

TESTING INTERVENTIONS TO IMPROVE ADHERENCE TO PHARMACOLOGICAL
TREATMENT REGIMENS

Release Date: January 19, 2000

RFA: OD-00-006

Office of Behavioral and Social Sciences Research
National Cancer Institute
National Human Genome Research Institute
National Heart, Lung, Blood Institute
National Institute on Aging
National Institute on Alcohol Abuse and Alcoholism
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Child Health and Human Development
National Institute of Dental and Craniofacial Research
National Institute of Diabetes and Digestive Disorders and Kidney Disease
National Institute on Drug Abuse
National Institute of Mental Health
National Institute of Nursing Research

Letter of Intent Receipt Date: March 6, 2000

Application Receipt Date: April 6, 2000

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 Office of Behavioral and Social Sciences Research, National Cancer Institute, National Human Genome Research Institute, National Heart, Lung, Blood Institute, National Institute on Aging, National Institute on Alcohol Abuse and Alcoholism, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institute of Child Health and Human Development, National Institute of Dental and Craniofacial Research, National Institute of Diabetes and Digestive Disorders and Kidney Disease, National Institute on Drug Abuse, National Institute of

Mental Health, and the National Institute of Nursing Research invite applications for research project (R01) grants in order to encourage behavioral and social research on the effectiveness of interventions to improve adherence to therapeutic regimens in various settings.

This RFA is responsive to Congressional Report Language for the FY 2000 Appropriations that urges “the Office of Behavioral and Social Sciences Research [and several NIH Institutes] to stress the need for all institutions to fund behavioral and social sciences research to improve adherence to medical regimes, exercise and weight reduction programs.” The RFA is consistent with and based upon recommendations in several recent reviews of the scientific literature and set forth by advisory groups to NIH Institutes and Centers.

Applications in response to this RFA must propose research on adherence to therapeutic treatment regimens where:

- 1) the therapeutic regimen includes a pharmacological treatment;
- 2) the therapeutic regimen must be for an existing illness or condition, whether acute or chronic, as opposed to a health promotion regimen;
- 3) the adherence intervention has been (a) demonstrated to be efficacious in controlled settings (e.g., laboratories, clinical trials), (b) tested only with limited populations (e.g., small samples or samples from restricted populations) or with short periods of follow-up, or (c) researched on a health condition or treatment regimen different from that in the proposed research;
- 4) the adherence intervention targets individuals, formal or informal health-care providers, and/or the social or institutional environment; and
- 5) there are measurements of (a) the delivery of the specified therapeutic regimen and adherence intervention (i.e., treatment fidelity) and of (b) adherence to the regimen.

In addition, applicants are encouraged to investigate how to adjust interventions to take into account the characteristics of different populations as well as people suffering from and receiving treatments for multiple acute and/or chronic illnesses and conditions. This RFA is an opportunity to conduct research cutting across the traditional boundaries of responsibility of the participating NIH Institutes and Centers (ICs).

HEALTHY PEOPLE 2000

Each NIH RFA addresses one or more of 22 Health Promotion and Disease Prevention priority areas. These areas can be found at <http://odphp.osophs.dhhs.gov/pubs/hp2000>.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by 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. Foreign organizations are not eligible. However, foreign organizations may participate if they are components of domestic, U.S. organizations or via contractual or consortium agreements with domestic, U.S. organizations. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as principal investigators. Questions about eligibility may be addressed to the program contacts listed in the INQUIRIES section.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) regular research grant (R01) mechanism. This mechanism supports the full range of research from basic to clinical intervention studies, as well as health services, policy and surveillance research. The Principal Investigator will be responsible for the planning, direction, and execution of the proposed research project. Awards will be administered according to the most recent NIH Grants Policy Statement.

Specific application instructions have been modified to reflect "MODULAR GRANT" and "JUST-IN-TIME" application procedures. Complete and detailed instructions and information on Modular Grant applications can be found at <http://grants.nih.gov/grants/funding/modular/modular.htm> and in the NIH Guide to Grants and Contracts, December 15, 1998 (<http://grants.nih.gov/grants/guide/notice-files/not98-178.html>). For this RFA, the budgetary maximum specified in these general instructions for Modular Grants should be disregarded. (See FUNDS AVAILABLE.)

FUNDS AVAILABLE

The Office of Behavioral and Social Research is making available \$3,000,000 for the support of approximately six new research grants in response to this RFA. The total project period for an application may not exceed five years. Direct costs in the first year of the award may not exceed \$350,000 and the accumulated direct costs over five years may not exceed \$1,750,000. Research projects with costs less than \$350,000 per year are encouraged.

