Interim
Guidelines

Specialized Programs of Research Excellence (SPOREs)

Organ Systems Branch
Office of Centers, Training, and Resources
Office of Centers and Special Programs
National Cancer Institute

February, 2005

Section I. Considerations for a SPORE

A. Introduction

Specialized Programs of Research Excellence (SPOREs) were conceived and implemented by the National Cancer Institute (NCI) through a special $20 million appropriation from Congress in Fiscal Year 1992. SPOREs evolved from the original NCI Organ Site Programs, which were organ-specific but without translational research focus, established shortly after the National Cancer Act of 1971. SPOREs represented a strategic response to the rapid expansion of information about cancer being developed through basic research. At that time, there was no funding mechanism designed exclusively to focus on translational research that would systematically explore the potential of basic research discoveries to impact upon human cancer. The SPORE Program was initiated by the NCI to address this need by promoting interactions between basic and applied scientists for the development of new approaches to the prevention, early detection, diagnosis and treatment of human cancer.

In FY92, the first Request for Applications (RFAs) resulted in the funding of eight SPOREs (four in breast cancer, two in prostate cancer and two in lung cancer). Since the objective of the SPORE program is to encourage a diversity of approaches to translational research, the P50 mechanism was chosen to support these grants. This mechanism has all of the features necessary to enable SPOREs to achieve translational goals—including the support of multiple translational research projects; co-leadership on all projects; specialized cores; flexibility to terminate and initiate new research projects without additional peer review; research engines to develop pilot projects as well as foster the development of translational scientists; and encouragement to combine resources and expertises between SPOREs to test new technologies and human applications.

Although the first P50 SPORE grants were funded for only three years, the translational research concept proved promising and the program was modified to allow requests for five years of support and expanded to include five organ sites: breast, prostate, lung, gastrointestinal and ovary. The limitation on the number of sites and the fact that RFAs only allowed the submission of applications every five years, however, meant the program was relatively closed and unable to capitalize on investigator-initiated scientific opportunities. In 1999, the NCI approved restructuring the SPORE program to one that utilized a program announcement (PA) and was open to grant applications for all major types of cancers on a scheduled competitive basis.

B. SPORE Definition of Translational Research

There is currently no consensus definition of translational research. The SPORE program defines it as follows: **translational research uses knowledge of human biology to develop and test the feasibility of cancer-relevant interventions in humans and/or determines the biological basis for observations made in individuals with cancer or in populations at risk for cancer**. "Interventions" is used in its broadest sense to include molecular assays, imaging techniques, drugs, biologicals and/or other methodologies applicable to the prevention, early detection, diagnosis, prognosis, or treatment of cancer. Translational research in SPOREs is always based upon human biology stemming from any cellular, molecular, structural, biochemical, genetic, or other appropriate experimental approach.

SPOREs conduct early-stage interventions to establish the feasibility or proof of principle of specific approaches in cancer. All research projects whose goal is the development and testing of an intervention are expected to reach the feasibility testing stage in humans within the anticipated five-year period of grant support. Similarly, studies that seek to determine the biological basis for an observation in human cancer should do so within five years. Some, but not all, types of behavioral research are appropriate for SPOREs. Biobehavioral research that clearly focuses on links between biological variables, processes, and mechanisms pertaining to behavior or psychosocial variables is appropriate. Psychosocial variables might include cognitions, affect, personality, or interpersonal context or processes (e.g., social support, familial interactions, physician-patient communication). Behavioral research that focuses on psychosocial processes or behavior change without a clear, specific linkage to a biological process (e.g., disease susceptibility, etiology, or progression) is not appropriate. SPOREs are also not the place for definitive validation of new interventions, which are supported by other programs within several divisions of the NCI.

Within the limits of the definitions and time frames outlined above, SPOREs have considerable flexibility in selecting and developing areas of research with the greatest anticipated potential for improving cancer outcomes. Investigators who question whether their research goals adhere to the above definition of translation and/or the expectations of the SPORE Program are advised to consult with NCI program staff in the Organ Systems Branch (OSB). A current listing of OSB program staff can be found at: http://spores.nci.nih.gov.

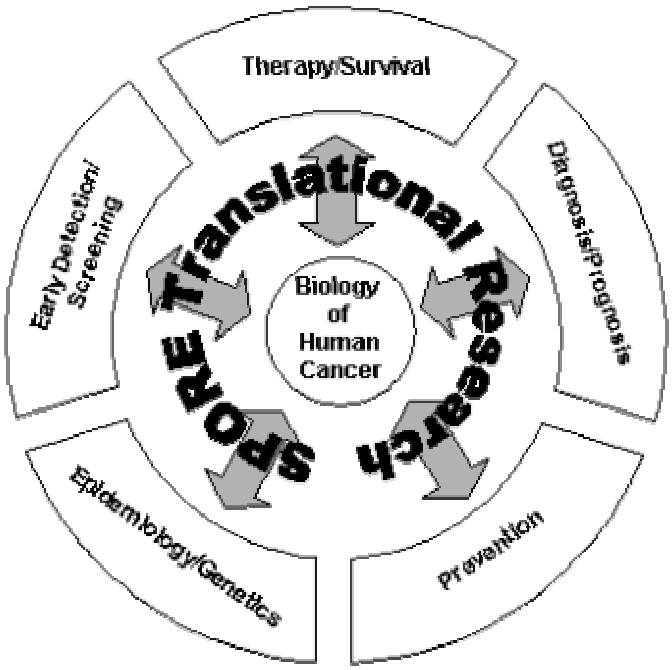

Figure 1. Translational research focus of a SPORE. Research projects should be designed to (a) test the relevance of a biological discovery in human cancer risk, prevention, diagnosis, prognosis, or treatment or (b) determine the biological basis of an observation made in the clinic or population within the five-year term of the grant.

C. General Description of the SPORE Program

SPOREs utilize the P50 grant mechanism to support interdisciplinary teams of investigators who are dedicated to translational research focused on an organ-specific human cancer (e.g., breast cancer) or a highly related group of human cancer types (e.g., gastrointestinal). SPOREs are open to any scientific approaches that can have an impact on the disease and are dependent upon team approaches in the design and implementation of the research. SPOREs differ from program project grants (P01s) by focusing exclusively on translational research and human disease, having a flexible approach to initiating and terminating research projects, supporting the critical acquisition and banking of human specimens, and encouraging the development of new translational opportunities through developmental programs. In addition to their organ-site orientation, the common features of all SPOREs are the following:

1. Translational Research Focus

All SPOREs focus on translational research that meets the definition provided in Section I.B. above. SPOREs are dedicated to capitalizing on research opportunities that have the potential to

impact upon the prevention, detection, diagnosis, and/or treatment of human cancer. SPORE projects can include some basic science objectives if they are relevant to human cancer and will lead to a human application during the five-year term of the grant. If a project has lost its translational focus or the likelihood of having an impact on human cancer, it should be discontinued as a SPORE project and another funding source sought.

2. Collaborative Design and Implementation of Research Projects

Every project in a SPORE is inherently translational because it is collaboratively designed and executed by basic scientists working at the cellular and molecular levels, physicians experienced in patient-oriented research, and population scientists experienced in studying the patterns of disease.

3. Flexibility to Change Research Direction/Team Approach

SPOREs continually select the most promising research approaches likely to have an immediate impact on improving cancer prevention, detection, diagnosis, prognosis and/or treatment. The flexibility of the SPORE program promotes the termination of research projects that demonstrate little or no translational progress and enables new projects with greater potential to be initiated. While the team of scientists that participates in the SPORE remains largely the same, the roles of co-leaders on projects may change through the course of the research.

The principal investigator of the SPORE is expected to make decisions about the continuation or discontinuation of projects in consultation with his/her internal and external advisors, as well as other lead investigators on the SPORE. The flexibility option is evoked only after the SPORE application has been awarded; a new project cannot be proposed for one that has overlap with an awarded or soon-to-be awarded PHS grant/application. Although it is acceptable for investigators to concurrently submit essentially the same proposal as a SPORE project and as an independent R01, R21, etc. application to the NIH, they must be prepared to relinquish the R01 (or single project) application if both are determined to be meritorious and moved forward for funding. It is against NIH policy to concurrently submit both a P01 and a P50 application requesting support for the same projects/activities as well as for an investigator(s) to submit a project proposal(s) that has significant overlap with an already funded activity. These latter types of potential overlaps will be screened for by NCI staff prior to review; submitted applications will be returned without review if they do not conform to these policies or fail to meet the minimal requirements of the SPORE Program. For additional information, please see PHS 398 Instructions (Rev. 09/2004; Part I, page 38) and Section E.4.f. below.

4. Specialized Research Infrastructure

SPOREs are expected to develop the critical research infrastructure needed to sustain translational research objectives for projects within the SPORE, as well as for potential collaborative research with other SPOREs and other research groups within the biomedical research community. SPOREs are expected to be in a position to facilitate the complex research objectives inherent in studying human cancer.

5. Fostering Translational Research Careers

SPOREs provide a unique environment for translational research that can be used to prepare new scientists for careers in this evolving field or provide the opportunity for established scientists to re-orient their research careers toward translational research.

6. Research Collaborations, Networks, and Consortia

SPOREs are expected to identify the kinds of research questions that can only be accomplished through collaborations, networks, and consortia. SPOREs collaborate with other scientists in the field to answer research questions that take full advantage of SPORE scientific expertise and infrastructure. Through the promotion of Inter-SPORE research, SPOREs also conceive and initiate research that is linked to other key programs of the NCI or NIH.

During the review process, the merit of all applications will partially depend upon the tangible interactions the SPORE investigators can demonstrate with other SPOREs, networks, and consortia. Re-competing SPOREs will be judged on their past and present Inter-SPORE activities, as well as collaborative activities with other NIH/NCI Networks. New applications will be judged on their demonstrated success to collaborate with other NIH/NCI Networks [e.g., with the cooperative groups, Early Detection Research Network, Mouse Models of Human Cancer Consortium, P01s, etc.] and potential or planned interactions with established SPOREs. The overall merit score for the application will be weighted to include the collaborative outreach capabilities of the SPORE team. For further information see Section G.5. below.

7. Sharing Information, Data, and Resources

SPOREs readily share information, data, and resources within their organ site network, as well as with other SPOREs, to take advantage of research results that are applicable to various cancer sites. Applications for SPORE grants are required to include a **data and research resources sharing plan**.

The plan should outline how final research data will be shared among the SPOREs, as well as the research community at large, or state why this is not possible. For additional information on the NIH Data Sharing Policy see: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html and PHS 398 Instructions (Rev. 09/2004; Part III, page 4).

The NIH also requires the timely sharing by grant recipients of biomedical resources. Therefore, the plan should also describe how unique research resources will be distributed, e.g., through the institution, a repository, or national coordinating center. If applicants plan to collaborate with third parties, the plan must explain how such collaborations will not restrict the SPOREs' ability to share research materials produced with NIH funding. If applicable, the plan should specifically address model organisms, both mammalian and non-mammalian. Research resources to be shared include genetically modified or mutant organisms, sperm, embryos, protocols for genetic and phenotypic screens, mutagenesis protocols, and genetic and phenotypic data for all mutant strains. For information regarding research resources sharing, see: http://grants1.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc546000132 and http://ott.od.nih.gov/NewPages/Rtguide_final.html. Additional information of the sharing of model organisms can be found at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html.

Reviewers of SPORE applications will not factor the proposed data and resources sharing plan into their determinations of scientific merit on individual project or cores, or the overall priority score. Program staff will be responsible for overseeing the data sharing policy and for assessing the appropriateness and adequacy of the proposed data and research resources sharing plan.

D. Award Adminstration Information

1. Grant Mechanism

This program is supported through the NIH specialized center grant (P50) mechanism. Applicants are responsible for the planning, direction, and execution of the proposed SPORE program. Awards can be made for up to five years and will be administered under NIH grants policy as stated in the NIH Grants Policy Statement (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-009.html).

2. Basis of Funding

Applications will be awarded on a competitive basis. The following will be considered in

making decisions:

- Quality of the application as determined by peer review
- Availability of funds
- Relevance to program priorities

3. Conversion to Planning Grants

Under special circumstances, the NCI may consider funding a P50 SPORE application at a reduced level for up to five years using the P20 planning grant mechanism. Circumstances leading to the funding of a P20 rather than a P50 include: (1) the research projects in the SPORE application have high scientific merit but other essential components of the application require further development; (2) the peer review criticisms can be readily addressed within the initial term of the award; and/or (3) the application meets important NCI program objectives (e.g., the organ site to be studied is under-represented). Applicants can not apply for a P20 grant directly.

4. Expanded Authorities

In accordance with NIH Grants Policy, Both NCI P50 and P20 grants may be administered by the awardee under Expanded Authorities which can be viewed at: http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600128. The expanded authorities allow additional flexibility to take advantage of research opportunities as they arise throughout the term of the grant. Under the expanded authorities, NIH has waived the requirement for its approval of specified actions and has provided the authorities to grantees to take such actions without NIH prior approval. In addition to the expanded authorities, the Organ Systems Branch has granted automatic carryover authority (up to 25% of total cost) to these P50s and P20s.

E. Eligibility and Required Components

Applications must meet all of the following eligibility criteria [items 1(a)-(d)] as well as contain the required components of a SPORE listed in items 2-9 below. Applications that are not responsive to these requirements will be returned to the applicant by NCI program staff and will not undergo scientific peer review.

