

BONE FORMATION AND CALCIFICATION IN CARDIOVASCULAR DISEASE

Release Date: January 2, 2001

RFA: RFA-HL-01-014

National Heart, Lung, and Blood Institute

(<http://www.nhlbi.nih.gov>)

National Institute of Arthritis and Musculoskeletal and Skin Diseases

(<http://www.nih.gov/niams/>)

Letter of Intent Receipt Date: February 15, 2001

Application Receipt Date: March 19, 2001

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

PURPOSE

The objective of this initiative is to stimulate research that addresses the pathophysiologic and molecular mechanisms of vascular calcification, and the possible links between vascular calcification, bone formation, and cardiovascular disease. Suggested research areas for this initiative include: (a) the relationship between cardiovascular disease, osteoporosis, and related pathologies and the delineation of potential mechanisms of vascular calcification and bone mineralization; and (b) the determination of the effects of statins, bisphosphonates, and other commonly used therapeutic agents on the skeleton and the cardiovascular system.

Collaborations among investigators from the cardiovascular and bone research communities are strongly encouraged as are multidisciplinary approaches including molecular, cellular and whole animal studies which can be applied to the human condition.

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 Request for Applications (RFA), "Bone Formation and Calcification in Cardiovascular

Disease", 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 domestic and foreign, 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

This RFA will use the National Institutes of Health (NIH) research project grant (R01) award mechanism. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for an application submitted in response to this RFA may not exceed four years. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures. The anticipated award date is September 30, 2001.

Specific application instructions have been modified to reflect "MODULAR GRANT" and "JUST-IN-TIME" streamlining efforts being examined by the NIH. Complete and detailed instructions and information on Modular Grant applications can be found at <http://grants.nih.gov/grants/funding/modular/modular.htm>.

FUNDS AVAILABLE

The National Heart, Lung, and Blood Institute (NHLBI) intends to commit approximately \$2.0 million total costs and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) intends to commit approximately \$1.0 million total costs in FY 2001 to fund up to 9 new grants in response to this RFA. An applicant may request a project period of up to four years and a budget for total direct costs of up to 10 modules (\$250,000) per year. Because the nature and scope of the research proposed may vary, it is anticipated that the size of each award will also vary. Although the financial plans of the NHLBI and NIAMS provide support for this program, awards pursuant to this RFA are contingent upon the availability of funds and the receipt of a

sufficient number of meritorious applications. At this time, it is not known if this RFA will be reissued.

RESEARCH OBJECTIVES

Background

The high visibility and commercialization of a non-invasive, more sensitive method to measure vascular calcification has focused national attention on the role of calcification in the development and progression of cardiovascular disease. Calcification is a common feature of atherosclerotic plaques and may lead to clinical complications, including myocardial infarction, impaired vascular tone, and coronary insufficiency caused by loss of aortic recoil. Calcification of valves is one of the leading reasons for valve replacement in patients with symptomatic aortic stenosis.

Recent intriguing observations suggest that rapid advancement in our understanding of the basic mechanisms involved in the initiation and progression of vascular and valvular calcification is now possible. Historically, this ectopic calcification was considered a degenerative process leading to passive precipitation of calcium phosphate. New findings strongly suggest that ectopic mineralization is part of an active ongoing process, rather than the result of passive degeneration. The concept of regulated vascular calcification suggests the presence of cellular and molecular determinants of ectopic calcification, natural inhibitors of ectopic calcification, and regulators of resorption.

Somewhat surprisingly, preliminary studies to probe the molecular mechanisms of vascular calcification have suggested parallels with bone formation. Cells with both osteoblastic (bone forming) and osteoclastic (bone resorbing) potential have been described in vascular tissue, and bone-related proteins have been identified in calcified arterial and valvular lesions. The recent progress in understanding the molecular mechanisms involved in bone formation and resorption suggest potential new mechanisms that may be involved in vascular calcification. Bone-related proteins also may play some protective role against vascular calcification since mice genetically engineered to be deficient in specific bone-related proteins have developed extensive vascular calcifications. Thus, the complex mechanisms involved in vascular calcification are not known, but if vascular calcification is regulated in a manner similar to bone and bone is constantly being remodeled, perhaps vascular calcification is also constantly being remodeled through similar complex processes.

