

# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific  
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NOTE: The NIH Guide for Grants and Contracts will not be published  
on August 9, 1991. The next issue will be August 16, 1991.

NOTICES

HUMAN SUBJECTS CERTIFICATIONS AND VERTEBRATE ANIMAL VERIFICATIONS IN  
APPLICATIONS FOR NON-COMPETING (TYPE 5) CONTINUATION OF PHS GRANT AWARDS

P.T. 34; K.W. 1014006, 1014003, 0783005

National Institutes of Health

It has come to the attention of the NIH Grants Policy Office and the Office for Protection from Research Risks that applicant organizations often submit applications for non-competing (Type 5) continuation support that are missing the required approvals for involvement of human subjects and/or vertebrate animals. The PHS 2590 application kit for non-competing (Type 5) continuation support instructs that in activities involving human subjects and/or vertebrate animals, the applicant organization is required to provide on the face page of the application the most recent date of approval by the Institutional Review Board (IRB) and/or Institutional Animal Care and Use Committee (IACUC). This information is to be provided at the time of application submission. The 60-day grace period, allowed for competing (Type 1 and 2) applications, may not be invoked for noncompeting (Type 5) continuation applications. (See related notice in this issue). Furthermore, no application for continuation support may be submitted until the necessary IRB certification and/or IACUC verification of review has been obtained (PHS 2590, page 9). Delay in submitting the required certification/verification will result in substantial delays in the award process.

Questions concerning this notice may be addressed to the Grants Management Office of the NIH awarding unit.

## COMMON RULE FOR THE PROTECTION OF HUMAN SUBJECTS

P.T. 34; K.W. 1014006, 0783005

National Institutes of Health

The Federal Policy for the Protection of Human Subjects was published in the Federal Register on June 18, 1991, as a final common rule (56CFR28004). The common rule applies to sixteen Federal departments and agencies conducting or supporting research involving human subjects. These include the Departments of Agriculture, Commerce, Defense, Education, Energy, Health and Human Services, Housing and Urban Development, Justice, Transportation, Veterans Affairs, and the Agency for International Development, Central Intelligence Agency, Consumer Product Safety Commission, Environmental Protection Agency, National Science Foundation, and National Aeronautics and Space Administration. In addition, the Food and Drug Administration simultaneously published modifications to its regulations to adopt provisions of the common rule.

Publication of the common rule implements a 1981 recommendation of the former President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. The recommendation called for a uniform policy governing federally conducted or supported research involving human subjects based on regulations for the protection of human subjects of the Department of Health and Human Services (HHS). An interagency committee developed the Federal policy under the auspices of the Office of Science and Technology Policy. The policy was first published in 1986 as a proposed "model policy," and then in 1988 as a Notice of Proposed Common Rule Making.

The common rule provides for protection mechanisms such as prospective and ongoing review of research by institutional review boards, assessment of risks and benefits of research to human subjects, an informed consent process, and a system of institutional assurances of compliance with regulatory requirements to protect human subjects.

Implementation of the common rule on the part of the departments and agencies will provide wider application of recognized protections for research subjects and a more consistent regulatory approach for institutions conducting Federally supported research.

The common rule is based on and replaces subpart A of the 1981 Department of Health and Human Services regulations for the protection of human subjects at Title 45 CFR Part 46 and is quite similar to those regulations. There are some important differences, however. For example:

### Grace Period:

The common rule does not explicitly incorporate the regulatory provision that is a part of the 1981 Department of Health and Human Services' regulations for a "60-day grace period" for Multiple Project Assurance Institutional Review Boards (IRBs) to certify IRB review and approval after a receipt of an application.

The grace period is not meaningful in the context of the review processes of other departments; hence, it is not appropriate to include it in a common rule. The preamble to the rule indicates that HHS intends to retain administratively the grace period, however.

