EARTH-BASED RESEARCH RELEVANT TO THE SPACE ENVIRONMENT

Release Date: April 6, 2000

PA NUMBER: PA-00-088

National Institute on Aging
National Institute on Alcohol Abuse and Alcoholism
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute on Deafness and Other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute on Drug Abuse
National Institute of Environmental Health Sciences
National Institute of General Medical Sciences
National Heart, Lung, and Blood Institute
National Institute of Neurological Disorders and Stroke
National Aeronautics and Space Administration

THIS PA USES THE "MODULAR GRANT" AND "JUST-IN-TIME" CONCEPTS. IT INCLUDES DETAILED MODIFICATIONS TO THE STANDARD APPLICATION INSTRUCTIONS THAT MUST BE USED WHEN PREPARING APPLICATIONS IN RESPONSE TO THIS PA.

PURPOSE

The purpose of this Program Announcement (PA) is to stimulate ground-based research on basic, applied, and clinical biomedical and behavioral problems that are relevant to human space flight or that could use the space environment as a laboratory. Although none of the research supported under this initiative would be conducted in space, it is anticipated that it would form a basis for future competitively reviewed studies which could be conducted on the International Space Station, or other space flight opportunities, by skilled on-board specialists.

HEALTHY PEOPLE 2010

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople/.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal government. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as principal investigators.

MECHANISM OF SUPPORT

The mechanism of support will be the individual research project grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. For all competing individual research R01 applications requesting up to $250,000 direct costs per year, specific application instructions have been modified to reflect "MODULAR GRANT" and "JUST-IN-TIME" streamlining efforts by NIH. Complete and detailed instructions and information on Modular Grant applications can be found at: http://grants.nih.gov/grants/funding/modular/modular.htm. Applications that request more than $250,000 in any year must use the standard PHS 398 (rev. 4/98) application instructions.

RESEARCH OBJECTIVES

Space flight affords a unique opportunity to study and characterize basic biological and behavioral mechanisms in the absence of gravity, one of the fundamental forces that shapes life on earth. In addition, space flight presents unique environmental stressors to the individual, and the study of responses to these stressors will provide new insights into how organisms adapt. Over the last several decades, space flight and ground-based research have been used to learn about basic biological mechanisms. Observations of astronauts have indicated a number of significant effects, such as post-flight orthostatic intolerance, cephalic shifts in fluid distribution, loss of muscle and bone mass, various sensory-motor changes, modifications of immunological functions, human factors challenges, and alterations in circadian and sleep rhythms. In some cases, changes associated with space flight are similar to clinical conditions on Earth and/or parallel changes associated with aging. A potent new laboratory for pursuing these and other questions will be the International Space Station (ISS). The ISS will permit long-term, uninterrupted access to the space environment to conduct basic biological, medical, and behavioral studies using skilled on-board specialists.

The major objective of this Program Announcement is to stimulate basic, applied, and clinical biomedical and behavioral ground-based research that is relevant to human space flight or to advancing our understanding of the effects of the space environment on biological systems. Potential areas of research could include neuroscience, musculoskeletal biology, immunology, cardiovascular functioning, integrative physiology, cognition and problem solving under stress and isolation, pharmacokinetics, drug metabolism and drug delivery, and the diagnosis and treatment of diseases or injury by both ground support and space flight crews. Use of hyper- or hypo-gravity, as research tools or models, is encouraged. Access to NASA facilities may be provided. Applicants interested in using NASA facilities should consult the "NASA Ground Facilities Information Package". This document provides description of available facilities and the NASA contacts for information and can be accessed at: http://peer1.nasaprs.com/peer_review/nra/life_science/00_OBPR_01/00_OBPR-01_GFIP.pdf. (Note: If typing this URL use underscores to connect the apparent spaces). Applicants wishing to use any of these facilities must contact the appropriateNASA official to plan their experiments. It is anticipated that ground-basedresearch supported through this PA may ultimately lead to the submission of space flight proposals to the National Aeronautics and Space Administration. Research proposals should take into account past biomedical and fundamental research already conducted during space flight. Applicants are advised to review literature sources specific to space flight such as the Spaceline website on Medline at http://spaceline.usuhs.mil/ and the Space Studies Board (SSB) report entitled "A Strategy for Research in Space Biology and Medicine in the New Century" available on-line at: http://bob.nap.edu/readingroom/books/spacebio/.

