July 2004

GUIDELINES FOR THE PROGRAM PROJECT GRANT OF THE NATIONAL CANCER INSTITUTE

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FORWARD

These Guidelines for the Program Project Grant of the National Cancer Institute are intended as a resource for prospective applicants and for reviewers of NCI program project (P01) applications. The Guidelines dated December 2003 are effective for all P01 applications submitted February 1, 2004 and later.

Program Projects constitute one of the major extramural research mechanisms supported by the National Cancer Institute (NCI). The NCI has found the P01 grant mechanism to be particularly effective and highly productive, especially in areas where interdisciplinary collaboration and specialized core resources are needed to achieve a larger objective than can be supported through the traditional single project R01 grant.

Submitting and reviewing a P01 application requires a substantial investment of effort by applicants, applicant organizations, NCI staff, and peer reviewers. To maximize the potential of this effort, prospective applicants are strongly encouraged to discuss their ideas with relevant NCI program staff prior to the submission of a formal application. Individuals should contact the NCI Referral Officer in the Division of Extramural Activities (DEA), NCI (E-mail: ncidearefof@dea.nci.nih.gov or 301-496-3428) for assistance in identifying appropriate NCI program areas and program staff.

Applicants must obtain approval from the NCI at least six weeks prior to the anticipated submission of a P01 application (including amended applications and requests for supplemental funds) requesting $500,000 or more in direct costs in any one year (NIH Guide to Grants and Contracts, dated October 16, 2001 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html).

In addition, for Type 2 (competing continuation) applications budget requests for direct costs for the first requested year must not exceed an increase of 20 percent over the direct costs awarded in the last non-competing (Type 5) year. Details of the restrictions on budget requests are provided at this web site: http://deainfo.nci.nih.gov/flash/NCIPolicy_p01_escalation.htm. To determine the base for calculation of the maximal allowed increase in the first continuation year, the principal investigator is strongly advised to contact appropriate NCI program staff for assistance.

It is a requirement that NCI P01 applications be prepared according to the instructions described in this document. The instructions for NCI application formatting refer to current procedures outlined in the Application for a Public Health Service Grant, PHS 398 (Rev. 5/01) as well as the latest changes in policies governing the submission, review and award of NCI P01s (see http://grants.nih.gov/grants/funding/phs398/phs398.html) (see http://grants.nih.gov/grants/funding). Applications not prepared using this or later versions of the PHS 398 application kit or not adhering to the instructions for preparation contained in this document may be returned without review.

Applications involving clinical research must meet the NIH requirement for addressing the protection of human subjects from research risk; the inclusion of women, minorities and children in the study populations; and the plan for data and safety monitoring (for research involving clinical trials). Expected accruals must be presented in tabular form for each clinical study proposed. Applicants should refer to the information in this document and the PHS 398 instructions. Failure to provide such information will result in the application being returned as non-responsive, or deferral of review until adequate information is provided.

Starting with the October 1, 2003 receipt date, investigators submitting an NIH application requesting research support of $500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why data sharing is not possible. This requirement is a reaffirmation of the NIH policy endorsing expedited translation of research results into knowledge, products and procedures to improve human health. Applicants should refer to the policy statements provided by the NIH Office of Extramural Research) (http://grants2.nih.gov/grants/policy/data_sharing/index.htm).

The NIH continues to evolve policies governing all extramural awards, including program projects. Applicants are strongly encouraged, therefore, to make certain to obtain the latest policy and procedure information as the first step in preparing a new or renewal P01 application. Updated information and additional copies of the P01 Guidelines may be obtained over the Internet by accessing the Home Page of the National Cancer Institute Division of Extramural Activities at: http://deainfo.nci.nih.gov/awards/P01.htm. Further information and guidance may also be obtained from the NCI Referral Officer (see contact information below), or for current grantees, from your NCI Program Director.

Referral Officer
Division of Extramural Activities
National Cancer Institute
6116 Executive Blvd., Room 8041
BETHESDA, MD 20892-8329
Rockville, MD 20852 (for courier delivery)
301-496-3428
301-402-0275 (FAX)
ncirefof@dea.nci.nih.gov

The process for submitting an NCI P01 application is different than that for most grant applications. All NCI P01 applications, including new, amended, supplemental and competing renewal applications, must be submitted on or before the P01 receipt dates February 1, June 1 or October 1. The original application and three copies are to be sent to the NIH Center for Scientific Review at the address provided in the PHS 398 form. Two copies of the application are to be sent directly to the NCI Referral Office at the above address.

BEGINNING WITH APPLICATIONS SUBMITTED FOR THE FEBRUARY 1, 2004 RECEIPT DATE, NCI IS DOING A 1-YEAR PILOT STUDY OF REVIEWING P01 APPLICATIONS CLUSTERED IN GROUPS ACCORDING TO SIMILAR TOPIC AND/OR APPROACH. IN THIS PROCESS, TWO TO FOUR APPLICATIONS ON RELATED TOPICS WILL BE REVIEWED BY ONE REVIEW PANEL ENCOMPASSING APPROPRIATE EXPERTISE. APPLICATIONS WILL BE GROUPED BASED ON COMMONALITY OF SCIENTIFIC RESEARCH AREAS AND GENERAL TECHNICAL APPROACHES IN A MANNER SIMILAR THAT USED IN THE STUDY SECTIONS OF THE NIH CENTER FOR SCIENTIFIC REVIEW. SITE VISITS WILL NOT BE CONDUCTED AS PART OF THE REVIEW PROCESS.

SUMMARY OF CHANGES

This page is a summary only. Detailed information is presented in the appropriate section.

Changes in Review Process

- Beginning with the February 1, 2004 receipt date, all NCI P01 applications will be reviewed by convened review panels meeting in the greater Washington, DC area
- Applications, grouped according to general research theme and approach, will be reviewed in clusters of two to four as appropriate
- New (Type 1), competing renewal (Type 2) and amended applications will be grouped together
- Amended applications will have a reasonable representation from the previous review panel
- Although site visits will be discontinued, applicants will have an opportunity to respond to review panel questions directly by telephone conference or by other means

Changes in Description of Application Preparation

- Directions for preparation of amended/revised applications have been clarified
- Directions for preparation of Type 3 applications (request for supplemental funds) have been presented in greater detail
- A plan for data sharing is now required for all grant applications submitted to the NIH
- Appendix materials may now be submitted as electronic files.

REMINDERS

- Communication with the NCI Referral Office via a Letter of Intent is required at least six weeks in advance of the projected submission date so that internal NCI approval can be obtained
- All NCI P01 applications are to be submitted February 1, June 1, or October 1
- The original application and three copies are to be sent to the Center for Scientific Review
- Two copies are to be sent to the NCI Referral Office

GUIDELINES FOR THE PROGRAM PROJECT GRANT OF THE NATIONAL CANCER INSTITUTE

I. INTRODUCTION

The Program Project (P01) grant is a mechanism for the support of an integrated, multiproject research program involving a number of independent investigators who share knowledge and common resources. This type of grant has a well-defined central research focus involving several disciplines or several aspects of one discipline. The individual projects are interrelated and synergistic; hence, they are expected to result in a greater contribution to program goals than if each project were pursued separately.

These Guidelines provide:

- Definitions, background and review criteria for National Cancer Institute (NCI) P01 grant applications.
- Instructions for the preparation of new, competing renewal, supplemental, amended and accelerated peer review (APR) P01 grant applications.
- Descriptions of the peer review process used for the evaluation of P01 grant applications.

II. DEFINITIONS and IMPORTANT URLs for GRANT POLICIES

Accelerated Peer Review (APR) - a mechanism for accelerated re-review of P01 applications that are rated as highly meritorious, but fall outside the IC=s P01 payline.

Awaiting Receipt of Application (ARA) - an internal NIH document submitted to CSR by NCI staff to indicate willingness to accept an application (a) requesting $500,000 or more in direct costs in any year, or (b) for programmatic relevance.

Core - a separately budgeted component of the P01 that provides essential facilities or services to two or more of the proposed research projects.

Draft Review Report - a preliminary compilation of reviewer critiques used by Scientific Review Groups to guide final discussion and assignment of overall priority scores to applications.

Grants Management Specialist - the NCI official who serves as the focal point for all business-related activities associated with the negotiation, award and administration of grants.

Letter of Intent - a non-binding notification submitted to NCI staff by a principal investigator indicating intent to submit an application.

National Cancer Advisory Board (NCAB) - a Presidential-appointed chartered advisory committee to the Secretary, DHHS and the Director, NCI, composed of both scientists and lay members, which performs the final advisory review of grant applications and advises on matters of significance to the policies, missions and goals of the NCI. The members include outstanding authorities knowledgeable in relevant programmatic areas that are especially concerned with the health needs of the American people.

National Cancer Institute Initial Review Group (NCI IRG) - a chartered advisory group composed primarily of non-Federal scientific experts who conduct the scientific and technical merit review (initial peer review) of grant applications and assign priority scores to meritorious applications. This large review committee is divided into a number of subcommittees or Scientific Review Groups (SRGs) that are analogous to study sections used throughout the NIH peer review system.

P01 - the NIH activity code which identifies a Program Project application or grant.