In response to the Notice of Proposed Rule Making, many institutions raised concerns about loss of the grace period. HHS, which includes the Public Health Service, will still honor the policy that within 60 days after the date of submission to HHS of an application or proposal, an institution with an approved assurance covering the proposed research shall certify that the application or proposal has been reviewed and approved by the IRB, except whenever there is a specific mandate and advisory to do so within a different time period, e.g., for certain HIV-related research (see NIH Guide for Grants and Contracts, Vol. 17, No. 13, April 8, 1998).

As provided in the regulations at Title 45 CFR Part 46.103(f), institutions without an assurance on file that covers the research to be conducted shall certify that the application or proposal has been approved by the IRB with 30 days after receipt of a request for an Assurance of Compliance from the Office for Protection from Research Risks. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

The above pertains to applications for competing awards. For information regarding applications for noncompeting continuation support, see other notice in this issue.

**Exemptions:**

The exemptions in Section 101, applicability, differ slightly from those in the 1981 regulations at Title 45 CFR Part 46.

Applicant institutions should become familiar with the exemptions and be certain to cite the correct exemption, if applicable, in the PHS 398 Public Health Service Grant Application and in other documents.

There are additional differences between the 1981 HHS regulations and the common rule with which researchers and administrators will want to become aware.

Copies of the common rule have been provided to Multiple Project Assurance Institutions and their Institutional Review Boards. For further information, contact:

The Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-7005

NOTICES OF AVAILABILITY (RFPs AND RFAs)

SHELF-LIFE EVALUATION OF CLINICAL DRUGS

RFP AVAILABLE: NCI-CM-27721-19

P.T. 34; K.W. 0740025, 1003008

National Cancer Institute

The Pharmaceutical Resources Branch of the Developmental Therapeutics Program, Division of Cancer Treatment, National Cancer Institute (NCI), is seeking a contractor experienced in analysis and evaluation of clinical pharmaceuticals to provide proper storage, adequate testing, and evaluation of the shelf-life of samples of investigational clinical drug formulations, including both injectable products and oral dosage forms, and report the results of such testing. Data provided in these reports will be used for providing NCI and its investigators with information regarding the proper storage and handling of various drug products under investigation, for determining appropriate expiration dates for the products, and to support NCI Investigational New Drug Applications (INDs) files with the Food and Drug Administration (FDA). Storage and inspection of reserve samples as defined by the FDA Current Good Manufacturing Practices Regulations shall be required. The contractor will be responsible for validating each of the analytical methods in conformance with FDA requirements prior to use.

RFP No. NCI-CM-27721-19 will be issued upon request to Zetherine Gore, Contract Specialist, on or about July 31, 1991. Proposals will be due approximately 45 days thereafter. The contract period is five years beginning approximately May 1992. The NCI expects to award one contract from this solicitation.

For a copy of RFP NCI-CM-27721-19, send a stamped, self-addressed envelope to:

Ms. Zetherine Gore  
Contract Specialist  
Developmental Therapeutics Program  
Division of Cancer Treatment  
National Cancer Institute  
Executive Plaza South, Room 603  
Bethesda, MD 20892

## ONGOING PROGRAM ANNOUNCEMENTS

### MULTI-INSTITUTIONAL COLLABORATIVE RESEARCH PROJECT

PA AVAILABLE: PA-91-81

P.T. 34; K.W. 0715095, 0715129

National Institute of Mental Health

The National Institute of Mental Health (NIMH) is accepting applications for Multi-Institutional Collaborative Research Projects (MICRPs). These are investigator-initiated and investigator-coordinated, multi-site projects. The purpose of the MICRP (R10) mechanism is to facilitate research that requires collaboration between or among organizationally distinct entities and that is best carried out if the independence of the investigators is maintained, while simultaneously providing a mechanism for coordination within the overall project. Unlike the cooperative agreement (U01) mechanism, the MICRPs will not have a Federal collaborator involved in planning or conducting the research. In contrast with the traditional research project (R01) award, no subcontracting will be required to support the collaborative research projects, and each site will have a Principal Investigator.

This announcement summarizes the guidelines for the preparation, review, and administration of multi-site collaborative studies in mental health. Interested parties are encouraged to obtain the Program Announcement (PA) from the NIMH staff contact listed below. Applications may be submitted by any public or private, non-profit or for-profit, organization, including units of State and local governments. Women and minority investigators are especially encouraged to apply.

