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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 16, No. 40
December 11, 1987
NOTICE

NIH REGIONAL WORKSHOPS ON IMPLEMENTATION OF THE PHS POLICY
ON HUMANE CARE AND USE OF LABORATORY ANIMALS

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NIH REGIONAL WORKSHOPS ON IMPLEMENTATION OF THE PHS POLICY ON HUMANE CARE AND USE OF LABORATORY ANIMALS

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The National Institutes of Health, Office for Protection from Research Risks, is continuing to sponsor a series of workshops in implementing the Public Health Service Policy on the Humane Care and Use of Laboratory Animals. The workshops are open to institutional administrators, members of animal care and use committees, laboratory animal veterinarians, investigators and other institutional staff who have responsibility for high-quality management of sound institutional animal care and use programs.

Date: January 28-29, 1988
Location: Albuquerque, New Mexico

Contact:
Ms. Rynda Gibbs
University of New Mexico School of Medicine
Continuing Medical Education
815 Vassar N.E.
Albuquerque, New Mexico 87131
Telephone: (505) 277-3942

Date: March 22-23, 1988
Location: Durham, North Carolina

Contact:
Ms. Sandy Huskins or
Ms. Pat McAdams
Duke University
Creative Conference Planners
2900 Harriman Avenue
Durham, North Carolina
Telephone: (800) 845-1054 or
(919) 782-1905

Other workshops are being planned and will be announced in future issues of the NIH Guide for Grants and Contracts.

For additional information contact:
Ms. Roberta Garfinkle
Executive Assistant for Animal Welfare Education
National Institutes of Health
Office for Protection from Research Risks
Building 31, Room 4B09
Bethesda, Maryland 20892

DATED ANNOUNCEMENTS (RFPs AND RFAs AVAILABLE)

CASE CONTROL STUDY OF INDOOR RADON LEVELS, CIGARETTE SMOKING EXPOSURE AND CANCER

RFP AVAILABLE: NIH-ES-88-05

P.T. 34; K.W. 0785055, 0715035, 0715165

National Institute of Environmental Health Sciences

The Division of Biometry and Risk Assessment, National Institute of Environmental Health Sciences, is planning to initiate a case-control study of the relationship between both active and passive smoking and alpha radiation from indoor radon pollution with respect to the onset of cancer of the lung and other potential target sites that have been identified in ecologic and industrial studies. Offerors will be required to define an appropriate
population for study and design a case-control study to assess the interaction between alpha radiation from indoor radon pollution and cigarette smoke in the onset of lung cancer and cancer at other specified sites. The estimated period of performance is thirty (30) months. This thirty-month period may involve approximately 1.30 person years of professional effort, approximately 5.80 person years of technical effort and approximately 1.20 person years of clerical effort. All responsible sources may submit a proposal. A maximum of two awards is planned.

This is an announcement of an anticipated Request for Proposals. RFP-NIH-ES-88-05 will be issued on or about January 11, 1988, with a closing date for receipt of proposals set for February 22, 1988.

To receive a copy of the RFP, please supply this office with two self-addressed mailing labels. All responsible sources may submit a proposal which will be considered by the agency. Requests for copies of the RFP will be honored if received within 20 calendar days after the scheduled issue date of the RFP. Requests received after this period will be filled on a first-come, first-served basis until the supply is exhausted. The RFP package will be available upon written request to:

Velvet M. Torain
Contract Specialist
National Institute of Environmental Health Sciences
P.O. Box 12874
79 T.W. Alexander Drive, 4401 Building
Research Triangle Park, North Carolina 27709

DEVELOPMENTAL TOXICITY TESTING AND RESEARCH

RFP AVAILABLE: NIH-ES-88-01

P.T. 34; K.W. 1007009, 0775030, 0775020

National Institute of Environmental Health Sciences

The purpose of this project is to test chemical agents for their potential to cause developmental and reproductive toxicity. This project will involve two tasks. Task I provides for the screening of developmental toxicants. Task II provides for the testing of chemical agents for their potential to cause teratogenicity and developmental toxicity. Task I will consist of developmental toxicity screen studies in which 75 chemicals will be tested over the 5-year period in two species each. A study is defined as the testing of one chemical in one species; one chemical studied in two species is counted as two studies. Thus, 150 studies will be conducted under Task I. The number of pregnant animals used and the endpoints examined shall be sufficient to indicate the potential for developmental toxicity and the dose levels that will be used in a definitive teratology study. Task I shall be conducted with rats, mice, and rabbits.