1. **Eligibility**

   (a) Institutional

   Applications may be submitted by domestic for-profit and non-profit organizations, either public or private, including universities, colleges, hospitals, laboratories, units of State

and local governments, and eligible agencies of the Federal government. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as principal investigators.

Because SPOREs are supported by the "specialized center grant" (P50) mechanism, foreign institutions cannot apply as a primary site. Center grants can only be awarded to institutions located within the United States. Consortium agreements with foreign institutions, however, can be proposed as long as the appropriate federal wide assurances for the protection of human subjects are in place (see: http://www.hhs.gov/ohrp/) and the activities at the foreign site(s) do not exceed 49% of the direct costs of the overall budget. NIH provides limited F&A cost (8% of total direct costs less equipment) to foreign institutions and international organizations to support the costs of compliance with NIH requirements, including, but not limited to, protection of human subjects, animal welfare, and research misconduct. See NIH Grants Policy Statement (Revised December 2003): http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part12.htm.

(b) Minimum Research Base

In order for a SPORE application to be accepted by NCI, the application must include four or more independent investigators who currently serve as principal investigators (or project leaders) on *peer-reviewed* research grants (e.g., R01, R21, P01, U01, U10, ACS, DOD, or equivalent) or are chairs/site chairpersons on active NCI cooperative group clinical trial(s) or committees **directly related to the cancer(s)** being investigated. Principal investigators supported by the NCI through K05, K22, K24 or K25 career development grants can also be included in the research base requirement if the career award is directly relevant to the cancer being investigated on the SPORE. Please note that an investigator who is a principal investigator on multiple qualified grants or clinical trials only counts once towards the research base and, in order to qualify, the investigator must be the principal investigator (*not* co-investigator) on the highlighted activity. The qualifying investigators also must have a significant role on the SPORE (i.e., greater or equal to a 5% contributed effort as a project co-leader, co-investigator, or core director); they cannot just serve as mentors within the proposed Career Development Program or be the project leader of a proposed Developmental Research project. The funded activities of the investigators who fulfill the requirements of a minimal research base should be included in the Program Description part of the SPORE application as discussed in Section II below.

(c) Cancer Patient Population

Each SPORE must document access to a substantial patient population in the cancer-site focus of the application and provide reasonable assurance that the patients and human specimens needed for translational research are readily available. If the appropriate patient population is not available at the applicant institution, a consortium agreement may be established with a different institution to provide adequate access to clinical specimens (e.g., tissues, blood, urine) and/or patients at another site.

(d) Budget Limitation

By NCI policy, all competing SPOREs are subject to both *direct cost and total cost budget caps, which currently are $1.5 million and $2.5 million, respectively*. Indirect costs related to subcontracts to other institutions or organizations do not apply toward the $1.5 million direct cost cap. The PHS 398 (Rev. 09/2004) budget forms allow for a clear distinction between direct costs (including all direct costs from consortia) and total costs (including all direct and indirect costs from all participating organizations). Consortium indirect costs must be included in the total costs which, overall, may not exceed the $2.5 million cap. Applications with requests exceeding these financial limits will be returned to the applicant without peer review. In non-competing years, applications can exceed these caps as a result of annual cost-of-living increases ($\leq$ 3% of direct costs) or as a result of special supplements approved by the NCI. An applicant should not submit an application anticipating the support of a critical or required activity by an administrative supplement. For more information about the budget cap in any given year, applicants must contact the Organ Systems Branch using the telephone number, fax number or e-mail address listed under INQUIRIES below.

2. Statement of Institutional Commitment

An institution applying for a SPORE grant should demonstrate a commitment to the proposed SPORE's stability and success by promising to incorporate the SPORE, if awarded, high within its institutional priorities. The application must provide a statement of commitment that includes a plan addressing how the institutional commitment will be established and sustained, how the institution will maintain accountability for promoting scientific excellence, and how the SPORE research effort will be given a high priority within the institution relative to other research efforts. The institutional commitment may be in the form of support for recruitment of scientific talent, provision of discretionary resources to the SPORE Director, assignment of specialized research space, cost sharing of resources, or other ways proposed by the applicant institution. *Letters from a high-level institution official(s) (e.g., Dean of the School of Medicine, President,*

VP for Research) and the Cancer Center Director should be attached confirming this commitment. In the case of a SPORE that involves a consortium arrangement between two or more institutions, the institution that submits the P50 application must receive a formal written agreement(s) from the other participant organization(s). This agreement should clearly delineate the institutional commitment of the participating organization(s) (in the ways outlined above) to the SPORE program.

The primary institution is strongly encouraged to demonstrate this commitment by providing financial support to the Developmental Research and Career Development Programs on an awarded SPORE, as well as other programmatic needs identified as high priority on the original application. Up to $50,000 of the SPORE direct costs budget per year may also be requested for use as discretionary funds by the principal investigator. The institution(s) is encouraged to match this request. These funds can be used to support anticipated, as well as unanticipated, activities such as a clinical trial in year two, pre-clinical testing of an agent in year three, etc. Discretionary funds should be justified in detail and requested within the Administrative Core. All financial commitments made by the institution to the SPORE will be monitored and are expected to be maintained during the entire term of the award.

3. Intellectual Property Rights

An **intellectual property management plan** must included in the application which discusses the plans for evaluation, protection, and commercialization of solely or jointly owned SPORE inventions, including any patenting and licensing strategies. This plan should be comprehensive for all proposed SPORE projects and be included in the Program Description as specified in Section II.

The institution should provide a written assurance that it will protect the intellectual property rights arising from inventions of the SPORE investigators and their collaborators and under no circumstances enter into agreements with commercial entities (e.g., pharmaceutical companies) that would compromise the ability of SPORE investigators to have unhampered access to institutional resources developed in SPORE-related research or participate fully in collaborations with any other researchers. The statement of commitment should also include a written assurance that in its interactions with commercial entities under sponsored research agreements, the SPORE institution(s) will comply with the requirements of the Bayh-Dole Act (37 CFR 401; https://s-edison.info.nih.gov/iEdison/37CFR401.jsp), the NIH Grants Policy Statement and any relevant NIH funding agreements while upholding basic principles of academic freedom.

Sponsored research agreements with commercial entities should be entered into by the SPORE institution(s) only upon due consideration of the points outlined in "Developing Sponsored Research Agreements: Considerations for Recipients of NIH Research Grants and Contracts (Federal Register, Vol. 59, No. 215, Tuesday, November 8, 1994, pp. 55674-55679)", a copy of which can be viewed at: http://ott.od.nih.gov/NewPages/text-com.htm.

The statement of commitment should also include a written assurance that the SPORE institution(s) will manage its interactions with third parties so that they do not restrict the SPORE's ability to receive and disseminate biomedical research materials developed with NIH funding from and to the scientific community. *Likewise, letters should be supplied by any relevant third parties (including any external co-investigators, collaborators, or consultants) confirming their adherence to these policies.* These letters should outline in detail the agreement made between the commercial entity with the SPORE institution.

Costs related to the patenting and/or licensing of intellectual property may be allowable as F&A costs. See: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-045.html.

4. Research Projects

Research projects may be conducted solely through the parent institution, or through collaborative associations that have been developed or are planned with other SPOREs or with other investigators in the biomedical research community. However, all SPOREs must meet the following requirements:

(a) **Each** proposed research project must meet the definition of translational research as described in Section I.B above. Investigators who are not certain about whether their project fits this definition are advised to consult with NCI program staff.

(b) Each proposed research project must be designed to test the relevance and/or potential importance of the research to human cancer **within the five-year term of the grant** (e.g., validation of a new screening mechanism or diagnostic test, early phase therapeutic trial, analysis of human tissues such as tumor or blood samples). Basic research projects, such as those employing animal models or cell lines, qualify as translational only if a human application is included in the specific aims of the research. A project(s) proposed in a competitive renewal application may focus solely upon the human application or laboratory effort if it marks the final stage of an ongoing translational SPORE study. *Applicants are encouraged to contact the Organ*

Systems Branch (see INQUIRIES below) if they have any questions concerning this essential requirement.

(c) **Each** proposed research project must be led by project co-leaders, one in basic biological sciences and one in applied sciences, who commit adequate percent efforts and who use their combined conceptual and experimental skills in designing and implementing the project. It should be evident from this collaboration that translational research objectives will be accelerated such that it will be possible to test the relevance of the underlying hypotheses or to generate new hypotheses relevant to human disease. It is not necessary that the co-leaders commit equal effort to the project. There are **NO** exceptions to this requirement.

(d) For most organ sites, at least **ONE** research project must focus on early detection, screening, prevention (primary or secondary), and/or population science research. See Table 1 below for a list of the organ sites supported by the SPORE program and which of these sites includes a requirement for a project focused on early detection, screening, prevention, or population science. If such a project is required, then at least one scored project in this category will be required for award (see REVIEW CONSIDERATIONS, Section G.1. below) and must be maintained throughout the entire term of the award.

Cancer sites where a project on early detection, screening, prevention, or population science is not a formal requirement (i.e., brain, GU, leukemia, lymphoma, myeloma, pancreas and endometrium) are still *strongly encouraged* to include a project focused on one of these four underserved areas. The SPORE may reach out to another institution to include them as a consortium to fulfill this requirement either because of the relevant expertise of an investigator(s) or patient base/population present at the additional site. A SPORE may also propose an early detection, screening, prevention, or population science project that capitalizes upon an existing or evolving Inter-SPORE collaboration or related research activity supported by another NCI/NIH Networks.

Table 1. SPORE Organ Sites

Organ Site(s)	*Includes the following cancers*:*	*Required Project?***
1. Brain	Brain, *not* PNS tumors	No
2. Breast	Breast	Yes
3. Gastrointestinal (GI)	Esophageal, Stomach, Intestinal, Colon Liver, Pancreatic	Yes
4. Genitourinary (GU)	Bladder, Kidney, Testicular, *not* Prostate	No
5. Gynecological (GYN)	Cervical, Endometrial, *not* Ovarian	Yes (cervical); No (endometrial)
6. Head and Neck	Salivary, Larynx, Nasopharyngeal, Oral, Thyroid	Yes
7. Leukemia	Leukemia, MDS	No
8. Lung	Lung	Yes
9. Lymphoma	Lymphoma (Hodgkin's, Non-Hodgkin's, CLL)	No
10. Myeloma	Myeloma, MGUS	No
11. Ovary	Ovarian	Yes
12. Pancreas	Pancreatic	No
13. Prostate	Prostate	Yes
14. Skin	Skin	Yes

*Not all inclusive; if proposing projects on other cancers, contact appropriate OSB program staff.

**Applications requiring a project focused on early detection, screening, prevention, or population science.

(e) A minimum of **four research projects** are required representing a **balance and diversity** of translational research objectives (e.g., screening, prevention, diagnosis, treatment). Applications with a specific theme (e.g., gene therapy in prostate cancer) are discouraged. (Note that four projects scored by the peer review group will be required for award, see REVIEW CONSIDERATIONS, Sections G.1. and G.5. below.)

(f) Research projects involving **HUMAN SUBJECTS** must include women, children, and members of minority groups and their subpopulations unless a clear and compelling rationale establishes inclusion is inappropriate with respect to the health

of the subjects, the purpose of the research, or another extenuating circumstance. Applicants are required to address this issue in developing a research design appropriate to the scientific objectives of their study. Instructions for responding to this issue are provided at: http://grants1.nih.gov/grants/funding/phs398/HumanSubjects.pdf or can be downloaded in MS Word format from http://grants1.nih.gov/grants/funding/phs398/phs398.html.

Each project/core that involves human subjects must also adequately address the protection of human subjects from risks, the overall benefit of the study to participants, the inclusion of women and minorities, and the inclusion/exclusion of children as instructed in the PHS 398 Instructions (Rev. 09/2004; Part II). A project proposing the involvement of human subjects in clinical research must also include a 5/01 Targeted/Planned Enrollment Table Format Page as discussed in the PHS 398 Instructions (Rev. 09/2004; Part II, page 14). The table is available at: http://grants.nih.gov/grants/funding/phs398/enrollment.pdf.

If applicable, competing renewal applications that include ongoing projects from the previous funding period must also provide Inclusion Enrollment Reports (http://grants.nih.gov/grants/funding/phs398/enrollmentreport.pdf) on any clinical research activity performed during the past 12 months. Any past difficulties encountered in the recruitment of women and minorities should be discussed, as well as new plans to enhance recruitment. All of these items should be included in the "Inclusion of Women and Minorities" section of the project and/or core proposals.

Only early (Phase I and Phase II) clinical trials may be supported by the SPORE mechanism. A plan for a clinical trial must include provisions for rigorous data management, quality assurance, and safety monitoring. These monitoring activities are distinct from the requirement for study review and approval by an Institutional Review Board (IRB). For details about the Policy of the NCI for Data Safety Monitoring of Clinical Trials see http://deainfo.nci.nih.gov/grantspolicies/datasafety.htm and the PHS 398 Instructions (Rev. 09/2004; Part II, page 34). Applicants should provide evidence that they will utilize Data and Safety Monitoring systems in place at their institution. A general description of the data and safety monitoring plans should be included in the application (see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html). This description should explain the rules and procedures for detecting, monitoring, and

reporting any adverse drug reaction or event during a clinical trial. *A copy of a draft or IRB-approved clinical trial protocol, along with informed consent forms and a specific DSM plan, are also required and should be included in an Appendix if the trial is already underway or is anticipated to begin within the first two years of an award.* If the trial will be performed during the latter part of the grant term, submission of these items to NCI program staff is required prior to the initiation of the trial.

