D., M.D.  
Director, Urology Program, DKUHD  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A-05  
Bethesda, MD 20892  
Telephone: (301) 496-7133  
FAX: (301) 496-9721

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.849. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 and Section 431 (b) (Public Law 78-410, as amended: 42 USC 241 and 42 USC 285c-5) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## SKIN DISEASES RESEARCH CORE CENTERS

RFA AVAILABLE: AR-92-01

P.T. 04; K.W. 0715185, 0710030

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Application Receipt Date: April 22, 1992

## BACKGROUND

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) announces the availability of a Request for Applications (RFA) for research core centers in skin diseases. The Skin Diseases Research Core Centers (SDRCs) will provide the resources for a number of established, currently funded investigators, often from different disciplines, to adopt a multidisciplinary approach to common research problems in skin diseases and to ensure greater productivity through interaction among the investigators of individually funded research projects. New research directions are encouraged through a pilot and feasibility component.

## RESEARCH GOALS AND SCOPE

Research in skin diseases is at a stage where broad advances can be effectively fostered by research core centers. Examples of advances include, but are not limited to:

- o stratum corneum: biochemistry, structure, function
- o epidermis: differentiation, keratinization, cellular constituents
- o dermal-epidermal junction: structure, functions, diseases
- o skin as an immunological organ
- o autoimmune skin diseases
- o dermis: structural components, diseases

The choice of research problems upon which the SDRC would focus is made by the Principal Investigator and collaborating currently funded investigators.

## ELIGIBILITY

Applications may be submitted by domestic, nonprofit, public and private organizations, such as universities, colleges, hospitals, laboratories, units of State or local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

The SDRC (P30) is a mechanism for integrating, coordinating, and fostering the interdisciplinary cooperation of a group of established investigators conducting programs of active, high-quality research that relate to a common theme. The SDRC provides support for:

- o Core resources and facilities to be used by investigators of individually supported research projects in order to enhance and coordinate their activities. This support may include personnel, equipment, supplies, services, and facilities.
- o Limited funds for pilot and feasibility studies.

- o Program enrichment activities.

The NIAMS intends to fund two Skin Disease Research Core Centers in FY 92, subject to the availability of resources and the receipt of sufficiently meritorious applications, each with a yearly direct cost budget of up to \$400,000. The funding period is five years.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### APPLICATION GUIDELINES

Applicants must contact the NIAMS staff for the detailed guidelines for the SDRC grant application. Applications must be submitted on Form PHS 398 (rev. 10/88), which is available in the institution's business office and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, 5333 Westbard Avenue, Bethesda, MD 20892, telephone 301/496-7441.

All PHS and NIH grant policies governing research project grants apply to applications received in response to this RFA.

#### DEADLINES

Letter of Intent receipt date: February 17, 1992  
Application receipt date: April 22, 1992  
Ad Hoc Study Section review: June/July 1992  
NIAMS Advisory Council Review: September 1992  
Anticipated award date: September 1992

#### INQUIRIES

Further information on the program, including the guidelines for the Skin Diseases Research Core Centers, may be obtained from:

Julia B. Freeman, Ph.D.  
Director, Centers Programs  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 496-7495

For fiscal and administrative matters, contact:

Mary Graham  
Grants Management Specialist  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 496-7495

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846. Grants are awarded under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal Regulations, most specifically at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or review by a Health Systems Agency.

#### OBESITY/NUTRITION RESEARCH CENTERS

RFA AVAILABLE: DK/HD-92-06

P.T. 04; K.W. 0715145, 0765020, 0710095, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases  
National Institute of Child Health and Human Development

Letter of Intent Receipt Date: January 15, 1992  
Application Receipt Date: March 25, 1992

## PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Child Health and Human Development (NICHD) announce the availability of a Request for Applications (RFA) entitled "Obesity/Nutrition Research Centers" for conducting basic and clinical research on obesity and in the related fields of energy metabolism, body composition, satiety, adipocyte metabolism, eating disorders, and weight management. These centers will be awarded in Fiscal Year 1992. The award of three Obesity/Nutrition Research Centers by NIDDK and one Obesity/Nutrition Research Center by NICHD is anticipated.