Paradoxically, patients with vascular calcification which has the same composition as bone mineral hydroxyapatite, may experience osteoporotic loss of bone mineral. The reciprocal build up and loss of the calcium mineral in two locations in the same patient suggests that neither process is attributable to simple systemic calcium excess or deficiency. The potential for involvement of the estrogen receptors, immune system, and/or collagen in the calcification process exists, but their roles in the calcification paradox are not known. Several studies have reported an association between low bone mass and cardiovascular disease. More recently, an association was found between low bone mass and the risk of mortality from cardiovascular disease later in life. Studies to determine if patients with cardiovascular disease have low bone mass due to osteoporosis are not available. The association between low bone mass and cardiovascular disease suggests that strategies to prevent osteoporosis might prevent the development of cardiovascular disease as well.

In some types of osteoporosis, there is an elevated number of marrow adipocytes and a paucity of osteoblasts. Since marrow stromal cells contain a common progenitor cell population for both adipocytes and osteoblasts, the observed cellular population of osteoporotic bone may be related to an increased adipogenic differentiation at the expense of osteogenic differentiation. Oxidized lipids, a known factor in atherogenesis, appear to promote adipogenesis and may stimulate osteoclasts resulting in enhanced bone resorption. Oxidized lipids, then, may be one potential mechanism for the paradoxical coincidence of vascular mineralization with bone loss. If significant in the human disease process, lipid-lowering drugs and antioxidants might have beneficial effects in individuals susceptible to osteoporotic bone loss.

Phenotypic expression of coronary calcium deposition in asymptomatic, but high-risk adult human subjects appears to be dependent on ethnic origin. A lower prevalence of coronary calcification is found in black subjects as compared with white subjects with a similar extent of atherosclerosis. Bone density and cardiovascular risk are known to differ by ethnicity. The mechanisms responsible for these ethnic differences are not known.

Preliminary results from inbred strains of mice suggest the presence of common factors that could determine susceptibility to atherosclerosis and osteoporosis. Strains of mice that are very susceptible to the development of atherosclerotic lesions have the lowest values for bone mineral density, whereas those resistant to the development of atherosclerotic lesions have the highest values for bone mineral density. The basic underlying mechanisms and the factors involved with these differences in atherosclerosis susceptibility and bone formation/resorption have not been identified.

Several members of the statin drug family, long recognized as effective in lowering cholesterol levels and reducing cardiovascular risk, recently have been shown to have significant effects on bone. Statins can directly induce new bone formation in cell cultures and animal models, and some studies suggest that statin use may reduce fracture risk. Though still preliminary, these findings suggest another possible link between cardiovascular disease and bone remodeling. Whether statins influence the development of vascular calcification is not known. The mechanism of the statin induction of bone formation remains unclear, but may be related to complex down-stream effects on sterol synthesis. Since the available drugs for treating osteoporosis generally only prevent further bone loss rather than stimulating new bone formation, these recent findings may open up new areas of research as well as a new era in the prevention and treatment of osteoporosis.

Amino-bisphosphonates are widely used to block bone resorption. Although the exact mechanism of action of amino-bisphosphonates is not well understood, there is evidence to suggest that they may act, in part, by inhibiting the lipid modification of signaling proteins. The anti-resorptive action of bisphosphonates, along with the observation of potentially resorptive cells in some instances of vascular calcification, raises the possibility that bisphosphonates could potentially exacerbate cardiovascular disease in some patients. Therefore, the overall health benefits of bisphosphonates, including both bone and cardiovascular effects, needs systematic investigation.

Although there are several lines of evidence linking vascular calcification, bone formation and cardiovascular disease; much of the evidence is suggestive, rather than definitive, and the mechanisms involved as well as their regulation are unknown. The basic cellular and molecular processes involved in the initiation and progression of vascular calcification need to be identified. At present, there is no direct way to prevent or treat the development of vascular calcification. Given the links between bone cell differentiation and cardiovascular disease, an entirely new approach to treating cardiovascular disease could emerge. Thus, this initiative should result in insights leading to new areas for disease prevention and intervention.