Research Goals and Scope

The National Institute on Aging (NIA), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Deafness and Other Communication Disorders (NIDCD), National Institute of Dental and Craniofacial Research (NIDCR), National Institute of Neurological Diseases and Stroke (NINDS), National Institute on Drug Abuse (NIDA), National Institute of Environmental Health Sciences (NIEHS), National Institute of General Medical Sciences (NIGMS), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Heart, Lung, and Blood Institute (NHLBI), and National Aeronautics and Space Administration (NASA) encourage submission of applications that include, but are not limited to, the following possible areas of ground-based research that may lead to future space flight experiments, utilizing both animal and human subjects.

Spatial Orientation and Sensory-Motor Processes

The space environment affects sensory perception, sensory-motor transformations, and motor performance. Examination of sensory systems on the single system or multisystem level, in both humans and animals, would serve to advance our understanding of how the nervous system integrates information, carries out sensory-motor transformations, and functions under normal conditions, across the life-span, as well as under the special conditions of space travel. Specific areas of research relevant to gravity and space flight could include:

- Role of binaural auditory cues in spatial orientation and localization;
- Role of gravity in development of the vestibular system and of balance control;
- Central adaptation of vestibular functions;
- Vestibular autonomic regulation and dysregulation;
- Role of vestibular inputs in spatially-directed and non-spatial human cognition;
- Sensory structures and neural pathways;
- Adaptation of sensory-motor systems;
- Eye movements, including vestibular-ocular responses and neural storage and integration of sensory-motor and spatial coordinate information;
- Postural control
- Spatial navigation;
- Sensory-motor integration, including ability to adapt to altered sensory and motor conditions, and temporal coordination of complex activities, such as gait and reaching.

Nervous System

Research grant applications are encouraged from the full spectrum of the neuroscience community. The essential feature of any proposal would be that it addresses fundamental questions of biology and health sciences that might be elucidated by further research in microgravity and/or be related to sustaining the human presence in space. Examples of potential topics or research areas include:

- Autonomic control of blood pressure;
- Development of the central nervous system;
- Cerebral homeostasis and intracranial pressure changes;
- Neuronal plasticity;
- Gene transfer gene delivery, gene targeting, and gene expression in the nervous system utilizing viral (retroviral, adenoviral, adeno-associated virus, lentivirus, and herpes simplex virus) and nonviral vectors (liposomes and naked DNA);
- Neuroendocrine function;

o Chemosensory (taste and smell) changes that might affect food intake and flavor perception of food during space flight.

Behavioral and Psychological Processes

Long-duration missions in space are likely to produce significant changes in individual, group, and organizational behavior. Future missions in space will involve longer periods of exposure to features of the physical environment unique to space and features of the psychosocial environment characteristic of isolated and confined environments. Relevant research conducted in ground-based analogue environments could include, but are not limited to:

o Development of noninvasive qualitative and quantitative techniques for the ongoing assessment of preflight, in-flight, and postflight behavior and performance;
o Investigation of the neurobiological and psychosocial mechanisms underlying the effects of physical and psychosocial environmental stressors on cognitive, affective, and psychophysiological measures of behavior and performance;
o Studies on the effects of the space flight environment, through ground-based analogues, upon higher cognitive function, learning, memory, reasoning, and associated physiological and neural models;
o Effects of space flight associated stress on behavior and performance;
o Research on the affective and cognitive responses to microgravity-related changes in perceptual and physiological systems and behavioral responses to perceived physical dangers, restricted privacy and personal space, and physical and social monotony;
o Research on specific coping strategies and behavioral and physiological indicators of coping-stage transitions during long-duration missions; associations between general and mission-specific personality characteristics and performance criteria of ability, stability, and compatibility; changes in problem-solving ability and other aspects of cognitive performance in flight; and changes in personality and behavior postflight;
o Studies on the influence of crew psychosocial heterogeneity on crew tension, cohesion, and performance during a mission; factors affecting ground-crew interactions; and the influence of different styles of leadership and decision-making procedures on group performance;
o Research on the effect of differences in the cultures of the participating agencies on individual and group performance and behavior; the association between mission duration and changes in behavior and performance; and the organizational requirements for effective management of long-duration missions as they relate to task scheduling and workload and to the distribution of authority and decision making.

