Full Text PAR-97-006

SMALL GRANTS FOR THERAPEUTIC CLINICAL TRIALS OF MALIGNANCIES

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PURPOSE

The Division of Cancer Treatment Diagnosis and Centers(DCTDC), National Cancer Institute (NCI) announces a small grants program to encourage the submission of small grant applications for new therapeutic clinical trials of malignancies that take advantage of recent laboratory developments. New and experienced investigators in relevant fields and disciplines (clinical, surgical, and radiation oncology) may apply for small grants to test new treatment strategies in patients or do pilot clinical studies.

This PA supersedes PAR-95-023, Small Grants for Therapeutic Clinical Trials of Malignancies, which was published in the NIH Guide for Grants and Contracts, Vol. 24, No. 3, January 27, 1995.

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, Small Grants for Therapeutic Clinical Trials, 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 Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/512-1800).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State or local governments, and eligible agencies of the Federal government. Applications may be from a single institution or several institutions (collaborating institutions, consortia, clinical trials cooperative groups), if appropriate. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as principal investigators.

MECHANISM OF SUPPORT

Support of the program will be through the National Institutes of Health (NIH) small grants (R03) mechanism. The small grants research program provides limited funds (maximum of $50,000 direct costs per year) for short-term (not to exceed two years) research projects. These grants are non-renewable and continuation of projects developed under this program will be through the regular grant program.

Applicants will be responsible for the planning, direction, and execution of the proposed project. Applications submitted in response to this program announcement will compete for funds with all other R03 grant applications assigned to the NCI. The award of grants in response to this program announcement is also contingent upon the availability of funds. Awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement (rev. 4/94).

RESEARCH OBJECTIVES

Background

The NCI supports an extensive network of clinical and laboratory research studies related to cancer therapy through contracts, grants, and cooperative agreements. At present, there is no mechanism targeted to stimulate the communication of promising and potentially relevant new developments between the laboratory and the clinical setting. There is a need for a mechanism to fund short-term clinical studies and obtain preliminary clinical data rapidly. It is expected that these R03 grants will serve as a basis for planning future clinical research grant applications (R01) or NCI cooperative clinical trial group studies.

The small grants (R03) mechanism provides research support specifically limited in time and amount for studies in categorical program areas (see Research Goals and Scope). Small grants provide flexibility for initiating preliminary, short-term studies and are non-renewable. Furthermore, the time interval from application to funding is shortened under the R03 mechanism, thus allowing new ideas to be investigated or pursued in a more expeditious manner. The Cancer Therapy Evaluation Program, DCTDC, NCI has targeted the use of the small grants mechanism to support single or several institutions to perform therapeutic clinical trials to test new ideas. Support is needed to encourage new, as well as, experienced investigators to test new treatment approaches.

Research Goals and Scope

The aim of this initiative is to support therapeutic clinical trials of malignancies to move new treatment strategies more rapidly from the laboratory into the clinic. Clinical studies must involve human subjects and be therapeutic in design. The clinical studies must be based on a strong rationale and preclinical data should support the underlying hypotheses. The research plan should be focused on the clinical trial proposed. New clinical therapeutic trials employing drugs, biologics, radiation, or surgery whether used as a single

agent/modality or in combination are appropriate. Investigators should be able to identify sufficient numbers of patients to complete the trial in a timely manner.

Laboratory studies may also be proposed to conduct pharmacokinetic, pharmacodynamic, immunologic, and other important correlative studies in the cancer patients receiving therapy. The laboratory studies should be in support of the clinical trial, such that their conduct leads to a greater understanding of the relationship between drug administration and biological changes in patients.

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 must be included with the application.

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 subpopulations 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 new policy results from the NIH Revitalization Act of 1993 (Section 4928 of Public Law 103-43) and supersedes and strengthens the previous policies (Concerning the Inclusion of Women in Study Populations, and Concerning the Inclusion of Minorities in Study Populations), which have been in effect since 1990. The new policy contains some provisions that are substantially different from the 1990 policies.

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 reprinted 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.

APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 5/95). Applications must be received by the following receipt dates: May 15, September 15, and January 15. Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Extramural Outreach and Information Resources, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone (301) 435-0714, email: asknih@odrockm1.od.nih.gov. The title and number of this Program Announcement must be typed in Section 2 on the face page of the application.

Submit a signed, typewritten original of the application, and three signed, exact photocopies, in one package:

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, two additional copies of the application must also be sent to:

Ms. Toby Friedberg
Division of Extramural Activities
National Cancer Institute
Executive Plaza North, Room 636
6130 Executive Boulevard
Bethesda, MD 20892
Rockville, MD 20852 (for express mail)

Special Instructions for the Completion of the PHS 398 Application

"Just-in-time" (JIT) is an initiative of the National Institutes of Health (NIH) Extramural Reinvention Laboratory under the auspices of the National Performance Review and government-wide efforts to create a government that works better and costs less. JIT postpones the collection of certain information that currently must be included in all competing applications when submitted. The information for the applications with a likelihood of funding is submitted "just-in time" for awards to be made. This program announcement is incorporating JIT procedures as described below.

In responding to the program announcement, the instructions given below should replace the normal instructions for specific sections of the PHS 398 application form (rev. 5/95). Some sections are modified and others in the application do not need to be completed for the submission of the application but WILL be requested if your application receives a priority score in the fundable range. For all other items in the application, follow the usual instructions in the PHS 398 booklet.

FACE PAGE (Form AA) - The title and number of the PA must be typed in line 2. Failure to do so could result in delayed processing of your application such that it may not reach the review committee in time for review. The Social Security Number (SSN) of the Principal Investigator should not be included on the Face Page. It should be provided along with the applicant's name at the top of the Personal Data form page only (Form KK).

FORM DD - PAGE 4 - DETAILED BUDGET PAGE FOR INITIAL BUDGET PERIOD Do not complete form page 4 of the PHS 398 (rev. 5/95). It is not required nor will it be accepted at the time of application.

Form EE - Page 5 - BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD - Do not complete the categorical budget table on form page 5 in the PHS 398 (rev. 5/95). Only the requested total direct costs for each year and

total direct costs for the entire proposed period of support should be shown. Begin the budget justification in the space provided, using continuation pages as needed.

Budget Justification

o List the name, role on project and percent effort for all project personnel(salaried or unsalaried) and provide a narrative justification for each person based on his/her role on the project and proposed level of effort.

o Identify all consultants by name and organizational affiliation and describe the services to be performed.

o Provide a narrative justification for any major budget items, other than personnel, that are requested for the conduct of the project that would be considered unusual for the scope of research. No specific costs for items or categories should be shown.

o Indirect costs will be calculated at the time of the award using the institution's actual indirect cost rate. Applicants will be asked to identify the indirect cost exclusions prior to award.

o If consortium/contractual costs are requested, provide the percentage of the subcontract total costs (direct and indirect) relative to the total direct costs of the overall project. The subcontract budget justification should be prepared following the instructions provided above.

Form FF - Page 6- BIOGRAPHICAL SKETCH

A biographical sketch is required for all key personnel, following the modified instructions below. Do not exceed the two-page limit for each person.

o Complete the education block at the top of the form page;
o List current position(s) and those previous positions directly relevant to the application;
o List selected peer-reviewed publications directly relevant to the proposed project, with full citation;
o Provide information on research projects completed and/or research grants participated in during the last five years that are relevant to the proposed project. Title, principal investigator, funding source, and role on project must be provided.

Form GG - Page 7 - OTHER SUPPORT - Do not complete. Updated information will be requested by NCI staff from only those applicants being considered for funding.

Form HH - Page 8 - RESOURCES AND ENVIRONMENT - Complete item(s) only if proposed research requires specialized resources unique for the proposed research.

SPECIFIC INSTRUCTIONS - RESEARCH PLAN (Booklet Pages 15-19) - Applications in response to this PA should be concise and substantially shorter than regular grant applications. Items 1-4 may not exceed 16 pages in total.

