

SEX-BASED DIFFERENCES IN THE IMMUNE RESPONSE

Release Date: February 12, 2001

RFA: RFA-AI-01-005

National Institute of Allergy and Infectious Diseases

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

National Institute of Neurological Disorders and Stroke

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

National Institute of Arthritis and Musculoskeletal and Skin Diseases

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

Office of Research on Women's Health, National Institutes of Health

(<http://www4.od.nih.gov/orwh/>)

National Multiple Sclerosis Society

(<http://www.nationalmssociety.org>)

Letter of Intent Receipt Date: June 03, 2001

Application Receipt Date: July 10, 2001

THIS RFA USES THE "MODULAR GRANT" AND "JUST-IN-TIME" CONCEPTS FOR R01 AND R21 GRANTS. IT INCLUDES DETAILED MODIFICATIONS TO STANDARD APPLICATION INSTRUCTIONS THAT MUST BE USED WHEN PREPARING APPLICATIONS IN RESPONSE TO THIS RFA.

P01 GRANT APPLICATIONS IN RESPONSE TO THIS RFA MUST BE PREPARED USING A MULTI-PROJECT GRANT APPLICATION FORMAT; SPECIFIC INSTRUCTIONS FOR COMPLETING THE APPLICATION ARE IN THE NIAID BROCHURE ENTITLED "INSTRUCTIONS FOR APPLICATIONS FOR MULTI-PROJECT AWARDS (August 2000)".

PURPOSE

The National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the Office of Research on Women's Health (ORWH) of the National Institutes of Health (NIH) and the National Multiple Sclerosis Society (NMSS) invite applications to identify, characterize, and define differences in the immune response between males and

females, including responses to exogenous and self-antigens, the innate and adaptive immune response, systemic and mucosal immune response, and regulation of the immune system by hormonal and non-hormonal sex differences. The intent of this Request for Applications (RFA) is to support multidisciplinary research on sex-based differences in immune responses that may be important in autoimmune diseases, including multiple sclerosis (MS), rheumatic diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and systemic sclerosis (SSc), as well as other immune mediated diseases, and the underlying mechanisms and clinical significance of such differences. Collaborative multidisciplinary research, involving investigators with expertise in various scientific disciplines and clinical specialties is encouraged. Both human studies and animal models with relevance to human disease are appropriate. Research that expands basic and clinical knowledge of the effect of sex, including hormonal and non-hormonal differences, on the immune response will facilitate development of improved therapeutic and preventive strategies for autoimmune diseases and other immune-mediated disorders. The focus of this RFA is the biological or physiological sex differences between males and females; studies of the cultural, social, and historical differences between males and females ("gender differences") are not responsive to this RFA.

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), "Sex-Based Differences in the Immune Response", is related to one or more of the focus 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 institutions, such as universities, colleges, hospitals, laboratories, units of State and local governments; and eligible agencies of the Federal government. Although foreign institutions are not eligible to apply for Program Project (P01) grants, they are permitted as subprojects. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as Principal Investigators.

MECHANISM OF SUPPORT

The mechanisms of support will be the Individual Research Project Grant (R01), the Exploratory/Developmental Research Project Grant (R21), and the Program Project Grant (P01). The total requested project period for an application submitted in response to this RFA may not exceed four years for an R01, three years for an R21, and five years for a P01 grant.

Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant.

R21 grants generally provide short-duration support for preliminary studies of a highly speculative nature, which are expected to yield, within this time frame, sufficient information upon which to base a well-planned and rigorous series of further investigations. R21 applications in response to this RFA may not request more than \$150,000 direct costs per year and duration may not exceed three years.

P01 grants are used to support broadly based multidisciplinary research programs that have a well-defined central research focus or objective. An important feature is that the interrelationships among the individual scientifically meritorious projects will result in a greater contribution to the overall program goals than if each project was pursued individually. The program project grant consists of a minimum of three interrelated individual research projects that contribute to the program objective. The award also can provide support for certain common resources termed cores. Such resources should be utilized by two or more projects within the award. A P01 application should be prepared using the guidance and instruction provided in the NIAID Information Brochure for Program Projects and Grants, available at: <http://www.niaid.nih.gov/ncn/tools/multibron.htm>.