Musculoskeletal System

Research is encouraged that elucidates the effects of gravity on the musculoskeletal system. Particular emphasis is placed on developing mechanism-related hypotheses encompassing basic, applied, and clinical science. While the ultimate research focus is on reduced gravity conditions, well-justified studies on musculoskeletal responses to forces greater than 1 g may be instrumental in predicting the pathogenesis of bone and skeletal muscle weakness and loss during exposure to microgravity environments. Examples of research activities include, but are not limited to the following:

o Studies addressing microgravity-induced osteopenia and skeletal muscle atrophy in whole animal and human experiments;

o Understanding the cellular mechanisms whereby alterations in the musculoskeletal system are evoked in response to external loading and loading histories;

o The role of mechanical forces, including weight, on cellular processes and regulatory factors that control turnover of matrix and contractile proteins;

o Characterization of bone loading in bed rest subjects and the effects of bed rest, inactivity, or disuse on older vs. younger subjects;

o Elucidating the etiology of the pathogenesis of bone loss and skeletal muscle weakness during exposure to an altered gravity environment and predictive indices for prevention and treatment of bone and skeletal muscle loss from microgravity exposure;

o Hormonal and growth factor effects on bone and muscle cell function and metabolism in relation to gravity effects;

o Bone and muscle cell responses to altered mechanical stress and gravity;

o Evaluation of 3-D structure and integrity of the musculoskeletal system and constituent tissues in response to changes in gravity;

o Bone and muscle cell gene expression, including characterization of cellular receptors, signal transduction, and messengers in response to gravity changes;

o Alterations in blood flow and its impact on cellular metabolism in microgravity;

o Development of therapeutic agents that restore bone, muscle, and cartilage function and mass lost due to space travel;

o Motor unit loss (mechanisms, degree of loss, and muscle fiber loss);

o Role of specific types of exercise and overload in preventing muscle loss and rehabilitation of muscle;

o Trophic (anabolic/catabolic) factors and their interactions with muscle activity;

o Role of nutrition on muscle mass;

o Effect of microgravity, bed rest, and aging on recruitment of muscle groups;

o Effects of changes in connective tissue on muscle function and fluid distribution;

o Role of neural vs. muscular changes on force production and balance;
o Comparison of the effects of aging on flexor, extensor, and grasping musculature, and how these changes relate to changing muscle activity patterns;
o Effects of bed rest, inactivity, or disuse on older vs. younger men and women;
o Interactions with other systems, including: a) Muscle forces and their influence on bone; b) Changes in proprioceptors; with aging and microgravity or bed rest; c) Role of muscle in defining total peripheral resistance as it relates to orthostatic hypotension;
o Changes in calciotropic hormones and calcium metabolism;
o Uncoupling of bone remodeling; decreased efficiency of intestinal calcium absorption;
o Enhanced propensity for falls and fractures (such as after return of space-flight crew members to Earth);
o The lighting environment and its influence on Vitamin D synthesis;
o How loading and exercise can maintain or modify bone density;
o Understanding the factors that regulate bone cell function and activity;
o Defining nutritional and environmental factors that maximize retention of bone;
o Developing countermeasures to bone loss;
o Influence of skeletal muscle chemical signals on bone growth;
o Vascularity of muscle fibers including blood vessel regression, remodeling, and adaptation;
o Basic research on the physiologic changes of bone and skeletal muscle in cell and tissue cultures that occur in a low or high gravity environment.

Pulmonary Function

Space flight causes changes in the pulmonary system by mechanisms that are not yet fully understood. Research is needed on lung defense mechanisms, such as immune and inflammatory responses to foreign substances, basic lung cell biologic activities, lung mechanisms, as well as on hemodynamic changes in the lung vasculature. For example, microgravity environments could help us understand the:
o Progression of pneumonia and other opportunistic lung infections;
o Basic cellular processes of chemotaxis, migration, proliferation, and phagocytosis; leukocyte transmigration, T-cell motility, and water and solute transport across lung alveolar cells;
o Defense mechanisms, such as cilia movement, mucus formation, bronchomotor tone, and motility as they relate to clearance of foreign substances from the lungs and airways;
o Cellular and molecular mechanisms of oxygen radical formation and antioxidant enzyme activity;
o Underlying processes of remodeling, cell-matrix interactions, and induction of the expression of differentiation-specific genes;

o Effect of microgravity on various lung cell types and how cell growth and repair is affected in this environment. Also, determine the effect of weightlessness on aerosol distribution throughout the airway and lung and how macrophages handle aerosol particles in zero gravity conditions using simulations and models;
o Pulmonary microvascular permeability changes that could lead to space flight-induced pulmonary edema;
o Pulmonary vascular tone and responsiveness to pulmonary vasoactive mediators;
o Whether fundamental neurobiological transduction properties from lung receptors are influenced or altered by microgravity;
o Basic mechanisms by which physical forces affect lung cells, including epithelial cells, fibroblasts, and pulmonary endothelial and smooth muscle cells.