Principal Investigator - the one person designated by, and responsible to, the applicant/awardee institution for the scientific and administrative direction and proper conduct of all aspects of the P01.

Program Director - the NCI scientist administrator responsible for the development of initiatives and for the scientific management of research programs sponsored by the NCI. This person serves as the focal point for all science-related activities associated with the negotiation, award and administration of grants.

Program Project Grant (P01) - an assistance award for the support of a broadly based multidisciplinary research program that has a well-defined central research focus or objective. It may also include support for common supporting resources (cores) required for the conduct of the component research projects. Interrelationships between projects are expected to result in a greater contribution to the program goals than if each project were pursued separately.

Project - a research component of the P01 application with a separate detailed budget.

Project Leader/Core Director - the investigator responsible for the scientific direction and conduct of an individual research project or of a core component of a P01.

R01 - the NIH activity code that identifies an individual, investigator-initiated research project application or grant.

Review Panel - an advisory group of scientific experts typically including representatives of an SRG subcommittee plus ad hoc members. These review panels perform the initial technical review of P01 applications and provide comments in the form of a Draft Review Report to the chartered SRG.

Scientific Review Administrator (SRA) - the NCI scientist administrator responsible for the organization, management and documentation of the initial review process for applications.

Scientific Review Groups (SRGs) - subdivisions of the larger Initial Review Group, analogous to study sections used throughout the NIH peer review system. Currently, Subcommittees C (Basic and Preclinical), D (Clinical Studies) and E (Cancer Epidemiology, Prevention and Control) of the NCI IRG are responsible for review of P01 grant applications for NCI. (see http://deainfo.nci.nih.gov/Advisory/irg/sub-comte/index.htm)

Special Emphasis Panel (SEP) - an advisory group of scientific experts chartered for the specific review or collection of reviews by a blanket chartering mechanism. The SEP is a second type of IRG.

Summary Statement - the official record of the evaluation and recommendations of the IRG.

Work Group - a review panel that reports to a parent committee. Work groups are commonly used to review multi-component applications such as P01s. The report from this review, a draft

review report, is provided to the SRG where the final merit scoring is made. A work group may also be referred to as a review panel.

Important URLs for Grants Policy

http://cancer.gov/ (NCI Web Site)
http://deainfo.nci.nih.gov/funding.htm (Extramural Funding Opportunities)
http://deainfo.nci.nih.gov/extra/notices/index.htm (NCI Notices related to Initiatives)
http://grants.nih.gov/grants/peer/peer.htm (OER: Peer Review Policy and Issues)
http://grants.nih.gov/funding/phs398/phs398.html (PHS 398 Form and Instructions)
http://grants.nih.gov/grants/peer/hs_review_inst.pdf (NIH Instructions to Reviewers for Evaluating Research Involving Human Subjects)
http://www-cdp.ims.nci.nih.gov/policy.html (Research on Human Specimens)
http://grants1.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm (NIH Data Sharing Policy and Implementation Guidance)
http://www.nih.gov/news/stemcell/stemcellguidelines.htm

III. BACKGROUND

The P01 grant is intended solely for the support of multi-disciplinary or multifaceted research programs having a strong central theme. There are several features that distinguish P01 grants from other assistance mechanisms. Each project within a P01 is similar to the traditional research grant application in the sense that each is reviewed for scientific merit compared to a standard of quality in a broader scientific discipline. However, a component project also is evaluated within the context of the special collaborative interrelationships and environment required for a P01. Interaction between projects should be such that the acquisition of knowledge is accelerated or of a quality beyond that expected from the same projects conducted separately, without combined leadership or a common theme. Individual investigators apply their specialized research capabilities to basic research projects, clinical research projects, cancer control and cancer prevention research projects or combinations of such projects as they relate to the focused, central theme of the overall P01. Thus the P01 funding mechanism offers a special way to achieve research synergy through the sharing of personnel, facilities, equipment, data, ideas and concepts.

A P01 should include a sufficient number of scientifically meritorious projects to promote an effective collaborative effort among the participating investigators. To be eligible for an award, a P01 must consist of a minimum of three scientifically meritorious projects. However, the P01 should not be so large that it exceeds the scientific and administrative leadership capability of the principal investigator, or that it loses a tight focus. Applicants should realize that the larger the program, the greater the likelihood that some components will be of lower quality. The inclusion of projects of lower quality or of peripheral relationship to the central theme will have a negative impact on the overall evaluation. The maximum number of research projects recommended, therefore, is six. Plans to submit applications with more than six projects should be discussed with the appropriate NCI Program Director. Alternatively, investigators considering research programs with a larger number of projects should consider submission of separate P01 applications each containing fewer projects. Please note that division of projects into subprojects in order to designate additional key investigators or to fragment the experimental approach is not permitted, nor are applicants permitted to incorporate projects or core components in the application for which no funds are requested. For Type 2/competing renewal applications, in particular, reference may be made to other non-P01 projects/activities to emphasize institutional resources and support. Finally, in P01 grants, neither are there allowances for unspecified developmental research funds (seed money) nor is there an allowance for developmental projects.

A P01 grant application may contain one or more core component(s), each with a separate budget, for administrative or research support services that are required for and shared solely within a particular P01. Core components should be important to the overall success of the program, and each core must serve at least two projects. Core components may include research designed to improve core services. If a P01 application originates from an institution that is supported by an NCI Cancer Center Support Grant (P30), or there are Special Programs of Research Excellence (SPORE) (P50) on related research topics, a list of existing Cancer Center Shared Resources/Cores and SPORE resources and cores should be provided. If cores proposed within the P01 application duplicate existing institutional resources, clear justification should be provided for such duplication. Funds may be requested to supplement existing facilities in accordance with the needs of the P01.

Central to the quality of a P01 is the leadership of the principal investigator and the other senior participating investigators. The principal investigator of the P01 should be an established scientist with a strong record of accomplishment who is substantially committed to, and exercises the responsibility for the scientific leadership, integration and administration of the entire P01. The principal investigator need not serve as a project leader or core director. The component projects should be directed by investigators who are experienced in the conduct of independent research as evidenced by grant awards and publications and whose backgrounds and interests relate sufficiently to one another to allow for integrated group pursuit of the proposed P01 goals and objectives. There is one designated project leader and one designated core director for each project and core. This named person is the one responsible for overall management and coordination of the component.

IV. REVIEW CRITERIA

Peer review emphasizes a synthesis of two major aspects of the P01 application: (1) review of the merit of each of the individual research projects and core components compared to a standard of quality in its broad scientific discipline and (2) review of the program as an integrated research effort focused on a central theme. In arriving at an overall merit priority score for the P01, Scientific Review Group (SRG) members also will consider the likelihood that the proposed research program will have a substantial impact on the scientific field.

The review criteria for both the overall program and the individual projects are the standard NIH review criteria of "Significance," "Approach," "Innovation," "Investigators," and "Environment" (NIH Guide, Vol. 26, Num. 22, June 27, 1997 [http://grants1.nih.gov/grants/guide/notice-files/not97-010.html]). The sections below give more detail about how these five criteria are applied to the overall program and the individual projects.

A. Review Criteria for the Overall Program

- **Significance**: The overall program should be assessed for its potential to advance knowledge in a global scientific area.

- **Approach**: The overall adequacy and quality of the experimental approaches proposed in the projects and the overall design of the P01.

- **Innovation**: The degree to which the overall program applies novel concepts and innovative approaches.

- **Investigators**: The qualifications of the principal investigator and other senior scientists.

- **Environment**: Scientific, organizational and administrative environment.

B. Program Leadership

The leadership of the principal investigator is assessed according to the following criteria:

The demonstrated ability of the principal investigator to provide effective scientific and administrative leadership, as demonstrated by selection of individual projects for scientific excellence and thematic relatedness and by promotion of effective interactions and collaborations.

The adequacy of the commitment (percent effort) of the principal investigator to the P01. There should be a specific commitment to both the scientific and administrative aspects of the P01. Though a common practice, it is not mandatory that the principal investigator be a project leader of an individual research project.

Although the scientific merit of the P01 is based on the overall quality of scored and rated projects and cores, any components Not Recommended for Further Consideration (NRFC) are considered in the peer review evaluation of the principal investigator=s leadership and program administration skills.

C. Program as an Integrated Effort

The integrated effort is assessed by considering the following criteria:

Evidence of coordination, interrelationships and synergy among the meritorious research projects and core components as related to the common theme of the P01.

The advantages or value added that could be realized by conducting the proposed research as a P01 rather than through separate research efforts.

The presence and quality of mechanisms for regular communication and coordination among investigators.

The mechanisms for quality control of the research (e.g., internal or external advisory committees).

For competing renewals, evidence of productive collaborations, such as joint publications, resulting from the P01 award.

D. Review Criteria for Projects

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?

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?

Innovation: Are novel concepts, approaches or methods included? Are the aims original and innovative? Will the study challenge existing paradigms or develop new methodologies or technologies?

Investigators: Is the project leader appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the project leader and other researchers (if any)?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

Projects may be "Not Recommended For Further Consideration@ (NRFC) based on seriously flawed research approach or on inclusion of research hazardous to human subjects. Cores may be NRFC if they do not serve two or more projects or lack sufficient evidence of technical expertise and experienced leadership.