Task II will involve primarily FDA Segment 2 teratology studies, although other studies such as multigeneration, FDA Segment 1 or 3, or other studies involving a research component may be required. The proposed research shall provide testing of chemical agents for their potential to cause teratogenicity and developmental toxicity. The number of studies (i.e., one conventional teratology study or its equivalent) to be carried out within the first year is estimated to be approximately 10-12. The types of chemicals may include, but not be limited to: industrial solvents, plasticizers, food preservatives and colorants, drugs, pesticides, and heavy metals. Certification of concentration of chemicals in the dosage form shall be required for 10-12 chemicals/year. Completion-type contracts are contemplated for both Task I and Task II. Proposals must be clearly identified as related to Task I or Task II. Tasks must be costed separately and separate awards may be made. A maximum of two awards is planned.

This is an announcement of an anticipated Request for Proposals. RFP-NIH-ES-88-01 is now available, with a closing date for receipt of proposals set for February 1, 1988.

Requests should reference RFP NIH-ES-88-01 and should be forwarded to:

National Institute of Environmental Health Sciences
Contracts Management Office, OAM
Attn: Ms. Elizabeth B. Ford
79 T.W. Alexander Drive, 4401 Building
P.O. Box 12874
Research Triangle Park, North Carolina 27709
AIDS involves multiple organ systems. In addition to the well known immunologic, pulmonary, gastrointestinal and neurologic manifestations of AIDS, endocrine dysfunction appears to play a significant role in the clinical picture of AIDS. Adrenal insufficiency has been reported in patients with AIDS and autopsy studies have shown evidence of adrenal necrosis and adrenal cytomegalovirus infection in some patients. Because even partial adrenal insufficiency can severely compromise recovery from catastrophic illness, such as the opportunistic infections complicating AIDS, screening of AIDS patients for adrenal insufficiency is often appropriate. Information is needed on methods and indications for optimal screening for adrenal insufficiency in AIDS patients.

In addition to dysfunction of endocrine systems in AIDS, investigation of the newly recognized endocrine-immune axis may contribute to our understanding of the pathogenesis of AIDS and other disorders of the immune system. Whereas glucocorticoids have a well established role in the immune response to infection, the ability of other hormones to directly modulate the immune response has just begun to be elucidated. Scientists have discovered that the immune and neuroendocrine systems share a set of receptors and hormones. Evidence of bidirectional communication between the endocrine and immune systems includes:

- Cells of the immune system synthesize biologically active neuroendocrine hormones in quantities adequate for physiologic significance.
- Leukocyte synthesis of ACTH and endorphins is regulated by immune stimulants, such as viruses, as well as by traditional pituitary regulators such as hypothalamic peptides and glucocorticoids.
- Leukocytes possess functional receptors for these neuropeptide hormones and the hormones specifically modulate immune responses such as antibody production, lymphocyte proliferation in response to T cell mitogens, natural killer cell activity, mononuclear cell chemotaxis, and lymphokine production.
- ACTH made by leukocytes directly influences adrenal function, and glucocorticoids have direct effects on T cell lysis and sequestration, and on lymphokine production.
- Prolactin is an immunoregulator with effects on T lymphocyte dependent antibody production, skin graft rejection, development of contact sensitivity and in vitro mixed lymphocyte reaction.
- Insulin receptors are present on T-lymphocytes and have been postulated to participate in regulation of immune responses.

The nature and mechanism of interactions between the pituitary-adrenal axis and the immune system is an important area for further investigation with direct relevance to AIDS and other disorders of immune function.

RESEARCH GOALS AND SCOPE

The goal of this RFA is to solicit multidisciplinary research in the interface between endocrinology and immunology, in order to advance our understanding of the pathogenesis of AIDS, help in the evaluation, classification, and diagnosis of AIDS, or lead to development of treatment modalities to retard the disease process and enhance immune function in patients with AIDS. Areas of investigations of interest to NIDDK include but are not limited to:

- Studies of the incidence of endocrine dysfunction in AIDS.
- Characterization of endocrine dysfunction in AIDS.
- Development of appropriate methods of diagnosis of endocrine dysfunction in AIDS.
Characterization of physiological interactions between the endocrine and immune systems including possible alterations in AIDS.

Studies of hormone production and its regulation in populations of immune cells including effects of AIDS on hormone synthesis by immune cells.

Studies of hormonal regulation of immune cell function including its alteration in AIDS.

Investigation of the immune-pituitary axis in response to somatic stimuli, such as infection, and the effects of AIDS on this process.