Cardiovascular Function

Exposure to microgravity degrades the cardiovascular system. One example is autonomic changes, such as altered baroreceptor reflex function, which contribute to post-flight orthostatic dysfunction. The conditions of the space environment can provide a novel laboratory to examine a number of basic and clinical problems, such as the following:
o Study of the biophysics of functional attributes of cell signaling pathways in the cardiovascular system, with particular emphasis on the effect of zero gravity on vicinal water at the macromolecular interface. This would require an integrated effort by molecular geneticists, protein chemists, biochemists, biophysicists, and physiologists to design a compact experiment(s) using nonlinear approaches to design and analysis;
o Prediction of the effects of space travel in human subjects on: mean arterial, systolic, and diastolic blood pressure and pulse pressure using noninvasive ambulatory blood pressure monitoring; serum lipid subfractions; body mass index; forearm vascular resistance; electrocardiographic parameters through cardiac noninvasive chest wall and limb leads, and assessing rhythmic changes (e.g., nocturnal dipping) over 24-hour periods of time;
o Microvascular permeability leading to space flight-induced plasma volume reduction;
o Vascularity of muscle fibers including blood vessel regression, remodeling, and adaptation;
o Vascular tone and responsiveness to vasoactive agonists;
o Cerebral cortical blood flow across the life span;
o The time-dependent development of high blood pressure in animal models at various ages and predictions of whether microgravity is protective or a risk factor for hypertension;
o Role of various intermediate phenotypes, such as salt sensitivity or sympathetic nerve activity (utilizing skin microneurography), on blood pressure regulation;

o Identify possible cardiovascular adaptations to microgravity during the early developmental stages of life during space flight and upon return to the earth;
o Autonomic function, including the baroreceptor reflex, arrhythmias, and responses to orthostatic stress;
o Peripheral vascular changes, including vascular/endothelial reactivity and stiffening;
o Vestibular/autonomic nervous system interaction;
o Interaction with circadian rhythms.

Sleep and Biological Rhythms

Poor sleep is common on space missions, and even on long-term missions, insomnia is prevalent to the extent of impairing judgment and the excessive use of hypnotic medications. Microgravity decreases the need to tonically activate upper airway muscles. Alterations in upper airway control may develop during space flight and increase the risk of hypoventilation during sleep and sleep fragmentation upon return to earth gravity. Research is needed to determine:
o The long and short-term adaptations of the airway to microgravity; the influence of zero gravity on automatic processes such as respiratory rate, heart rate, and circadian rhythms;
o The occurrence and mechanisms of periodic breathing, dyspnea, and sleep apnea in space; continued characterization of sleep parameters, circadian processes, and the role of sleeping medications;
o Whether the responses of the circadian and sleep-wake systems to the altered gravity environment characteristic of space flight change with age;
o Will altering circadian/sleep cycles change the response of the organism to the new gravity environment;
o What are the precise neurobehavioral deficits associated with the sleep loss and/or circadian disruptions of space flight and aging;
o What are the behavioral and pharmacological interventions/countermeasures to attenuate/reverse the circadian rhythm and sleep effects characteristic of aging and space flight.

Immunology

Space flight causes changes in the immune system by mechanisms that are not yet fully understood. Most of the data examining the effects of space flight on immune function have examined T-cell function, primarily the proliferatve response to mitogens. For example, microgravity environments could help us understand the:

o Factors in the space environment and aging that cause immunological change, such as altered T-cell responses, as evidenced by decreased proliferation and decreased DTH responses, and altered cytokine production;
o Use of space flight to provide a unique opportunity to investigate the initiation of immune dysregulation and its reversibility, and to determine whether the cumulative effects of prolonged space flight result in long-term or irreversible conditions similar to aging;
o Assessment of changes in immune response, time course, and resistance to opportunistic infection;
o Study of the relationship between immune responses and neuroendocrine parameters regulated by the circadian and sleep systems;
o Effects of microgravity on immune responses in cellular and animal models of disease.

Pharmacodynamics/Pharmacokinetics

While the complex biobehavioral effects of pharmacological compounds generally have been well characterized in ground-based studies, the cognitive, psychomotor, and other biobehavioral effects of drugs may be quite different when they are ingested during space flight. Because it is known that astronauts ingest a wide variety of pharmacological agents during space flight for conditions including nausea, anxiety, sleep disturbances, pain, and headache, it will be important to characterize their effects in microgravity environments. Research is needed in such issues as:
o Detecting current or recent medication use events;
o Monitoring physiological sequelae of medication use in ambulatory humans for the occurrence of disorientation, cardiovascular, or respiratory instability after medication or other drug use in space;
o Monitoring and assessing behavioral and cognitive ability in weightless conditions;
o Assessing the pharmacokinetics of pharmacological compounds in space;
o Effects of microgravity on drug delivery; novel drug delivery systems designed for the unique conditions of space flight.