(NOTE: Synergy and thematic relatedness between the projects and cores, and the significance of the project for the program as a whole, will be evaluated under "Program as an Integrated Effort@ and/or in the "Overall Critique@ sections.)

E. Additional Review Criteria for Projects involving Human Subjects

For P01s that involve human subjects, reviewers will examine (a) whether the applicant has adequately addressed the protection of human subjects and (b) whether the involvement of minorities and children and the gender characteristics of the study population are scientifically acceptable and consistent with the aims of the project. Deficiencies in the application with respect to these issues will be considered in assessing merit of the research approach, and may impact on the recommended scientific merit rating of individual projects.

If human subjects are involved, applicants should consult the instructions in the PHS 398 package as well as the on-line "NIH Policy and Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research".
(http://grants.nih.gov/grants/funding/phs398/section_1.html)
(http://grants.nih.gov/grants/funding/women_min/women_min.htm).

For P01s that involve NIH-defined clinical research, investigators must report ethnic/racial enrollment in tabular form, as specified in the PHS 398 application. For those projects that involve clinical trials, investigators must include a general description of the Data and Safety Monitoring Plan in the application. (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html)

F. Review Criteria For Core(s)

The utility of the core to the P01. Each core must provide essential facilities or services for two or more projects judged to have substantial merit.

The quality of the facilities or services provided by this core (including procedures, techniques, and criteria for prioritization).

The qualifications, experience, and commitment of the personnel involved in this core.

The appropriateness of the budget, and accountability for distribution of costs to projects. A realistic budget reflects the core director's understanding of the scope of the work.

When appropriate, adequacy of the proposed plan to augment and/or complement an existing shared resource supported by an NCI Cancer Center Support Grant (P30).
For an Administrative Core: The quality of administrative resources, the decision-making process for the allocation of resources and funds, and the plans for the evaluation of progress

and future directions of the P01. Although not required, if an External Advisory Board is identified, there should be plans for meeting with and use of recommendations resulting from the meeting.

G. Additional Criteria for Competing Renewal Applications

- The progress and achievements specific to this P01 since the previous competitive review. Both continuing and discontinued projects and cores should be assessed.
- Evidence that scientific synergy has occurred as indicated by joint publications and new collaborative aims and/or projects.
- Evidence that the previous specific aims have been accomplished and that the new research goals are logical extensions.
- The previous performance and cost-effectiveness of the core(s).
- The justification for adding new projects or cores or deleting previous components.

H. Additional Criterion for Amended Applications

Amended applications should be assessed based on the overall merit of the application including any progress made and the quality of changes made in response to the previous critique. An amended application may be improved, the same as, or worse than the previous application.

V. ADVANCE COMMUNICATIONS with NCI STAFF

A. Initial Communications with NCI Staff

Research groups planning to submit a P01 application have found it useful to establish advance communications with relevant NCI staff. Such communications should begin at least three months prior to submission date.

Specific issues that might be discussed include:

- The theme or focus of the P01.
- The size and scope of the program and the optimal number of projects.
- The rationale for choosing the P01 mechanism for support of the planned research.
- For each project within the program, the tentative title, name of the project leader, and a brief summary of goals and relationship to the central theme.
- A brief description of the core component(s) and how each one supports the overall program.
- The estimated budget for the program. NOTE: If the budget for a competitive renewal application exceeds 120 percent of the last budget period, the application may be returned if NCI approval has not been obtained and documented.
- The methods to be used to stimulate communication and interaction among program participants.

Other related support.

For competing renewal applications, an identification of components to be discontinued and new components that might be added to the P01.

B. Letter of Intent

Applicants must obtain approval from the NCI at least 6 weeks prior to the anticipated submission of any P01 grant application, including requests for supplemental funds, requesting $500,000 or more in direct costs in any one year (NIH Guide to Grants and Contracts, dated October 16, 2001 [http:/grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html]. **This rule also applies to amended applications and applications that have been delayed to a later submission date.**

An informative Letter of Intent, as described below, will assist NCI staff in preparing the ARA, the NIH internal document required for such approval, in a timely manner. Communications about intent to submit a P01 application should be with the NCI Referral Office. If the application is received without prior staff concurrence and identification of program staff contacted, it will be returned to the applicant without review. All applications including amended applications must have this permission six weeks in advance of the planned receipt date. If application submission is delayed, a new communication to the NCI Referral Office must be made to update NCI staff regarding the intent to submit the application.

Although the Letter of Intent is not binding either for the planned submission date or for final detailed research content, the information provided also allows NCI review staff to estimate the potential review workload and to avoid conflict of interest in the review. The Letter of Intent should include at a minimum:

1. The names of the principal investigator and principal collaborators.
2. A descriptive title of the potential application and a list of titles for the anticipated components of the P01.
3. Identification of the organization(s) involved.
4. Announcement (if any) to which the potential application is responsive.

Letters of Intent should be sent to:

Referral Officer
Division of Extramural Activities
National Cancer Institute
6116 Executive Blvd., Room 8041
BETHESDA, MD 20892-8329
Rockville, MD 20852 (for courier delivery)
301-496-3428
301-402-0275 7(FAX)
ncirefof@dea.nci.nih.gov

The Referral Office will send a copy to the Chief, Research Programs Review Branch and to the appropriate NCI program director. If you have previously been in communication with an NCI program director, please provide their name in the letter and forward them a copy of the letter.

VI. SPECIAL INSTRUCTIONS for PREPARATION of PROGRAM PROJECT APPLICATIONS

General instructions for the preparation of the P01 grant application are contained in the Grant Application Form PHS 398 (Revised 05/01). Please note that the instructions provided in the PHS 398 document are designed primarily for traditional research project (R01) applications. P01 applications require additional information as outlined below. Clear and concise organization of the document is essential to the efficient study and review of the application. Page limitations are presented in the PHS 398 instructions; these should be followed closely for each individual project and core unless otherwise noted. Page limitations for the sections relating to the overall program are noted under the specific categories.

When submitting the application, please attach a cover letter that includes the following information: the institute (NCI) which has agreed to accept the application (see NIH Policy), the name of the NCI program director, and response to a Program Announcement or RFA (if applicable),

A. Face Page (PHS 398 Form Page 1; Instructions for PHS 398, Section I-C1)

   Type "PROGRAM PROJECT" in the top left-hand corner of the face page immediately above the words "GRANT APPLICATION." Complete all items on the face page of the application as in a traditional research grant application. This is page 1 of the application; all succeeding pages should be numbered consecutively.

B. Description, Performance Sites and Key Personnel (PHS 398 Form Page 2 and Continuation Pages; Instructions for PHS 398, Section I-C2)

   State concisely the overall goals of the entire P01 and clearly state the contribution of each component to the overall theme and goals. Under Performance Sites, list the applicant institution and all other sites where work described in the research plan will be conducted. Key personnel for the entire P01, including consultants and consortium collaborators, if any, should be listed alphabetically. To aid in the review of the application, include information concerning the distribution of effort of key personnel on each project and core. This could be presented in a tabular form such as that shown in Appendix B: Sample Table of Distribution of Professional Effort, NCI P01 Guidelines.

C. Table of Contents (PHS 398 Research Grant Table of Contents Form Page 3; Instructions for PHS 398, Section I-C3)

   Prepare a detailed table of contents that enables reviewers to find specific information readily. Identify projects by number, title and responsible investigator. Identify cores by letter, title and responsible investigator. A sample Table of Contents is included at the end of these Guidelines as an example of how the order and format of the application could be organized (see Appendix A, NCI P01 Guidelines). For Type 2/competing renewal or amended/revised applications, in the event an existing project or core is discontinued or deleted, all projects and cores should be renumbered in sequence.

D. Overall Budget for Program Project

   The PHS 398 Instructions (Sections 1-C4 and 1-C5) should be followed closely in preparing a detailed composite budget for all requested support for the first year using page 4 of the PHS 398 application. A summary budget for the entire proposed period of support should be prepared using page 5 of the PHS 398 application. The composite budgets should summarize all project/core expenses by category, i.e., personnel, equipment, and supplies.

   Budget requests for direct costs for Type 2/competing renewal P01 grant applications must not exceed an increase of 20 percent over the direct costs to be awarded in the last non-competing (Type 5) year. The Notice of Grant Award for the last grant period (Type 5) now

includes an estimate of the budget cap allowed for the competing renewal application. The principal investigator is encouraged to contact NCI program staff for assistance in preparing budgets. (http://deainfo.nci.nih.gov/flash/NCIPolicy_p01_escalation.htm).

E. Biographical Sketch and Other Research Support Information (PHS 398 Format Page; Instructions for PHS 398, Section I-C6)

Follow the instructions on the "Biographical Sketch Format Page". Biographical sketches are required for all KEY personnel participating in individual projects and cores and for all consultants. In arranging the biographical sketches, the principal investigator should be listed first, with other key personnel in alphabetical order. Each sketch may not exceed four pages. Item A (Positions and Honors) and Item B (Selected Publications) may not exceed two of the four-page limit.

Information on other support beyond that required in the biographical sketch should not be submitted with the application. Specifically, do not list award amounts or percent effort in projects, nor address potential scientific and/or budgetary overlap.