Studies on the immune-adrenal axis and its alteration in AIDS.

Investigation into the nature and mechanisms of corticosteroid regulation of the immune system in AIDS.

MECHANISM OF SUPPORT

The mechanism of support for this program will be the grant-in-aid (R01). Although this solicitation is included in the funding plans for Fiscal Year 1988 for NIDDK, support is contingent upon receipt of appropriated funds for this purpose. The NIDDK plans to designate a total of $1,500,000 (direct and indirect costs) for the support of applications submitted in response to this solicitation; however, the specific amount to be funded will depend upon the overall merit and scope of the applications received. It is anticipated that approximately 10 to 15 grants will be awarded under this solicitation.

REVIEW PROCEDURES AND CRITERIA

Upon receipt, applications will be reviewed by staff for their responsiveness to the objectives of this RFA. If the application is considered unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or have it considered for the regular grant program of the NIH.

Applications in response to this solicitation will be reviewed on a nationwide basis and in accord with the usual NIH peer review procedures. Applications will first be reviewed for scientific and technical merit by an Initial Review Group, which will be arranged by the Review Branch, Division of Extramural Activities, NIDDK. This group will be composed primarily of non-federal scientific consultants. The applications will then be reviewed by the National Advisory Council of NIDDK.

METHOD OF APPLYING

Applications should be submitted on form PHS 398(revised 9/86), which is available from an applicant institution's Office of Sponsored Research or from the NIH Division of Research Grants. Use the conventional format for research project grant applications and ensure that the points identified in this announcement are fulfilled. To identify the application as a response to this RFA, check "yes" on item two of page one of the application and enter the title "Endocrine Aspects of AIDS" and the RFA Number 88-DK-05. The RFA label available in the 9/86 revision of Application Form 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of your application such that it may not reach the review committee in time for review.

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

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

Two additional copies of the application are to be sent to:

Review Branch
National Institute of Diabetes and Digestive and Kidney Diseases, NIH
Westwood Building, Room 406
Bethesda, Maryland 20892**

= 4
Prospective applicants are encouraged to submit a one-page letter of intent. This letter should be received no later than February 1, 1988 and should be sent to program staff identified under inquiries below.

Applications must be received by March 15. Any applications not received by this date will be considered ineligible for this special solicitation.

APPLICATION     INITIAL COUNCIL EARLIEST
RECEIPT         REVIEW REVIEW START DATE

For further information, investigators are encouraged to contact the following office:

Judith Fradkin, M.D.
Chief, Endocrine and Metabolic Diseases Programs Branch
Division of Diabetes, Endocrinology, and Metabolic Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 603
Bethesda, Maryland 20892

Telephone: (301) 496-7791

ENDOCRINE BASIS OF WASTING IN AIDS

RFA AVAILABLE: 88-DK-06
P.T. 34; K.W. 0785050, 0715120, 0715085
National Institute of Diabetes and Digestive and Kidney Diseases
Application Receipt Date: March 15, 1988

BACKGROUND:

Wasting is a hallmark of AIDS. AIDS patients frequently experience diarrhea and malabsorption which may result from a variety of gastrointestinal pathologies including infectious agents, neoplasms and inflammatory changes. However, severe and relentless tissue wasting is seen in patients with AIDS with modest intestinal dysfunction and without diarrhea. The pathophysiology of the severe weight loss common in AIDS is poorly understood and is likely to involve mechanisms other than gastrointestinal dysfunction.

Patients with malignancy, chronic inflammatory illness or immunodeficiency are often cachetic. The cachexia may occur when the tumor or parasite burden is small and may persist despite adequate caloric intake. There is a growing awareness that endogenous mediators are essential elements in the pathogenesis of wasting diatheses. Cachexin (tumor necrosis factor) is a macrophage hormone originally isolated in the course of studies aimed at delineating basic mechanisms of cachexia in chronic disease. Its metabolic effects include suppression of the expression of lipoprotein lipase (LPL) and several other adipose specific enzymes. Cachexin thus prevents the uptake and storage of exogenous triglyceride and causes a net loss of triglyceride from fat. Cachexin is not the only monokine which suppresses LPL; interleukin-1 also has this effect. Tumors produce a variety of hormones that exert metabolic effects and result in well-recognized paraneoplastic syndromes. Tumor-derived growth factors also affect the metabolic responses of target cells. Whether cell derived peptides play a role in mediating the wasting diathesis of AIDS remains to be established.