Hemodynamics

Many components of hematologic system are affected by microgravity. Loss of red blood cell mass and hemoglobin content is a consistent response to near-weightlessness. Changes in lymphocyte function and a resulting weakening of the immune system are also known to occur:

o Microgravity may be used in developing models of innovative regulatory mechanisms affecting gene expression, such as the production of cells of hematopoietic lineage originating in the spleen and bone marrow;
o Regulation of hemoglobin S gene expression as it is altered by several DNA-binding substances, and the control of the deleterious effects of hemoglobin S production;
o Regulation of globin gene expression relevant to sickle cell disease and other hemoglobinopathies;
o Determine the formation of platelet microaggregates, platelet activation, and effects of weightlessness on endothelial function;
o Platelets stored in a microgravity environment display superior structural and functional integrity as compared to platelets stored under normal gravitational conditions. Research into the storage of the formed elements of the blood under microgravity conditions could potentially be useful for extending viability of transfusion products.

Injury

Organ systems and tissues function synergistically. A greater understanding is needed of integrative physiology, particularly the normal homeostatic mechanisms and how they are altered in individuals under the stress of hostile environments like space flight. Also, even under ideal situations, severe injury produces alterations in the integrative physiology of a host and many of the biological processes listed elsewhere in this Program Announcement. The probability of serious trauma on a prolonged space mission is high. The appropriate treatment on earth may be inappropriate under the extreme environmental conditions presented in space. Thus, research is needed to understand how the physical and psychological realities of microgravity and space flight will intersect with the body's response to injury. Research is encouraged on the basic science principles of the clinical management of injury during space flight including, but not limited to:
o Fluid and cardiovascular resuscitation;
o The physiology of all forms of shock and compensatory mechanisms;
o Surrogate markers for routine clinical assessments;
o Bioengineering principles allowing detailed monitoring of physiological processes either on site or from remote settings;
o Delineation of the physiological changes dictating the shift from acute to long-term responses to injury, including shunting of regional blood flow, hyper-metabolic responses, altered nutritional needs, compromised gut function including changes in intestinal microflora, pulmonary considerations such as ventilation requirements and techniques and acid aspiration, hepatobilliary function including drug metabolism and response to toxic agents;

o The initiation of and response to infection (either localized to the wound or systemic), including host defense mechanisms and increased understanding how the physical nature of microbial growth in humans (biofilms) may be altered by microgravity;
o Better understanding of the common complications of injured or critically ill patients, including Systemic Inflammatory Response Syndrome (SIRS), sepsis, Acute Respiratory Distress Syndrome (ARDS), and Multiple Organ Dysfunction Syndrome (MODS);
o Analysis and control of wound healing and tissue repair of soft and hard tissue;
o Use of tissue engineering principles towards fostering and promoting healing and restoration of normal function following injury;
o Consideration of the psychological, emotional, and cognitive aspects of the response to injury.

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and in the NIH Guide for Grants and Contracts, Volume23, Number 11, March 18, 1994, and is available on the web at the following URL address:
http://grants.nih.gov/grants/guide/notice-files/not94-100.html

Investigators also may obtain copies of the policy from the program staff listed under INQUIRIES. Program staff may provide additional information concerning the policy.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS.

It is the policy of NIH that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" that was published in the NIH Guide for Grants and Contracts, March 6, 1998, and is available at the following URL address: http://grants.nih.gov/grants/guide/notice-files/not98-024.html.

NOTE FOR APPLICATIONS FOCUSED ON AGING RESEARCH

Some applications received in response to this program announcement are expected to focus on scientific issues related to aging and to aging-related aspects of disease. In describing the plan to recruit human subjects investigators may cite a focus on aging or on aging-related aspects of disease as the justification for why children will be excluded. In this regard applicants may use Justification 1, the research topic to be studied is irrelevant to children, from the policy announcement.

URLS IN NIH GRANT APPLICATIONS OR APPENDICES

All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Reviewers are cautioned that their anonymity may be compromised when they directly access an Internet site.

APPLICATION PROCEDURES

Applications are to be submitted on grant application form PHS 398 (rev. 4/98). and will be accepted at the standard application deadlines as indicated in the application kit. Application kits are available at most institutional offices of sponsored research and may be obtained from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, Phone (301) 435-0714, Email: GRANTSINFO@NIH.GOV. Applications are also available on the internet at http://grants.nih.gov/grants/funding/phs398/phs398.html.