In order to facilitate financial planning of the NIH, applicants are strongly encouraged to develop budgets with the same number of modules in each year of the award. That is, it is highly desirable

to have “flat” or “even” budgeting across the years of support. Deviations from even budgeting should be well justified. The anticipated award date for all applications is September 29, 2000. Funding in response to this RFA is dependent upon the receipt of a sufficient number of applications of high scientific merit. At this time, it is not known if this RFA will be reissued at a future date.

RESEARCH OBJECTIVES

(1) Background

Several recent reports and literature reviews point to the continuing need for improving adherence to therapeutic regimens. (See REFERENCES.) Adherence rates vary considerably across diseases and treatments, measuring instruments, and populations, with rates ranging from 30% to 60% in many instances. Most researchers agree that at least 50% of persons for whom drugs are prescribed fail to receive the full benefit through inadequate adherence. As noted by the American Heart Association (1997), “the rationale for enhancing [adherence] is based on the premise that the patient will get well or stay well if the physician, other healthcare providers, and the healthcare organization make appropriate recommendations, providing the patient has the requisite knowledge, motivation, skills, and resources to follow the recommendations.” Lack of adherence to therapeutic regimens may result in poorer health for individuals as well as economic costs for their health-care organizations and the broader society.

The reasons for non-adherence are multifaceted and not fully understood. Health-care providers, organizational systems, and personal factors all play a role in adherence to therapeutic regimens. Thus, to understand and eventually improve adherence, conceptual frameworks and interventions need to take into account institutional, system, situational, interpersonal, and personal factors as well as the characteristics of the illness or condition and of the treatment regimen.

Research has demonstrated the efficacy of a variety of approaches to improving adherence to therapeutic regimens in controlled laboratory or field experimental situations, in small, selected samples, or over limited periods of time. Less is known about the effectiveness of interventions when they are moved from controlled research settings to where health care is actually practiced with individuals of varied backgrounds over extensive periods of time. How does the success of interventions to improve adherence vary across types of health-care providers, settings, and persons of varying educational, economic, and ethnic backgrounds? What adjustments may be needed to implement interventions in the “real world” of health care and under what circumstances?

In addition to research on effectiveness, opportunities may exist for research on adapting and assessing the efficacy of promising intervention strategies that have been used successfully to improve adherence, but in small, selected (e.g., unrepresentative) samples. Similarly, behavior-change strategies that have been successful in one domain may hold promise for improving adherence to therapeutic regimens for other illnesses or health conditions.

(2) Areas of Emphasis

In order to concentrate available resources, this RFA stipulates five requirements for research on adherence. Research grant applications must address all five requirements to be considered responsive to this RFA. Subsequent funding initiatives may be issued to address other aspects of adherence. Special emphasis is given to adherence research in diverse racial/ethnic and socioeconomic status populations.

1. The therapeutic regimen must include a pharmacological treatment. This treatment may be combined with behavioral or other kinds of treatments of illnesses or conditions.
2. The therapeutic regimen must be for an existing illness or condition as opposed to health promotion regimens. See below for examples of diseases or conditions of interest to the participating NIH Institutes. While research on changing behaviors to promote health is important, it lies outside of the purview of this RFA. The NIH does continue to encourage such research. Most recently, several ICs joined to solicit such research through the RFA on Innovative Approaches to Disease Prevention through Behavior Change, NIH Guide to Grants and Contracts, Volume 26, Number 36, October 24, 1997 (<http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-98-002.html>).
3. The research must address either (a) the translation of interventions already demonstrated to be efficacious in controlled experimental situations to “field” or practice settings or (b) the further development of efficacious interventions previously tested in small, selected samples or with specific diseases and health conditions. The major emphasis of the RFA is on “effectiveness” research as opposed to “efficacy” research. The research should be aimed at determining if and how efficacious interventions may be transported to clinical and community settings. Research on testing the applicability or generalizability of interventions to broader groups of individuals (e.g., differing in socioeconomic status, race, ethnicity, in medical conditions and illnesses) is also appropriate. However, proposals to develop interventions de novo (i.e., those without a prior history of development in any treatment area) fall outside the scope of this RFA.

4. The intervention may target individuals, formal or informal health-care providers, and/or the social or health-care environments. Interventions may operate on multiple levels and targets in order to improve adherence. For example, interventions may attempt to enhance adherence by increasing people's knowledge, skills, and motivation, by instructing health-care providers on how to better provide information, guidance, or monitoring, by involving the individual's social network, or by altering aspects of the health-care system.