Item 1 - Specific Aims - In one page or less, list in priority order, the broad, long-range objectives. Describe concisely and realistically the hypothesis to be tested and what the specific research described in this application is intended to accomplish.

Item 2 - Background and Significance - In three pages or less, use this section to describe (a) how the proposed research will contribute to meeting the goals and objectives of the PA; and, (b) explain the rationale for the selection of the general methods and approaches proposed to accomplish your specific aims.

Items 3-4 - Progress Report/Preliminary Studies, Research Design and Methods - In twelve pages or less, complete as instructed on pages 16-17 of the PHS 398 booklet. The investigator may use this section to address the following:

o preliminary studies pertinent to the application;

o rationale and hypothesis for the clinical trial and laboratory studies.

o general methods that will be utilized; provide specific details for those techniques which are unique or where a significant departure from a generally accepted technique is important for reviewers to know;

o outcome measures that will be used to assess the success or failure of each set of experiments (include statistical analyses for laboratory and clinical studies);

o plans for the rigorous data management and verification of research data;

o potential pitfalls in the experimental design and alternative studies that will be done if the proposed experiments fail.

Items 5-6 - Human Subjects, Vertebrate Animals - Complete as described on pages 17-18. State clearly the plans for early detection of and protection against adverse effects on human subjects. Describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection of such subjects. Use a format like the Annual Report Format for Gender and Minority Inclusion on pg. 31.

Item 7 - Consultants/Collaborators - Biographical sketches should conform to the brief format described previously for Form FF.

Item 8 - Consortium, Contractual Arrangements - In one page or less, provide a brief explanation of the programmatic, fiscal, and administrative arrangements made with collaborating organizations.

Item 9 - Literature Cited - In two pages or less, give full literature citations including the title of the article.

SPECIFIC INSTRUCTIONS - APPENDIX (Page 19) - Up to five publications, manuscripts submitted or accepted for publication, patents, invention

reports should be provided. Clinical protocol(s) must be included in this section.

SPECIFIC INSTRUCTIONS - CHECKLIST (Form II) - Do not complete. Information will be requested by NCI staff from only those applicants being considered for funding.

If you or your business office have any questions regarding these instructions, please contact program staff listed under INQUIRIES.

REVIEW CONSIDERATIONS

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by an appropriate review group at the Division of Extramural Activities, National Cancer Institute, in accordance with standard peer review procedures. Foreign grant applications will also be reviewed by the National Cancer Advisory Board.

Applications that are complete and responsive to the program announcement will be evaluated for scientific and technical merit by an appropriate peer review group in accordance with 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 will be discussed and assigned a priority score.

Review Criteria

o Importance, timeliness, and clinical merit of the clinical trials

o Scientific and technical merit and relevance of proposed patient monitoring or laboratory studies

o Appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research

o Qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research

o Availability of the resources necessary to perform the research

o Quality of data verification and management plans and statistical analysis

The initial research group will also examine the provisions for the protection of human and animal subjects, the safety of the research environment, and conformance with the NIH Guidelines for the Inclusion of Women and Minorities as Subjects in Clinical Research.

AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to the NCI. The following will be considered in making funding decisions: Quality of the proposed project as determined by peer review, availability of funds, and program

priority.

INQUIRIES

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

Direct inquiries regarding programmatic issues to:

Ms. Diane Bronzert or Dr. Roy Wu
Division of Cancer Treatment
National Cancer Institute
Executive Plaza North, Room 734
Bethesda, MD 20892
Telephone: (301) 496-8866
FAX: (301) 480-4663
Email: BRONZERD@DCT.NCI.NIH.GOV
WUR@DCT.NCI.NIH.GOV

Direct inquiries regarding fiscal matters to:

Ms. Victoria Price
Grants Administration Branch
National Cancer Institute
Executive Plaza South, Room 252
Bethesda, MD 20892
Telephone: (301) 496-7800, ext. 56
FAX: (301) 496-8601
Email: PRICEV@GAB.NCI.NIH.GOV

AUTHORITY AND REGULATIONS

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, Title IV, Part A (Public Law 78-410, as amended, Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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