## OBJECTIVE AND SCOPE

The objectives of the Core Center are to encourage a multidisciplinary approach to research in the nutritional sciences and to bring together, on a cooperative basis, clinical and basic science investigators in a manner that will enhance and extend the effectiveness of nutritional research being conducted in the field of obesity, eating disorders, and energy regulation. To accomplish the overall goal of these centers, there must be in existence at the applicant's institution an ongoing program of excellence in biomedical research related to the study of obesity. The research base in the nutritional sciences need not be exclusively in obesity and can include a focus on eating disorders, energy metabolism, cell biology, or nutrient metabolism. It would be highly desirable that the Principal Investigator, as well as the applicant institution, have a commitment to the treatment and prevention of obesity. The availability of a clinic population with adequate representation of women and minorities which can be readily utilized by investigators will play a major role in attracting investigators to the field of obesity research and to serve as a resource in the design of pilot and feasibility projects.

## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## MECHANISM OF SUPPORT

Support of this program will be by the Core Center Grant (P30) mechanism. An average Center may include about three to five pilot/feasibility projects and two to four core units. However, the actual cost of the Center will vary depending on the needs of the Center. In no case shall direct costs requested exceed \$600,000 per year, nor shall the direct costs awarded exceed \$500,000 per year per Center. The anticipated awards will be for five years and are contingent upon the availability of appropriated funds. Currently, funds totalling approximately \$2.0 million (total costs) are available for support of this announcement. The award of three new Obesity/ Nutrition Research Centers by NIDDK and one Obesity/Nutrition Research Center by NICHD is anticipated.

## METHOD OF APPLYING

### Letter of Intent

Potential applicants are requested to submit a letter of intent by January 15, 1992. The letter of intent is non-binding, is not a necessary requirement for submission of an application, and is not a precondition for an award. Letters of intent are requested for review planning purposes. The NIDDK and NICHD will not specifically respond to such letters. Include in the letter of intent the name(s) of the Principal Investigator and principal collaborators, descriptive titles of the core facilities and pilot/feasibility projects, and the institution(s) involved. Letters of intent are to be sent to:

Robert Hammond, Ph.D.  
Chief, Review Branch  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 406  
Bethesda, MD 20892

Applications must be submitted using PHS 398 (rev. 10/88). Applications are available from the business or grants offices of most academic or research institutions and from the Office of Grants Inquiries, division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

## INQUIRIES

It is essential that prospective applicants obtain the RFA and the general description and guidelines for the Obesity Research/Nutrition Centers from:



Van S. Hubbard, M.D., Ph.D.  
Director, Nutritional Sciences Branch  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A18B  
Bethesda, MD 20892  
Telephone: (301) 496-7823  
FAX: (301) 402-1278

Gilman Grave, M.D.  
Endocrinology, Nutrition and Growth Branch  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 637A  
6130 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 496-5593  
FAX: (301) 402-2085

#### BUSINESS INFORMATION

Nancy Dixon  
Supervisory Grants Management Specialist  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 639  
Bethesda, MD 20892  
Telephone: (301) 496-7467

E. Douglas Shawver  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 501  
6130 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 496-1303

#### REVIEW PROCEDURES

Applications for the Obesity/Nutrition Research Center Grants will be evaluated for scientific merit by the NIH grant peer review process and subsequently by either the NIDDK or NICHD Advisory Council for program relevance and policy issues before awards for meritorious applications are made. The special single receipt date for submissions in response to this announcement is March 25, 1992, with the earliest funding being September 1992.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93. 848. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 and Section 431 (b) (Public Law 78-410, as amended: 42 USC 241 and 42 USC 285c-5) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### DEVELOPMENT OF BIOMARKERS OF AGING

RFA AVAILABLE: AG-91-17

P.T. 34; K.W. 0710010, 0760003, 0755018

National Institute on Aging

Letter of Intent Receipt Date: December 16, 1991  
Application Receipt Date: February 19, 1992

#### PURPOSE

The Biology of Aging Program (BAP), National Institute on Aging (NIA), announces the availability of a Request for Applications (RFA) for the development of biomarkers of aging using rodent animal models supplied by the NIA. The major goal of the research to be supported is to continue the development of a panel of rodent biomarkers of aging constituted from the biomarkers developed in response to this and a previously announced RFA (see Development of Biomarkers of Aging, NIH GUIDE For Grants and Contracts, Vol. 16, No. 19, June 5, 1987). To achieve this goal, two separate types of applications are solicited in this RFA: one type addresses the assessment of potential biomarkers of aging, and the other type addresses the statistical analyses of these potential biomarkers to provide a panel of statistically valid biomarkers useful for testing future interventions in the aging process.