The NIH also requires that all investigators proposing research involving human subjects are educated on the protection of human research participants. For information relating to this requirement, see the following notices (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html and http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html), and Frequently Asked Questions found at: http://grants.nih.gov/grants/policy/hs_educ_faq.htm.

5. Shared Cores

(a) Specimen Core (*Required*)

Each SPORE must have a dedicated core for collecting and distributing **human cancer site-specific and/or related specimens**. Specimens include fixed tissue, frozen tissue, paraffin blocks, slides, preserved cells, serum, plasma, urine, sputum samples, or other body fluids. This should be a specialized specimen resource that can be used for novel and robust biomarker development and accurate testing of translational hypotheses with minimal preanalytical concerns. Each specimen should have detailed annotation of parameters of collection and preservation that are pertinent to the preanalytic and analytic considerations of potential studies. The specimen core should also include the essential pathological, clinical, and family history information needed for conducting a wide range of translational research activities. Appropriate informatics capability for tracking, as well as linkage to clinical and follow-up data sets, should be demonstrated. Networking with informatic systems at other SPORE sites is encouraged. The development, acquisition, storage, and usage of standardized reference specimens and materials are also strongly encouraged.

This core may also provide services related to the analysis of specimens (e.g., tissue microdissection, immunohistochemistry). Other research activities may also be included if they are designed to improve core services that are of obvious benefit to the SPORE.

This core should be essential to the research activities of the SPORE, as well as those of other scientists within and outside the parent institution who are invested in translational research. A

plan must be proposed for prioritizing distribution of biospecimens to SPORE scientists and others [inside and outside the parent/consortium institution(s)] based on the merit of the proposed translational cancer research projects. Competing renewal applications should also include a list of the studies or collaborations that benefited from this core, as well as a summary listing the numbers and types of specimens accrued and distributed during the previous funding period.

(b) Other Cores (*Optional*)
Additional shared cores (e.g., administrative, clinical, biostatistical, animal) may also be proposed that are supportive of one or more of the research projects of the SPORE. These cores should provide essential services to *at least one* SPORE project and may also include other analytical or non-hypothesis driven research activities designed to enhance a service. Administrative, clinical, and biostatistical cores are strongly encouraged.

For all non-administrative cores, the application must document that the proposed cores will not duplicate pre-existing resources at the institution. A proposed SPORE core must include a budgetary request. If the SPORE is benefiting from a *funded* institutional, local, or national resource/consortium, the benefit to the SPORE should be described in the overall Program Description (see Section II). The utilization of this pre-existing resource will factor into the merit of the institutional commitment or the collaborative interactions component of the application. Additional instructions for applicants located at institutions supported by NCI Cancer Center Support Grants (CCSGs) are provided under E.9. below.

All non-administrative core directors are expected to provide a brief description of related cores at their Cancer Center or institution. This includes cores or resources supported by P01, P20, other P50 grants, and Cancer Center cores dedicated to a similar activity. If there are no related cores at the Cancer Center or institution, this should be stated. Descriptions should briefly outline the activities of the already funded core(s) or resource(s), the staff available to support these activities, and any charge backs to investigators who utilize the core/resource(s). For competing renewal applications, utilization of an ongoing core that was previously supported by the SPORE should also be clearly documented. Details should be provided on the services the core provided to projects supported in the previous funding period, including those supported by the DRP and CDP. A list of joint publications, including investigators from both the projects and the cores, should also be included in the preliminary studies/progress report for the core.

If an Administrative Core is proposed, costs to cover the travel of 10 SPORE investigators to the

annual SPORE Workshop (see below) and some additional support for Inter-SPORE meetings can be requested within this core. In addition, any requests for discretionary funds (up to $50,000 direct costs per year) should also be discussed within the administrative core; institutions are encouraged to match this request. See Section II for additional guidance.

If a Clinical Core is proposed, the Director of this core should discuss its integration with Cancer Center resources and discuss how duplication in the reporting of clinical trial data to the NCI will be avoided.

6. Developmental Research Program

Every SPORE must allocate a significant effort to support pilot projects that take maximum advantage of new research opportunities. Such projects may be collaborative among scientists within one or more SPOREs, or with scientists outside the SPORE environment. The SPORE application should propose an institutional review process for funding pilot projects that generate feasibility data and have the most promising translational research potential. These funds are intended to remain flexible and to support studies of a limited duration, of two years or less. The expectation is that successful feasibility studies will replace full projects that are not progressing satisfactorily with regard to translational research objectives within the SPORE (see above). New applicants may supply a short description (1-2 page(s) maximum) of eligible projects as examples. Competing renewal applicants should supply their track record of funding pilot projects, ongoing pilot projects, and short descriptions of other potentially eligible projects.

A Developmental Research Program (DRP), as a required element of a SPORE, must be maintained throughout the entire term of the grant. A *minimum commitment of $50,000 direct costs per year* from SPORE funds must be proposed. Matching funds of $50,000 or more are also, generally, promised by the parent institution. Most SPORE DRPs have commitments between $100,000 to $300,000 direct costs per year, including the contribution made by the parent and/or consortium institutions. The NCI will monitor the activities of both SPORE and institutionally sponsored DRP projects during non-competitive years to assure the institutional commitment is being maintained and there is adherence to the translational intention of the SPORE program during the term of the award. SPORE DRP funds should be utilized for research activities and not for the purchase of large pieces of equipment.

7. Career Development Program

The SPORE must demonstrate a consistent and significant commitment to a career development program in translational cancer research. Funds from this program may be used to support

advanced post-doctoral or clinical fellows (who will be independent investigators within the next year), junior faculty, or established investigators who wish to develop or refocus their careers on translational research. SPORE career development programs are not intended for predoctoral candidates or junior level post-docs and clinical fellows. Investigators supported by NCI career development awards (K series) may also be eligible for support through this program.

A minimum of $50,000 direct costs per year from the SPORE budget must be dedicated to this program and be utilized to support the salary and research costs of candidates with outstanding potential. Each junior level candidate (senior post-docs, clinical fellows, and assistant professors) should have a mentor(s) and devote a significant percentage of his/her effort to translational research. The description of this program should include the policies, criteria, and processes for selecting candidates, including **special efforts to recruit qualified women and minorities**. The plan should include the number and types of positions (e.g., advanced post-docs, junior faculty, and established investigators) that will be made available, the criteria for eligibility and selection of candidates, and a description of the selection process. New applicants should provide a list and short description of potential candidates, as well as the names and research activities of mentors. Renewal applicants should provide this in addition to the track record of awardees supported on the SPORE, in addition to addressing past performance on recruiting women and minorities. Similar to the DRP, support of a career development awardee should not exceed two years.

A Career Development Program (CDP), as a required element of a SPORE, must be maintained throughout the entire term of the grant. A financial commitment of $50,000 or more direct costs per year from the parent and/or consortium institutions is also encouraged. Funds from the CDP should be utilized to support research activities, including partial salary support for the candidate, his/her personnel, supplies, travel, and other expenses. CDP funds should not be used for the purchase of large pieces of equipment; these items should be purchased by other means (e.g., equipment grants or institutional start-up funds).

8. SPORE Workshop and Meetings

(a) Annual SPORE Workshop

SPORE investigators will be expected to participate in an annual workshop organized by the Organ Systems Branch of the NCI to share positive and negative results with other SPOREs, share materials, assess progress, identify new research opportunities, as well as establish interactions, research priorities, and collaborations that will maximize the impact of the research on reducing incidence and mortality, and improving survival. A statement of commitment to

attend this workshop should be included within the Program Description. Travel funds for the Principal Investigator and nine selected SPORE investigators and collaborators should be budgeted for this purpose. Support for attendance at the SPORE Workshop can be requested within the Administrative Core or projects of the SPORE.

(b) Additional Inter-SPORE and NCI/NIH Network Meetings

SPORE investigators are also expected to attend additional meetings during each year designed to foster or support collaborative activities across SPOREs or NCI/NIH Networks. SPORE PIs may also be requested to attend or participate in planning or review activities by the NCI leadership. A small amount of funds ($\leq$$5,000 direct costs) can be requested within the Administrative Core and/or projects to support attendance at these meetings.

Because of the collaborative nature of the SPORE Program, an unwillingness or routine inability of a PI or SPORE group to attend these required meetings may be basis for termination of the grant. As stated within Section I.C.4., SPOREs are expected to develop the infrastructure necessary to quickly address translational needs and should be able to, as a group, rapidly test new biomarkers or agents for the advancement of clinical applications.

9. Other Provisions

If a SPORE application originates from an institution that is supported by an NCI Cancer Center Support Grant (CCSG; P30), the following items should also be addressed (within the Program Description).

(a) Once a SPORE is funded, the Principal Investigator of the SPORE should become a senior leader in the Cancer Center. The Principal Investigator of the SPORE may or may not be the Cancer Center Director.

(b) Lines of authority should be clearly indicated such that the SPORE is an integral part of the Cancer Center but does not interfere with the P30 chain of authority. **A letter of commitment which delineates these organizational relationships is required.** This letter must be signed by the proposed Principal Investigator of the SPORE, as well as the Cancer Center Director.

(c) The applicant should discuss how the SPORE will interact synergistically with existing P30 programs in order to maximize both SPORE and Cancer Center research objectives. While the SPORE is expected to become an integral element within the

NCI-designated Cancer Center, a distinct institutional commitment to the SPORE must still be maintained throughout the term of the SPORE grant (see Section E.2. above).

(d) The proposed cores within the SPORE should not duplicate any available facility already in place and supported by another granting mechanism (e.g., P30, P01, U01, U10, DOD, etc.). Applicants can, however, use SPORE funds to augment pre-existing Cancer Center resources in order to direct these activities towards more effectively fulfilling the requirements of the SPORE. This is especially true of the SPORE specimen core, which should be designed to prioritize the needs of SPORE investigators over those of others. The SPORE should also utilize the IRB, Data and Safety Monitoring Board(s), as well as clinical resources available throughout the Cancer Center whenever possible.

Directors of SPORE cores are expected to discuss the integration and relationship of their core to any other *related* Cancer Center core(s) as outlined above and discussed in detail, again, in Section II. A brief description of any related CCSG core must be provided in the SPORE core description, along with its staffing commitments and capabilities, as well as any fees charged to investigators for its use. At a Cancer Center with two or more pre-existing SPORE awards, an additional section must address how related (e.g., specimen banking) activities are coordinated across all SPOREs, as well as the Cancer Center. It is anticipated that a request to support a Specimen Core at an institution with a CCSG and substantial pre-existing SPORE support should be smaller based on the infrastructure already in existence at the institution. Prior to an award, NCI will carefully review proposed SPORE core activities and budgets for overlaps with pre-existing CCSG and SPORE cores. It should be the objective of all involved core directors to make sure specimen-related, biostatistical, bioinformatic, and clinical activities are performed in a cost effective and coordinated manner.

F. Submission Requirements and Receipt Dates

1. Pre-application Consultation (Strongly Recommended)

NCI program staff strongly encourages each prospective applicant to schedule a pre-application consultation. The consultation should be scheduled **four to six months** in advance of the due date for submission and is intended to help the applicant (**along with one or more of his/her**

intended co-investigators) understand the SPORE Program and discuss strategies for preparing a competitive application. NCI staff will clarify the intent of the guidelines, discuss funding trends, and describe the peer-review process. The applicant can define which issues would be most helpful to discuss and then work with NCI program staff to decide what information should be provided. The following are examples of items that help NCI program staff understand the plans of applicants:

- A brief description of the background and proposed responsibilities of the SPORE Director and key senior leaders of the SPORE.

- A diagram showing the proposed reporting, programmatic, and advisory structure of the SPORE and how it relates to the structure of the institution as a whole.

- A brief description (1-2 pages) of the proposed translational research projects, along with their specific aims and the names of project co-leaders.

- Estimated budgets for each component (i.e., full projects, resources, developmental/career programs) of the anticipated SPORE application.

- A list of active peer-reviewed research grants, cooperative agreements, and contracts that form the research base of the scientific leaders of the SPORE.

2. Letter of Intent

Although it is not required and does not enter into the review of an application, all prospective applicants are requested to submit a letter of intent **at least 60 days prior to the receipt date** for the application. The letter of intent should include an overall title of the proposed application, the name, address, and telephone number of the principal investigator, the identities of other key personnel and all participating institutions, and the number and title of the PA in response to which the application will be submitted. Specific aims for each of the intended projects, along with a title of the project and its co-leaders, should also be provided. This information allows NCI staff to estimate the potential review workload, begin to identify potential reviewers, and avoid conflict of interest in the review. Furthermore, NCI staff can make sure applicants are fully aware of all applicable NIH and NCI policies, meet eligibility requirements, and understand the peer review process before the application is submitted.

The letter of intent should be sent to the NCI program director assigned to the organ site of

interest (see http://spores.nci.nih.gov for current program director assignments) at the following address:

Organ Systems Branch
OCTR, ODDES, NCI
6116 Executive Blvd., Suite 7013
Rockville, MD 20852 (if hand or express delivered)
Bethesda, MD 20892 (if delivered by US Postal Service)

Alternatively, the letter of intent can be sent as an e-mail attachment directly to the appropriate program director within the Organ Systems Branch.