RESEARCH GOALS AND SCOPE

In some chronic diseases, the timing of death is likely to be determined as much by the body's energy reserve as by the activity of the disease process itself. Severe weight loss of itself can impair the function of the immune system and affect the susceptibility of individuals to infection. Thus severe weight loss contributes significantly to the morbidity and mortality of AIDS.

This RFA is intended to stimulate research which will elucidate the endocrine and metabolic basis of wasting in AIDS with the ultimate goal of developing strategies to reverse the wasting diathesis of AIDS.

Areas of investigation of interest to NIDDK include but are not limited to:

- The role of cachexin and/or other monokines in the pathogenesis of wasting in AIDS and other chronic diseases;
Identification of hormones, growth factors, lipid mobilizing factors or other peptides which may contribute to wasting in AIDS;

Identification and characterization of aberrant metabolic patterns in AIDS such as homeostatic responses to decreased fuel intake;

Regulation of lipolysis and lipogenesis in AIDS and identification and characterization of specific abnormalities of lipid metabolism;

Regulation of muscle mass and nitrogen balance in AIDS;

Studies of whether abnormalities in insulin secretion or sensitivity may be involved in decreased fat stores in AIDS.

MECHANISM OF SUPPORT

The mechanism of support for this program will be the grant-in-aid (R01). Although this solicitation is included in the funding plans for Fiscal Year 1988 for NIDDK, support is contingent upon receipt of appropriated funds for this purpose. The NIDDK plans to designate a total of $750,000 (direct and indirect costs) for the support of applications submitted in response to this solicitation; however, the specific amount to be funded will depend upon the overall merit and scope of the applications received. It is anticipated that approximately 5 to 8 grants will be awarded under this solicitation.

REVIEW PROCEDURES AND CRITERIA

Upon receipt, applications will be reviewed by staff for their responsiveness to the objectives of this RFA. If the application is considered unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or have it considered for the regular grant program of the NIH.

Applications in response to this solicitation will be reviewed on a nationwide basis and in accord with the usual NIH peer review procedures. Applications will first be reviewed for scientific and technical merit by an Initial Review Group, which will be arranged by the Review Branch, Division of Extramural Activities, NIDDK. The applications will then be reviewed by the National Advisory Council of NIDDK.

METHOD OF APPLYING

Applications should be submitted on form PHS 398 (revised 9/86), which is available from an applicant institution's Office of Sponsored Research or from the NIH Division of Research Grants. Use the conventional format for research project grant applications and ensure that the points identified in this announcement are fulfilled. To identify the application as a response to this RFA, check "yes" on item two of page one of the application and enter the title "Endocrine Basis of Wasting in AIDS" and the RFA Number 88-DK-06. The RFA label available in the 9/86 revision of Application Form 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of your application such that it may not reach the review committee in time for review.

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

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

Two additional copies of the application are to be sent to:

Review Branch
National Institute of Diabetes and Digestive and Kidney Diseases, NIH
Westwood Building, Room 406
Bethesda, Maryland 20892XX

Prospective applicants are encouraged to submit a one-page letter of intent. This letter should be received no later than February 1, 1988 and should be sent to program staff identified under inquiries below.

Applications must be received by March 15. Any applications not received by this date will be considered ineligible for this special solicitation.
APPLICATION INITIAL COUNCIL EARLIEST RECEIPT REVIEW REVIEW START DATE

For further information, investigators are encouraged to contact the following office:

Judith Fradkin, M.D.
Chief, Endocrine and Metabolic Diseases Programs Branch
Division of Diabetes, Endocrinology, and Metabolic Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 603
Bethesda, Maryland 20892
Telephone: (301) 496-7791

NIH SMALL INSTRUMENTS GRANTS PROGRAM
P.T. 34; K.W. 0735000
National Institutes of Health
Application Receipt Date: February 16, 1988

BACKGROUND

In its appropriation for the NIH for Fiscal Year 1987, the Congress included a total of $16 million to be spent by the respective Bureaus, Institutes, and Divisions (BIDs) for the funding of grants to purchase small instruments costing between $5,000 and $60,000. This action was in response to several recent studies of the problem of obsolete biomedical research instrumentation indicating that the state of biomedical research instrumentation has seriously eroded over the last ten years and that this situation is retarding the progress of biomedical research. The most significant need identified in these studies is for the relatively low-cost pieces of equipment in the price range of approximately $5,000 to $60,000.

It is anticipated that funds, at approximately last year's level, will be available for small instrumentation grants this year.