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and nonprofit, public and private, such as universities, colleges, hospitals, laboratories, units of State or local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

For the purposes of continuity and to receive the full benefit of 10 years of focus and support in biomarkers of aging research, applications will be accepted from investigators in either of the following two categories related to experience with Biomarkers of Aging Research: investigators currently conducting NIA-funded Biomarkers of Aging research projects, or investigators who can demonstrate an active research focus for the previous four or more years on biomarkers of aging, regardless of the source of research support, using the same rodent genotypes as are available from the NIA/National Center for Technological Research biomarker colony described below, are able and willing to use animals from the NIA/NCTR biomarker colony, and have suitable facilities for housing these animals.

There are no similar experience restrictions on the investigators applying for the statistical analyses of biomarkers of aging research.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) research project (R01) grant funding mechanism. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Awards will be administered under PHS grants policy as stated in the Public Health Service Policy Statement, DHHS Publication No. (OASH) 82-50,000, revised October 1, 1990.

## FUNDS AVAILABLE

A total of \$2,000,000 is expected to be available for this program in FY 1993. Funds for subsequent years are expected to range from \$1,500,000 to \$2,000,000 per year. It is anticipated that individual awards will range from \$75,000 to \$150,000 per year in direct costs. Collaborative applications or applications to test more than one type of potential biomarker may request more than \$150,000 per year in direct costs with sufficient justification. A maximum of 14 awards for the Biomarker of Aging Research and one award for the Statistical Analysis of the Biomarkers of Aging Research are anticipated.

The award of grants pursuant to this RFA is contingent upon receipt of appropriated funds for this purpose. This RFA is a one-time invitation. There are no plans for future reissuance. The duration of proposed projects may be up to five years. The start date for funded projects will be approximately April 1, 1993.

## RESEARCH OBJECTIVES

This RFA is to encourage the continued development of research projects that utilize the available colony of rodents to conduct biomarker research. Two types of applications will be considered:

**Applications for Biomarkers of Aging Research:** The objective of applications submitted in response to this request must be the continued development and testing of one or more biomarkers of aging using genetically defined mice and/or rats obtained from the NIA/NCTR biomarker research colony. In order to allow for the development of a broadly based panel of biomarkers, applications are solicited from a wide variety of possible approaches.

By the final year of the proposed project, the investigator will be expected to obtain data for the proposed biomarker using non-invasive methods, and the proposed biomarker must be applicable to the human population.

The research plan for biomarker development must include evaluation of each potential biomarker for reproducibility, sensitivity, significance of rate of change over the lifespan, temporal pattern of changes, non-lethality, degree of invasiveness required, potential functional importance to human aging, simplicity, and cost-effectiveness.

As one step in a plan to implement testing of potential biomarkers, the NIA, in collaboration with the NCTR, has available a colony of four mouse genotypes and three rat genotypes as a resource for rodent biomarker research. Mice available in this colony include C57BL/6NNIA, DBA2/NNIA, B6D2F1 (C56BL/6NNIA X DBA2/NNIA), B6C3F1 (C57BL/6 X C3H) ranging in age from three to 30 months (approximately 22,000/year). Available rats include Fischer 344, Brown-Norway, and F344 X BN hybrids ranging in age from three to 24 months (approximately 6,000/year). Both male and female rodents are available. This major animal resource has provided a suitable test population for 14 investigator-initiated biomarker research projects over the previous four years. In order to allow testing of biomarker sensitivity to interventions that alter lifespan, and since dietary restriction is the only currently available intervention that reliably alters lifespan in rodents, ad libitum fed and dietary restricted animals of each genotype will be available. Diets used in the NIA/NCTR colony will be made available for shipment to investigators to assure diet continuity for all animals. Applications must include funds for diet acquisition and shipment. All NIA/NCTR animals are maintained in Specific Pathogen Free barrier facilities. Applicants must demonstrate their ability to house animals received from this colony in similar or equivalent barrier conditions. This can be achieved either with existing barrier facilities that can

be devoted to this activity, or by the use of laminar flow caging in non-barrier rooms devoted solely to this project.