It is the policy of the NCI that meritorious projects reviewed as part of the P01 be funded as part of the P01 even though other funding (e.g., in the form of an R01 grant) may be available.

F. Program Narrative: Overall Program Project (PHS 398 Continuation Pages)

The narrative for the P01 should provide explicitly the required information in the order noted below. Efforts should be made to keep the narrative as concise as possible. **Typically, eight to twelve pages are sufficient.**

1. Goals and Significance: Present the general scientific or medical area to be studied, the overall long-term objectives of the research described in this application, and any hypotheses to be tested. In addition, the overall significance of the research effort should be described.

2. Theme: A P01 is a confederation of interrelated research projects. It is important to establish the programmatic theme in this section and to address the issue of the integration of components, demonstrating how each individual component benefits from and contributes to the overall P01. A diagram illustrating the interactions between components may be helpful to reviewers.

3. Research Plan: This section delineates the research effort as a whole and explains the strategic approach to the problem, briefly mentioning each project as it relates to the overall P01. Descriptions of prior collaborative efforts among investigators in the group, as well as the sequence of events leading to the current application, may also be included in this section. It is important to discuss the advantages expected from a group effort, e.g., how the projects are mutually reinforcing, how collectively they further the goals of the proposed research, etc.

4. Preliminary Studies (for new applications): This section should focus on ongoing research and current accomplishments of the investigators. More detailed preliminary reports should be included separately under each individual project. Items to be included are:

   # A summary of major accomplishments attributed to the participating investigators that relate to the overall theme of the P01.

   # A list of all publications and manuscripts accepted for publication already produced by the interaction(s) of the participating investigators.

5. Progress Report (for Type 2/ competing renewal applications): This section should describe achievements in the current funding period. Separate progress reports are included in the individual research projects, so the information in the program narrative should focus on the overall P01 rather than reiterating information provided in each component. Items to be included are:

    # A summary of major accomplishments that can be attributed to the P01 grant. Accomplishments involving more than one project leader should be noted.

    # A list of all publications and completed manuscripts that have resulted from the P01 grant. With an asterisk, denote each publication that is a result of formal collaborations among different projects within the program.

    # A list of project and core components in tabular form (by title, investigator and previous number/letter) that denotes which projects have been discontinued or completed since the last review. Also include projects that are continuing, are new, or are substantially modified. Explain the decision to discontinue, substantially modify, or start new projects.

6. Institutional Environment and Resources: Briefly describe the institutional environment and resources that are relevant to effective implementation of the P01. This may include statements about clinical and laboratory facilities, participating and affiliated units, patient population, geographic distribution of space and personnel, consultative resources and relevant collaborations with investigators currently funded under other mechanisms.

7. Organization and Administrative Structure: Several kinds of information are required in this section:

    # Describe in detail, and by diagram, the chain of authority for decision making and administration, beginning at the level of the principal investigator. Include investigators responsible for individual components (project leaders) and how the projects are planned, coordinated, and evaluated. If internal or external advisory groups are to be used, list the membership and describe the role of each.

    # List in a separate table all consultants, and their institutional affiliations, both paid and unpaid.

    # Describe relationships between the P01 and other research, academic, and administrative units of the institution (such as centers, institutes, departments) and the central administration.

8. Literature cited: List <u>complete</u> literature citations at the end of the program narrative. Each should include names of <u>all</u> authors, <u>full title</u>, name of book or journal, volume, pages and year of publication.

G. <u>Individual Research Projects</u> (Research Plan, Instructions for PHS 398, Section I-C8)

Describe each project **in sufficient detail to enable reviewers to judge the scientific merit from the written application**. Be explicit enough to enable experts in other areas to follow the main objective of the project. All projects are to have a single theme, project leader and budget. Separately numbered subprojects (i.e., such as Subprojects 3A and 3B) are not allowed.

1. Title Page (PHS 398 Continuation Page). Clearly denote the project number, the title of the project, the project leader=s name, and educational degrees.

2. Description/List of Key Personnel (PHS 398 Form Page 2). The title of "Principal Investigator" is reserved for the director of the overall application. The directors of individual projects should be referred to as "project leaders" and directors of cores should be referred to as "core directors."

3. Omit the PHS 398 Table of Contents form.

4. Detailed Budget (PHS 398 Form Pages 4 and 5; Instructions for PHS 398). A detailed budget is required for the first year and a budget summary for the future years. The budget justifications should be explicit, including those for any increases or changes for future years.

   In the upper left-hand corner of the initial year and total budget forms, identify the project or core. The PHS 398 Instructions (Sections 1-C4 and 1-C5) should be followed closely in preparing the budgets for individual projects and cores. If collaborative efforts or "purchased services" involving other institutions or organizations are anticipated, itemize all costs associated with such third-party participation, including any applicable indirect costs, on separate budget pages and enter the total under the "Consortium/ Contracted Costs" direct costs budget category. For details, refer to "Consortium Agreements," available on the Web at http://grants2.nih.gov/grants/policy/nihgps/part_iii_htm#Consortium

   The budget pages for the subcontracts should be identified by project or core and the name of the sub-contractual institution. They should be placed in the application in sequence after the main budget pages for the project or core.

   Pay particular attention to the specific instructions for justifying budget requests as NIH cost containment policies encourage the deletion of unreasonable or unjustified expenditures. All budget items and increases in future years, whether standard cost of living or projected special requirements, should be stated explicitly and justified clearly.

5. Omit Biographical Sketches and Other Support because these are grouped together elsewhere in the application.

6. Resources (PHS 398 Format Page). Follow the instructions on the PHS 398 Resources Format Page. List only those resources specific to the individual project or core.

7. Research Plan: (PHS 398 Continuation Pages; Instructions for PHS 398, Section I-C8). Do not exceed 25 pages for items a-d.

   a. Specific Aims. One to two pages are recommended.
   b. Background and Significance. Two to three pages are recommended.
   c. Preliminary Studies/Progress Report. Six to eight pages are recommended.
   d. Research Design and Methods. Limited by the 25 page maximum for items a-d.

8. Human Subjects Research (PHS 398 Continuation Pages; Instructions for PHS 398, Section I-C8, Item e).

   For P01s that involve human subjects, applicants must address (a) the protection of human subjects from research risk, (b) the inclusion of women, minorities and children in the study population, and (c) the plan for data and safety monitoring (for projects involving any type of clinical trials), in accordance with information provided in the ANIH Instructions

to Reviewers For Evaluating Research Involving Human Subjects in Grant and Cooperative Agreement Applications@ (http://grants.nih.gov/grants/peer/hs_review_inst.pdf). Deficiencies in the application with respect to these issues will be considered in evaluating the research approach, and may impact on the recommended scientific merit rating of individual projects.

For P01s that involve NIH-defined clinical research, investigators must report ethnic/racial enrollment in TABULAR form, as specified in the PHS 398 application. For those projects that involve phase I and/or phase II clinical trials, investigators must include a general description of the Data and Safety Monitoring Plan in the application. If a phase III clinical trial is proposed, a Data and Safety Monitoring Board is required.

9. Vertebrate Animals (PHS 398 Continuation Pages; Instructions for PHS 398, Section I-C8, Item f). Self-explanatory.

   NIH policy requires the submission of Institutional Animal Care and Use Committee (IACUC) approval when animal studies are involved. The certification must be submitted with the application or within 60 days after the application receipt date. Otherwise, the application will be considered incomplete and deferred to the next review cycle.

10. Literature Cited (PHS 398 Continuation Pages; Instructions for PHS 398, Item g). List complete literature citations at the end of each project. Each citation must include the names of all authors, full title, name of book or journal, volume, pages and year of publication.

11. Consortium/Contractual Arrangements (PHS 398 Continuation Pages; Instructions for PHS 398, Item h). Self-explanatory.

12. Consultants (PHS 398 Continuation Pages; Instructions for PHS 398, Item i). List consultants specific to this project but external to the P01. For each consultant, include within the application a letter of support detailing the nature and extent of participation. **Do not include these letters in the Appendix.**

13. Data Sharing Plan (PHS 398 Continuation Pages; Instructions for PHS 398, Item j). This description does not count toward the Research Plan page limits.

14. Do not include a checklist for each project.

15. If a Personnel Report is submitted with a competing continuation (Type 2) application, Personnel Report Forms should be identified by project/core and grouped at the end of the application.

16. Appendix **(Procedures differ from PHS 398 Instructions)**

    Do not submit appendix materials with the application. The SRA for the review will give applicants a specific deadline for submitting the appropriate number of **collated sets** of appendix materials in the initial communication. The appendix material is to be sent directly to the SRA by the stated deadline. An exception is for P01s submitted in response to an RFA. In this instance, the appendix material should be submitted with the application. Appendix materials must be received in time to distribute to reviewers. Appendix materials submitted later than the date specified by the Scientific Review Administrator will be returned to the applicants. Appendix material can be submitted as electronic documents. However, all material should be submitted on one CD if possible. Details of electronic submission procedures will be provided by the SRA.