SPORE applicants are exempt from the requirement to seek approval 6 weeks prior to submitting an application requesting $500,000 or more in direct costs. (See: http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html). This requirement is only for the submission of *unsolicited* grant applications. Applicants, however, must adhere to the budgetary cap restrictions of the SPORE program as outlined in Section I.E.1.(d) to avoid return of their application without review.

3. Application Procedures

The NIH PHS 398 (Rev. 09/2004) application forms are to be used in applying for these grants. Application forms and instructions are available through: http://grants1.nih.gov/grants/funding/phs398/phs398.html or may be obtained electronically by e-mail from grantsinfo@nih.gov.

Effective October 1, 2003, applications for Federal grants or cooperative agreements must also have a Dun and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as a Universal Identifier. For more details, see: http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-03-055.html. A DUNS number can be obtained by calling (866) 705-5711 or through the web site at http://www.dunandbradstreet.com/. The DUNS number should be entered on line 11 of the face page of the PHS 398 form. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: grantsinfo@nih.gov.

Copies of the SPORE guidelines and program announcements are available at the following URL addresses, respectively: http://spores.nci.nih.gov and http://grants1.nih.gov/grants/guide/pa-files/index.html. Instructions in these documents must be

followed in preparing a SPORE application. On line 2 of the face page of the application form, the applicant should provide the Program Announcement (PA) number, the title "Specialized Program of Research Excellence", and check the YES box.

At the time of submission, the **original signed application**, including the checklist, and **three exact single-sided copies (without appendices)** should be sent to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Suite 1040
Bethesda, MD 20892-7710
(use 20817 zip code for express service)
Ph. (301) 435-0715

Two additional copies of the application must also be sent to:

Referral Officer
Division of Extramural Activities
National Cancer Institute
6116 Executive Blvd., Room 8041, MSC 8329
Rockville, MD 20852 (if hand or express delivered)
Bethesda, MD 20892-8329 (if delivered by US Postal Service)

Appendix material should NOT be sent in either of these two packages. The Scientific Review Administrator (SRA) will contact the applicant at a later date and request these materials.

The applicant is encouraged to keep documentation of their mailing date(s) rather than contact the Center for Scientific Review (CSR) or the Division of Extramural Activities (DEA) for confirmation of receipt. The CSR will not accept any application that is essentially the same as one previously reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique. Applications must meet all eligibility requirements as described above and must address all programmatic requirements (see ELIGIBILITY AND REQUIRED COMPONENTS, Section I.E.) in these guidelines.

NCI program staff will review applications for responsiveness to SPORE Guidelines prior to acceptance for review. Any component of the application found to be funded through another NIH grant or contracting mechanism will not be counted towards fulfilling an essential requirement. For example, a SPORE project that proposes activities that duplicate those already funded by an R01 grant will be considered *non*-responsive. If the application, as a whole, has less than the four responsive projects, it will be returned without review. Any application that does not meet the minimal requirements as outlined in the SPORE Guidelines will be returned without review.

4. Application Receipt Dates

Due to the logistical problems that would be created by simultaneously accepting and reviewing grant applications for all cancer sites, the NCI has implemented a schedule for the solicitation of SPORE applications for each organ site.

Receipt dates for cancer sites will be announced each year with a formal program announcement in the NIH Guide (http://grants1.nih.gov/grants/guide/pa-files/index.html). Applicants should check the posted program announcement to determine what organ sites are being solicited in the current year. The 14 organ sites solicited by the SPORE program are listed in Table 1 (Section I.E.4.(d), above]. If the organ site of interest is not listed in the current program announcement, applicants are encouraged to contact OSB program staff to obtain information about the next possible receipt date for that organ site.

Applications for a given organ site will be accepted only on a solicited receipt date. Incomplete applications will be returned without peer-review (see ELIGIBILITY AND REQUIRED COMPONENTS, above). For competing renewal applications, consultation with NCI program staff is encouraged to ensure adherence to the organ-specific submission schedule and avoid gaps in funding.

5. Protection of Human Subjects

Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. See http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm.

Investigators proposing research involving human subjects are required to demonstrate that they

have been trained in the protection of human research participants according to the policy published in the NIH Guide for Grants and Contracts, June 5, 2000 (Revised August 25, 2000), available at the following URL address: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html and http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html. A continuing education program in the protection of human participants in research is available at: http://cme.nci.nih.gov.

Research components involving Phase I and II clinical trials must include provisions for assessment of patient eligibility and status, rigorous data management, quality assurance, and auditing procedures. In addition, it is NIH policy that all clinical trials require data and safety monitoring, with the method and degree of monitoring being commensurate with the risks (see NIH Policy for Data and Safety Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: http://grants.nih.gov/grants/guide/notice-files/not98-084.html and further guidance in http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html). Details on the Policy of the NCI for Data and Safety Monitoring of Clinical trials is available at: http://deainfo.nci.nih.gov/grantspolicies/datasafety.htm and information concerning essential elements of data safety monitoring plans for clinical trials funded by the NCI is available at: http://www.cancer.gov/clinicaltrials/conducting/dsm-guidelines.

Data and safety monitoring plans must be included along with a draft or IRB-approved clinical protocol for all projects that propose to perform a Phase I or II clinical trial *within the first two years* of the award. A general description of the monitoring plan should be provided in the "*Human Subjects Research*" section at the end of each project description following the subsection on "*Inclusion of Children*". The clinical protocol, consent forms, as well as a more detailed data and safety monitoring plan, should be provided in an Appendix. See the PHS 398 Instructions (Rev. 09/2004; Part II and Part I, page 35) for further guidance.

6. Inclusion of Women and Minorities in Research Involving Human Subjects

It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

As part of the scientific and technical merit evaluation of the research plan, reviewers are instructed to consider the adequacy of the plan for including women, minorities, and children.

Omission of this information (including reasons for exclusion) can have a negative impact on the priority score of a specific project and/or the overall application. In preparing these sections of the application, investigators are encouraged to follow the additional instructions provided directly below as well as under Section I.E.7.

All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines are available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. Investigators should provide a Targeted/Planned Enrollment Table for each proposed clinical study and address, at minimum, the four points outlined in the PHS 398 Instructions under "Inclusion of Women and Minorities in Clinical Research" (Rev. 09/2004; Part II, page 14). Ongoing projects proposed in competing renewals applications should also include an Inclusion Enrollment Report(s) (http://grants.nih.gov/grants/funding/phs398/enrollmentreport.pdf) for any clinical research performed in the past 12 months and discuss any difficulties encountered during the previous funding period in the recruitment of women and minorities and/or describe new plans to enhance recruitment.

7. Inclusion of Children in Research Involving Human Subjects

The NIH maintains a policy that children (i.e., *individuals under the age of 21*) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at http://grants.nih.gov/grants/funding/children/children.htm and http://grants.nih.gov/grants/guide/notice-files/not98-024.html. The PHS 398 Instructions also provide additional guidance on the inclusion or exclusion of children in research studies (Rev. 09/2004; Part II, page 19-20). Each proposed SPORE project should include a section that addresses this issue.

8. Standards for Privacy of Individually Identifiable Health Information

The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information," the "Privacy Rule," on

August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

9. Research Involving Human Embryonic Stem Cells

Criteria for federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html. Guidance for investigators and institutional review boards regarding research involving human embryonic stem cells, germ cells, and stem cell-derived test articles can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-044.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see http://escr.nih.gov). It is the responsibility of the applicant to provide on PHS 398 form page 2 (Rev. 09/2004) the registration number for any hESC line(s) to be used in the proposed research. Stem cell registration numbers can be found at: http://stemcells.nih.gov/registry/index.asp. Applications that do not provide this information will be returned without review.

10. Sharing Research Data

Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year are expected to include a plan for data-sharing (http://grants.nih.gov/grants/policy/data_sharing) or state why this is not possible. Investigators should seek guidance from their institutions, on issues related to institutional policies, local IRB rules, as well as local, State, and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data-sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

For SPOREs, this plan should be global in nature to include research data generated by projects and/or SPORE supported cores.

The plan should also describe how unique research resources will be shared in a timely manner and confirm that industry collaborations will not restrict the ability to share these resources (http://grants1.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc546000132 and http://ott.od.nih.gov/NewPages/Rtguide_final.html). If applicable, this plan should also discuss how model organisms generated through the SPORE will be shared (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html). A comprehensive **data and resources sharing plan** should be presented in the Program Description; individual projects and cores must also include a brief description on data and resource sharing pertinent to their activities or discuss why sharing is not possible. See Section I.C.7. above and Section II below for more detailed guidance.

11. Public Access to Research Data Through the Freedom of Information Act

The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

12. URLS in NIH Grant Applications or Appendices

All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Reviewers are cautioned that their anonymity may be compromised when they directly access an Internet site.

G. Review Considerations

1. Review Policies

Upon receipt of an application, the Scientific Review Administrator (SRA) in the NCI Division of Extramural Activities (DEA) reviews it for completeness and conformance to NIH policies. The application is then evaluated for responsiveness to all required components in the PA by OSB program staff. Applications that are incomplete or are non-responsive to the NCI SPORE Guidelines will be returned to the applicant without further consideration (See Section I.E. above).

Applications that are complete and responsive will be evaluated for scientific and technical merit by a peer review group convened by the National Cancer Institute and informed of the review criteria provided below. While all eligible applications will receive a written critique, some may be removed from further consideration (i.e., triaged) by the peer review group in the initial stages of the merit review process and will be unscored. In these instances, only applications deemed to have the highest scientific merit will be fully discussed by the review panel. In addition, if a required component(s) of an otherwise meritorious SPORE application is of such low merit that it is not recommended for further consideration (NRFC) by the peer review committee, the entire application will be NRFC. See Section I.E. of this document for a description of the required components of a SPORE application. Applications that receive a full discussion are assigned a priority score and undergo a second level of review by the National Cancer Advisory Board (NCAB).

2. Application Receipt and Referral

SPORE applications, like all other PHS applications, are received and initially processed by the NIH Center for Scientific Review (CSR). Following the current NCI referral guidelines, the application is assigned to NCI and subsequently to the Organ Systems Branch and SPORE program area. An SRA in the Research Programs Review Branch in the NCI Division of Extramural Activities will be assigned to manage the review.

After application submission, all correspondence should be directed to the SRA. Applicants are expected to submit complete applications (with the exception of Appendix material) by the specified receipt dates. The SRA will contact the applicant at a later time about the submission of Appendices and will also decide whether or not to allow submission of additional supplementary materials prior to the review.

3. Review Procedures

As the manager of the review process, the SRA serves as the resource for both applicants and reviewers with respect to NIH review policies, guidelines, rules, regulations, options available, procedures, etc. He or she ensures that the review is conducted in accordance with NIH and NCI policies. The NCI program director serves as a resource, as needed, concerning the history, intent and development of the program, changes in program direction, objectives, and any other relevant programmatic matters.

The scientific merit of a SPORE application is initially assessed by a peer review committee. This committee includes senior scientists with extensive review experience, a broad perspective on cancer research, and a wide variety of expertise. Because of the multi-disciplinary nature of SPORE applications, breadth is a necessary component of the review committee. Patient advocates also serve as members on these committees since they provide unique and important perspectives on translational research conducted by SPOREs. Beginning in 2005, review of SPORE applications will be performed by a standing Special Emphasis Panel (SEP) that will include experienced SPORE reviewers committed to continuous participation in SPORE reviews for a term of up to four years. These standing members will assist in ensuring consistency in the review process across all organ sites.

Applicants should take into account the fact that their application is reviewed by multiple individuals. Any piece of information that is critical to a particular project, resource, or program should be presented within the section designated for that activity (and not just within the overall "Program Description", for example).

Following assignment of a priority score by the review committee, a second level of review by the NCAB completes the peer-review process.

4. Review Criteria

The evaluation of applications is based on the following:

(a) Full Projects

Within the SPORE concept of translational research (see definition in Section I.B. above), reviewers will evaluate each research project using the recently updated five review criteria (see: http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-05-002.html) and additional factors noted below. Each criterion will be considered by the

reviewers in assigning the overall merit score of the project, although a project does not need to be strong in **all** criteria in order to be viewed as meritorious.

(a.1) Significance

Does this study address an important translational research goal or barrier? Is it likely the study will be completed within the project period? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the **impact** of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? If a project is ongoing, did it achieve its goals within the previous funding period; is scientific progress adequate?

(a.2) Approach

Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Is there clear **evidence of co-leadership** between both a basic biological and applied or clinical scientist in the conception, design, and proposed implementation of the project? Do the project co-leaders acknowledge potential problem areas and consider alternative tactics? If the project is ongoing and has changed research direction, is there appropriate rationale for the new approach?

(a.3) Innovation

Is the project original and innovative in the context of translational research? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this organ site?

(a.4) Investigators

Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level and time commitments of the co-leaders and co-investigators on the project? Does the investigative team bring complementary and integrated expertise to the project?

(a.5) Environment

Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the

scientific environment, or subject populations, or employ useful collaborative arrangements? If applicable, is there evidence of effective use of SPORE cores?

For competing renewal applications, adequate progress should be demonstrated on projects that are ongoing. Any difficulties in achieving the previously proposed specific aims should be addressed and the new research goals should be logical extensions for the project. There should be clear evidence that such a project reached its anticipated human application(s) during the previous funding period and the continuation of the project will lead to new translational findings. It should also be evident that the investigative team, especially the project co-leaders, established a productive working relationship during the past performance period and have published or submitted manuscripts describing their previous findings. For research projects that will not be continuing in the renewal, a progress report should be provided including the reasons why the project was discontinued in the SPORE. This information should also be detailed within the Program Description under Planning and Evaluation Activities.