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>. A notice of modification and update (OD-00-046) regarding modular grants was released on 7/24/00 and can be found at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-046.html>.

This RFA is a one-time solicitation. Future competing renewal applications will compete with all investigator-initiated applications and will be reviewed according to customary referral and review procedures.

FUNDS AVAILABLE

The estimated total funds (direct and Facilities and Administrative (F&A) costs) available for the first year of support for all awards made under this RFA will be \$4,450,000: \$2,000,000 from the NIAID, \$750,000 from NINDS, \$500,000 from NIAMS, \$200,000 from ORWH and \$1,000,000 from NMSS. NINDS will fund grants with relevance to the central and peripheral nervous system. Applications considered for co-funding with the NMSS must have relevance to multiple sclerosis or a relevant model system for MS, although collaborative projects including expertise from a variety of scientific and clinical disciplines are encouraged. The NMSS will determine fulfillment of this requirement. Although this program is provided for in the financial plans of the NIH and NMSS, awards pursuant to this RFA are contingent upon the availability of funds for this purpose and the receipt of a sufficient number of applications of high scientific merit, and for the NMSS sufficient applications with relevance to multiple sclerosis. In Fiscal Year 2002, the NIH and NMSS plan to fund approximately 5 to 10 awards. Although the NIH and NMSS intend to co-fund applications, separate notices of grant award will be sent to successful applicants by each organization indicating the independent commitment by each organization. Funding rules and policies, including the determination of allowable indirect costs, of each funding organization will be applicable. Information on current policies for NMSS and NIH can be found at (<http://www.nationalmssociety.org/nmssupload/pdf/PoliciesAndProcedures.pdf>) and <http://grants.nih.gov/grants/policy/nihgps/> respectively. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years and availability of funds. Post-award administration will conform to current policies that govern the research grants programs of the NIH and the NMSS as appropriate.

RESEARCH OBJECTIVES

Background

Sexual dimorphism in various aspects of the immune response has long been appreciated. In general, women mount a more vigorous immune response than men to infections, which may partially explain why women tend to live longer. However, women are also more likely than men to suffer from autoimmune diseases. In multiple sclerosis, rheumatoid arthritis, and systemic sclerosis, for example, the female to male ratio is between 2:1 and 3:1 and in systemic lupus erythematosus approximately nine times as many women as men are affected. As a result, of the 14 million people with autoimmune diseases in the United States, the majority are women. Although autoimmune diseases are more common in women, disease severity may be worse in

men. Recent analyses of multiple sclerosis patients suggest men experience acceleration of disease and increased mortality compared to women.

The precise reasons for the sex-based differences seen in immune responses are unclear. The increased incidence of many autoimmune diseases after puberty, as well as the effect of pregnancy on the course of disease, suggest a role for sex hormones in these illnesses. Clinical remissions often occur during pregnancy in patients with multiple sclerosis and rheumatoid arthritis, whereas postpartum disease activity is increased. In contrast, pregnancy may either precipitate or ameliorate symptoms in patients with systemic lupus erythematosus. Estrogen administration induces a systemic lupus erythematosus-like phenotype in non-autoimmune mice transgenic for the heavy chain of a pathogenic DNA-specific antibody. In addition, estrogen enhances the efficacy of a T cell receptor-based immunotherapy for experimental autoimmune encephalomyelitis, an animal model of multiple sclerosis. Therefore evidence from a variety of sources implicates a role for sex hormones in modulating the incidence, course and severity of autoimmune disease.

Sex hormones also appear to influence infectious diseases. Malaria is one of the most serious complications of pregnancy for women living in endemic areas. Both estrogen and testosterone have been shown to suppress immunity to this disease, although pre-existing protective immunity is not affected by testosterone. Recent evidence also suggests that estrogens and progesterone regulate antigen presentation in the female reproductive tract and may affect susceptibility to sexually transmitted diseases. Unique defensins, components of the innate immune response produced in the male and female reproductive tract, may play a role in preventing sexually transmitted diseases including HIV infection.