ELIGIBILITY AND TERMS OF AWARD

Each institution that received support under the Biomedical Research Support Grant (BRSG) Program in Fiscal Year 1987 and currently has active NIH research grants is eligible to apply. Only one application may be submitted from each eligible institution or organizational unit. Each institution may establish its own procedures for identifying equipment requests to be included.

The small instrumentation award will be restricted to the purchase of equipment costing between $5,000 and $60,000. Awards will be made on or before September 30, 1988. The amount of the award will be based upon a percentage of the institution's Biomedical Research Support Grant award for Fiscal Year 1987 or $5,000, whichever is greater. Specific funding decisions will depend on available BID appropriations as well as the appropriateness of the request. Institutions will be notified of the maximum amount for which they may apply.

METHOD OF APPLYING

Letters of instruction have been mailed to eligible institutions.

Completed applications must be received by February 16, 1988.

Investigators interested in participating in their institution's application must contact the institution's Biomedical Research Support Grant Program Director. Institutional officials who expect to be involved in preparing an application are requested to review the letter of instruction prior to contacting NIH.
BIOMEDICAL RESEARCH SUPPORT GRANT APPLICATIONS FOR FISCAL YEAR 1988

P.T. 34; K.W. 0710030, 1014002
Division of Research Resources
Application Receipt Date: January 6, 1988

BACKGROUND

The Biomedical Research Support Grant (BRSG) Program is designed to provide funds to eligible institutions (i.e., those heavily engaged in health-related research) to strengthen their programs by allowing flexibility to meet emerging opportunities in research; to explore new and unorthodox ideas; and to use these research funds in ways and for purposes which, in the judgment of the grantee institution, would contribute most effectively to the furtherance of their research program.

ELIGIBILITY

Awards are made to non-profit institutions, not directly to individual investigators. Health professional schools, other academic institutions, hospitals, state and municipal health agencies, and research organizations may apply, if during FY 1987 (October 1, 1986 through September 30, 1987), the institution was awarded a minimum of three allowable PHS biomedical or health-related behavioral research grants and/or cooperative agreements, totaling $200,000 (including direct and indirect costs). Federal institutions, foreign institutions, and profit-making institutions are not eligible.

NOTE: "Other academic institutions" includes, as a single eligible component, all other schools, departments, colleges and free-standing institutes of the institution other than the health professional schools of a university.

AWARD CONDITIONS

The BRSG award is for one year with eligibility determined annually. The start date is April 1. Awards are contingent upon the availability of funds.

The amount of each BRSG award is based upon a formula that is applied to the total costs awarded for allowable PHS research grants.

METHOD OF APPLYING

BRSG application kits (Form NIH-147-1) will be mailed on or about November 27 to institutions that, according to NIH records, are eligible to apply for a BRSG.

Completed BRSG applications must be received by January 6, 1988.

If an institution believes that it is eligible and has not received an application kit, please submit a letter of request to:

Mrs. Gilda Polletto
Grants Management Specialist
Office of Grants and Contracts Management
Division of Research Resources
Building 31, Room 5B32
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

This program is described in the Catalog of Federal Domestic Assistance, No. 13.337, Biomedical Research Support. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (a)(3); Public Law 86-798, (42 USC 241) and administered under PHS grant policies and Federal Regulations 45 CFR Part 74 and the Biomedical Research Support Grant Information Statement and Administrative Guidelines. This program is not subject to the intergovernmental review requirements of the Executive Order 12372 or Health Systems Agency review.
SMALL GRANTS FOR INNOVATIVE TECHNOLOGY

P.T. 34; K.W. 0706000, 0735000, 1004000, 1013020

Division of Research Resources

Application Receipt Dates: February 1, October 1

The Biomedical Research Technology (BRT) Program identifies and develops advanced technologies needed in biomedical research. Through grants and contracts, it supports an extremely broad and innovative array of technologies. Areas of emphasis in the Program are biomedical computing, biomedical engineering, and technologies for the study of biomolecular and cellular structure and function. To further its mission, the BRT Program supports a small grant award for support of pilot studies in relevant biomedical technologies.

DESCRIPTION OF THE AWARD

This is a one-year, non-renewable award for a pilot project in a high technology in engineering, instrumentation, physics or computer science related to biomedical research. The project should involve a feasibility study of an innovative or high risk idea in a high technology. Innovative is considered to be an unusually imaginative or a drastically different approach to a problem. High risk is having uncertain chances for success because no historical base exists for a proposed technological approach. High technology is defined here as working at the limits of understanding of a technology. The project should be oriented towards new instrumental or methodological approaches and provide a basis for more extended research in the project's technology.