(b) Cores

(b.1) Specimen Core

- Adequacy of the proposed plan and/or track record to develop, annotate, and maintain a human cancer site-specific specimen resource, including linkage of specimens with preanalytical parameters and pathological, clinical, and family history data that maximize their potential use in translational research.

- Adequacy of the proposed plan and/or track record to prioritize the distribution of specimens within and outside the SPORE. *For competing renewal applications*, there should be clear documentation of the use of specimens by SPORE investigators within full and developmental projects, as well as details, if applicable, about the distribution and use of SPORE collected specimens outside of the SPORE and/or institution.

- If applicable, adequacy of the proposed plan and/or track record to perform analyses on specimens (e.g., tissue microdissection, immunochemistry) and/or develop new technologies and methodologies that enhance or benefit activities of the SPORE. *For competing renewal applications*, there should be clear documentation that demonstrates these analyses were critical to the success of certain projects and are worthy of continued support, if requested.

- Evidence of experienced and available personnel dedicated to the activities of specimen collection, annotation, quality control, storage, distribution, and analysis; as well as overseeing the collection of initial and follow-up clinical information, data entry, and maintenance of database and computer networks. *For competing renewal applications*, the performance and relative time commitments of these individuals should also be evaluated based on the past accomplishments of the core.

- Adequacy of the proposed plan and/or track record to demonstrate that the activities of the core are well integrated with those of the projects and the investigators within the projects are working closely with those of the core to meet project objectives.

- When appropriate, adequacy of the proposed plan/track record to augment and/or complement any existing specimen resource supported by a Cancer Center Support Grant (CCSG; P30) or other funding mechanism(s) to avoid duplication and maximize productivity. Investigators applying from institutions with a CCSG and *multiple* SPORE grants should address how their core will benefit from already established infrastructure, databases, etc. that will enable this proposed specimen core to be more cost effective and efficient.

- Adequacy of the proposed plan and/or track record to obtain informed written consent for all prospectively collected tissues/specimens and protect confidentiality.

(b.2) Other Cores

- Degree to which plans and/or track record indicate that shared resources (will) effectively and efficiently support the research of the SPORE in a manner that can not be supported through other available (institutional or outside) resources.

- Adequacy of the plan and/or track record to demonstrate that the activities of the core are essential to one or more SPORE projects. *For competing renewal applications,* demonstrated use of each core by SPORE projects during the previous funding period.

- Adequacy of the proposed plan and/or track record to demonstrate that the activities of the core are well integrated with those of the projects and the investigators within the projects are working closely with those of the core to meet project objectives.

- If applicable, adequacy of the plan and/or track record to demonstrate the activities of the core related to the performance of specialized analyses or development of technologies or methodologies that enhance and benefit the projects.

- When appropriate, adequacy of the proposed plan/track record to augment and/or complement an existing shared resource supported by an NCI Cancer Center Support Grant (P30) or other funding mechanism. There should be adequate details within the core description to assure there is no duplication of services with pre-existing cores at the Cancer Center or institution.

- Adequacy of qualifications, past performance (if applicable), and time commitments of resource directors.

- All proposed cores must include a budgetary request from SPORE funds.

(c) Developmental Research Program

(c.1) Adequacy of the process and/or track record for attracting new ideas and pilot studies within and outside of the SPORE institution. The outreach capabilities of a SPORE are often demonstrated within this program.

(c.2) Adequacy of the proposed process and/or track record for continuously reviewing and funding a spectrum of pilot projects with translational research potential. *For competing renewal applications,* this program should also be evaluated on the SPORE's ability to promote outstanding translational pilot projects to full projects and/or demonstrate the successful competition of these projects for outside funds.

(c.3) A minimum of $50,000 direct costs per year must be allocated from SPORE funds.

(d) Career Development Program

(d.1) Adequacy of the process and/or track record for selecting promising candidates for independent careers (academic, industrial, governmental) in translational cancer research.

(d.2) Adequacy of the procedures and/or track record to seek out and include qualified women and minorities.

(d.3) *For competing renewal applications,* current status and research activities of individuals who have been supported by the career development program. This may include the promotion of outstanding career development projects to full projects within the SPOREs and involve the continuing support and integration of successful career development awardees as project co-leaders or co-investigators.

(d.5) A minimum of $50,000 direct costs per year must be allocated from SPORE funds.

(e) Overall Program Organization and Capability

All of these items should be addressed within the Program Description part of the application.

(e.1) Leadership

Scientific qualifications and involvement of the SPORE principal investigator as well as his/her demonstrated scientific and administrative leadership capabilities and time commitment.

(e.2) Institutional Commitment

Adequacy of and/or demonstrated institutional commitment for facilitating the research objectives of the SPORE (e.g., special facilities, recruitments, discretionary resources such as dollars and space).

(e.3) Integration within the SPORE and the Institution

Effectiveness of and/or plans for integrating the activities of SPORE projects with proposed cores, as well as integrating SPORE research and cores with existing Cancer Center/institutional resources (e.g., use of clinical data and safety management systems, biostatistical cores, etc.). SPORE projects are *not* required to interact with each other.

(e.4) Cancer Patient Population

Adequacy of access to patients and populations for conducting current and projected therapeutic, prevention, detection, and control research. *For competing renewal applications*, documentation of accomplished translational goals, including

evidence of human subjects enrollment on clinical/population research studies during the past funding period.

(e.5) Planning and Evaluation of Activities

Adequacy of the plan and/or track record to evaluate the translational research productivity of existing projects and cores; discontinue activities of low productivity; initiate new activities in response to important translational research opportunities; establish collaborations; and utilize the advice of internal and external advisors.

(e.6) Collaborations

Evidence of tangible interactions with other SPOREs and/or NIH/NCI Networks. Willingness to interact with other SPOREs and with the NIH/NCI in sharing information, participating in committees, and collaborating on activities of mutual interest. *For competing renewal applications*, contributions and outcomes from annual SPORE Workshop and other related SPORE or NIH/NCI meetings during the term of the award.

(e.7) Intellectual Property Management Plan

Adequacy of a plan and/or track record for the management of intellectual property generated by SPORE projects. There should be evidence for the appropriate evaluation, protection, and commercialization of SPORE inventions. Engagement of the institution's technology transfer office should be documented and established or proposed assurances should be provided outlining any pre-existing agreements with commercial entities. Related or ongoing activities with industrial sponsors may also be discussed to demonstrate collaborative potential and provide assurance that the SPORE is poised to move human applications forward into the next appropriate clinical or population setting.

(e.8) Data Management

Adequacy of and/or track record for the overall data management or bioinformatics capabilities of the SPORE as they related to the Cancer Center, institution, or activities of other NIH/NCI initiatives.

(e.9) *Progress (for Competitive Renewal Applications)*

The progress and achievements specific to the application and relevant to

translational research since the previous competitive review. Adequacy of the justification for adding new projects or cores or deleting previous components.

(f) *Additional Review Criteria and Considerations*

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the priority score:

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated (see the Research Plan, Section E on Human Subjects in the PHS Form 398.)

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the five items described under Section F of the PHS Form 398 research grant application instructions will be assessed.

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed activity. The priority score should not be affected by the evaluation of the budget.

5. Overall Evaluation and Scoring of Applications

A single numerical priority score will be assigned to the SPORE application as a whole after discussing all of the review elements listed above. The score will be based on the overall quality of the research projects (using the SPORE definition of translational research in Section I.B.) and career development and developmental research programs, the overall effectiveness and adequacy of shared cores, the overall program organization and capability including plans or productivity of interactions with other SPOREs and/or NIH/NCI Networks.

The final overall priority score for the application will be weighted as follows:

70% scientific merit of the projects and shared cores, including the likelihood of achieving the proposed translational research objectives

30% overall programmatic organization and capabilities, including developmental programs (Career Development and Developmental Research)

If a required component(s) of an otherwise meritorious SPORE application is of such low merit that it is not recommended for further consideration (NRFC) by the peer review committee, the entire application will also receive a NRFC.

6. Summary Statements

The findings and recommendations of the reviewers are summarized in a written report (i.e., Summary Statement) which conveys the evaluation of the P50 application. This Summary Statement is transmitted to the NCAB for second level 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.

7. Award

Final funding decisions are made by NCI based on overall priority scores of the applications as determined by peer review, recommendations by the NCAB, the availability of funds, and NCI research priorities during each fiscal year.

The NCI may consider funding a P50 application as a P20 planning grant. Applications considered for P20 awards will be funded on the basis of their scientific merit and NCI programmatic priorities.

The award and administration of the P50 and P20 grants are subject to the same policies and procedures as other research grants. These policies and cost principles are set forth in the current NIH Grants Policy Statement, other NIH and NCI issuances and Federal legislation and regulations.

H. Inquiries

For further clarification of the different topics contained in the present guidelines, individuals may contact the Organ Systems Branch by e-mail (nciosb-r@mail.nih.gov), phone (301-496-8528), or fax (301-402-5319). Direct e-mail addresses are also listed for current OSB program staff on the Internet site: http://spores.nci.nih.gov.

Section II. Instructions for Preparing a Competing SPORE Grant Application

These instructions provide information needed for the preparation of either a new or competing renewal grant application for a Specialized Program of Research Excellence (SPORE). The application receipt dates are specified in an annual program announcement (PA) which is accessible through the program Internet site: http://spores.nci.nih.gov.

A. General Information

General instructions for the preparation of an NIH grant application (PHS 398, Rev. 09/2004) are available at: http://grants1.nih.gov/grants/funding/phs398/phs398.html. Although the PHS 398 application is intended primarily for a single research project grant (i.e. R01), many of the general instructions and forms also apply to SPORE grant applications. However, as outlined in Section I, SPORE grants have unique requirements and review criteria. Accordingly, the special instructions in this document were prepared for use along with the PHS 398 forms.

Revised applications are only accepted in response to published Program Announcements for the specific organ site. The SPORE program adheres to the same general policy for revised (amended) applications as issued by the NIH (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-041.html) with the following points of clarification:

1. Applications submitted within two years of the previous submission will be reviewed as amended applications regardless of whether the scientific direction of the projects has changed significantly or there have been other noteworthy changes in the leadership or infrastructure of the SPORE. In this case, the peer reviewers will be provided with a copy of the previous Summary Statement.

2. In many instances, a SPORE applicant will not be able to re-apply within two years

due to the schedule of organ site solicitations. There may be a gap of two to four years before an applicant can consider submitting an amended application. Any application submitted more than two years after the original or previous submission will be considered a new application if more than 50% of the research projects have changed significantly in direction. Significant changes include the deletion of a previous project and addition of a new project with completely different aims and, potentially, led by different investigators. If less than 50% of the research projects have changed then the application will be considered a revised application. Changes in direction that are the result of the normal progression of a project over time would not be considered as significant changes in direction. Projects that have received funding under another award mechanism (such as R01, P01, etc.) during the interim are not eligible for inclusion. Up to two amended applications can be submitted in adhering to these criteria.

B. Detailed Directions

1. Face Page

The face page is the same as the face page (form page 1) in a PHS 398 grant application (Rev. 09/2004). In item 1, enter the title "SPORE in (Organ-Specific) Cancer". In item 2, insert the PA number, and enter the title "Specialized Program of Research Excellence". In item 3, indicate the name, degree, and position (or equivalent) title of the SPORE Principal Investigator. Complete the rest of the page according to the PHS 398 instructions, including the signature of the appropriate institution official(s).

2. Description, Performance Sites, and Key Personnel (Page 2)

Page 2 is the same as form page 2 for a PHS 398 grant application (Rev. 09/2004). Provide a brief description of the proposed SPORE in the space provided, specifically addressing each project and proposed resource core. Fill in all the performance sites and all key professional personnel including all project and core leaders and key personnel of the Developmental Research and Career Development Programs, using form page 2-continued if required.

3. Table of Contents (Page 3)

Instead of using form page 3 of the PHS 398 grant application, prepare a Table of Contents that identifies by page number all major parts of the SPORE application so that they can be readily located. When listing individual projects and core components, identify each by a project or core number, title and responsible investigator(s) in the order in which they appear in the application.

It is recommended that all applicants follow a format similar to that outlined below:

I. Face Page (PHS 398 Form Page 1)
II. Description, Performance Sites, Key Personnel (PHS 398 Form Page 2)
III. Table of Contents (PHS 398 Form Page 3)
IV. Initial Budget (PHS 398 Form Page 4; see item 4 below)
V. Summary Budget (PHS 398 Form Page 5; see item 5 below)
VI. Biographical Sketches
VII. Resources (see item 7 below)
VIII. Eligibility Statement (see item 8 below)
IX. Program Description (see item 9 below)
    A. Introduction
    B. Institutional Commitment
    C. Scientific and Administrative Leadership
    D. Relationship to Cancer Center
    E. Scientific Integration - Interactions and Collaborations
    F. Cancer Patient Population
    G. Translational Research Objectives
    H. Planning and Evaluation Activities
    I. Intellectual Property Management Plan
    J. Data Management
    K. Data and Research Resources Sharing Plan
X. Research Projects (Minimum of four projects required; see item 10 below)

For competing renewals, outline the scientific accomplishments and discuss the potential impact on the disease for each project completed in the last grant period. Publications should be restricted to those that cite support from the SPORE grant. With the exception of the publication list, this information should be incorporated into the Preliminary Studies/Progress Report of each project and count towards the 25 page limit according to the PHS 398 instructions (Rev. 09/2004; Part I, page 31).