Research Scope

This RFA will support research into the pathophysiology and molecular mechanisms of vascular calcification, and the possible links between vascular calcification, bone formation, and cardiovascular disease. It is expected that progress in these areas will require the integration of insights from both vascular biology and skeletal biology. Thus, to be considered responsive to

this initiative, applications must demonstrate the potential to draw on techniques, concepts, existing information, or new investigations from both the skeletal and vascular areas of research.

This interdisciplinary character may be achieved in a number of different ways. For example, the efforts of investigators with complementary expertise may be integrated within a single application, using sub-contracts if necessary to extend support to scientists at different institutions. Alternatively, if a substantial body of work already exists in one tissue or disease area, a team specializing in the other area may be able to meet the standard of responsiveness without proposing overtly interdisciplinary studies. For example, proposed studies of cardiovascular physiology or atherosclerosis that would take place in an existing clinical cohort that was originally developed for studies of the skeletal system would be responsive if results can be correlated with the skeletal parameters that have already been determined. Similarly, it may be valuable to study the skeletal system of a genetically modified animal model developed for studies of atherosclerosis that is already well characterized with respect to its cardiovascular phenotype.

The following areas are of interest. This list is illustrative and is not intended to exclude other investigations that are consistent with the overall purpose of this initiative.

- o Differences and similarities between the mechanisms of vascular mineralization and bone formation (e.g., cell types involved, gene expression patterns, regulatory factors). Variation of this comparison with different types of vascular mineralization (e.g. atherosclerotic lesions, valve implants).

- o Influence of lipid metabolism on bone, and parallels with its influence on calcification in vascular tissue. Role of oxidized lipids in bone metabolism and vascular calcification.

- o Possible parallels and interactions between bone remodeling and vascular maintenance and repair. Possible presence of osteoclast-like resorptive function in vascular tissue.

- o Comparison of bone and vascular responses to pharmacological agents with beneficial effects in one of these diseases such as statins and bisphosphonates with emphasis on mechanistic studies and early responses as well as pathophysiology. Determine whether bisphosphonates exacerbate or reduce vascular calcification.

o Studies to determine whether osteoporosis (bone loss) and vascular calcification or atherosclerosis progress in parallel. Correlations between cardiovascular disease and osteoporosis with respect to incidence, progression, or outcomes. Dependence of correlation on gender, race, or ethnicity; common and distinguishing genetic and environmental risk factors.

EXCLUSIONS

This RFA is intended to support R01 programs that draw on techniques, concepts, existing information, or new investigations from both the skeletal and vascular areas of research. Therefore, proposed research examining only vascular calcification or only bone development will not be considered responsive to this RFA. New epidemiological studies or large clinical trials are beyond the scope of this initiative. Ancillary studies to ongoing clinical trials or epidemiologic studies would be considered. Proposed research examining lipids or lipid oxidation and atherosclerosis or calcification without including a connection to osteoporosis or bone development will not be considered responsive to this RFA.

SPECIAL REQUIREMENTS

Upon initiation of the program, annual meetings will be held in Bethesda, MD, to encourage exchange of information among investigators who participate in this program. A major goal of these meetings is to facilitate progress by providing a forum that will lead to sharing ideas, technology, data, skills, and biological materials. Applicants must budget for travel funds that will allow Principal Investigators and other key research scientists as appropriate to participate in these meetings.

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 are provided indicating 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 UPDATED "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research," published in the NIH Guide for Grants and Contracts on August 2, 2000

(<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html>); a complete copy of the updated Guidelines are available at http://grants.nih.gov/grants/funding/women_min/guidelines_update.htm. The revisions relate to NIH defined Phase III clinical trials and require: a) all applications or proposals and/or protocols to provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) all investigators to report accrual, and to conduct and report analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

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>.

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

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.

LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NHLBI and NIAMS staff to estimate the potential review workload and plan the review.