Separate applications must be submitted from each participating institution, and applicants must use the form PHS 398 (revised 10/88). All applications comprising the MICRP must be submitted for the same receipt deadline and have identical titles. Complete item 2 of the face page by typing the title and number of this announcement.

Applications for NIMH grants and cooperative agreements are required to include both women and minorities in study populations for clinical research, unless compelling scientific or other justification for not including either women or minorities is provided. This requirement is intended to ensure that research findings will be of benefit to all persons at risk of the disease, disorder, or condition under study. For the purpose of these policies, clinical research involves human studies of etiology, treatment, diagnosis, prevention, or epidemiology of diseases, disorders, or conditions, including but not limited to clinical trials; and minorities include U.S. racial/ethnic minority populations (specifically, American Indians or Alaskan Natives, Asian/Pacific Islanders, Blacks, and Hispanics). NIMH recognizes that it may not be feasible or appropriate in all clinical research projects to include representation of the full array of U.S. racial/ethnic minority populations. However, applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups in the project as a whole.

Applications should include a description of the composition of the proposed study population by gender and racial/ethnic group, and the rationale for the numbers and kinds of people selected to participate. This information should be included in the form PHS 398 in Section 2, A-D, of the Research Plan AND summarized in Section 2, E, Human Subjects.

Applications should incorporate in their study design gender and/or minority representation appropriate to the scientific objectives of the work proposed. If representation of women or minorities in sufficient numbers to permit assessment of differential effects is not feasible or is not appropriate, the reasons for this must be explained and justified. The rationale may relate to the purpose of the research, the health of the subjects, or other compelling circumstances (e.g., if in the only study population available there is a disproportionate representation in terms of age distribution, risk factors, incidence/prevalence, etc., of one gender or minority/majority group).

If the required information is not contained within the application, the review will be deferred until it is complete. Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If gender and/or minority representation/justification are judged to be inadequate, reviewers will consider this as a deficiency in assigning the priority score to the application.

All applications/proposals for clinical research are required to address these policies. NIMH will not award grants that do not comply with these policies.

Applications will be received according to the standard PHS review schedules. All applications will be reviewed for scientific and technical merit by an initial review group (IRG), composed primarily of non-Federal scientific experts, and by the appropriate Advisory Council. By law, only projects recommended for approval by the IRG and Council may be considered for funding.

Each application within the R10 will be evaluated on the merit of the overall project plan, the merit of each site's individual contributions, and the relationship between these two aspects. The priority score assigned to each application will be based on the IRG evaluation of the merits of the entire project (all sites) proposed for the MICRP as well as the merit of the individual sites. Reviewers may decide that the project can be successfully completed as proposed and recommend approval with identical priority scores for each application. The IRG may also determine that all applications within the proposed MICRP are not equally meritorious or necessary to accomplish the goals.

Support may be requested for expenses clearly related and necessary to conduct the research, including both direct and allowable indirect costs. Applicants may request support for up to five years. A competing continuation (renewal) application may be submitted near the end of a grant period in order to request funds for the continuation of the project.

Because of the complex nature of collaborative studies and budgeting constraints, potential applicants are strongly encouraged to seek information and consultation from NIMH staff members as listed in the PA. Copies of the PA are available from:

Anne Cooley  
Division of Extramural Activities  
National Institute of Mental Health  
Parklawn Building, Room 9-97  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-4673

For further information on grants management issues, contact:

Stephen J. Hudak  
Chief, Grants Management Section  
National Institute of Mental Health  
Parklawn Building, Room 7C-23  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-4596

This program is described in the Catalog of Federal Domestic Assistance No. 93.242. Awards are made under authority of Section 301 of the Public Health Service Act (42 USC 241), as amended. Grants must be administered in accordance with the "PHS Grants Policy Statement (revised October 1990)."