Project 1

1. Title Page with **Project Co-Leaders**
2. Abstract Page
3. Budget/Budget Justification Pages
4. Research Proposal (If an ongoing project, discuss scientific progress within the original five-year time frame)
5. Human Subjects Research

a. Data Safety and Monitoring Plan

6. Women and Minority Inclusion
    a. Targeted/Planned Enrollment Table
    b. Inclusion Enrollment Report Table (competing continuation)
7. Inclusion/Exclusion of Children
8. Vertebrate Animals
9. Literature Cited
10. Consortium/Contractual Arrangements
11. Resource Sharing
12. Consultants/Commercial Agreements

Project 2

1. Title Page with **Project Co-Leaders**
2. Abstract Page
3. Budget/Budget Justification Pages
4. Research Proposal (If an ongoing project, discuss scientific progress within the original five-year time frame)
5. Human Subjects Research
    a. Data Safety and Monitoring Plan
6. Women and Minority Inclusion
    a. Targeted/Planned Enrollment Table
    b. Inclusion Enrollment Report Table (competing continuation)
7. Inclusion/Exclusion of Children
8. Vertebrate Animals
9. Literature Cited
10. Consortium/Contractual Arrangements
11. Resource Sharing
12. Consultants/Commercial Agreements

ETC.

XI. Cores (Specimen Core is required; see item 11 below)

Specimen Core

1. Title Page with Director(s)
2. Abstract Page
3. Budget/Budget Justifications
4. Plan/Interactions/Progress (for competing renewals)
5. Human Subjects and Vertebrate Animals
6.

Other Cores

1. Title Page with Director(s)
2. Abstract Page
3. Budget/Budget Justifications
4. Plan/Interactions/Progress (for competing renewals)
5. Human Subjects and Vertebrate Animals

ETC.

XII. Developmental Research Program (see item 12 below)

1. Title Page with Director(s)
2. Budget/Budget Justification Pages
3. Plan/Examples
4. For competing renewals describe each project funded during the last grant period and the outcome of each project relative to the SPORE objectives.

XIII. Career Development Program (see item 13 below)

1. Title Page with Director(s)/Leader(s)
2. Budget/Budget Justification Pages
3. Plan/Examples
4. For competing renewals, denote individuals supported during the last grant period, their scientific accomplishments while supported by the SPORE, and how SPORE support has advanced their translational research careers.

XIV. Checklist (see item 14 below)

XV. Appendix Material (see item 15 below)

Amended/revised applications should include additional sections prior to the Program Description, as well as each revised research project, core, and development program that address the critiques from the previous review. These sections should be limited to three pages or less and be entitled as "Introduction to Amended/Revised Application", "Introduction to Amended/Revised Project", etc.

4. Summary Program Budget for the Initial Budget Period

Use form page 4 of the PHS 398 application to present the summary budget for the first year. For each category, show separately the total amounts requested for each research project and core.

If the grant application includes research activities that involve institutions other than the applicant organization, the proposed program represents a consortium effort. It is essential to

explain the programmatic, fiscal, and administrative arrangements for such activities. These matters should be discussed in general terms in the program introduction, and more specifically within descriptions for pertinent projects. Include in the designated blocks on this page the total (direct and indirect) costs associated with such third party participation. The PHS 398 form page 4 (Rev. 09/2004) has recently been modified to separate total direct costs (from the parent institution and any consortium sites) from all indirect costs. Details on policies governing consortia are available at: http://grants1.nih.gov/grants/policy/policy.htm.

5. Summary Program Budget for Entire Project Period

Use form page 5 of the PHS 398 application to show the total SPORE budget requested for each of the five years. Justifications for increases in succeeding years should not be included here; they should be delineated in the detailed budgets for individual projects (as described below in item 10). Note that current NIH practice limits overall budget escalation per year to 3% cost-of-living. Also note that NCI policy for SPORE grants establishes an annual **direct cost cap of $1.5 million** and maximum annual **total cost cap of $2.5 million** for new and competing applications. Indirect costs related to subcontracts to other institutions or organizations do not apply toward the $1.5 million direct cost cap. Form pages 4 and 5 of the PHS 398 application (Rev. 09/2004) now provide a subtotal line for direct costs from all participating sites. Consortium indirect costs, however, must be included in the total costs which, overall, may not exceed the $2.5 million cap. In non-competing years, applications can exceed these caps as a result of the standard cost-of-living increases or special supplements approved by the NCI. An applicant should not submit an application anticipating the support of a critical or required activity by an administrative supplement.

6. Biographical Sketches

Prepare biographical sketches as described in the PHS 398 instructions (Rev. 09/2004). Begin with the Principal Investigator/SPORE Director and then proceed in alphabetical order. Biographical sketches are required for all professional personnel participating in the individual SPORE projects and core(s). The "Biographical Sketch Format Page" and “Continuation Format Page” should be used. Information on current Research Support must be provided within the four page limit. This information is assessed by NCI program staff to determine if the application meets the Minimal Research Base eligibility requirement [see Section I.E.1.(b)]. Significant overlap between a proposed SPORE component and a funded grant is not allowed and could result in the return of an application that fails to meet minimal program requirements.

7. Resources

Complete "Resources Format Page" as instructed. If applicable, additional Resource pages should be provided in consortia projects or cores and may be desirable in certain projects that capitalize upon unique resources or infrastructures present at the parent institution. An extensive discussion of the institution's commitment to the SPORE is also required in item 9c below.

8. Eligibility Statement

In considerable detail, specifically address how this application meets the eligibility requirements under ELIGIBILITY AND REQUIRED COMPONENTS, Section I.E.1." above.

9. Program Description

(a) Introduction

Describe the purpose and intent of the research program; the overall breadth of the scientific capabilities of the program to address critical issues in the *organ-specific* human cancer from basic laboratory to clinical to prevention and control research; the organization of the SPORE to maximize the potential of the institution to achieve translational research objectives. Applicants for *competing renewal* grants should address overall progress of the SPORE in meeting these objectives, as well as the evolution of project goals over time.

(b) *Scientific and Administrative Leadership*

Describe the authority, scientific experience, and administrative experience of the principal investigator to provide leadership and direction to the SPORE. Similarly, describe the responsibilities of other senior scientific leaders and administrators and their qualifications to meet these responsibilities. Describe the processes and chain of responsibility for scientific decision making and day-to-day administration and management of the SPORE. *For competing renewal applications*, discuss any changes in the leadership of the SPORE and additions or deletions of key personnel since the last submission. Specify how these changes have strengthened the current activities of the SPORE. If these changes have resulted in any hardships or deficiencies, discuss how the leadership of the SPORE have addressed or propose to manage these problems.

(c) Institutional Commitment

Describe how the institution will and/or has made the SPORE an area of high priority. Describe the space, personnel and all other resources that the institution will and/or has committed to ensure that the SPORE exists in an appropriate environment for conducting

an effective translational research program. Outline plans for any future commitments in space or personnel to strengthen the research capability of the SPORE. The application should describe how the institution will (continue to) participate in overseeing research progress, identifying research needs, and generally assuming a high level of accountability for the success of the SPORE in achieving research goals and objectives. Fiscal support from the institution is strongly encouraged. Examples of such support include providing matching funds to the Developmental Research and/or Career Development Programs, as well as providing discretionary funds to the principal investigator or executive committee of the SPORE to enhance project activities during the term of the award. *Competing renewal applications* should outline in detail how any institutional funds were utilized during the previous funding period to enhance SPORE activities.

(d) Relationship to Cancer Center

If the SPORE application is being submitted from an institution already designated as a NCI Clinical or Comprehensive Cancer Center, a special section under this heading should clearly delineate the relationship of the SPORE (P50) to the Cancer Center (P30) as noted under "ELIGIBILITY AND REQUIRED COMPONENTS, Section I.E.9," above. A statement(s) signed by the appropriate institutional official(s), Cancer Center Director and SPORE principal investigator confirming and agreeing to this relationship must be included in the application, at the end of the section on Program Description.

A copy of the approved Comprehensive Cancer Center Data Safety and Monitoring Plan should also be provided at the end of the Program Description section.

(e) Cancer Patient Population

Describe how the clinical patient care and service resources will be integrated with the research activities of the SPORE. Delineate the number and distribution of stages of cancer patients relevant to this organ cancer SPORE that are routinely cared for and how this patient population will meet all current and anticipated research needs. If the care and service facility is not part of the parent institution, the consortium arrangements should be clearly stated and officially confirmed as noted under "ELIGIBILITY AND REQUIRED COMPONENTS", Section I.E.1.c. above. If human subjects from foreign countries are involved in the proposed studies, evidence that the foreign institution operates under or has applied for a federal wide assurance (FWA) should be provided and, if applicable, clearance by the State Department and Foreign Embassy. See the

following Internet sites for additional information: http://www.hhs.gov/ohrp/ and http://www.fic.nih.gov/.

(f) Scientific Integration - Interactions within the SPORE, Cancer Center, and Institution
Specifically discuss how interactions will be and/or have been maintained between basic and more applied researchers within the research projects to foster a truly collaborative atmosphere that takes maximum advantage of research opportunities. Describe how the SPORE has and/or will operate collectively to maximize research objectives. Discuss any critical interactions with additional scientists within or outside of the institution that have enhanced or are proposed to enhance the overall research objectives of the SPORE.

Describe how the core services have been and/or will be integrated effectively with the project and how these cores augment any pre-existing activity within the Cancer Center (if applicable) and/or institution.

(g) Translational Research Objectives
It is critical that the application delineate in considerable detail how the program will focus on translational research objectives in moving basic research findings into studies for improving the detection, diagnosis, treatment and prevention of human cancer, or moving clinical observations into the laboratory environment (see Section I.B. for SPORE DEFINITION OF TRANSLATIONAL RESEARCH). Describe how the SPORE will strengthen its research capability through the use of developmental funds to explore innovative research ideas. *For competing renewal applications*, a summary should be included that discusses translational outcomes from the previous funding period. Specifically, a brief description of all clinical trials and interventions sponsored or co-sponsored with SPORE funds should be provided, including those supported by administrative supplements. More detailed progress should be provided on trials/interventions performed during the past 12 months. This information is critical for demonstrating the past successes of the SPORE in accomplishing translational endpoints.

(h) Planning and Evaluation Activities
Describe how the SPORE will measure research progress collectively, identify new translational research opportunities, and terminate projects that are not achieving their translational research objectives. A plan must be provided for evaluating the scientific progress and translational potential of all projects and replacing them as necessary. This plan should outline how the SPORE will utilize internal and external advisors for this

activity. During the period of award, replacement projects will be reviewed by the SPORE and NCI program staff, but will not undergo additional peer review. *Competing renewal applications* will be evaluated based on their track record for fostering and promoting significant translational research during the prior grant period. Details should also be provided in this section on the past 12 months of progress on projects that were *not* chosen for continuation in the current application. It should be clear whether or not these projects will be supported by other means or have been terminated permanently.

(i) Collaborations

Provide a plan of how the SPORE will or does utilize the annual SPORE Workshop most effectively for sharing data, establishing new collaborations, and setting priorities for future research. *All applicants are required to include a statement within this section that indicates their commitment to attend the annual SPORE Workshop, along with nine of their key investigators.* This statement fulfills a critical requirement of the SPORE program (see Section I.E.8. above). *Competing renewal applications* should also describe how the annual workshop, as well as other meetings throughout the year, have fostered collaborations between SPOREs and/or other NIH/NCI Networks and highlight their specific contributions to these meetings during the past term.

Discuss in detail ongoing or completed collaborative activities SPORE investigators have participated in with other SPOREs and/or NIH/NCI networks to advance translational goals. Collaborating on projects to advance their clinical application is a key feature of the SPORE program. New applicants should discuss any relevant past or ongoing collaborative activity with an NIH or NCI Network which is likely to enhance SPORE activities. Competing renewal applicants should discuss the SPORE's involvement in Inter-SPORE activities during the previous funding period and provide detailed progress on collaborative activities performed during the past 12 months.

(j) *Intellectual Property Management Plan*

Provide a comprehensive plan for managing the intellectual property resulting from all SPORE activities. This plan should discuss any ongoing or planned collaborations with commercial entities and outline, in detail, their particular contributions to the research activity. Information should also be provided on the process by which solely or jointly owned inventions of SPORE institutions are evaluated and moved forward for patent applications. The application should describe the individuals and office responsible for evaluating and protecting SPORE inventions and whether or not is potential or immediate

plans for commercializing the technology, including any proposed licensing strategies. If more than one commercial entity is involved in a project, a plan for how these entities will or might interact should also be provided.

A letter signed by an official from the technology transfer/intellectual property management/licensing officer or equivalent at the principal investigator's institution must be included to assure that the proposed plan is acceptable and follows legal guidelines for the handling of intellectual property. The letter should be responsive to the specific programmatic objectives of the SPORE described within the application. The letter should also confirm the written agreement with this intellectual property management plan by the institutions of any external co-investigators, collaborators, consultants, and industry partners.

(k) *Data Management*

Provide an overview of the data management and bioinformatics capabilities of the Cancer Center and institution(s) as they relate to SPORE activities. This includes describing the types and capabilities of existing databases, the integration of clinical and basic research databases, and protections in place to assure the confidentiality of information obtained on human subjects. *Competing renewal* applicants should also highlight any changes in the management of data since the last submission such as the addition of new databases, integration with other sites, etc.