Applicants planning to submit an investigator-initiated new (type 1), competing continuation (type 2), competing supplement, or any amended/revised version of the preceding grant application types requesting $500,000 or more in direct costs for any year are advised that they must contact the Institute or Center (IC) program staff before submitting the application,

i.e., as plans for the study are being developed. Furthermore, applicants must obtain agreement from the IC staff that the IC will accept the application for consideration for award. Finally, applicants must identify, in a cover letter sent with the application, the staff member and Institute or Center who agreed to accept assignment of the application.

This policy requires applicants to obtain agreement for acceptance of both any such application and any such subsequent amendment. Refer to the NIH Guide for Grants and Contracts, March 20, 1998 at: http://grants.nih.gov/grants/guide/notice-files/not98-030.html

The program announcement title and number must be typed on line 2 of the face page of the application form and the YES box must be marked.

USE OF NASA FACILITIES. Proposals that include the use of NASA facilities must be accompanied by a letter from the appropriate NASA official certifying that the proposed use of the facilities is feasible and can be implemented. The cost for the use of the NASA facilities must be included in the proposal budget.

Submit a signed, typewritten, original of the application, including the checklist and five signed photocopies in one package to:

CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040-MSC 7710
BETHESDA, MD 20892-7710
BETHESDA, MD 20817 (for express/courier service)

SPECIFIC APPLICATION INSTRUCTIONS FOR MODULAR GRANTS

The modular grant concept establishes specific modules in which direct costs may be requested as well as a maximum level for requested budgets. Only limited budgetary information is required under this approach. The just-in-time concept allows applicants to submit certain information only when there is a possibility for an award. It is anticipated that these changes will reduce the administrative burden for the applicants, reviewers and Institute staff. The research grant application form PHS 398 (rev. 4/98) is to be used in applying for these grants, with the modifications noted below.

BUDGET INSTRUCTIONS

Modular Grant applications will request direct costs in $25,000 modules, up to a total direct cost request of $250,000 per year. (Applications that request more than $250,000 direct costs in any year must follow the traditional PHS 398 application instructions.) The total direct costs must be requested in accordance with the program guidelines and the modifications made to the standard PHS 398 application instructions described below:

PHS 398

o FACE PAGE: Items 7a and 7b should be completed, indicating Direct Costs (in $25,000 increments up to a maximum of $250,000) and Total Costs [Modular Total Direct plus Facilities and Administrative (F&A) costs] for the initial budget period. Items 8a and 8b should be completed indicating the Direct and Total Costs for the entire proposed period of support.

o DETAILED BUDGET FOR THE INITIAL BUDGET PERIOD - Do not complete Form Page 4 of the PHS 398. It is not required and will not be accepted with the application.

o BUDGET FOR THE ENTIRE PROPOSED PERIOD OF SUPPORT - Do not complete the categorical budget table on Form Page 5 of the PHS 398. It is not required and will not be accepted with the application.

o NARRATIVE BUDGET JUSTIFICATION - Prepare a Modular Grant Budget Narrative page. (See http://grants.nih.gov/grants/funding/modular/modular.htm for sample pages.) At the top of the page, enter the total direct costs requested for each year. This is not a Form page.

o Under Personnel, list key project personnel, including their names, percent of effort, and roles on the project. No individual salary information should be provided. However, the applicant should use the NIH appropriation language salary cap and the NIH policy for graduate student compensation in developing the budget request.

For Consortium/Contractual costs, provide an estimate of total costs (direct plus facilities and administrative) for each year, each rounded to the nearest $1,000. List the individuals/ organizations with whom consortium or contractual arrangements have been made, the percent effort of key personnel, and the role on the project. Indicate whether the collaborating institution

is foreign or domestic. The total cost for a consortium/contractual arrangement is included in the overall requested modular direct cost amount. Include the Letter of Intent to establish a consortium.

Provide an additional narrative budget justification for any variation in the number of modules requested.

o BIOGRAPHICAL SKETCH - The Biographical Sketch provides information used by reviewers in the assessment of each individual's qualifications for a specific role in the proposed project, as well as to evaluate the overall qualifications of the research team. A biographical sketch is required for all key personnel, following the instructions below. No more than three pages may be used for each person. A sample biographical sketch may be viewed at: http://grants.nih.gov/grants/funding/modular/modular.htm.