ASSOCIATION OF ARTHRITIS, INFLAMMATORY MUSCLE DISEASES AND OTHER RHEUMATIC MANIFESTATIONS WITH HIV POSITIVITY AND AIDS

PA: PA-91-82

P.T. 34; K.W. 0715008, 0715010, 0715026, 0715136

National Institute of Arthritis and Musculoskeletal and Skin Diseases

The Arthritis and Muscle Biology Programs of the National Institute of Arthritis and Musculoskeletal and Skin Diseases invite research grant applications to study arthritis and inflammatory muscle and other rheumatic conditions associated with HIV infection and/or AIDS. This program announcement is to encourage research grant applications for basic, clinical, and epidemiologic research. Research mechanisms to support these investigations include traditional research grants (R01), Clinical Investigator Awards (K08), and First Independent Research Support and Transition (FIRST) Awards (R29).

Several investigators have reported the co-occurrence of HIV antibody positivity or frank AIDS with Reiter's Syndrome and other rheumatic disorders. It is unknown whether a causal biological connection exists between certain

arthritis and HIV infection or some of these co-occurrences are merely coincidental.

Certain arthritis and inflammatory muscle diseases and other rheumatic disorders may be found more frequently in HIV-positive individuals and AIDS patients than in the general population, according to reported observations. The frequency, spectrum, and natural history of these conditions in HIV-positive individuals, including AIDS cases, are unknown. It has also been noted that a spectrum of disease encompassing Reiter's syndrome and psoriasis, in particular, appears to be more severe and increasingly difficult to control as signs of immunodeficiency develop. Myositis may be an early presenting feature of HIV infection, and myopathy secondary to zidovudine therapy has been reported.

Safety and efficacy of drugs used in the management of arthritis, inflammatory muscle diseases, and other rheumatic disorders have not been formally assessed in HIV-positive individuals. Recent case reports have suggested that immunosuppressive drugs, particularly methotrexate, used widely at present in the management of rheumatoid arthritis and psoriatic arthritis, may accelerate AIDS in HIV-infected individuals.

A previous program announcement (see NIH Guide for Grants and Contracts, Vol. 17, No. 12, April 1, 1988) was published to encourage research in this area. The current solicitation is intended to further stimulate basic, clinical, and epidemiologic research related to arthritis, inflammatory muscle diseases, and other rheumatic manifestations in HIV-positive individuals, including those who have AIDS. In addition, it is expected that the increased frequency of these diseases in HIV-positive individuals will provide unusual opportunities for research on the pathogenesis and accelerating factors in Reiter's syndrome, myositis, and other rheumatic diseases of uncertain etiology.

Among the broad spectrum of basic research projects encouraged are studies of disease pathophysiology and genetics. Clinical studies may include prevention of morbidity and mortality or amelioration of arthritis, inflammatory muscle disease, and other rheumatic complications. Epidemiologic studies may focus on etiology, risk factors for disease development and severity, natural history of disease, and prognosis for developing disease. This includes AIDS and arthritis, inflammatory myopathy, and other rheumatic syndromes as well as descriptive studies of incidence, prevalence, morbidity, and mortality.

Investigators are encouraged to work with existing, or proposed, longitudinal data collection resources and cohorts of patients. Populations that may be included are those at increased risk for HIV infection, as well as HIV-positive cohorts who are clearly defined by their source of exposure. Investigators are encouraged to use existing cohorts, such as the Multicenter AIDS Cohort Study (MACS), the HIV Pulmonary Complications Study, and the AIDS Clinical Trials Group patients.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects. Applicants/offers are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority populations groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' population, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### ELIGIBILITY

Nonprofit organizations and institutions, governments and their agencies, for-profit organizations, and individuals are eligible to apply. Foreign institutions are eligible to apply.

#### APPLICATION PROCEDURES

Applications will be accepted in accordance with the announced receipt dates for unsolicited AIDS R01 and R29 applications, January 2, May 1, and September 1 of each year. AIDS investigator-initiated applications received on these dates by the Division of Research Grants will undergo expedited review. Applicants for the K08 award must submit applications to meet the receipt dates listed in the instructions for that mechanism.