Appendices should be clearly identified by project number and investigator, and may consist of the following materials:

a. Sets of supplementary graphs, diagrams, tables, photographs and charts directly pertinent to the application. Keep such material to a minimum; if it is essential to the evaluation of a project or of the application, incorporate it in the application. The appendix is not to be used to circumvent the page limitations in the application. Normally only the assigned reviewers for a project receive the appendix material for the project.

b. Publications and manuscripts accepted for publication. No more than 10 publications and/or accepted/@in press@ manuscripts may be submitted for each project. As stated in the 5/01 PHS 398 instructions, "submitted@ manuscripts or manuscripts "in preparation@ are not allowed.

I. Cores (PHS 398 Continuation Pages; Instructions for PHS 398)

The cores of a P01 may include laboratory and clinical facilities, equipment, and services that will be shared by two or more projects of the P01. A core may also include support for administration, such as the costs of fiscal and business management, consultant, secretarial and clinical services associated with the P01 unless these items are included in the institution's indirect cost rate.

1. Title Page. (Form PHS 398 Continuation Page) Clearly denote the core letter, the title of the core, and the core director's name and educational degree(s). If there is to be more than one core component, prepare a separate section for each core (i.e., Core A, Core B, etc.).

2. For each core component, follow the specific instructions for the individual Research Project, Section VI. In place of Item H. 7., Research Plan, describe the role of the core component as a resource to the P01 as a whole. The core service plan should include a description of the services to be provided and the background and significance for the inclusion of the core. The applicant should present a clear description of methods and services to be provided and (if appropriate) discussion of human subjects protection and inclusion, as well as a data safety monitoring plan/board. Cores may contain a non-hypothesis driven research activity, provided that the research is designed to improve core services. For competing renewal applications, a progress report/summary of services in the current funding period should be provided. This may include reference to publications from the completed research effort. Clearly present the facilities, resources, and professional skills that the core component provides.

   For Administrative Cores (if included in the P01), the services to be provided may encompass such functions as fiscal management, clerical support, manuscript preparation, meeting organization, data management, and quality control and planning/evaluation. The latter may include plans to establish internal and/or external advisory committees. If an Administrative Core is not part of the P01, these issues must be discussed under "Organization and Administrative Structure" in the Program Narrative (see Section VI, G.7 of these Guidelines). In particular, the principal investigator should include a discussion of the decision-making processes involved in the program and the planned mechanisms for promoting communication and collaboration among program investigators.

3. To aid in the review, it is suggested that a table showing the estimated or actual proportional use of this core component by each project be included in the application. (See Appendix C: Sample Table of Distribution of Core Resources). Justify each core

component by discussing ways in which these centralized services improve quality control, produce an economy of effort, and/or save overall costs compared to their inclusion as part of each project in the program.

4. The resources (or cores) within the P01 should not duplicate any available shared core facilities available to the research group. If duplication is necessary, justification should be provided along with an explanation as to why these institutional resources cannot be used for the P01 activities. For a P01 application originating from an institution that is supported by an NCI Cancer Center Support Grant (P30), a list of existing Cancer Center Shared Resources/Cores should be included as part of the institutional resources. P01 funds can be requested to augment pre-existing P30 Cancer Center or other such resources in order to direct these core support activities towards more effectively fulfilling the needs of the P01. The P01 should, where practical, use the Internal Review Board, Data and Safety Monitoring Boards (s), as well as clinical resources available throughout the Cancer Center.

5. For a competing renewal application, summarize core activities carried out during the preceding performance period.

J. Checklist for overall application (Use PHS 398 Checklist Form Page; Instructions for PHS 398). Self-explanatory.

VII. SPECIAL INSTRUCTIONS for AMENDED/REVISED APPLICATIONS

Prepare an amended/revised application according to instructions provided in Section VI of these Guidelines. An amended application will be returned without review if substantive changes are not clearly apparent and identified.

A. For an amended application, a telephone call or e-mail message to the NCI Referral Office may take the place of the Letter of Intent. Even though an application has been reviewed previously, NCI program staff will need to file another ARA notice if funds are requested in excess of $500,000 first year direct costs.

B. Acceptance of an amended application automatically withdraws the prior application.

C. Adjust the Table of Contents to include a listing for the “Introduction to the Amended/Revised Application” before the Program Narrative. Similarly, add an “Introduction to the Amended/Revised Application” before the Research Plan for the individual projects and cores.

D. Before the Program Narrative for the overall P01, provide an Introduction that summarizes the additions, deletions and changes that have been made. This new section should not exceed three pages.

E. Preceding the Research Plan, in each project and core, provide an introduction that delineates in greater detail the changes made in the research plan. This new section should not exceed two pages.

F. Incorporate in the Progress Report/Preliminary Results a discussion of any work done since the previous review.

G. Throughout the application text, amended portions or passages must be clearly identified to facilitate the review of the amended aspects of the application. The preferred method is to

use a vertical line in the left margin to mark amended areas of the application. An easily differentiable font, such as italics, of size required in the PHS 398 form, also may be used.

VIII. SPECIAL INSTRUCTIONS for COMPETING SUPPLEMENTAL APPLICATIONS

Requests for supplemental funds maybe submitted only for grants with at least two years of support remaining in the current award. A supplemental application is not accepted before the original application is awarded funding. The request for supplemental funds needs to have a well-founded basis, such as unexpected costs and/or pursuance of an unanticipated scientific opportunity or continuation of a currently funded project/core. It should contain sufficient detail to permit an adequate evaluation of the requested expansion of the overall P01. A supplemental application will not be accepted if (a) it is to restore administrative cuts or (b) it does not fit within the scope of the existing P01 or extend the program=s scope in a clear and logical manner. If the request for supplemental funds exceeds $500,000, the NCI Referral Office must be notified by a letter of intent or direct communication with Referral Office staff. Consultation with the program director of the original application may precede the submission of a competing supplement application.

All the information requested in these Guidelines (Section VI) should be included in the application, but adjusted to the requirements of the supplement as follows:

A. Face Page (PHS 398 Form Page 1; Instructions for PHS 398, Section I-C1)

Type “PROGRAM PROJECT” in the top left-hand corner of the face page immediately above the words “GRANT APPLICATION.” Complete all items on the face page of the application as in a traditional research grant application. This is page 1 of the application; all succeeding pages should be numbered consecutively.

B. Description, Performance Sites and Key Personnel (PHS 398 Form Page 2 and Continuation Pages; Instructions for PHS 398, Section I-C2)

Use the Description for the overall funded program as given in the original P01 application or state concisely the overall goals of the entire P01 and clearly state the contribution of each component to the overall theme and goals. Under Performance Sites, list the applicant institution and all other sites where work described in the research plan will be conducted. Key personnel for the entire P01, including consultants and consortium collaborators, if any, should be listed alphabetically. Investigators added specifically for the supplemental funds request should be identified by an asterisk (*) with annotation.

C. Table of Contents (PHS 398 Research Grant Table of Contents Form Page 3; Instructions for PHS 398, Section I-C3) A Table of Contents is optional, depending on the complexity of the Type 3 application.

D. Detailed Budget Award for Program Project Initial Budget Period (PHS 398 Form Page 5; Instructions for PHS 398, Section 1-C4)

Present a detailed composite budget table for all years of the P01 award. Label the composite budget table page in the upper left hand corner: CURRENT PROGRAM BUDGET

F. Biographical Sketch and Other Research Support Information (PHS 398 Format Page; Instructions for PHS 398, Section I-C6) Follow the instructions on the ‘‘Biographical Sketch Format Page.” Biographical sketches are required only for the P01 Principal Investigator and for individuals whose efforts are newly included in the request for supplemental funds. In arranging the biographical sketches, the principal investigator should be listed first, with other personnel in alphabetical order. Each sketch may not exceed four pages and should be prepared according to PHS 398 instructions. Item A (Positions and Honors) and Item B

(Selected Publications) may not exceed two of the four-page limit. Information on other support beyond that required in the biographical sketch should not be submitted with the application. Specifically, do not list award amounts or percent effort in projects, nor address potential scientific and/or budgetary overlap.

G. Program Narrative: Overall Program Project (PHS 398 Continuation Pages)

The program narrative for a Type 3 (request for supplemental funds) application should summarize briefly the theme and research goals of the funded program. The narrative also should include the justification for requesting additional supplemental funds. Progress made in the current funding period should be summarized for each project and core including numbers of publications and identification of completed aims. The description of the proposed research should include the goal of the entire P01 in addition to a summary of the supplemental request and the rationale for the request. The research plan should include rationale for how the requested funds will augment the funded program or the reasons for the urgent need for supplemental support.

If the supplemental request is for one or more new projects or for an extension of time for ongoing projects, each project should be described in detail. Particular emphasis should be placed on the relationship of each new project to the goals of the P01. **Typically, four or five pages are sufficient for the Overall Narrative.** Appendix material should be held until called for by the SRA. Appendix material may be submitted in electronic form on a CD. Instructions for formatting of the CD will be provided by the SRA.

H. Format for the Research Plan.

1. Additional project or core

   If the request is for a new project or core, the application format should follow the instructions for a project or core as described for a new P01 application (See Section VI). Describe the project **in sufficient detail to enable reviewers to judge the scientific merit from the written application**. Be explicit enough to enable experts in other areas to follow the main objective of the project. Include a Title Page or PHS 398 Face Page; Description/List of Key Personnel; Detailed Budget for initial year and Summary Budget for subsequent years; Biographical Sketches and Other Support for investigators included specifically for the new studies; Resources; Research Plan; Human Subjects Research; Vertebrate Animals; Literature Cited; Consortium/Contractual Arrangements; Consultants; and Data Sharing Plan. Include a checklist for the application.