- Complete the educational block at the top of the form page;
- List position(s) and any honors;
- Provide information, including overall goals and responsibilities, on research projects ongoing or completed during the last three years;
- List selected peer-reviewed publications, with full citations.

o CHECKLIST - This page should be completed and submitted with the application. If the F&A rate agreement has been established, indicate the type of agreement and the date. All appropriate exclusions must be applied in the calculation of the F&A costs for the initial budget period and all future budget years.

o The applicant should provide the name and phone number of the individual to contact concerning fiscal and administrative issues if additional information is necessary following the initial review.

REVIEW CONSIDERATIONS

Applications will be assigned on the basis of established Public Health Service referral guidelines. Applications that are complete will be evaluated for scientific and technical merit by an appropriate peer review group convened in accordance with NIH peer review procedures. As part of the initial merit review, all applications will receive a written critique and undergo a process in which only those applications deemed to have the highest scientific merit, generally the top half of

applications under review, will be discussed, assigned a priority score, and receive a second level review by the appropriate national advisory council or board.

Special Note

As described in APPLICATION PROCEDURES, proposals that include the use of NASA facilities will be accompanied by a letter from the appropriate NASA official certifying that the proposed use of the facilities is feasible and can be implemented. The cost for the use of the NASA facilities will be included in the proposal budget. The ground-based studies selected for funding through this initiative should form the basis for future space flight research. However, at the appropriate time, NIH PIs will be provided the format for flight proposals and invited to submit space-based applications to NASA. International Science Merit Panels will review these and those found to be scientifically meritorious would go through International Technical Review. Both NIH and NASA then will prioritize them based upon merit, technical risk, program relevance, and funding availability.

Review Criteria

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments reviewers will be asked to discuss the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, weighting them as appropriate for each application. Note that the application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

Significance: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

Approach: Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

Innovation: Does the project employ novel concepts, approaches or method? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

Investigator: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

The initial review group will also examine: the appropriateness of proposed project budget and duration; the adequacy of plans to include both genders, children and minorities and their subgroups as appropriate for the scientific goals of the research, or the justification for their exclusion; plans for the recruitment and retention of subjects; the provisions for the protection of human and animal subjects; and the safety of the research environment.

AWARD CRITERIA

Applications will compete for available funds with all other recommended applications. The following will be considered in making funding decisions:

- Quality of the proposed project as determined by peer review
- Availability of funds
- Program priority
- Relevance and technical feasibility of proposed research for future space applications.

INQUIRIES

Inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Andrew A. Monjan, Ph.D., M.P.H.

Neurobiology of Aging Branch
Neuroscience and Neuropsychology of Aging Program
National Institute on Aging
7201 Wisconsin Avenue, Suite 3C307, MSC- 9205
Bethesda, MD 20892-92-5
Telephone: (301) 496-9350
FAX: (301) 496-1494
Email: am39m@nih.gov

Daniel A. Sklare, Ph.D.
Hearing and Balance/Vestibular Sciences Branch
Division of Extramural Research
National Institute on Deafness and Other Communication Disorders
Executive Plaza South, Room 400C
6120 Executive Blvd., MSC-7180
Bethesda, MD 20892-7180 (for regular mail)
Rockville, MD 20852 (for express/courier mail)
Telephone: (301) 496-1804
FAX: (301) 402-6251
Email: daniel_sklare@nih.gov

Richard W. Lymn, Ph.D.
Muscle Biology Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS49E
Bethesda, MD 20892-6500
Telephone: (301) 594-5128
FAX: (301) 480-4543
Email: lymnr@exchange.nih.gov

James P. Kiley, Ph.D.
Director, Division of Lung Diseases
National Heart, Lung and Blood Institute
6701 Rockledge Drive, Room 10018
Bethesda, MD 20892-7952
Telephone: (301) 435-0233
FAX: (301) 480-3557

Email: kileyj@nih.gov

Jaylan S. Turkkan, Ph.D.
Chief, Behavioral Sciences Research Branch
National Institute on Drug Abuse
6001 Executive Blvd, MSC 9555
Bethesda, MD 20897
Telephone: (301) 435-1318
FAX: (301) 594-6043
Email: jturkkan@nida.nih.gov

Antonio Noronha, Ph.D.
Division of Basic Research
National Institute on Alcohol Abuse and Alcoholism
6000 Executive Blvd., MSC 7003
Bethesda, MD 20892-7003
Telephone: (301) 443-7722
FAX: (301) 594-0673
Email: anoronha@mail.nih.gov

Scott D. Somers, Ph.D.
Division of Pharmacology, Physiology, and Biological Chemistry
National Institute of General Medical Sciences
Natcher Building, Room 2As.49A
45 Center Drive, MSC 6200
Bethesda, MD 20892-6200
Telephone: (301) 594-5560
FAX: (301) 480-2802
Email: somerss@nigms.nih.gov