All applications must be submitted on form PHS 398 (rev. 10/88). Application kits are available in the business or grants and contract office at most research and academic institutions. Additional application kits may be obtained from the office of Grants Inquiries, Division of Research Grants (DRG), NIH, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The phrase, "Association of Arthritis, Inflammatory Muscle Diseases and Other Rheumatic Manifestations with HIV Positivity and AIDS, PA-91-82" must be typed at item 2 of the face page of the application form 398 (rev. 10/88). The original and 24 copies for receipt dates of an R01 or R29 application submitted for expedited review must be sent to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES AND CRITERIA

Applications in response to this solicitation will be reviewed in competition with other research grant applications and in accord with the expedited NIH peer review procedures for AIDS-related research. To expedite the review, investigators must submit PHS human subject certifications and animal verifications with the applications. Applications will be reviewed first for technical merit by initial review groups and then by an appropriate national advisory council. The review criteria customarily employed by the NIH for research grant applications will prevail.

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. In such



a case, a letter of agreement from the Program Director of the GCRC must be included with the application material.

All PHS and NIH grant policies governing research project grants apply to applications received in response to this program announcement. Applications will be referred in accordance with customary procedures of the DRG.

For further information contact:

Lawrence M. Petrucelli, Ph.D.  
Arthritis Program Director  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 405  
Bethesda, MD 20892  
Telephone: (301) 496-7326

Richard W. Lymn, Ph.D.  
Muscle Biology Program Director  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403B  
Bethesda, MD 20892  
Telephone: (301) 496-7495

Reva C. Lawrence, M.P.H.  
Epidemiology/Data Systems Program Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Building 31, Room 4C13  
Bethesda, MD 20892  
Telephone: (301) 496-0434

For administrative and fiscal matters, contact:

Diane Watson  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 407-A  
Bethesda, MD 20892  
Telephone: (301) 496-7495

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 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.

#### CANCER THERAPY RESEARCH IN LUNG CANCER

PA: PA-91-83

P.T. 34; K.W. 0715035, 0715165, 0745045, 0745062, 0740015, 0765012

National Cancer Institute

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

#### I. PURPOSE

The National Cancer Institute (NCI) seeks grant applications to conduct therapeutic studies in lung cancer in human subjects. This Program Announcement (PA) encompasses a full range of therapeutic studies and clinical trials employing surgery, radiation, chemotherapies, or biologic response modifiers. The intent of the announcement is to encourage clinical researchers to translate new insights in the biology of lung cancer into clinical trials of innovative cancer therapies.

This type of grant solicitation, a Program Announcement, is used to encourage investigator-initiated research projects in areas of special importance to the NCI.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Clinical Cancer Therapy Research, is related to the priority area of cancer. Potential applicants may

obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202/783-3238).

## II. BACKGROUND INFORMATION

In the past several years, research efforts into understanding the biology of lung cancer have been productive. Laboratory associations with both dominant (ras, myc) and suppressor (p53, Rb) oncogenes, growth factors and their receptors (EGF, HerB/neu), and recurrent cytogenetic abnormalities (3p deletion) have been made with either small cell or non-small cell lung cancer. At the same time, promising developments have occurred in both pre-existing treatment modalities such as cytotoxics (new combinations of agents) and radiation therapy (new techniques of administration, radiosensitization and radioprotection), as well as new approaches such as differentiating agents/retinoids, biologic response modifiers, and photodynamic therapy and new drugs (taxol). Unfortunately, neither the basic nor the therapeutic advances have yet translated into marked improvement in the treatment of lung cancer. Therefore, it is essential to facilitate collaborations between basic scientists and clinical investigators in order to promote the rapid incorporation of promising scientific advances into research on a well-characterized lung cancer patient population.

## III. RESEARCH GOALS AND SCOPE

The Division of Cancer Treatment (DCT) is requesting qualified investigators to develop research grant (R01) applications and First Independent Research Support and Transition (FIRST) Award (R29) applications involving therapeutic studies of lung cancer patients. Studies should involve human subjects and be designed to ultimately improve lung cancer treatment. The applications may include single or multi-institutional (e.g., consortia, cooperative groups) research studies with appropriate biological correlates linked to these studies. New therapeutic studies may involve drugs, radiation, surgery, or biologic response modifiers, alone or in combination. Biological correlate studies that have clinical relevance to lung cancer therapies are also appropriate.