The purposes of the small grants program are to:

1. Provide an opportunity to test new ideas in a high technology that will lead to a larger research project or implementation of the technology in a working environment; or

2. Develop significant changes in an existing high technology important to biomedical research; or

3. Translate scientific notions into a basis for a future technology.

The award may not be used to supplement support for an ongoing project. Because of the high risk, feasibility nature of the proposals, support of stipends for student dissertation research is discouraged.

ELIGIBLE APPLICANTS

This program is open to both non-profit and for profit organizations and is designed to support engineers and other scientists for work in high technological projects in the biomedical research area.

APPLICATION AND REVIEW PROCEDURE

Applications should be submitted on Form PHS 398, available at most institutional business offices or from the Division of Research Grants, NIH. Because the format for preparing this application is different from that used for regular research grants, additional information and instructions should be obtained from the BRT Program staff contact listed below. Applications must adhere to this format to be responsive. Unresponsive applications will be returned to the applicant without review. The review schedule is:

<table>
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<tr>
<th>Receipt Date</th>
<th>Institute Committee</th>
<th>Council</th>
<th>Earliest Date</th>
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<td>October 1</td>
<td>November-December</td>
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REVIEW CRITERIA

Applications will be evaluated using the following criteria: adequacy of scientific merit; characterization as an innovative or high risk pilot project in a high technology in engineering, instrumentation, physics or computer science related to biomedical research; probability the study will provide a basis for more extended research in the relevant technology; adequacy of
proposed experimental methods, equipment or materials; adequacy of the investigator's background and training; adequacy of the available and requested facilities; and adequacy of budget justifications.

Those criteria which are emphasized in the review of small grant applications are:

- adequacy of scientific merit,
- degree of innovation evident in the proposed approach, and
- degree of risk or uncertain chance of success because no historical base exists for the proposed technological approach.

FUNDING CRITERIA

Applications will compete with each other in accordance with the purposes of the small grant program. Approximately 10 to 20 awards are made per year, contingent on receipt of meritorious applications and appropriated funds.

TERMS OF THE AWARD

The award will provide a maximum of $25,000 (direct costs) for personnel, consultants, supplies, small equipment, and travel required by the project. The award will be for one year, and in most cases can be extended for an additional year without additional funds.

INSTRUCTIONS FOR APPLICANTS

Additional instructions are needed to prepare a small grant application. These are supplementary to those given with PHS 398 (Rev. 9/86). To receive these instructions, please contact:

Caroline Holloway, Ph.D.
Head, Biological Structure Section
Biomedical Research Technology Program
Division of Research Resources
National Institutes of Health
Building 31 - Room 5B41
9000 Rockville Pike
Bethesda, Maryland 20892
Telephone: (301) 496-5411

This program is described in the Catalog of Federal Domestic Assistance No. 13.371, Biotechnology Research. Awards will be made under the authority of the Public Health Service Act, Title 111, 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 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency reviews.

ALCOHOL AND ENDOCRINOLOGICAL DEVELOPMENT IN ADOLESCENTS

P.T. 34, AA; K.W. 0404003, 0785050

National Institute on Alcohol Abuse and Alcoholism
Alcohol, Drug Abuse, and Mental Health Administration

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

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) seeks grant applications for the support of research addressing problems related to the effects of alcohol on endocrine and psychosexual development and on normal reproduction, growth and brain function as they relate to endocrine function in adolescents.

BACKGROUND

The prevalence of adolescent drinking is a major cause for concern, because alcohol abuse in this special population may have adverse physiological and developmental consequences with far-reaching effects into adulthood. The initiation of puberty involves a complex cascade of events in the hypothalamic-pituitary-gonadal axis. Animal studies suggest that chronic ethanol ingestion by juveniles and adolescents can affect one or more components of the system, leading to delayed sexual maturation and/or impaired reproductive function. Other aspects of adolescent development such as physical growth are also under endocrine control and may be affected by exposure to alcohol. Research is needed to further our understanding of endocrine processes and the impact of ethanol on them.
RESEARCH GOALS

The purpose of this announcement is to encourage research proposals which will examine the consequences of adolescent alcohol consumption on endocrine development and functioning, and on the processes regulated by the endocrine system, including sexual maturation and reproductive functions, growth, and behavioral functions. Basic studies utilizing appropriate animal models may focus on endocrine development at the organ, cellular, and molecular levels with emphasis on progressive changes with age, from weaning to maturity. Clinical studies may focus on basic or applied research on the etiology and pathogenesis of alcohol-induced endocrine dysfunction and related disorders in adolescent populations. The inclusion of young women and minorities in the study populations, where appropriate, is encouraged.