Not all sex-based differences in immune responses are necessarily hormonally related. Recent studies show increased incidence and numbers of fetus-derived cells in blood and affected tissues of postpartum women with scleroderma as compared to healthy women, suggesting a role for microchimerism in the pathogenesis of autoimmune disease. In addition, human and animal studies suggest sex-related factors may interact with susceptibility genes leading to differential expression of autoimmune disease in males and females. Thus, both hormonal and non-hormonal factors appear to contribute to sex-based differences in the immune response, however, the mechanisms remain unclear.

In 1995 the NIH sponsored a meeting on Gender and Autoimmunity and recently participated in a Task Force on Gender, MS and Autoimmunity organized by the National Multiple Sclerosis Society. The latter resulted in a major review article entitled "A Gender Gap in Autoimmunity"

(Science 283:1277, 1999, and the Science web site <http://www.sciencemag.org/feature/data/983519.shi>). Both workshops recommended increased support for basic and clinical research on sex-based differences in the immune response. This RFA is in response to these recommendations and expands upon a 1996 NIH Program Announcement "Gender in the Pathogenesis of Autoimmune Diseases: Mechanisms."

Research Objectives and Scope

While both the NIH and the NMSS are currently supporting some sex-based research, this new program will: (1) target basic and clinical investigation of sex differences in all aspects of the immune response, (2) encourage new and established investigators to address existing gaps, and (3) foster multidisciplinary research collaborations to focus on existing opportunities.

Research topics of interest include, but are not limited to the following:

- o Mechanisms that underlie sex-based differences in susceptibility to and severity of autoimmunity, infectious diseases, or other immune-mediated diseases.
- o Molecular basis for differences between males and females in the immune response, including the adaptive, innate, and mucosal immune systems.
- o Differences between males and females in adaptive immune responses including, but not limited to, T and B cell development, tolerance induction, antibody production, antigen presentation and processing, and immune regulation.
- o Differences in the triggering or response mechanisms in innate immunity that may be responsible for the sexual dimorphism observed in response to pathogens.
- o Differences in the immune response to infections of the central and peripheral nervous system.
- o Mechanisms of sex hormone regulation of the immune response in normal and disease states in males and females.
- o The effect of pregnancy on the immune response and identification of postpartum changes that are responsible for either protection from or provocation of autoimmunity.
- o Mechanisms of microchimerism in the etiopathogenesis of autoimmune disease.

- o The genetic basis for sex differences in autoimmunity.

The above examples of research topics are not meant to be all-inclusive or restrictive. Investigators are encouraged to develop their own innovative hypothesis-driven approaches to achieve the goals of this RFA.

SPECIAL REQUIREMENTS

The NIH and the NMSS plan to sponsor an annual meeting to encourage the exchange of information among investigators supported under this RFA, foster collaborative efforts, and identify resources that would enhance the productivity of this research program. Applications should include a statement indicating the willingness of the applicant institution to participate in such annual meetings. For this purpose, travel funds for an annual two-day meeting, to be held in the Washington DC area should be included in the budget request.

TERMS AND CONDITIONS OF AWARD

When clinical studies or trials are a component of the research proposed, NIAID policy requires that studies be monitored commensurate with the degree of potential risk to study subjects and the complexity of the study. In such cases, specific Terms and Conditions of Award will apply.

NIAID policy was announced in the NIH Guide on February 24, 2000 and is available at:

<http://grants.nih.gov/grants/guide/notice-files/NOT-AI-00-003.html>.

The full policy including terms and conditions of award are available at:

<http://www.niaid.nih.gov/ncn/pdf/clinterm.pdf>

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, compelling rationale, and justification are 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 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.

NIH POLICY AND GUIDELINES ON THE INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH:

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 which is available at the following URL address:

<http://grants.nih.gov/grants/guide/notice-files/not98-024.html>.

Investigators may obtain copies from these sources or from the program staff listed in INQUIRIES below who 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, by June 03, 2001, a letter of intent that includes a descriptive title of the overall proposed research; the name, address and telephone number of the Principal Investigator; and the number and title of this RFA. Although the letter of intent is not required, is not binding, does not commit the sender to submit an application, and does not enter into the review of a subsequent application, the information that it contains allows NIAID staff to estimate the potential review workload and to plan the review. The letter of intent is to be sent to Dr. Nasrin Nabavi at the address listed under INQUIRIES.