Collaborative research applications from investigators will be accepted where biomarker development requires multiple research skills not available in a single institution, where collaboration enhances the value of the research conducted at the cooperating institutions or where multiple use of animals is scientifically feasible and allows significant research cost economies.

The applicant is permitted to propose studies leading to the elucidation of the physiologic or molecular mechanism(s) by which the biomarker studied constitutes a biomarker of aging, or the mechanism(s) by which caloric restriction produces lifespan extension in these animals.

Applications must clearly state the type, number, and use schedule of all animals needed for the proposed research. Where multiple or shared uses of animals are proposed, each relevant application must clearly show which animals are shared and which are not. Animals from the NIA/NCTR biomarker colony will be shipped to investigators by preferred air freight. Only costs for investigator-reared animals, if required by the proposed research design, must be included in the application. Applications that include the use of investigator-reared animals must show a clear rationale for using such animals in addition to NIA/NCTR colony animals. Applications that do not propose biomarker of aging research or that do not include the use of NIA/NCTR colony animals will not be accepted.

Applications for the Statistical Analysis of Biomarkers of Aging Research: The goal of this segment of the RFA is to bring together the results of all of the research conducted as a result of this Biomarkers of Aging Research RFA, using the procedures of mathematical statistics, to permit a statistically valid assessment of the gerontologic age of rodents of the genotype specified herein using a panel of applicable biomarkers of aging. Applicants may obtain a description of ongoing research supported by the NIA Biomarkers of Aging program from the program administrator listed in INQUIRIES of this RFA. It is anticipated that a single successful applicant will be able to accomplish this task, consequently a single award will be made.

#### SPECIAL REQUIREMENTS

In order to facilitate the achievement of this goal, the Principal Investigators of successful applications will be expected to meet annually to exchange information and to address progress and problems. Applications in response to this request should include funds for one trip each year lasting approximately three days to attend this meeting in addition to any other travel requirements.

#### REVIEW CONSIDERATIONS

Applications will be received by the NIH Division of Research Grants (DRG) and will be assigned to the NIA. Applications responsive to this RFA will be evaluated for scientific and technical merit by an initial review group that will be convened solely to review these applications. Applications judged by the NIA to be non-responsive (those not directed at the goals of this RFA) will be returned to the applicant without review. Applications may first receive a preliminary review by a subcommittee of the review panel to establish those applications deemed to be competitive. Those applications judged non-competitive will be so designated, and an abbreviated summary statement noting the major areas of concern will be sent to the Principal Investigator. Applications judged to be competitive will be given full review. Following review by the initial review group, the applications will be considered by the National Advisory Council on Aging.

The factors to be considered in the evaluation of the scientific merit of each application will be the responsiveness to the intent of this RFA, and those factors used in the review of traditional research-project grant applications and the past record of performance in biomarkers of aging research. Awards will be made on the basis of scientific merit and the need to fund applications that provide a broad spectrum of potential biomarkers.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 10/88, reprinted 9/89) must be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441; and from the NIH program administrator named below.

The RFA label available in the 10/88-9/89 revision of PHS 398 application form must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title, "Development of Biomarkers of Aging" and number must be typed on line 2 of the face page of the application form and check the YES box.

Submit a signed typewritten original of the application, including the Checklist, and four signed, exact photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892 \*\*

At time of submission, two additional copies of the application must also be sent to:

Chief SRO/OEA  
National Institute on Aging  
7201 Wisconsin Avenue  
Bethesda, MD 20892

Applications must be received by February 19, 1992. If an application is received after that date, or if it is incomplete, it will be returned to the applicant. Additional or revised material will not be accepted after the receipt date. Also, the DRG will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. Nor will the DRG accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

#### LETTER OF INTENT

Prospective applicants are encouraged to submit to the program administrator indicated below a non-binding letter of intent to apply, post-marked no later than December 16, 1991, that includes a descriptive title of the proposed research, the name, address and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of this RFA. The letter of intent is not mandatory and does not influence the review or funding decisions, but it will enable the NIA to plan the review.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Richard L. Sprott, Ph.D.  
Associate Director, BAP  
National Institute on Aging  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-4996

Direct inquiries regarding fiscal matters to:

Ms. Mary Burton  
Grants Management Specialist, GCMO  
National Institute on Aging  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-1472

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.866, Aging Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants 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.