Examples of potential research under this announcement include, but are not limited to, the following:

- Studies on the induction, progression, or reversibility of alcohol-induced hormone imbalance in the hypothalamic-pituitary-gonadal axis and the impact on sexual maturation of prepubertal males and females
- Epidemiological studies on the influence of alcohol on age of menarche and prevalence of menstrual disorders in adolescent girls
- The impact of prepubertal alcohol exposure on reproductive function following puberty
- Relationship between prepubertal alcohol exposure and abnormal endocrine-related emotional and behavioral development associated with sexual maturation
- Studies to determine the nature and severity of endocrine dysfunction in relation to the age at which drinking begins and the duration of alcohol exposure
- The role of impaired or altered endocrine functioning, subsequent to prepubertal or adolescent alcohol exposure, on the modulation of alcohol consumption behaviors and on the addictive potential of alcohol
- The influence of alcohol on bone growth and skeletal muscle development of adolescents
- Nutritional consequences of adolescent alcohol abuse as it relates to altered endocrine functioning and manifestations of abnormal organ system function
- Studies to determine the relationship between neuroendocrine modulation of neurotransmitter processes and ethanol-induced cognitive and affective impairment in adolescents
- The impact of alcohol consumption in juveniles and adolescents on neuroendocrine regulation of immune system reactivity

APPLICATION AND REVIEW PROCEDURES

Applications may be submitted by any public or private nonprofit or profit-making organization and by eligible agencies of the Federal government. Women and minority investigators are encouraged to apply. Support may be requested for a period of up to 5 years. Annual awards will be made subject to continued availability of funds and progress achieved. Grant funds may be used for expenses clearly related to and necessary to carry out the research project. Research grant support is not provided to establish, add a component to, or operate a prevention, intervention or treatment program. Grants must be administered in accordance with the PHS Grants Policy Statement (Rev. 1/87).

Applications should be submitted on form PHS-398, available from the National Clearinghouse for Alcohol and Drug Information, Reference Department, 6000 Executive Boulevard, Suite 402, Rockville, Maryland 20852 or at most academic and research institutions.

Applications will be accepted in accordance with the usual receipt dates for new applications on an indefinite basis.
Grant Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
533 Westbard Avenue
Bethesda, Maryland 20892

Applications recommended for approval by the National Advisory Council on Alcohol Abuse and Alcoholism will be considered for funding on the basis of overall scientific and technical merits as determined by peer review, NIAAA programs needs and balance, and the availability of funds. In FY 1988 approximately $500,000 will be available to support approximately 4 grants under this announcement. Applications of high scientific merit which cannot be funded under this announcement may be considered for funding under the Institute's regular research grant programs.

Further information and consultation on program requirements can be obtained from:

Helen M. Chao, Ph.D.
Chief, Biomedical Research Branch
Division of Basic Research, NIAAA
5600 Fishers Lane, Room 14C-20
Rockville, Maryland 20857
Telephone: (301) 443-4223

This program is described in the Catalog of Federal Domestic Assistance No. 13.273. Grant awards are made under the authority of Section 301 of the Public Health Service Act (42 USC 241, 290bb and 290cc). Applications submitted in response to this announcement are not subject to the intergovernmental review requirements of Executive Order 12372, as implemented through Department of Health and Human Service regulations at 45 CFR Part 100.

RESEARCH GRANTS RELATED TO BATTEN DISEASE AND OTHER NEURONAL CEROID LIPOFUSCINOSES

P.T. 34; K.W. 0705055, 0715000, 0755030, 1002019, 0745020, 0785165

National Institute of Neurological and Communicative Disorders and Stroke

This solicitation is a reissuance of the announcement that appeared in this Guide on October 10, 1986.

The Developmental Neurology Branch, Division of Convulsive, Developmental and Neuromuscular Disorders, National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) encourages the submission of traditional research project grant applications (R01) related to the etiology, developmental embryology, pathogenesis, genetics and prevention of the ceroid lipofuscinoses, particularly the juvenile type known as Batten disease or Spielberg-Sjogren disease.

BACKGROUND

The ceroid lipofuscinoses are a group of hereditary degenerative diseases in which an autofluorescent lipopigment, ceroid, accumulates in the central nervous system and other tissue. Clinically they are characterized by a progressive encephalopathy, loss of vision, seizures, and a downhill course. There are three childhood types of ceroid lipofuscinosis and one, possibly two, adult types. Although in general these types are clinically distinct, combined and transitional forms occur. The ceroid lipofuscinoses are inherited in autosomal recessive fashion with the exception of one rare adult type which shows autosomal dominant transmission.