2. Continuation of a funded project or core

   If the request is for continuation of a project or core funded for a period less than the overall program, a detailed research plan, including a budget, for the requested years should be presented in the format described above. It is important to address those factors that contributed to the recommendation for a reduced funding period. Progress reports and key preliminary data should be provided, as well as justification for the time extension.

3. Special requests for unique opportunity or additional resources

   In addition to items A through G above, the application should include justification for the request based on recent research findings. Requests for funds to purchase equipment to support research effort should also include verification of the requested cost.

IX. SPECIAL INSTRUCTIONS for PREPARATION of an ACCELERATED PEER REVIEW (APR) DOCUMENT

The National Cancer Institute (NCI) has established a procedure for the accelerated peer review (APR) of P01 applications. Applications that receive a highly favorable merit priority score but are not awarded funding may be eligible for an accelerated peer review. To be eligible for the APR process, the concerns noted in the summary statement must be addressable in a concise and straightforward manner. Examples would include deletion of a weak project or core, moderate changes in specific experiments or methods, addition of key preliminary data or expertise, or recent acquisition of an essential reagent. Inclusion of new projects or cores is not allowed. If a project is deleted, the amended P01 must still include a minimum of three research projects and the proposed cores must still serve two or more projects.

Applicants will be notified by NCI program staff of their eligibility to submit an APR document in response to the previous review critique, in lieu of a fully amended application. The APR document will be considered by the P01 SRG or by a SEP prior to the next scheduled National Cancer Advisory Board meeting. This procedure, designed for applications requiring minimal amending, will normally save the time of one review cycle. The APR response submitted for consideration will count as one of the two amended application submissions currently allowed by the NIH. The NCI APR procedure, therefore, is available for new and competing renewal applications and applications that have been amended no more than one time. (Applications that have been amended twice are no longer eligible for additional reviews under current NIH rules.) (see the NIH Guide for Grants and Contracts [http://grants1.nih.gov/grants/guide/notice-files/not98-142.html]).

NCI program staff will notify eligible principal investigators of the opportunity to submit an APR document in response to the summary statement critique (as described below) in lieu of an amended application. Specific dates for submission of a letter of intent and the receipt of the APR document for review will be clearly stated in the notification letter sent by NCI program staff. It is expected that this procedure will save time for applicants in the preparation of their responses and in the time involved in the peer review process. The APR review format will reduce the amended application review cycle from eight to approximately four months. However, all applicants eligible for APR will still have the option to decline the accelerated review process, to amend fully their application in the usual way, and resubmit in time for the next standard P01 application receipt date (February 1, June 1, or October 1).

A. Face Page (PHS 398 Form Page 1: Instructions for PHA 398, Section 1-C1).

   Type “PROGRAM PROJECT APR” in the top left-hand corner of the face page immediately above the words “GRANT APPLICATION.” Complete all items on the face page as in a traditional research grant application. This is page 1 of the APR document; all succeeding pages should be numbered consecutively.

B. Description, Performance Sites and Key Personnel (PHS 398 Form Page 2 and continuation pages; Instructions for PHS 398, Section 1-C2)

   Page 2 from the previous application may be used, if it is still appropriate. If new key personnel are included as part of the application group, their names should be added to the Key Personnel section.

C. Detailed Budget for Program Project Initial Budget Period (PHS 398 Form Page 4; Instructions for PHS 398, Section 1-C4)

If there are no changes in the requested budget, only the Detailed Composite Budget for all requested support for the first year, and the Summary Composite Budget for the total requested years should be submitted. If the requested budget has been modified in response to the previous summary statement, new summary budgets for the overall program and modified budgets for all projects and cores should be submitted.

D. Biographical Sketch and Other Research Support Information (PHS 398 Format Page; Instructions for PHS 398, Section 1-C6). Follow the instructions as given on the "Biographical Sketch Format Page". Submit Biographical Sketches only for new key personnel.

E. The text of the response is not to exceed 20 pages excluding revised budget pages and biographical sketches, if any. Human Subjects issues also should be addressed within the 20-page document.

   There is no specific format for the 20-page text. However, the document should have headings for each component of the application addressed in the APR response. It is anticipated that space allocation will be concentrated on those projects/cores or sections of the research plan needing the most revision. Allocation of space within the 20-pages is vested with the applicant group.

F. Collated sets of appendix material, such as new data from key experiments or new publications and/or in press publications, may be submitted along with the original and five copies of the APR document. The number of sets should be discussed with the assigned SRA. A cover letter stating that the application is being submitted under the APR process should be included in the package. Submission of electronic copies of the appendix material is now allowed. Details of the formatting will be provided by the SRA.

THE ORIGINAL APR DOCUMENT, FIVE COPIES AND ALL APPENDIX MATERIAL MUST BE SENT DIRECTLY TO THE FOLLOWING ADDRESS BY THE DATE INDICATED IN THE APR INVITATION LETTER:

Referral Officer
Division of Extramural Activities
National Cancer Institute
6116 Executive Blvd., Room 804
BETHESDA, MD 20892-8329
Rockville, MD 20852 (for courier delivery)
301-496-3428
301-402-0275 (FAX)
ncirefof@dea.nci.nih.gov

X. APPLICATION SUBMISSION PROCESS (for all applications except APRs)

A. Receipt deadlines and review schedules for all P01 applications submitted to the NCI, including all new, competing renewal, amended, and supplemental applications, are presented in the table below. Incomplete applications will be deferred to the next review cycle or administratively withdrawn and returned to the applicant without review. All competing renewal applications should be submitted in a timely fashion to avoid a possible gap in support for the program. Please note that the NCI Executive Committee has reaffirmed that applicants must submit competing continuation applications only on the originally scheduled submission date (ordinarily nine months prior to the end date of the award), in order to assure that applications are considered for funding with their proper cohort and to conserve NCI staff resources. Therefore, the Division of Extramural Activities will defer to the appropriate later round(s), the review of all renewal applications submitted prematurely.

Communication with NCI Referral Office*	Receipt Date for Applications	Initial Review**	NCAB Review	Earliest Possible Start Date
December15	February 1	Mid April to Early June	September	December 1
May 15	June 1	Mid August to Early October	February	April 1
August 15	October 1	January to early March	May	July 1

*Applicants must notify the NCI Referral Office, preferably by means of a Letter Of Intent, if the application has a requested budget in excess of $500,000 direct costs in any year. This notification must be repeated each time the application is submitted or if the application is delayed to a subsequent review cycle.
**Requests For Applications announcements may prescribe different Letter of Intent, receipt and review dates.

B. Mail the **original** and **three copies** of the complete application to the NIH Center for Scientific Review (CSR) using the address label included in the application kit. DO NOT BIND SECTIONS OF LARGE APPLICATIONS SEPARATELY. This will cause problems with processing the application in the CSR. Applications must be sent by U.S. mail or by commercial carrier. Hand-delivered packages will not be accepted by the CSR mailroom.

C. In addition, **send two complete copies under separate cover to:**

Referral Officer
Division of Extramural Activities
National Cancer Institute
6116 Executive Blvd., Room 8041
BETHESDA, MD 20892-8329
Rockville, MD 20852 (for courier delivery)
301-496-3428
301-402-0275 (FAX)
ncirefof@dea.nci.nih.gov

It is to the advantage of the applicant to be certain that the Referral Office copies are submitted separately; this allows NCI staff to direct early attention to such issues as review scheduling and the need for additional information or materials required for peer review.

D. **Do NOT send appendix material with the application**. The SRA will request the appropriate number of sets directly from the applicant after assignment (see page 17).

E. For applications responsive to Requests for Applications (RFAs), the RFA label available in the 5/01 revision of Application Form 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review.

XI. REVIEW PROCEDURES

A. Policies

The Scientific Review Administrator (SRA) serves as the Designated Federal Official (DFO) with legal responsibility for managing the review and ensuring that the review is conducted according to relevant laws, regulations, policy, and established NIH and NCI policies and procedures. The SRA provides guidance and direction with respect to review procedures and criteria; the need for a well-documented review; the functions of the NCI staff; conflicts of interest policies; implications of the Privacy Act; the need for confidentiality of the proceedings; the necessity of addressing gender, minority and children representation in clinical study populations; and other policy and logistic matters. The NCI program director serves as a resource, as needed, concerning the history and development of the program, changes in program direction and other relevant program matters.

The NCI is committed to the conduct of impartial, quality peer review of grant applications submitted by the scientific community and to the maintenance of an objective review process.

The Research Programs Review Branch, Division of Extramural Activities, which is responsible for managing the peer review of NCI P01 applications, is organizationally independent from the NCI extramural program units. The Research Programs Review Branch has responsibility for, and autonomy in, the conduct of initial review activities.

The conduct of peer review by one of the NCI IRG Scientific Review Groups (SRG) or by a Special Emphasis Panel (SEP) shall be in all particulars consistent with, and subject to, NIH and PHS peer review practices and policies.