5. Explicit conceptualization and measurement of the therapeutic regimen (i.e., health treatment delivery), the intervention(s) to improve adherence, and of adherence behaviors are essential. Research projects should include appropriate measures of the delivery of the specified therapeutic regimen and adherence intervention as well as measures of adherence.

In addition to the preceding five emphases, research projects may address such issues as the following:

- o How should the intervention be adjusted to take into account the characteristics of different populations? Interventions may not work equally well for all persons depending on their educational, economic, and cultural backgrounds and circumstances. Are particular groups at high risk for non-adherence? How should the intervention take this into account?

- o What are the consequences for adherence, if any, of an individual suffering from and receiving treatments for multiple illnesses and conditions? An intervention may improve adherence for one treatment aimed at a specific condition, but it may interfere with adherence to a regimen for treating another condition. How do interventions to improve adherence to acute conditions interface with therapeutic regimens for treating chronic illnesses or conditions (and vice versa)? Research investigating situations of multiple morbidity cutting across the traditional boundaries of NIH ICs is particularly encouraged.

- o How can the proposed intervention be improved based upon research results? Research proposals may include provisions making adjustments to the intervention based upon assessing the effectiveness of the interventions midway through the grant period. That is, the research may be divided into two phases. The first phase would consist of a test of the intervention as originally proposed in the application. During the second phase, based upon research results obtained during the first phase, the researchers may "fine tune" the intervention and assess the results of this adjustment.

Several NIH Institutes have joined with OBSSR to support this initiative. Examples of topics of interest to specific NIH Institutes are given below. These examples are not meant to be an

exhaustive list of the research of interest to the NIH. Additional topical areas and approaches designed to better understand and increase adherence to pharmacological therapeutic regimens are welcomed.

NATIONAL CANCER INSTITUTE

NCI is interested in behavioral and social sciences research on promoting adherence to therapeutic regimens effective in the management of cancer. Therapeutic regimens are broadly defined to include not only active anticancer treatments but also post-chemotherapeutic administration of compounds to prevent/minimize recurrence and prevent post-treatment toxicities (e.g., steroid and growth factor administration or reduce sun light exposure post-photodynamic therapy). Examples of therapeutic regimens that pose particular problems in adherence include but not limited to interferon treatment for melanoma, topical application of drugs in mycosis fungoides, oral maintenance therapy for ALL and oral treatment regimens in CLL. NCI has special interest in promoting research that may lower barriers to effective therapy for children and the aged as well as for the underserved.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

As human genetic research progresses and as more is learned about the role that genes play in the development of common disorders, it will become increasingly possible to provide individuals with information about the genetic contribution to their disorder. Currently, there is no data on the impact of genetic information on individuals' adherence to therapeutic regimens. Will individuals who are found to have genes or genetic markers associated with their own disorder be more, equally, or less likely to adhere to proposed therapeutic regimens? The NHGRI, through its Ethical, Legal, and Social Implications Research (ELSI) program, is interested in supporting research to explore what impact individualized information about the genetic contribution to particular disorders, including common complex adult-onset disorders, will have on an individual's adherence to therapeutic regimens. For example, women who are known to be at increased risk to develop breast cancer, due to family history, BRCA mutations, or other factors, may be put on a regimen of tamoxifen or raloxifen. What impact will knowledge of BRCA1 mutation status have on an individual's adherence to a tamoxifen or raloxifen regimen? Special consideration will be given to studies that examine the impact of this information on individuals from different socio-cultural and socioeconomic groups.

NATIONAL HEART, LUNG, BLOOD INSTITUTE

The NHLBI supports studies that seek to improve rates of adherence to medical and behavioral regimens used in preventing and treating heart, lung, blood and sleep diseases and disorders.

The NHLBI is also interested in studies that investigate how psychological, social, behavioral, biological, cultural and health care systems factors influence adherence. Examples of therapies and conditions where adherence poses special problems include antihypertensive therapies, cholesterol-lowering medications, medications used to treat myocardial infarction and congestive heart failure, and treatments for asthma, tuberculosis and sickle cell disease. Areas of special interest include effectiveness studies involving development and testing of adherence-enhancing interventions in health-care and community settings; investigations of the cultural, social and health care system factors that affect adherence; research on the determinants of and optimal approaches to changing provider behavior and practices; and use of new technologies (e.g., computer-based approaches) in the measurement and promotion of adherence.