The juvenile type, or Batten disease, exemplifies the devastating effects that these disorders have on affected individuals and their families. Onset is between 5 and 10 years usually with visual failure and seizures, and the...
The course is that of a slowly progressive encephalopathy leading to death in 8-10 years. Pathologically the brain shows moderate atrophy. There is massive accumulation of ceroid in neurons and macrophages, in the ganglionic layer of the retina, and in other tissues. The etiology of Batten disease is unknown; its incidence is about 3 per 100,000 births. There is no effective therapy.

RESEARCH GOALS AND SCOPE.

The goal of this program announcement is to encourage research to delineate clinical and genetic types of the ceroid lipofuscinoses, to identify and localize the gene(s) responsible for them, to determine the biochemical defects that result from the action of these genes, and to develop measures for the prevention, early diagnosis and treatment of these disorders.

The research scope of this program encompasses the developmental, genetic and biochemical aspects of the ceroid lipofuscinoses, particularly the juvenile type or Batten disease, and a variety of experimental approaches and methods. Some examples are given below, but applications are not limited to them, and proposals with new ideas and initiatives would be welcome.

1. Subjects

These may include experimental animals and human subjects. Animal mutants in particular could greatly facilitate research and provide direct and crucial information about the etiology, developmental embryology, pathogenesis and genetics of the ceroid lipofuscinoses. Animal models exactly comparable to the human disease should also make possible the determination of the basic metabolic defect, detection of early biochemical changes, characterization of the chemical pathology and recognition of the heterozygous carriers.

2. Pathology

Precise characterization of the pathological changes is highly desirable. Examination by computerized scanning procedures and neuroimaging techniques may be useful in identifying early intracranial changes.

3. Biochemistry

Very little is known about the biochemistry of the ceroid lipofuscinoses in general and Batten disease in particular. It is not known if the presence of lipofuscin, which is normally found in the brain of older individuals, is a causal or associated defect. A disturbance of dolichol metabolism has been reported in patients with Batten disease, but its relation to the presence of lipofuscin or to the disease itself is not clear. Biochemical studies should be pursued at the cellular and molecular level with state-of-the-art precise and sensitive techniques of immunochemistry and membrane microchemistry, tissue culture, and the high resolution methodology of rapid flow microfluorimetry and two-dimensional electrophoresis.

4. Genetics

Classical genetic studies have not resolved whether or not the conventional clinical classification, based mainly on age of onset, represents different forms of the same genetic disorder. Further genetic studies, using advanced molecular and biochemical genetic techniques are needed to resolve this question, and to identify and map the gene or genes involved.

5. Detection of the genetic carrier

Identification of a biochemical marker should make possible heterozygote detection, prenatal diagnosis and early clinical recognition of cases, and thus lead to prudent management and treatment.

MECHANISM OF SUPPORT

Support for this program will be through the traditional research grant-in-aid. Successful applicants will direct and carry out the individual research projects. Applicants from institutions which have a General Clinical Research Center (GCRC) funded by the NIH Division of Research Resources may wish to identify the Center as a resource for conducting the proposed research. In such a case, a letter of agreement from the GCRC Program Director should be included in the application material.
APPLICATION AND REVIEW PROCEDURES

Applications should be prepared on Form PHS 398 (revised 9/86) according to instructions contained in the application kit. Application kits are available from most institutional business offices, or may be obtained from the Division of Research Grants (DRG), at the address given below. Check "Yes" in item 2 on the face sheet of the application and type "Grants related to Batten Disease" in the space provided.

The original and six copies of the application should be mailed to the following address:

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

Deadline dates for the receipt of individual research grant (R01) applications are October 1, February 1, and June 1.

For further information applicants may contact:

Dr. Ntinos C. Myrianthopoulos
National Institute of Neurological and Communicative Disorders and Stroke
National Institutes of Health
Federal Building - Room 8C-04
Bethesda, Maryland 20892
Telephone: (301) 496-5820

This program is described in the Catalog of Federal Domestic Assistance No. 13.853, Clinical Basis Research, NINCDS. Awards will be made under the authority of the Public Health Service Act, Title IV, 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. This program is not subject to Health Systems Agency Review.

***THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:

5333 Westbard Avenue
Bethesda, Maryland 20816