Some examples of therapeutic studies include, but are not limited to:

- o immunotherapies based on surgically obtained tumor specimens;
- o therapies with novel mechanisms of action (e.g., retinoids);
- o new radiation therapies, or radiation modifiers, to enhance cell kill or protect normal tissues;
- o biologic response modifiers (e.g., monoclonal antibodies, cytokines, tumor vaccines) alone or in combination with other therapies;
- o studies of drug- or radiation-resistance and reversal;
- o therapies aimed at interfering with growth factor action (e.g., suramin, bombesin analogs);
- o innovative surgically based multimodality studies.

Some examples of biological correlate studies include:

- o phenotypic or genotypic alterations that appear to correlate with the development of drug- or radiation-resistance;
- o oncogenes, growth factors, and specific antigen expression on tumor cells;
- o pharmacokinetic and pharmacodynamic measurements;
- o biochemical pharmacologic parameters;
- o imaging studies to assess efficacy of treatment.

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. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator must be included with the application.

## IV. MECHANISM OF SUPPORT

Support of this program will be by the research project (R01) and the First Independent Research Support and Transition (FIRST) Award (R29). Applicants will be responsible for the planning, direction, and execution of the proposed project. All PHS and NIH grants policies will apply to applications received in response to this announcement. Domestic applicants may request no more than five years of support, and foreign applicants may request no more than three years. Applications submitted in response to this PA will compete for

funds with all other investigator-initiated applications. The award of grants in response to this PA is also contingent upon the availability of funds.

## V. ELIGIBILITY REQUIREMENTS

Non-profit and for-profit organizations and institutions, governments and their agencies, and occasionally individuals are eligible to apply. Both domestic and foreign applicants may apply. Applications may be submitted from a single institution or may include arrangements with multiple institutions (e.g., consortia, clinical cooperative group) if appropriate. Applications from minority individuals and women are encouraged.

## VI. REVIEW PROCEDURES AND CRITERIA

### A. REVIEW PROCEDURE

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by an appropriate peer review group convened by the DRG. Following peer review, the applications will receive a second-level review by the appropriate national advisory council/board.

### B. SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including not but limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population

is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### VII. METHOD OF APPLYING

The research grant application form PHS 398 (revised 10/88) must be used in applying for these grants and will be accepted at the standard application deadlines. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, Bethesda, MD 20892; and from the NCI Program Director named below. The title and number of this announcement must be typed in line 2 on the face page of the application. The typed original application and six signed exact single-sided photocopies must be submitted or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### IX. INQUIRIES

Written or telephone inquiries concerning the objectives and scope of this PA and inquiries about whether or not specified proposed research would be responsive are encouraged and should be directed to the Program Directors, Ms. Diane Bronzert and Dr. Roy Wu, at the address below. The Program Directors welcome the opportunity to clarify any issues or questions from potential applicants.

##### For Technical Information:

Ms. Diane A. Bronzert or  
Dr. Roy S. Wu  
Program Directors  
Cancer Therapy Evaluation Program  
Division of Cancer Treatment  
National Cancer Institute  
EPN, Room 734  
Bethesda, MD 20892  
Telephone: (301) 496-8866  
FAX: (301) 480-4663

##### For Business Information:

Ms. Carolyn Mason  
Grants Management Specialist  
National Cancer Institute  
EPS, Room 242  
Bethesda, MD 20892  
Telephone: (301) 496-7800 ext. 59

This program is described in the Catalog of Federal Domestic Assistance No 93.395, Cancer Treatment Research. Awards are made under the authorization of the Public Health Service Act, Sections 301, 410, and 411 (Public Law 78-410, 42 USC 241 as amended, Public Law 99-158, 42 USC 285a) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 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.

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

5333 Westbard Avenue  
Bethesda, Maryland 20816