Review staff are responsible for managing the scientific and technical review of P01 applications, including the selection of reviewers; management of SRGs, SRG-associated work groups/review panels, or SEPS; and the documentation of review panel findings and recommendations.

The responsibility for communications between the applicant and NCI staff changes during the various phases of the application process. Prior to submission of the application, NCI extramural program staff are the appropriate contact. From submission of the application until the initial peer review has been completed at the SRG meeting, all contacts should be made through the SRA. Following the SRG peer review and assignment of the priority score, program staff again become the contact for communications with the applicant.

Effort is made to avoid both the fact and appearance of conflict of interest in obtaining advice concerning P01 applications. In addition, the confidentiality of both the review materials and deliberations is maintained. Under no circumstances should there be direct contact between applicants and reviewers; instead, any questions or concerns should be brought to the attention of appropriate NCI staff as indicated above.

To maintain the integrity of the peer review process in its focus on scientific merit, current pay lines and funding policies are not discussed.

Amendments of the application in the interim between the review by the work group/review panel and scoring by the SRG are not allowed.

B. Application Receipt and Referral

Program project applications, like all other PHS grant applications, are received and initially processed by the NIH Center for Scientific Review (CSR). Following the current National Cancer Institute referral guidelines, the application is assigned to NCI and subsequently to a program area and to an SRA who manages the review. Applications that do not meet the referral guidelines for NCI programs are referred to another NIH institute.

C. Application Administrative Review

Upon receipt, the SRA reviews the application for conformance to NIH policies and NCI Guidelines and discusses concerns with NCI program staff. If the deficiencies can be resolved easily post-submission, then the principal investigator is notified and remedial action is taken. If the deficiencies are extensive or cannot be resolved quickly, the application will be returned to the applicant without further consideration.

D. Review Format

Beginning with applications submitted for the February 1, 2004 receipt date, NCI is undertaking a 1-year pilot study of reviewing P01 applications clustered according to similar topic and/or approach. In this new review process, SITE VISITS WILL NOT BE CONDUCTED. Thus, the success or failure of an application will depend first and foremost on how well the application text conveys the intent, merit and impact of the proposed research. Applications must be complete as submitted so that they can be reviewed without communication between the applicant and review groups. However, applicants will have an opportunity to respond to questions from the review panel, generally via teleconferencing.

One review panel will review two to four applications on related topics. Applications will be grouped based on commonality of scientific research areas and general technical approaches in a manner similar to that used in the study sections of the NIH Center for Scientific Review. New, competing renewal and amended applications will, therefore, be reviewed together. Clusters may contain applications addressing a continuum of basic, translation or clinical related projects on closely related topics. Applications will be assessed according to a standard of P01 quality as defined in the P01 review criteria.

The review panel will include senior investigators who can view the proposed science in a global perspective, specialists for specific scientific areas, and members of the three NCI P01 parent review committees for guidance in P01 review standards. Key members of the previous review panel will be included for continuity of review of the amended applications. In organizing the review panel membership, conflicts of interest, either real or perceived, will be avoided.

Generally, applications submitted for review will be assigned to one of the three P01 SRGs: SRG-C (Basic Sciences), SRG-D (Clinical and Translational Studies) or SRG-E (Cancer Epidemiology, Prevention and Control). For those applications assigned to a SRG, a review of technical merit by a SRG work group/review panel typically precedes the final review and assignment of merit priority score by the SRG. An application will be reviewed by a Special Emphasis Panel (SEP) if a member of the applicant group is a current or recent member of the appropriate SRG. In the latter case, both technical merit evaluation and assignment of an overall program merit priority score will be the responsibility of the SEP.

The review panel meeting date will be determined by the SRA according to the availability of suitable chairpersons and senior investigators. The applicants will be informed of the review date in advance. When possible, applicant schedules will be considered particularly with respect to the time zone. Applicant groups will be contacted by teleconference during the application review so that specific questions that impact program merit can be answered. Applicants may be given an opportunity to respond to key questions in writing prior to the review meeting. New data may be submitted with appendix material prior to the mailing of review materials to the panel members.

The review panel will convene in a face-to-face meeting in the Washington, D.C. metropolitan area or elsewhere at the convenience of the reviewers. The agenda for the meeting will include an introductory orientation and planning session conducted by the SRA to discuss administrative and logistic matters relating to the review. Then, for each application, a preliminary discussion will be held to identify key information that needs to be obtained from the applicant group during a brief telephone conference. **The telephone conference will be restricted to reviewer questions only. Formal presentations by applicants will not be permitted during the telephone conference.** Major changes in projects, cores or aims will not be allowed either during the course of the telephone conference or before the final scoring of the application at the SRG meeting. After the telephone conference, the final discussion and technical assessment of the research plan and overall program will be completed.

For those reviews conducted as an NCI SRG activity (work group/review panel), the reviewers' comments will be assembled as a Draft Review Report (DRR) that includes summaries of discussions of project/core merit, human subjects, and other review issues. These reports are forwarded to the NCI SRG for use in final discussion and assignment of overall merit priority score. Discussions of the NCI SRG are summarized and added to the DRR to form the final summary statement. If the review is conducted as a SEP, the reviewers' comments directly constitute the summary statement.

E. Communications with the Principal Investigator

The SRA will contact the principal investigator concerning background information relevant to the application, names of investigators in collaboration with the members of the applicant group, other investigators who may be in conflict with the group, and the number of collated copies of appendix materials required for the review.

The SRA will provide a deadline for receipt of appendix materials and any supplemental data obtained after submission of the application. This deadline, generally, will be five to six weeks prior to the review so that all materials related to the application(s) can be mailed to the reviewers in a timely manner. Major changes in scope or documentation that cannot be readily assimilated in the review process may result in deferral of review.

F. Communications with NCI Staff

Shortly after receipt of the application, the SRA contacts appropriate NCI program staff and other individuals for supplemental information and recommendations for prospective reviewers where appropriate. Program and/or grants management staff members discuss with the SRA any unusual features of the application which might require additional material for reviewers, or any special problems that they anticipate in the review of the application. All review-related communications with actual or potential reviewers are through the SRA.

G. Selection of Reviewers

The size and composition of each SRG work group (or SEP review panel) will be determined by the particular details of the applications to be reviewed. It is the responsibility of the SRA

to make these determinations based upon thorough review of the applications and consultation with program and review staff. In identifying prospective qualified reviewers, the SRA takes full advantage of many available resources, including existing databases of experienced reviewers, lists of grantees and contractors, and consultation with recognized authorities in the scientific community. The SRA, as well as program staff, will identify reviewers who, because of collaboration, affiliation, or bias, should be excluded from the review. Applicants are prohibited from suggesting names of prospective reviewers. However, applicants may suggest expertise areas appropriate for inclusion in the review panel. Amended applications will have a core of membership from the previous review but there also will be new reviewers assigned to the application.

The chairperson of the review panel, usually a SRG member, will be a senior investigator experienced in the review of complex multidisciplinary applications and generally knowledgeable in the broad scientific areas to be reviewed. The review panel membership will reflect a balance in terms of experience, expertise, and specialty so as to afford peer review of the separate components as well as the overall P01s in the cluster. A consultant experienced in management and fiscal administration may be needed when large P01s are reviewed. In most cases, this consultant does not vote on the scientific merit of the components or assign a priority score for the application, but does express opinion of the overall program administration. For relevant applications including clinical trials or population studies, a patient advocate/consumer will be included in the review group. These individuals, who have full scoring privileges, will speak to the importance of the research to the patient community and comment on human subject issues.

The SRA may contact the principal investigator to discuss the specific disciplines or specialty areas of expertise that the principal investigator feels are required to review the application properly. However, as noted above, names of potential reviewers are <u>not</u> to be directly or indirectly solicited from the principal investigator by either the SRA or the program director assigned to the application.

A limited number of individuals who, in the opinion of the principal investigator, may not be able to give an unbiased review may be submitted to the SRA. Full consideration is given to valid reasons presented by the principal investigator requesting that a particular reviewer not be invited, but the final decision rests with the SRA responsible for the review. The principal investigator should discuss these issues fully with co-investigators before communicating this information to the SRA.

When the arrangements for the review are completed, the SRA will advise the principal investigator and the program director in writing of the details, including the roster of the SEP or SRG review panel.

H. <u>Scientific Review Procedures</u>

1. Initial Technical Review by Work Groups/Review Panels

   Although the NCI Scientific Review Groups (SRG-C, -D, and -E) assess the overall merit of P01 applications that have been submitted for consideration for funding in a given review cycle, the applications first undergo review for scientific merit of their individual components and for program integration by a work group/review panel of experts in the specific scientific discipline. Representatives from the different SRGs participate in this initial phase of application evaluation to provide guidance to work group members relative to standards of review and general program merit.

