Division of Extramural Activities

Report of the National Cancer Institute Cancer Centers Program Review Group

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Executive Summary

One person in three eventually will develop cancer. Due to the aging of the population and reductions in heart disease and other major causes of death, the proportion of Americans dying of cancer is increasing. Cancer threatens our society in numerous ways, from the pain and suffering it causes patients and their families to its economic costs. There are, however, important reasons for optimism in the battle against cancer. The treatments for cancer--surgery, radiation, chemotherapy, immunotherapy, and bone marrow transplantation--have each, and in combination, had major impacts on survival and new approaches to understanding the cancer cell have unlocked even greater potential for preventing, diagnosing, and treating the disease.

Despite these notable advances in understanding, however, cancer remains a formidable disease in the United States, requiring an aggressive and long-term commitment to research. Progress in prevention, diagnosis, and treatment has been possible only because of the existence of a strong cancer research infrastructure, which is the result of public investment. And because the best treatment results require the close, prospective collaboration of several specialists, progress has also depended on multidisciplinary research efforts in basic, clinical, and population-based research. The centerpiece for these efforts is the National Cancer Institute (NCI) supported cancer centers, which continue to be the principal sites where these integrated research activities take place.

A cancer center is a nationally visible and stabilizing organization. To become an NCI-designated cancer research center requires that the institution already has in place a substantial and broad portfolio of peer-reviewed cancer research support and a scientific staff recognized for its cancer research skills in a wide array of scientific areas. An NCI-designated cancer research center is more than a collection of good research grants. It is a setting in which shared resources, multidisciplinary staff, and common research goals synergistically affect cancer investigation and provides a means for drawing in and promoting vestigial cancer activities in an institution.

The Cancer Centers Program Review Group, convened to review the current status and future of the NCI cancer centers program, believes that the centers program

remains a central and significant component of the nation's cancer research investment. The stability and centralized support provided by the program allows an institution to conduct a wide array of investigations into the etiology and treatment of cancers. In a turbulent era when clinical research must adjust to the new realities of managed care, cancer center support is especially critical in ensuring that there is a place where cutting-edge cancer research can be conducted. And, at a time when advances in the science have enlarged our focus to include asymptomatic as well as symptomatic individuals, and genetic susceptibility and early detection can play a key role in risk reduction, clinical investigations will require an even broader array of researchers and access to greater numbers of research participants. The Program Review Group strongly believes that the NCI cancer research centers will play a leading role in meeting these diverse challenges.

To meet the challenges of the future, there must be flexibility in the system. Cancer centers must be able to expediently expand or contract research programs as the need arises and redirect resources to meet new challenges and opportunities. In addition, opportunities must exist for the creation of new types of cancer research centers, which might not be recognizable by today's standards, and phasing out of those centers which are no longer responsive to the demands of research. Finally, to improve the quality of all centers, the criteria by which they are reviewed must be re-evaluated and realigned. This will require a major overhaul of the guidelines, review criteria and review process currently in place. In a view toward the future, the Program Review Group also proposes an expanded role for cancer centers as regional and national resources.

The Program Review Group made several major recommendations regarding the designation, structure, function, review of cancer centers, as well as the distribution and use of cancer center funds. The following major recommendations are made in the spirit of enhancing and strengthening the ability of cancer centers to conduct research which will reduce the incidence and mortality of cancer. In general, they aim to reward research excellence, provide for stringent quality review, increase flexibility, enhance productivity, streamline administrative responsibilities, and improve communication among cancer centers and NCI.

- Centers should be primarily reviewed for the quality of science, and the value added by the center grant to the advancement of excellence in all appropriate areas of cancer research.
- Two, rather than three, types of cancer centers should be designated by NCI: comprehensive cancer research centers and cancer research centers. There should be no separate review of comprehensiveness, and the issue of comprehensiveness should not be separated from grant review.
- The review process and guidelines should be consistent with an increased flexibility in the percent of funds that can be applied to different categories.
- The excessive and rigid record keeping expected in the application for a center grant, in the letter of intent, and in the noncompeting renewals should be dramatically reduced.
- NCI program administration should be further separated from the review

process.