NATIONAL INSTITUTE ON AGING

The NIA seeks research on biological, behavioral, cognitive, social and economic factors that affect adherence to medications and other behavioral regimens in the middle and later years. NIA is interested in adherence behavior to both acute and chronic treatment recommendations for a broad range of co-morbidities prevalent in old age (e.g., Alzheimer's disease, arthritis, cancer, diabetes, heart disease, infectious diseases, stroke). Of special interest is an examination of age-related processes and conditions (e.g., multiple medication use, multiple morbidities, cognitive changes, transitions in living arrangements and social supports, and the nature of provider-patient interactions and clinical decision-making) that affect adherence behaviors and that are important in the design of appropriate adherence interventions for older adults. Psychosocial and economic mediators and outcomes of multi-level intervention approaches should be considered.

For background material and emphasis areas see NIA's recent program announcement PA-99-07 on Diversity in Medication Use and Outcomes in Aging Populations - May 1999 that can be found on the Web at <http://www.nih.gov/nia/resfund/bsr.htm>.

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

The NIAAA is the lead federal agency responsible for research on the causes, consequences, prevention and treatment of alcohol-related problems. Research is currently being funded to develop and test pharmaceutical agents to treat alcoholism. Of interest is the identification of practical, effective techniques to enhance adherence to medication regimens, given alone or in combination with psychosocial therapy, for the treatment of alcohol abuse and alcohol problems.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

NIAMS is interested in behavioral and social sciences research on promoting adherence to therapeutic regimens effective in the management of arthritis and other rheumatic diseases, muscle diseases, musculoskeletal disorders, bone diseases including osteoporosis, and skin diseases. NIAMS has special interest in promoting research which may lower barriers to effective therapy for underserved populations.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

NICHHD is interested in research to elucidate behavioral mechanisms involved in adherence to medical and therapeutic regimens for children and adolescents with acute and chronic illnesses, injuries, stress and pain as well as behavioral and attentional disorders. Of interest are intervention studies examining motivational factors and deterrents to adherence in children, their parents/caretakers, and health care providers.

NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

NIDCR is interested in the development and translation of effective interventions to increase adherence to fluoride, antimicrobial, antibiotic, analgesic, or other pharmacological regimens used in treating oral diseases such as dental caries, periodontal diseases, salivary disorders and xerostomia, TMJ disorders, and trigeminal neuralgia or other orofacial pain disorders as well as the pain, swelling, or inflammation associated with dental procedures or with surgeries to correct craniofacial defects. NIDCR is also interested in research to increase adherence to treatment regimen involving pharmacological approaches to reduce oral complications of systemic diseases, such as diabetes or HIV, or oral complications of medical interventions, such as chemotherapy or radiation. In addition, research projects utilizing oral biomarkers, such as salivary measures, to assess or enhance adherence to pharmacological regimens are of specific interest to NIDCR.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE DISORDERS AND KIDNEY DISEASE

NIDDK is interested in development and translation of effective interventions to increase adherence to medical regimens for diabetes, obesity, genetic metabolic diseases and endocrine, renal, urologic, hematologic, digestive, and liver diseases. Examples of topics of interest to NIDDK include: interventions to increase adherence behaviors affecting glycemic control and other diabetes outcomes; interventions to improve post-transplant medication compliance; improved treatment of depression in patients with diabetes or on dialysis; interventions targeted at increasing compliance in adolescents; development of interventions in the context of ethnicity,

culture and SES; and studies of interactions between care providers and patients leading to improved adherence and outcome.

NATIONAL INSTITUTE ON DRUG ABUSE

NIDA is interested in research aimed at improving interventions that promote adherence to medication in individuals who are addicted to drugs (including but not limited to cocaine, nicotine, opiates, marijuana, prescription drugs, etc.). Of particular interest is research that integrates new developments in basic behavioral, cognitive, or clinical science to refine, test and improve the effectiveness of adherence interventions. Adherence to medication for drug addiction or adherence to medication for a co-morbid physical and/or mental health problem may be the focus of the research. A related announcement, delineating a "Stage Model" for behavioral intervention research, "Behavioral Therapies Development Program," NIDA PA-99-107, can be found at <http://grants.nih.gov/grants/guide/pa-files/PA-99-107.html>.