   In keeping with the focus of NIH review on five explicit review criteria, the <u>individual</u> research projects will be evaluated for Significance, Approach, Innovation, Investigators

and Environment. (See Section IV and the NIH Guide, Vol. 26, Num. 22, June 27, 1997 (http://grants1.nih.gov/grants/guide/notice-files/not97-010.html). In evaluating Environment for each project, reviewers will consider the extent of institutional commitment, as well as the quality and effective use of research facilities and other resources. In addition, each project will be evaluated for its contribution to the overall program. These comments will be summarized under "Program as an Integrated Effort" (see below). For competing renewal applications (Type 2) applications, the reviewers also will evaluate the progress in the current funding period, both for the overall program and for each continuing or discontinued project. Amended applications will be assessed by taking into consideration the fundamental merit of the research plans along with changes made in response to the critique in the summary statement from the previous review. Reviewers will indicate whether the amended application is improved, is the same as, or is worse than the previous application. Note that under current NIH policy, an application may only be amended twice.

Individual projects in a NCI P01 are scored using a two-digit numerical rating from 1.0 to 5.0, based on an assessment of where the project ranks in the general field of research that the project addresses. Cores are rated as "Satisfactory" or "Superior" without numerical scores. Plans to include women, minorities, and children are part of the merit assessment for all research that uses human subjects. Reviewers may vote a project or core as "Not Recommended for Further Consideration" (NRFC) should the proposed research or function lack significant and substantial merit, or when serious human subject, animal welfare, or other concerns are identified. If the core does not support at least two projects, it is automatically deleted. After assigning a merit score, reviewers critically examine the requested budget for each component and recommend a budget and research duration appropriate for the proposed activities.

It is the view of the NCI that the P01 should be a cohesive, synergistic research effort focused on a central theme. Consequently, criteria related to the review of the program as an integrated effort are brought together in one section of the summary statement. Reviewers will discuss this aspect of the application, and assign a rating "Highly Integrated", "Integrated" or "Not Integrated."

The strengths and weaknesses of the overall program relative to global significance, general research approach, innovation, investigator qualifications, environment, and potential scientific impact are then discussed. Program leadership, including administrative ability and qualifications of the principal investigator and adequacy of commitment to the P01, is also assessed. Finally, the work group discusses and makes a recommendation for duration of the overall P01.

The reviewers' comments are assembled as a Draft Review Report (DRR). Summaries of discussion for each project/core are included in the Overall Critique of the application. A copy of the DRR is sent to the principal investigator prior to the NCI SRG meeting. The DRRs for all applications assigned to an SRG are forwarded to the NCI SRG for use in final discussion and assignment of overall merit priority score.

2. Final Discussion and Scoring by Scientific Review Groups (SRGs)

The primary role of the SRG is to provide a global perspective on overall P01 quality, and to assign an overall merit priority score to the application. At the SRG meeting, reporters (individuals who participated in the work group/review panel) present the outcome of the initial review in a balanced and impartial manner. Discussion is focused on evaluating the overall P01 in terms of the specific criteria provided in these Guidelines (see Section IV). These criteria include Significance, Approach, Innovation, Investigators and Environment, as well as overall progress in the current funding period for Type 2/competing renewal

applications. In addition, attention is given to considering the value added in conducting the proposed research as a coordinated effort, as well as the potential scientific impact of the program. For those applications that contain translational and clinical components, the potential impact on the standard of patient care is also discussed.
Peer reviewers will consider all of the above elements in assigning a single numerical score for the overall P01. Reviewers also will consider the likelihood that the proposed research will have a substantial impact on the scientific field under study. Since a single priority score is assigned to the program as a whole, applicants should keep in mind that inclusion of projects of lower quality or having only peripheral relationship to the central theme will have a negative impact on the overall evaluation. It is recommended, therefore, that applications include no more than six projects. Research programs requiring a larger number of projects should be considered for submission as two smaller, more focused P01 applications.

Reviewers will focus on the meritorious projects and cores of the program (excluding any components not recommended for further consideration) in assigning a merit priority score. Components of the P01 that are not recommended for further consideration will not be considered in the scientific evaluation of the overall program. Nevertheless, inclusion of components that are of poor quality or are unrelated to the P01 will be considered as evidence of a deficiency in judgment on the part of the principal investigator and on overall program administration. It should be noted that reviewers do not have the option of selecting only the better components of the program in order to improve the overall score.

Following discussion of the application, SRG members (both permanent as well as temporary) privately assign a merit priority score to the application. The merit priority score, along with the findings and recommendations of the initial work group, are incorporated into a written report that accurately conveys the evaluation of the P01. This summary statement is transmitted to the NCAB for advisory review, to the NCI official file and to the appropriate NCI staff. NCI program staff will automatically send a copy to the principal investigator as soon as the final document is available.

3. Review by Special Emphasis Panel (SEP)

   There are instances in which it may not be appropriate for the SRG to review a P01 application. For example, this is the case when the principal investigator, project leaders, or core directors are permanent members of the SRG to which the application would normally be assigned. Under these circumstances, the review is conducted by a Special Emphasis Panel (SEP) that performs all the functions associated with the initial work group (i.e., assess the merit of the individual components) and the SRG (i.e., assign an overall merit priority score). For those reviews conducted as a SEP, the reviewers' comments directly constitute the summary statement.

XII. SUMMARY STATEMENT

The findings and recommendations of the reviewers are summarized in a written report called the summary statement that accurately conveys the evaluation of the P01. This summary statement is transmitted to the NCAB for advisory review, to the NCI official file and to the appropriate NCI staff. NCI program staff will automatically send a copy to the principal investigator as soon as the final document is available.

XIII. AWARD

Following review by the NCAB, scored applications are considered for funding by NCI program staff and the NCI Executive Committee. When an award is made, it is the policy of NCI that meritorious projects reviewed as part of the P01 be funded as part of the P01 even though other funding may be available. Under no circumstances is duplicate funding awarded.
NCI program staff may administratively delete funding or reduce the duration of support for components of P01s that are judged by peer review to be less meritorious and/or non-essential to the conduct of the P01.

The award and administration of P01s are subject to the same policies and procedures as other research grants. These policies and cost principles are set forth in the current PHS Grants Policy Statement, other NIH and NCI issuances and Federal legislation and regulations.

Questions related to NCI P01 review may be directed to:

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Deputy Chief
Research Programs Review Branch
Division of Extramural Activities
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APPENDIX A: SAMPLE TABLE OF CONTENTS

SECTION I

Face Page
Description, Performance Sites, and Personnel
Table of Contents
Detailed Summary Budget for Program Project Initial Budget Period
Budget for Entire Proposed Program Project Period Direct Costs Only
Biographical Sketches

SECTION II

Overall Program Project
- Goals
- Theme of the Program Project
- Research Plan
- Progress Report/Preliminary Studies
- Institutional Environment and Resources
- Organization and Administrative Structure
- Literature Cited with complete titles and authors

Individual Research Project 1
- Title Page (Title, Project Leader, Degree)
- Description of Research Plan, Performance Sites, and Key Personnel
- Detailed Budget for First 12-Month Period
- Budget Estimate for Each Year of Requested Support
- Resources and Environment
  - Detailed Budget for First 12-Month Period for Consortium/Subcontract Arrangement
  - Budget Estimate for Each Year of Requested Support for Consortium/Subcontract Arrangement
- Resources and Environment for Consortium/Subcontract Arrangement
- Research Plan
  - A. Specific Aims
  - B. Background and Significance
  - C. Preliminary Studies/Progress Report
  - D. Research Design and Methods
  - E. Human Subjects
    - Protection of Human Subjects
    - Inclusion of Women
    - Inclusion of Minorities
    - Inclusion of Children
    - Data and Safety Monitoring Plan/Board
  - F. Vertebrate Animals
  - G. Literature Cited
  - H. Consortium/Contractual Arrangements
  - I. Consultants/Collaborators

Core Component A
- Title Page (Title, Core Director, Degree)
- Description of Core Service Plan/Key Personnel
- Budget for the First 12-Month Period
- Budget Estimate for Each Year of Requested Support
- Core Services Plan
  - A. Specific Aims

B. Background and Significance
C. Progress Report/Summary of Services in Current Funding Period
D. Methods and Services to be provided
E. Human Subjects
    Protection of Human Subjects
    Inclusion of Women
        Inclusion of Minorities
        Inclusion of Children
    Data and Safety Monitoring Plan
F. Vertebrate Animals
G. Literature Cited
H. Consortium/Contractual Arrangements
I. Consultants/Collaborators

Checklist

APPENDIX B

(SAMPLE TABLE)
DISTRIBUTION OF PROFESSIONAL EFFORT (%)
ON THIS APPLICATION

Participating Investigator	Project 1	Project 2	Project 3	Project 4	Core A	Core B	Core C	Application Total
Dr. A. (Principal Investigator)	20*		15		15*			50
Dr. B.						10*		10
Dr. C.		25*	10				20*	55
Dr. D.				30*				30
Dr. E.	30		30*					60
Dr. F.						30		30
Dr. G.		25					25	50
Dr. H.							25	25
Dr. I.				50				50

*Project Leader/Core Director
First lines should be reserved for project and core directors; other investigators should follow thereafter.

APPENDIX C

(SAMPLE TABLE)
PERCENTAGE DISTRIBUTION OF SCIENTIFIC CORE
RESEARCH RESOURCES TO PROJECTS

Project	Project 1	Project 2	Project 3	Project 4	Project 5	Total (100%)
Core A: Bioinformatics	20		40	40		100
Core B: Animal Maintenance	50			50		100
Core C: Administration		30	40		30	100