(l) Data and Research Resources Sharing Plan

Provide a plan for the sharing of research data generated by the SPORE. This plan can include the use of or be linked to the SPORE program Internet site (http://spores.nci.nih.gov) and should be comprehensive for all components of the SPORE. Additional guidance can be obtained from: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html and http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm.

The plan should also discuss how unique research resources will be shared in a timely manner and confirm that industry collaborations will not restrict the ability to share these resources (http://grants1.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600132; and http://ott.od.nih.gov/NewPages/Rtguide_final.html). If applicable, this plan should also discuss how model organisms generated through the SPORE will be shared

(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html). *Competing renewals applications* should include a discussion on resources, data, and information that was shared (and how) during the previous funding period. As stated in Sections I.C.7. and I.F.10 above, the evaluation of this plan does not factor into the overall merit or priority score for the application.

10. Translational Research Projects

As previously discussed, for the purposes of this program, the NCI has defined translational research as follows: **"Translational research uses knowledge of human biology to develop and test the feasibility of cancer-relevant interventions in humans and/or determines the biological basis for observations made in individuals with cancer or in populations at risk for cancer"**. The term "interventions" is used in its broadest sense to include molecular assays, imaging techniques, drugs, biologicals and/or other methodologies that are relevant to the prevention, early detection, diagnosis, prognosis or treatment of cancer. Translational research in SPOREs is always based upon human biology stemming from any form of cellular, molecular, structural, biochemical, genetic, or other appropriate experimental approach.

SPOREs conduct early-stage interventions to establish the feasibility or proof of principle of specific approaches in cancer. All research projects whose goal is the development and testing of an intervention are expected to reach the feasibility testing stage in human subjects within the anticipated five-year period of grant support. Similarly, studies that seek to determine the biological basis for an observation in human cancer should do so within five years. SPOREs are not the place for definitive validation of new interventions, which are supported by other programs in several divisions of the NCI.

Questions regarding the definition of translational research and its applicability to specific research projects should be directed to OSB program staff (see INQUIRIES, Section I.H. above).

A SPORE application cannot include projects that significantly overlap activities that are already or soon-to-be awarded by the NIH or another PHS mechanism. Prior to review, SPORE applications will be scrutinized by NCI staff for responsiveness to this requirement by screening internal NIH databases for other related applications submitted by the same team of investigators. Projects that are already supported by the NIH or have overlap with other funded activities will not be considered. The SPORE application, as a whole, will be viewed as non-responsive and returned to the applicant prior to review if the minimal number of *unfunded* projects falls below four.

For each research project provide the following as noted below. Page limitations specified for individual (R01) grant applications in the PHS 398 application (Rev. 09/2004) must be followed for individual project and core unit research plans. Unnecessarily long, wordy or confusing presentations are usually perceived as indicators of premature or poorly planned research.

(a) A title page with a project number, a title for the project and the project co-leaders on a plain piece of paper.

(b) A "Description of the Research Plan" using form page 2 of the PHS 398 application (Rev. 09/2004). The top section should contain a succinct summary of the research project. The bottom section should include performance sites and all key professional personnel as instructed. If human embryonic stem cells are utilized in the project, the registration number(s) of the cell line(s) must be provided.

(c) Budget Pages
The detailed budget for the first 12 months and the overall budgets for each succeeding year for each research project should be presented using the PHS 398 application form pages 4 and 5 (Rev. 09/2004). For each category or individual listed on form page 4, provide a rationale in the budget justification. SPORE project budgets are exempt from the modular format.

(d) Research Plan
Following the budget pages, use continuation pages to address the (a) Specific Aims, (b) Background and Significance, (c) Preliminary Studies/Progress Report, and (d) Research Design and Methods sections as outlined in the PHS 398 instructions (Rev. 09/2004). For continuation of ongoing SPORE projects, scientific progress over the past term of the grant should be delineated in the Preliminary Studies/Progress Report section. Reasons as to why a project has not completed its previously proposed objectives should also be discussed in this section.

Page limitations are the same as those delineated in the PHS 398 instructions; no more than 25 pages should be used for sections a-d of the Research Plan for each project proposed within the SPORE application. The 25-page limit also applies to all other self-contained components of the application, e.g., each Shared Core Resource, the Developmental Research Program, and the Career Development Program.

Amended/revised applications should include additional introductory sections addressing previous reviewer critiques of up to 3 pages before the Research Plan for projects, Resource Description for cores, and Program Summary for developmental programs.

(e) Human Subjects Research

For each SPORE project, which are required to include the involvement of human subjects and/or utilize human specimens, applicants must determine what level of detail needs to be provided to address the protection of human subjects from research risks, as well as include the participation of women, minorities, and children in the research. The PHS 398 instructions provides a decision tree which should be utilized to determine which of the five scenarios (B-F) best matches the research proposed in the SPORE project (Rev. 09/2004; Part I, page 33). For all projects, which are not exempt from HHS human subjects regulations, investigators must include after the "Research Design and Methods" section a discussion on how human subjects will be protected from research risks, details on the inclusion of women and minorities, and reasons for the inclusion or exclusion of children (individuals under the age of 21), respectively. Importantly, Targeted/Planned Enrollment Tables for new studies and Inclusion Enrollment Report Tables for competing continuations are required for *all* studies identified as "clinical research". **Clinical research** is defined by the NIH as:

Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies.

If the project includes a clinical trial, then a Data Safety Monitoring Plan must also be included in the project proposal. The NIH defines a **clinical trial** as a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

All applicants are encouraged to review the PHS 398 "Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan" (Rev. 09/2004; Part II)

in composing their responses to these critical sections of the application. Applications that contain proposed projects that fail to address the appropriate required items on human subjects will be designated incomplete and may be returned to the applicant without peer review. As indicated in Section I.G.4.f., a draft or IRB-approved clinical protocol, along with appropriate consent forms, should also be included in the Appendix for all projects that propose to perform a clinical trial within the first two years of the award. Assessment of all human subject materials is factored into the project/core/program peer reviewer evaluations and can impact on the merit score assigned for each of these components, as well as the overall priority score assigned to the application.

(f) Vertebrate Animals

If applicable, provide a brief description of any animal protocol. When research involving vertebrate animals will take place at a collaborating site, this should be indicated. The five points for vertebrate animals listed below should also be addressed:

(1) Provide a detailed description of the proposed use of the animals in the work outlined in the "Research Design and Methods" section. Identify the species, strains, ages, sex and numbers of animals to be used in the proposed work.

(2) Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.

(3) Provide information on the veterinary care of the animals involved.

(4) Describe the procedures for ensuring that discomfort, distress, pain and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize the discomfort, distress, pain, and injury.

(5) Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If not, present a justification for not following the recommendations.

(g) Literature Cited
List all references. This list may include, but should not replace, the list of publications required in the Progress Report section for competing continuation applications. Follow the format provided in the PHS 398 instructions (Rev. 09/2004; Part I, page 35).

(h) Consortium/Contractual Arrangements
Follow instructions as outlined in the PHS 398 application (Rev. 09/2004; Part I, page 35).

(i) Resource Sharing
Investigators should highlight, in a brief one paragraph description, how final research data will be shared or explain why data-sharing is not possible. If the development of a model organism is anticipated, investigators should also include the sharing of this model in their plan. This section should focus on research data that are unique to the project and may refer back to the comprehensive Data and Research Resources Sharing Plan provided within the Program Description. Additional information on data, resource, and model organism sharing is provided in Section I.C.7. of these guidelines and can be found within the PHS 398 instructions (Rev. 09/2004; Part I, pages 8, 9, and 35).

(j) Consultants/Commercial Agreements
Attach letters from individuals or commercial entities documenting their roles in the projects. Letter from individuals representing a commercial entity should be detailed and outline the exact relationship between the commercial entity with the project investigators and address how intellectual property will be handled. Adherence to the Bayh-Dole Act is required as outlined in Section I.E.3 above.

11. Cores

Cores should *not* duplicate services or resources that are fundamentally available through any other mechanism (including P30s, P01s, and other P50s) or national resources supported by the NCI or NIH. The SPORE, however, may augment a pre-existing resource to enhance its capacity to serve SPORE research objectives. Cores can be proposed for supportive activities that clearly enhance the specialized research of the SPORE and must serve at least one full project. For each proposed Core provide the following information:

(a) A title page with the Core Number, Title, and Director(s) on a plain piece of paper.

(b) An abstract of the Core, using form page 2 of the PHS 398 application (Rev. 09/2004). The abstract should describe the nature and purpose of the resource.

(c) Budget Pages
Use same format as in item 10, above, for research projects. A budgetary request must be made to justify the existence of a SPORE Core.

(d) Core Description

(d.1) Describe the nature and activities of the core and its importance to the specialized research of the SPORE. Discuss in detail how the core will augment any pre-existing activities of related resources available at the institution or cancer center. Specifically, list related resources/cores and briefly describe their activities, staffing, and pre-existing level of support provided to investigators. If the resources charge for their services, provide a list of the charges.

(d.2) For a *competing renewal application*, describe how the core has performed in the past in relationship to accomplishing SPORE related services or goals. Detailed progress should be provided on activities performed during the past 12 months.

(d.3) Describe the facilities and space available and the qualifications of the professional expertise assigned to operate the core.

(d.4) Discuss past (for competitive renewal applications) and projected use of the core by individual research projects within the SPORE and any SPORE collaborators within or outside of the parent institution.

(d.5) Describe the projected operation, placing special emphasis on cost effectiveness and/or quality control factors.

(e) Human Subjects and Vertebrate Animals
If applicable, address human subject and vertebrate animal issues as outlined above for the research projects and detailed within the PHS 398 instructions (Rev. 09/2004; Parts I and II).

(f) The required *Specimen Core* description should include details on how the core will

collect, storage, and distribute specimens, as well as provide anticipated numbers for the different types of specimens processed and outline the quality control measures that will be implemented. A description of the data management system should also be provided and the level of detail with which specimens are annotated with preanalytical parameters and clinical data should be specified. For *competing renewal applications*, inclusion of a comprehensive table listing tissues/specimens accrued to date is encouraged. The distribution and utilization of these specimens by inside/outside investigators during the previous funding period should also be discussed.

(g) If an *Administrative Core* is proposed, requests to support the travel of 10 SPORE investigators (including the principal investigator) to the SPORE Workshop and other Inter-SPORE meetings during the year can be made within this core. Travel requests for support to attend additional Inter-SPORE meetings should be limited to $\leq$$5,000 direct costs per year. In addition, the principal investigator can request discretionary funds of up to $50,000 direct costs per year. The institution(s) is encouraged to match requests for discretionary funds. A detailed plan for the proposed and/or previous use of discretionary funds should also be included within the Administrative Core.

(h) If a *Clinical Core* existed on the previous submission, a list of the trials/interventions performed within the SPORE during this past funding period must be provided in a continuing core description. Inclusion Enrollment Report Tables should also be provided for clinical research activities performed by the core during the past 12 months.

12. Developmental Research Program

This program should primarily be used to promote the exploration of innovative ideas through the funding of pilot projects proposed by independent investigators. This program does not support projects proposed by postdoctoral/clinical fellows or graduate students and should not be used, in general, to extend the activities of a full project. DRP funds can, however, also be used to initiate a new shared resource, establish short-term collaborations, and/or contract services required by the SPORE. This required component of the SPORE must be maintained for the duration of the grant period. This section of the application should include:

(a) A Title Page with "Developmental Research Program" on a plain piece of paper.

(b) Budget Pages

Use same format as for research projects in item 10, above. A minimum commitment

of $50,000 direct costs must be proposed from SPORE funds for the support of pilot projects (does not include any charges for administrative oversight). Institutions are encouraged to match this request. See Section I.E.6. for further guidance.

(c) A Program Summary containing the following elements:

(c.1) A description of the process used by the SPORE for identifying and selectively funding innovative, pilot studies within and outside of the SPORE institution.

(c.2) *For competing renewal applications*, a summary identifying the achievements of all projects (ongoing or completed) supported during the last project period, the investigators associated with each project, and the publications and grant submissions resulting from the research. For all previously supported projects, specifically discuss whether they were promoted to a full project in the SPORE, led to other grant applications (either by SPORE investigators or SPORE collaborators), or were terminated because of lack of success. For ongoing activities during the past 12 months, report on progress.

(c.3) Brief examples of projects (1-2 pages) that may be supported during the grant period.

(c.4.) A description of the process by which projects will be (or have been) promoted to full translational research projects within the SPORE.

13. Career Development Program

The Career Development Program (CDP) within a SPORE is used to prepare new investigators or established investigators for careers in translational cancer research. It is *not* a training program for graduate students, postdoctoral fellows, or clinical fellows. This section of the application should include:

(a) A title page using instructions in item 12, above.

(b) Budget Pages

Use same format as in item 10, above, for research projects. A minimum commitment of $50,000 direct costs must be proposed from SPORE funds for the support of career development candidates (does not include any charges for

administrative oversight). Institutions are encouraged to match this request. See Section I.E.6. for further guidance.

(c) A Program Summary containing the following elements:

(c.1) Describe the process for selecting candidates and how the program will place special emphasis on recruiting qualified women and minorities. A career development candidate should not already be designated as a full project co-leader on the SPORE. Full project co-leaders should already be considered translational scientists. It is acceptable, however, for career development candidates to be listed as co-investigators on full projects.