LETTER OF AUTHORIZATION

This RFA is co-sponsored by the NMSS. In order for an application to be considered for funding by the NMSS, applicants must submit a brief letter of authorization co-signed by the Principal Investigator and the Business Official of the applicant institution authorizing release of any letter of intent, the application, priority score, and summary statement to the NMSS. This letter of authorization should be submitted directly to Dr. Denise Wiesch at the address listed under INQUIRIES.

APPLICATION PROCEDURES

Applicants are strongly encouraged to call NIAID, NINDS, or NIAMS program staff with any questions regarding the responsiveness of their proposed project to the goals of this RFA.

The research grant application form PHS 398 (rev. 4/98) is to be used in applying for these grants. Application kits 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. Applications are also available on the World Wide Web at <http://grants.nih.gov/grants/forms.htm>.

For purposes of identification and processing, item 2a on the face page of the application must be marked "YES" and the RFA number "AI-01-005" and the words "SEX-BASED DIFFERENCES IN THE IMMUNE RESPONSE" must be typed in.

The RFA label and line 2 of the application should both indicate the RFA number. The RFA label must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review.

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.

Applications must be received by July 10, 2001. Applications that are not received as a single package on the receipt date or that do not conform to the instructions contained in PHS 398 (rev. 4/98) Application Kit (as modified in, and superseded by, the NIAID BROCHURE ENTITLED "INSTRUCTIONS FOR APPLICATIONS FOR MULTI-PROJECT AWARDS") will be judged non-responsive and will be returned to the applicant.

If the application submitted in response to this RFA is substantially similar to a grant application already submitted to the NIH for review, but that has not yet been reviewed, the applicant will be asked to withdraw either the pending application or the new one. Simultaneous submission of identical applications will not be allowed, nor will essentially identical applications be reviewed by different review committees. Therefore, an application that is essentially identical to one that has already been reviewed cannot be submitted in response to this RFA. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, exact, single-sided 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 mail or courier service)

At the time of submission, two additional exact copies of the grant application and all five sets of any appendix material must be sent to:

Dr. Nasrin Nabavi
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Room 2212
6700-B Rockledge Drive
Bethesda, MD 20892

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.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. If so, a letter of agreement from either the GCRC Program Director or Principal Investigator should be included with the application.

SPECIAL INSTRUCTIONS FOR COMPLETION OF P01 GRANT APPLICATIONS IN RESPONSE TO THIS RFA

Applicants for P01 grants must follow special application guidelines in the NIAID Brochure entitled INSTRUCTIONS FOR APPLICATIONS FOR MULTI-PROJECT AWARDS (August 2000); this brochure is available via the WWW at:

<http://www.niaid.nih.gov/ncn/tools/multibron.htm>.

The brochure presents specific instructions for sections of the PHS 398 (rev. 4/98) application form that should be completed differently than usual. For all other items in the application, follow the usual instructions in the PHS 398.

Concurrent submissions of a component research project of a multi-project (P01) grant application as a traditional individual research project (R01) to this RFA is prohibited. However, investigators may submit a component research project to NIH as an unsolicited R01 recognizing that if both are found competitive and approved for award the P01 will be awarded and the unsolicited R01 must be withdrawn by the applicant.

SPECIFIC INSTRUCTIONS FOR R01 and R21 GRANT APPLICATIONS

R01 and R21 applications in response to this RFA should use the modular grant format. R21 applications in response to this RFA may request up to \$150,000 direct costs and duration may not exceed three years. 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:

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 BUDGET NARRATIVE 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.

Under Personnel, provide budget narrative for ALL personnel by position, role and level of effort. This includes consultants and any "to be appointed" positions. 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 a Letter of Commitment or Intent if there is or is to be a subcontract/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, including consultants, 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. Applicant institutions should calculate the Facilities and Administration (F&A) costs using the current negotiated F&A rate, less exclusions, for the initial budget period and all future budget periods. It is not necessary to list the exclusions on the Checklist nor anywhere in 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.

Effective for the receipt dates beginning September 1, 2000, R01 and R21 applications not in compliance with the modular application instructions will be returned to the applicant institution.