The letter of intent is to be faxed, E-mailed, or mailed to Dr. Deborah Beebe at the address listed under INQUIRIES by February 15, 2001.

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 4/98) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301/435-0714, email: GrantsInfo@nih.gov.

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.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS

BUDGET INSTRUCTIONS

Modular Grant applications will request direct costs in \$25,000 modules, up to a total direct cost request of 10 modules (\$250,000) per year. 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 all 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 all 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.

The RFA label available in the PHS 398 (rev. 4/98) application form must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked.

The sample RFA label available at: <http://grants.nih.gov/grants/funding/phs398/label-bk.pdf> has been modified to allow for this change. Please note this is in pdf format.

Submit a signed typewritten original of the application, including the Checklist, and three 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)

At the time of submission, two additional copies of the application must be sent to Dr. Deborah Beebe at the listing under INQUIRIES.

Applications must be received by the application receipt date listed in the heading of this RFA. If an application is received after that date, it will be returned to the applicant without review.

The Center for Scientific Review (CSR) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the NHLBI and NIAMS. Incomplete and/or non-responsive applications will be returned to the applicant without further consideration.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the NHLBI in accordance with the review criteria stated below. 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 will be discussed, assigned a priority score, and receive a second level review by the National Heart, Lung, and Blood National Advisory Council and/or the National Institute of Arthritis and Musculoskeletal and Skin Diseases Advisory Council.

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 their 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.

(1) 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?

(2) 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?

(3) 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?

(4) 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)?

(5) 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?

In addition to the above criteria, in accordance with NIH policy, all applications will also be reviewed with respect to the following:

- o The adequacy of plans to include both genders, minorities and their subgroups, and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated.

- o The reasonableness of the proposed budget and duration in relation to the proposed research.

- o The adequacy of the proposed protection for humans, animals or the environment, to the extent they may be adversely affected by the project proposed in the application.

Schedule

Letter of Intent Receipt Date: February 15, 2001
Application Receipt Date: March 19, 2001
Peer Review Date: June/July, 2001
Council Review: September 6-7, 2001
Earliest Anticipated Start Date: September 30, 2001

AWARD CRITERIA

Award criteria that will be used to make award decisions include:

- o scientific merit (as determined by peer review)
- o availability of funds
- o programmatic priorities.

INQUIRIES

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

Direct inquiries regarding NHLBI programmatic issues to:

Deborah Applebaum-Bowden, Ph.D.
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
6701 Rockledge Drive, Suite 10184, MSC 7956
Bethesda, MD 20892-7956
Telephone: (301) 435-0550
FAX: (301) 480-2858
Email: applebad@nhlbi.nih.gov

Direct inquiries regarding NIAMS programmatic issues to:

William J. Sharrock, Ph.D.
Musculoskeletal Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
45 Center Drive, Natcher Building, Room 5AS-37A, MSC 6500

Bethesda, MD 20892-6500
Telephone: (301) 594-5055
FAX: (301) 480-4543
Email: ws19h@nih.gov

Direct inquiries regarding review matters, letters of intent, and two copies of the application to:

Deborah Beebe, Ph.D.
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
6701 Rockledge Drive, Room 7178, MSC 7924
Bethesda, Maryland 20892-7924 (20817 for express mail)
Telephone: (301) 435-0270
FAX: (301) 480-3541
E-mail: beebed@nhlbi.nih.gov

Direct inquiries regarding fiscal matters to:

Ms. Michelle Gosha
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
6701 Rockledge Drive, Room 7136, MSC 7926
Bethesda, MD 20892-7926
Telephone: (301) 435-0177
FAX: (301) 480-0422
E-mail: gosham@nhlbi.nih.gov

Ms. Melinda Nelson
Grants Management Officer
National Institute of Arthritis and Musculoskeletal and Skin Diseases
45 Center Drive, Natcher Bldg. Rm. 5A49, MSC 6500
Bethesda Md 20892-6500
Telephone: (301) 594-3535
FAX (301) 480-5450
Email: mn23z@nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.837 and No. 93.846. 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 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](#)