(c.2) Provide a short description of prospective mentors/consultants who have experience in translational research and who will interact directly with career development candidates. A list of mentors is not required for the DRP since these projects should be led by independent investigators.

(c.3) Describe any candidates that have already been selected for support under this program and the rationale for these selections. Provide biosketches using the PHS 398 (Rev. 09/2004) format, if available. Highlight candidates who are women or minorities.

(c.4) *For competing renewal applications*, list all of the individuals supported by this program during the past term of the grant. The present position and recent accomplishments of these individuals (e.g., funded grants, publications) should also be described that clearly demonstrate how the SPORE has contributed to their careers in translational research. If applicable, describe the process by which a career development project has been promoted or incorporated into the full translational research projects within the SPORE.

14. Checklist

Complete the checklist as required for a PHS 398 application (Rev. 09/2004).

15. Appendix Material

The application should be a complete document that includes all essential information necessary for its evaluation. Additional appropriate material (e.g., clinical protocols, consent forms,

publications) may be submitted as appendices. There is no page limitation on appendices. However, appendices should not be used to bypass page limitations in the application because only selected reviewers will receive copies of the appendices. Follow the guidance in the PHS 398 instructions (Rev. 09/2004; Part I, pages 35-36) regarding appendices, in particular noting what types of material may be included in an appendix. As stated previously, Appendix material should *not* be submitted with the application. This material will be requested at a later time by the SRA.

Section III. Instructions for Preparing a Non-Competing Continuation SPORE Grant Application

A. Introduction

These instructions are supplemental to those provided with the Form PHS 2590 (rev. 9/04), "Application for Continuation of a Grant," which is required each year in order to receive continuing support. In general, you should follow the "Information and Instructions for Using Form PHS 2590 to Apply for Continuation of a Grant Award"(**http://grants.nih.gov/grants/funding/2590/2590.htm**). Please note that *non-competing SPORE applications are not eligible for the* ***streamlined non-competing award process (SNAP)***. In order to avoid a gap in funding, non-competing continuation applications should be received **60 days** prior to the anniversary date of the award.

Additional guidance important for the preparation of a SPORE non-competing continuation application (Type 5) is provided to you in this section.

*****IMPORTANT CHANGES TO THE PHS 2590*****

- The submission requirement has been changed – grantees need only submit a signed original and one signed copy to the centralized mailing address:

  Division of Extramural Activities Support, OER
  National Institutes of Health
  6705 Rockledge Drive, Room 2207, MSC 7987
  Bethesda, MD 20892-7987 (for regular or US Postal Service Express mail)
  Bethesda, MD 20817 (for other courier/express mail delivery only)
  Phone Number: (301) 594-6584

- For additional information visit **http://grants.nih.gov/grants/funding/2590/2590.htm**. and **http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-007.html**

- Throughout the instruction, the **refined definition of Key Personnel** has been incorporated: Individuals who contribute no measurable effort on the project/core should be designated as a "Significant Contributor".
- On the Key Personnel Report, the request for a Social Security Number is now limited to the last four digits.

B. Overall Organization of Progress Report

The NCI advocates flexibility and innovation in the use of SPORE funds to achieve translational research objectives and will administer these grants accordingly. Nevertheless it is important to highlight and explain changes in the component budgets that differ significantly from the approved peer-reviewed budget levels of the original competing application. Areas requiring explanation and justification are as follows:

- Any proposed increase or decrease in the level of effort of key personnel by >5% of total effort.
- Substitution, addition, or deletion of key personnel (e.g., Project Co-Leader, Core Director).
- Redistribution of dollars among budget components (NOTE: this is encouraged in a SPORE when it is done to place greater emphasis on more promising *translational* research activities).
- New research activities not included in the competing application and not peer reviewed (NOTE: this is encouraged, especially in the use of developmental funds, to pursue the feasibility of new hypotheses of potential importance to translational research).

The following organizational format is required for all non-competing continuation grants:

- Face page (see "eRA Commons" at **https://commons.era.nih.gov/commons/index.jsp**)
- Table of Contents
- Composite Budget
- Director's Overview
- Research Projects
- Cores
- Developmental Research Projects
- Career Development Projects
- Supplemental Research Projects

- Checklists
- Personnel Report

For forms and detailed instructions on the preparation of Budgets, Biographical Sketches, Progress Report Summaries, Checklists, and Personnel Report please see: http://grants.nih.gov/grants/funding/2590/2590.htm.

C. Director's Overview

The intent is to explain how the team of SPORE scientists at the basic and applied levels is pursuing research objectives using integrated, innovative, and flexible strategies thereby maximizing the unique capabilities of the SPORE to achieve translational research objectives.

1. **Scientific Achievement of the SPORE Program**
   Describe the single most significant translational research achievement in the last year of support. Indicate the project, the achievement, and its potential impact on human cancer in one or two paragraphs.

2. **Integration within the SPORE**
   The levels at which applied researchers (e.g., clinical researchers, epidemiologists) interact with basic investigators in the design and implementation of research that is most likely to have an impact on human cancer (i.e. reducing mortality, improving quality of life).

3. **Translational Research Objectives**
   Discuss the specific research activities that appear the most, or least, promising in achieving translational research objectives. Also report on any new ideas, technical breakthroughs, etc. that have occurred to advance a translational goal.

4. **Advisory Committee Activities**
   Discuss how recommendations of the External Advisory Committee, Internal Advisory Committee, and SPORE leadership have impacted upon the modification, discontinuation, or initiation of any projects or cores.

5. **Collaborations**

   Important collaborative efforts including formal Inter-SPORE activities established within and outside the SPORE institution. Please indicate if these activities use developmental or supplemental funds and address interactions with other NCI or NIH networks.

   (a) Outreach Activities - Special efforts to recognize **unique research opportunities** of the SPORE and/or to enhance the research capability of the SPORE through interactions with outside individuals, organizations, and institutions (local, national or international).

6. **Emerging and Derivative Projects**

   Discuss research opportunities or studies that have emerged from SPORE scientists, the SPORE environment and/or SPORE collaborative efforts resulting in the submission of grant applications (e.g., R01s) and/or attracting additional support from other sources (e.g. foundations, industry) which are likely to advance fundamental studies in this cancer site. Please list in tabular form grant applications that have been submitted, where and when submitted, and whether pending, funded or not funded.

7. **Intellectual Property Management and Industrial Relations**

   Discuss any opportunities or problems that arose in moving a discovery forward for commercialization during the past year. Report on any patent or licensing activities related to the translational research supported by the SPORE.

D. Research Projects

This section includes materials pertaining to each individual (full) project on the SPORE, including a title page, proposed budget for the upcoming year, budget justification, any biosketches on new personnel, other support and a progress report for the past year. The Progress Report Summary Form Page 5 from the PHS 2590 application and instructions (pages 10-14) should be followed. The "*Studies and Results*" and "*Plans*" sections of the progress report should be relevant to accomplishments of the past year and not the same at those reported in previous years. Please use the following format when reporting on each full project on the SPORE:

1. Title page
2. Detailed Budget
3. Budget Justification (add Biosketches for new personnel)
4. Other Support (for Key Personnel)
5. Progress Report Summary

(a) Specific Aims (no more that 500 words)

Briefly describe the specific aims of the project as originally funded and how basic/clinical interactions have been employed in the design, implementation, and interpretation of experiments. Provide a short rationale for any changes in specific aims that have occurred over the past year.

(b) Studies and Results (no more than 750 words)

For the past year, describe important positive and/or negative results associated with each specific aim. Describe any changes in approach that may have resulted from technical barriers or discoveries in the field. For those projects that involve clinical research, briefly describe the status of each study. NIH defines clinical research as *"Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies."*

Provide information on clinical studies and/or vertebrate animals in sections (e) and (f) listed below.

(c) Significance

Explain in lay terms the importance and intent of the research in terms of translational research objectives that may impact on the disease in a reasonable time span.

(d) Plans

Summarize plans for the next year to pursue existing specific aims and/or new

or modified aims that may have a greater impact on the translational research objectives of the SPORE.

(e) Human Subjects
(http://grants1.nih.gov/grants/funding/phs398/HumanSubjects.pdf)

i. For all projects involving human subjects or tissue resources please include status of patient/specimen accrual and recruitment of gender and minorities where applicable. *A clinical protocol, consent forms, DSM plan and IRB approval must be on file with the NCI prior to the initiation of any new clinical trial.* **Please submit the clinical trials protocol(s) to the SPORE website via a portal at http://sporesprotocols.nci.nih.gov/spores.**

ii. An updated Gender and Minority Inclusion Enrollment Report Table is required each year for each individual project. This table is provided at: http://grants.nih.gov/grants/funding/2590/enrollmentreport.pdf. Final assessment of closed or completed studies and pertinent publications and reports should also be included. The format of these forms should not be **altered** or **modified**. Review all enrollment information so that the totals in different sections are internally consistent and accurate. All updates or changes to clinical trial protocols, consent forms and DSM plans should also be attached.

(f) Vertebrate Animal Studies

If there has been no change, check "No Change" on the Progress Report page.

If vertebrate animals were not involved in the last application but are now to be included, or if significant changes regarding the use of animals are now proposed, provide a description of the intended involvement of animals in accord with the PHS policy for use of vertebrate animals in research and check "Change" on the Progress Report page. Examples of significant changes might include substituting one animal model for another or changing from noninvasive to invasive procedures. If studies

involving Vertebrate Animals are planned, and they were not part of the originally proposed research design, then you must comply with the requirements of Section F. "Vertebrate Animals" described in the PHS 398 instructions (Rev. 09/2004) and provide the required information to NIH.

(g) Publications

Provide **one copy** of each publication not previously submitted. List the complete citation (author(s), title, journal or book, volume, page number, year) of all publications not previously reported. This includes manuscripts submitted or accepted for publication. **Report only those publications resulting directly from this grant.** State if there have been **no** publications.

(h) Project-Generated Resources

Please list resources developed from this project such as patents, data, research materials (e.g., cell lines, microarrays, DNA probes, animal models), protocols, software, or other unique information available to be shared with other investigators. Describe the resource(s) and how it may be accessed. Provide updates to and any explanations for changes made to the original Data and Resources Sharing Plan for the project.

E. Cores

1. Core Director(s) should describe progress in establishing and maintaining the high-quality operation of each core outlined in the original competitive application.
2. Discuss any structural, organizational, logistical, or administrative changes; or problems that have developed in the operation of the core.
3. Discuss the usage of the core by SPORE investigators and outside investigators.
4. Describe how the core supports individual research projects, developmental projects, and career developmental projects – provide details on usage.

F. Developmental Research Program

The director(s) of the Developmental Research Program should first give an overview describing the overall process of selection of meritorious projects during the past year. Give the breakdown of funds (SPORE and institutional matching funds) devoted to each project. The information requested below should be provided for projects supported by

SPORE funds, as well as those supported by matching funds committed to the SPORE by the institution(s).

1. Give a brief description of new projects, including a title, project leader(s), and specific aims. Include Gender and Minority Enrollment Report Tables and/or clinical protocols, consent forms, and DSM plans on relevant projects as discussed under III.D.5.(e)i. above.
2. Use the PHS 2590 report summary form for reporting progress on (1) ongoing projects and (2) completed/finished projects. Summaries on developmental projects do not need to be as explicit or in-depth as those required for full research projects. Provide appropriate information on clinical interventions, including completed Gender and Minority Inclusion Enrollment Report Tables
3. Discuss developmental projects that have been converted to full translational research projects in the past year; or that have resulted in research grant application (e.g. R01s).

G. Career Development Program

The director(s) of the Career Developmental Program should first give an overview describing the overall process for selection of meritorious candidates in the past year. Give the breakdown of funds (SPORE and institutional matching funds) supporting these candidates. The information requested below should be provided for candidates supported by SPORE funds, as well as those supported by matching funds committed to the SPORE by the institution(s).

1. Provide brief background information on each newly supported candidate. Describe how each individual is being prepared to pursue a career in translational research. Include a title, specific aims, and a brief description of their translational research project, along with an NIH biosketch.
2. Use the PHS 2590 report summary form for reporting progress on (1) ongoing career development projects and (2) completed/finished projects. Summaries on developmental projects do not need to be as explicit or in-depth as those required for full research projects. Provide appropriate information on clinical interventions, along with completed Gender and Minority Inclusion Enrollment Report Tables.
3. Highlight any changes or significant advancements in the careers of individuals who previously received support from this SPORE program in the past.

H. Supplemental Activities

A progress report is also required on all activities that were supported during the last year by administrative supplement funds provided through the SPORE program. Please list all supplements (e.g. Minority supplement, Early-Phase Clinical Intervention, Inter-SPORE, or AVON-NCI Progress for Patients) and utilize the "Progress Report Summary" form and instructions (pages 10-14) provided for a PHS2590 application.

1. For all projects involving human subjects or tissue resources please include status of patient/specimen accrual and recruitment of gender and minorities where applicable. *A clinical protocol, consent forms, DSM plan, and IRB approval must be on file with the NCI prior to the initiation of any new clinical trials. This documentation should be sent to your program director and grants management specialist at the NCI.* An updated Gender and Minority Inclusion Enrollment Report Table is required each year on each clinical trial or intervention. This table is provided at: http://grants1.nih.gov/grants/funding/2590/enrollmentreport.pdf.

2. A Progress Report Summary should also be provided on any supplemental study that were closed or completed during the previous year. Pertinent publications and/or summary reports should also be included.