An R01 and R21 application will be considered NON-COMPLIANT if:

1. The requested direct cost budget is not in modules of \$25,000 for all years of support for requests up to \$250,000 per year.
2. A detailed itemized categorical budget is provided.
3. The Budget Narrative Justification page includes an itemized justification for one or more of the following: equipment, supplies, travel, other expenses, etc. but the number of modules requested in each year is the same, or the information is not intended to explain the request for a different number of modules in one or more years.

4. OTHER SUPPORT pages are supplied, in addition to or in the absence of the section in the Biographical Sketch identifying "Research Projects Ongoing or Completed During the Last Three Years."

5. The Biographical Sketch lists "Current and Pending Support" instead of or in addition to the required information.

REVIEW INFORMATION

Review Procedures

Upon receipt, applications will be reviewed for completeness by the NIH Center for Scientific Review and for responsiveness by NIAID staff. Incomplete and/or non-responsive applications will be returned to the applicant without further consideration.

Review Considerations

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 Division of Extramural Activities, NIAID in accordance with the review criteria stated below. As part of the initial merit review, all applications will be discussed, be assigned a priority score, receive a written critique and a second level of review provided by the appropriate NIH advisory council. The NMSS's Research Programs Advisory Committee will review all projects considered for NMSS co-funding.

The initial review group will examine: the appropriateness of proposed project budget and duration; the adequacy of plans to include children and both genders and minorities and their subgroups as appropriate for the scientific goals of the research and 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.

Review Criteria for P01 grant applications

The general criteria for P01 grant applications are presented in the NIAID brochure entitled INSTRUCTIONS FOR APPLICATIONS FOR MULTI-PROJECT AWARDS (August 2000).

Review Criteria for R01 and R21 grant applications

The criteria to be used in the evaluation of R01 and R21 grant applications are listed below. To put those criteria in context, the following information is contained in instructions to the peer reviewers.

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. The reviewers will comment on the following aspects of the application in their written critiques 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 by the reviewers 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 a 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?

Schedule

Letter of Intent Receipt Date: June 03, 2001
Application Receipt Date: July 10, 2001
Scientific Peer Review Date: November 15, 2001
Advisory Council Date: February 15, 2002
Earliest Anticipated Award date: April 01, 2002

AWARD CRITERIA

Funding decisions will be made on the basis of scientific and technical merit as determined by peer review, programmatic priorities, and the availability of funds. The earliest anticipated date of award is April 01, 2002.

INQUIRIES

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

Direct inquiries regarding programmatic (research scope and eligibility) issues to:

Denise Wiesch, Ph.D.
Program Officer, Clinical Immunology Branch
Division of Allergy, Immunology and Transplantation
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Room 5253, MSC-7640
6700-B Rockledge Drive
Bethesda, MD 20892-7640
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E-Mail: dwiesch@niaid.nih.gov

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Bethesda, MD 20892-9521
Telephone: 301-496-1431

FAX: 301-402-2060

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J. Elizabeth Gretz, Ph.D.

Extramural Program Director,
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Lisa Begg, Dr.P.H.

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1 Center Dr., Bethesda, MD, 20892

Telephone: 301/402-1770

FAX: 301.402.1798

E-mail: beggl@od.nih.gov

Direct inquiries regarding review issues; address the letter of intent to; and mail two copies of the application and all five sets of appendices to:

Nasrin Nabavi, Ph.D.

Division of Extramural Activities

National Institute of Allergy and Infectious Diseases

Room 2212

6700-B Rockledge Drive

Bethesda, MD 20892

Telephone: (301) 496-2550

FAX: (301) 402-2638

E-Mail: nnabavi@niaid.nih.gov

Direct inquiries regarding fiscal matters to:

Karen McVay

Division of Extramural Activities

National Institute of Allergy and Infectious Diseases

Room 2252
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Melinda Nelson
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45 Center Drive, Natcher Building Rm 5As49f
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AUTHORITY AND REGULATIONS

This program is described in the Catalogue of Federal Domestic Assistance No. 93.855 - Immunology, Allergy, and Transplantation research, No. 93.853 - Extramural Programs in the Neurosciences and Neurological Disorders, and No. 93.846 - Arthritis, Musculoskeletal and Skin Diseases Research. 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.

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