NATIONAL INSTITUTE OF MENTAL HEALTH

NIMH is interested in expanding research on adherence and behavior change that integrates findings from the basic behavioral sciences with interventions for mental disorders, symptoms, or related disability. Included are studies of mechanisms and processes that enhance and/or interfere with adherence to preventive, pharmacological, psychosocial, and rehabilitative treatments. Potential research topics germane to adherence to interventions for mental disorders are listed in NIMH PA-00-16 "Research on Adherence to Interventions for Mental Disorders" which can be found on the Web at <http://www.nimh.nih.gov/grants/pamenu.htm>.

NATIONAL INSTITUTE OF NURSING RESEARCH

NINR is interested in research studies that involve nursing interventions or that have a direct impact on client adherence by a health team. NINR promotes research in health care and outcomes across all ages, in diverse populations, and for a wide variety of acute and chronic health conditions. NINR is interested in studies involving interventions to promote adherence behaviors. In addition to the client group, interventions may involve health care providers, family members, or other key individuals or groups involved in the process of promoting adherence. NINR encourages applications that include both pharmacological and other adherence interventions.

REFERENCES

American Heart Association, The Multilevel Compliance Challenge: Recommendations for a Call to Action, *Circulation*, 1997; 95:1085-1090. D. L. Roter, J. A. Hall, R. Merisca, B. Nordstrom, D. Cretin, and B. Svarstad, Effectiveness of interventions to improve patient compliance, *Medical Care*, 36, 8, 1998, pp. 1138-1161. Center for the Advancement of Health, Health Care Financing Administration, and National Institute on Aging, Interventions to Improve Adherence to Medical Regimens in the Elderly. Washington, DC: Center for Advancement of Health, 1999.

R. B. Haynes, K. A. McKibbin, R. Kanani, M. C. Brouwers, and T. Oliver, Interventions for helping patients to follow prescriptions for medications, *The Cochrane Library*, 1999, Issue 1.

SPECIAL REQUIREMENTS

(a) DATA AND SAFETY MONITORING. A clinical trial entails a relationship between participants and investigators, both of whom must fulfill certain obligations for the effort to succeed. Participants must be fully informed of the study requirements throughout the conduct of the trial and should comply with the rigors of the research protocol or be allowed the opportunity to withdraw from participation. The investigators must protect the health and safety of participants, inform participants of information relevant to their continued participation, and pursue the research objectives with scientific diligence. In 1994, the NIH Office of Extramural Research established the Committee on Clinical Trial Monitoring to review the oversight and management practices of the ICs for phase III clinical trials. One of the outcomes of this Committee's review was a strong recommendation that "all trials, even those that pose little likelihood of harm, should consider an external monitoring body." Applicants should describe and budget for the organizational structures and procedures they will employ to ensure the safety of participants and the validity and integrity of the data. (For a statement of issues and concerns, see "NIH Policy for Data and Safety Monitoring," NIH Guide to Grants and Contracts, Release Date: June 10, 1998, <http://grants.nih.gov/grants/guide/notice-files/not98-084.html>.) At the time of the award, applicants should be prepared to make adjustments to their procedures based upon the policies of the NIH Institute/Center administering their grant.

(b) SAMPLE SIZE/DATA ANALYSIS. Assumptions and steps used to arrive at the proposed sample size must be described. Discussion should be devoted to analytic features of the study including primary endpoint specification, statistical power estimates, randomization procedures, statistical methods, and use of the intention-to-treat principle (i.e. whether the primary analysis will be carried out based on the original treatment assignment versus treatment administered), as applicable.

(c) LEVERAGING. Applicants should consider taking advantage of other research projects (e.g., clinical trials about to be implemented) that could be expanded by adding a research component on adherence. Such projects might provide access to subject populations or settings as well as reduce the costs of conducting research.

(d) ANNUAL MEETINGS AND COLLABORATION. Successful applicants will be asked to participate in yearly meetings to report progress, discuss problems, and share information related to the conduct of their grants. Previous experience with such meetings has shown that they can provide opportunities for grantees to work collaboratively in various areas such as measurement of treatment fidelity and adherence, techniques for participant recruitment and retention, development and implementation of interventions, and data archiving and sharing. Cooperation across funded studies increases their value by facilitating the accumulation of comparable knowledge and experience. Applicants should include in their budget funds for two or three investigators to attend the annual collaborative meetings to be held in Bethesda, MD, at the NIH. The first of these meetings will be held in November or December 2000.

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, Volume 23, Number 11, March 18, 1994.

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

NIH POLICY AND GUIDELINES ON THE 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 to exclude them. (See NIH Guide to Grants and Contracts, March 6, 1998 or <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.