William J. Heetderks, M.D., Ph.D.
Neural Prosthesis Program
National Institute of Neurological Disorders and Stroke
Neuroscience Center, Room 2207
6001 Executive Boulevard
Bethesda, MD 20892-9525
Telephone: (301) 496-1447

FAX: (301) 480-1080
Email: Heet@nih.gov

Kenneth Gruber, Ph.D.
Chronic Diseases Branch
National Institute of Dental and Craniofacial Research
Natcher Building, Room 4AN-24
Bethesda, MD 20892-6402
Telephone: (301) 594-4800
FAX: (301) 480-8318
Email: Kenneth.Gruber@nih.gov

Carol Shreffler, Ph.D.
Program Administrator, Training and Career Development Programs
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-1445
FAX: (919) 541-5064
Email: shreffl1@niehs.nih.gov

David R. Liskowsky, Ph.D.
Lead Scientist
Fundamental Biology Program
Life Sciences Division, Code UL
National Aeronautics and Space Administration
300 E Street, SW
Washington, DC 20546
Telephone: (202) 358-1963
FAX: (301) 358-4186
Email: dliskows@hq.nasa.gov

Direct inquiries regarding fiscal matters to:

Joe Ellis
Grants and Contracts Management Office

National Institute on Aging
7201 Wisconsin Avenue, Suite 2N212, MSC 9205
Bethesda, MD 20892-9205
Telephone: (301) 496-1472
FAX: (301) 402-3672
Email: ellisj@exmur.nia.nih.gov

Sharon Hunt
Grants Management Branch
Division of Extramural Research
National Institute on Deafness and Other Communication Disorders
Executive Plaza South, Room 400C
6120 Executive Blvd., MSC-7180
Bethesda, MD 20892-7180 (for regular mail)
Rockville, MD 20852 (for express/courier mail)
Telephone: (301) 402-0909
FAX: (301) 402-1758
Email: sh79f@nih.gov

Sally A. Nichols
Grants Management Officer
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS 49F
Bethesda, MD 20892-6500
Telephone: (301) 594-3535
FAX: (301) 480-5450
Email: nicholss@exchange.nih.gov

Raymond Zimmerman
Grants Operation Branch
Division of Extramural Affairs
National Heart, Lung and Blood Institute
6701 Rockledge Drive, Room 7154
Bethesda, MD 20892-7926
Telephone: (301) 435-0171
FAX: (301) 480-3310
Email: zimmermr@nih.gov

Gary Fleming, J.D., M.A.
Grants Management Branch
National Institute on Drug Abuse
6001 Executive Blvd., Room 3131, MSC 9541
Bethesda, MD 20892-9541
Telephone: (301) 443-6710
FAX: (301) 594-6847
Email: gf6s@nih.gov

Antoinette Holland
Grants Management Office
National Institute of General Medical Sciences
Natcher Building, Room 2AN50B
45 Center Drive, MSC 6200
Bethesda, MD 20892-6200
Telephone: (301) 594-5132
FAX: (301) 480-1852
Email: hollanda@nigms.nih.gov

Judy Simon
Grants Management Branch
National Institute on Alcohol Abuse and Alcoholism
6000 Executive Blvd., MSC 7003
Bethesda, MD 20892-7003
Telephone: (301) 443-2434
FAX: (301) 443-3891
Email: js182@nih.gov

Brenda Kibler
Grants Management Specialist
National Institute of Neurological Diseases and Stroke
Neuroscience Center, Room 3268
6001 Executive Boulevard
Bethesda, MD 20892
Telephone: (301) 496-7441
FAX: (301) 402-0219

Email: bk29j@nih.gov

Martin Rubinstein
Office of Grants Management
National Institute of Dental and Craniofacial Research
Natcher Building, Room 4AN-44A
Bethesda, MD 20892-6402
Telephone : (301) 594-4800
FAX : (301) 480-8301
Email : Martin.Rubinstein@nih.gov

Dorothy G. Duke
Chief Grants Management Officer
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709
Telephone : (919) 541-274
FAX: (919) 541-2860
Email: duke3@niehs.nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.866 (NIA), 93-846 (NIAMS), 93.837, 93.838, 93.839 (NHLBI), 93.273 (NIAAA), 93.853 (NINDS), 93.279 (NIDA), 93.173 (NIDCD), 93.113 (NIEHS), 93.859 (NIGMS) and 93.121 (NIDCR). Awards are made under authorization of sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and administered under NIH grants policies and Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant and contract recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Return to Volume Index

Return to NIH Guide Main Index