LETTER OF INTENT

Prospective applicants are asked to submit, by March 6, 2000, 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 (including research project collaborators and consultants) and participating institutions, and the number and title of this RFA. Although a letter of intent is not binding and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and avoid conflict of interest in the review.

The letter of intent should be sent to:

Dr. Ronald P. Abeles
Office of Behavioral and Social Sciences Research
National Institutes of Health
Gateway Building, Rm. 2C234
7201 Wisconsin Ave., MSC 9205
Bethesda, MD 20892-9205
Telephone: 301-496-7859
Fax: 301-435-8779
E-mail: Abeles@nih.gov

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 4/98) must be used in applying for these grants, with the modifications noted below. Applications 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, E-mail: GrantsInfo@nih.gov. Applications are also available on the World Wide Web at <http://grants.nih.gov/grants/forms.htm>.

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.

MODULAR GRANT applications request direct costs in \$25,000 modules, up to a total direct cost request of \$350,000 per year. For the purposes of this RFA, the usual maximum of \$250,000 for modular awards does NOT apply. 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:

(a) PHS 398

- o FACE PAGE: Items 7a and 7b should be completed, indicating Direct Costs (in \$25,000 increments up to a maximum of \$350,000) 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.

Applications should include in their budgets funds for attending an annual meeting of research projects funded under this RFA. For budgeting purposes, applicants should assume that the meetings would be for two days in Bethesda, Maryland at the National Institutes of Health and require the attendance of two or three investigators per funded project. (See SPECIAL REQUIREMENTS, (d) ANNUAL MEETINGS AND COLLABORATION.)

- 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.

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.

Applicants are strongly encouraged to request the same number of modules for each year of funding. 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.

(b) Mailing Procedures

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.

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, original of the application, including the Checklist, and four (4) signed photocopies of the application in one package to:

CENTER FOR SCIENTIFIC REVIEW (formerly Division of Research Grants)
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, send one (1) additional copies of the application to:

Dr. Ronald P. Abeles
Office of Behavioral and Social Sciences Research
National Institutes of Health
Gateway Building, Rm. 2C234
7201 Wisconsin Ave., MSC 9205
Bethesda, MD 20892-9205

It is important to send this copy at the same time that the original and four copies are sent to the Center for Scientific Review (CSR).

Applications must be received by April 6, 2000. 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 CSR and responsiveness by the participating NIH entities. Incomplete and nonresponsive 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 CSR in accordance with the review criteria stated below. As part of the initial merit review, all applications will receive a written critique and may 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.

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. In addition to the criteria list below, the initial review group will examine: the appropriateness of proposed project budget and duration; the adequacy of plans to include both genders, minorities (and their subgroups), and children 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.

(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? For Pilot Research Projects, what is the likelihood that the research will contribute to the development of interdisciplinary programs or more mature research endeavors?

(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) INVESTIGATORS: Is each 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 of the project? Do the proposed studies take advantage of unique features of the scientific environment or employ useful collaborative arrangements?

AWARD CRITERIA

Applications will compete for available funds with all other approved applications submitted in response to this RFA. The following will be considered in making funding decisions:

The quality of the proposed project as determined by peer review

- o Availability of funds

- o The research priorities of the participating NIH Institutes.

INQUIRIES

Inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Applicants may also subscribe to the OBSSR's automated e-mail service in order to obtain subsequent information about this RFA. To subscribe, please send a message addressed to listserv@list.nih.gov. The message should read SUBscribe RFA-ADHERENCE-L [your full name]. The message is case sensitive; so capitalize as indicated! Do not include the brackets. For example, for Robin Smith to subscribe, the message would read "SUBscribe RFA-ADHERENCE-L Robin Smith" (omit the quotation marks). The subject line

should be blank. Subscribers will receive a confirmation of their subscription along with instructions on how to use the LISTSERV and how to unsubscribe. Information concerning the RFA, including "Frequently Asked Questions and Answers," will be posted on the OBSSR HomePage at <http://www1.od.nih.gov/obssr/adherence.htm>.

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AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.395 (NCI), 93.172 (NHGRI), 93.937 (NHLBI), 93.866 (NIA), 93.891 (NIAAA), 93.846 (NIAMS), 93.929 (NICHD), 93.121 (NIDCR), 93.279 (NIDA), 93.847/848/849 (NIDDK), 93.859 (NIGMS), 93.242 (NIMH), and 93.361 (NINR). Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410), as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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