- Each peer review committee should be constituted with the best available people, among whom should be individuals who are knowledgeable in the nature of cancer centers and the center grant mechanism.
- To facilitate better relative review, all grants of a particular designation (comprehensive cancer research center or cancer research center) should be reviewed at a single meeting of the parent review committee each cycle.
- An alternative approach to funding competitive grant renewals of cancer centers should be considered: all centers, regardless of existing grant size, may apply to increase their level of funding by a capped amount ($500,000, for example); all cancer centers would have the potential to expand their research support and excellent smaller centers would potentially be able to grow more rapidly.
- Funding for the lowest ranked centers should be discontinued through a phasing out mechanism.
- Centers with outstanding priority scores should receive 100 percent of the recommended amounts, whereas centers with lesser priority scores should receive lesser percentages of the recommended amounts.
- If the planning grant mechanism used by prospective centers to prepare an application for a center grant is to be continued, despite the low rate of success, its use for that purpose should be formally reviewed and the standards for initial grant review should be raised.
- A robust informatics program should be developed by NCI to facilitate the exchange of information between NCI and cancer research centers, among NCI-designated cancer research centers, and between cancer research centers and the public.

The Program Review Group believes that if NCI considers and implements the recommendations outlined in this report, the overall structure and performance of the nation's cancer centers will be vastly improved, further facilitating progress toward reductions in the morbidity and mortality of cancer.

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BACKGROUND AND OPPORTUNITIES

One person in three eventually will develop cancer. Due to the aging of the population and reductions in heart disease and other major causes of death, the proportion of Americans dying of cancer is increasing. Americans are also increasingly diagnosed with cancer. In 1970 there were 625,000 new cases and 331,000 deaths; this rose to 1,359,000 new cases and 555,000 deaths in 1996. Cancer threatens our society in numerous ways, from the pain and suffering it causes patients and their families to its economic costs.

Cancer also challenges the scientist and the clinician in its complexity. It is not one but many diseases. At least 65 specific types of cancer can be identified, although we are moving toward discovering common features for many. The treatments for

cancer--surgery, radiation, chemotherapy, immunotherapy, and bone marrow transplantation--have each, and in combination, had major impacts on the outcome of cancer. New approaches to understanding the cancer cell have unlocked even greater potential for preventing, diagnosing, and treating the disease. Mortality from most cancers has been reduced, and for some these reductions are very large.

There are important reasons for this optimism in the battle against cancer. For example, through revelations in molecular biology we now have a better understanding of how cancer cells develop and proliferate, and what might be used to stop their growth. Recent discoveries have yielded a vast amount of information about the genetics of cancer, the actions of carcinogens, and the roles of tumor viruses, viral oncogenes, proto-oncogenes, and tumor suppressor genes in cancer causation. Scientists are now able for the first time to begin to understand the molecular events which actually cause cancer. During the past decade the identification and cloning of human disease genes has advanced our understanding of the genetic aspects of cancer susceptibility, with over a dozen genes currently identified, most notably for the highly prevalent breast and colorectal cancers. In addition, the development of molecular epidemiology is crucial to cancer prevention efforts, including definition of high-risk individuals and development of molecularly based screening techniques and interventions.

Despite these notable advances in understanding, however, cancer remains a formidable disease in the United States, requiring an aggressive and long-term commitment to research. Mortality from cancer continues to increase and there remain important differences in age-, racial-, and ethnic-specific incidence rates and mortality that add complexity. For example, cancer is more common in those age 65 and over than in younger age groups; cancers in children are generally more curable than cancers common in adults; and socio-economic deprivation has an adverse affect on cancer survival rates.

In recent years there has been a shift in the way scientists and physicians view cancer. Investigators now recognize that there are multiple strategies available to reduce the burden of cancer. Strategies include: primary prevention through reduction of risk factors such as smoking; chemoprevention; early detection (e.g., mammography, pap smears, sigmoidoscopy); treatment advances (i.e., testicular cancer, hematologic malignancies); and progress in pain control and symptom management. If society could only successfully address the growing problem of lung cancer--85 percent or more of which is due to tobacco use--overall cancer mortality would have decreased significantly in the past 25 years. Recent reductions in lung cancer among U.S. males and in hepatobiliary cancer in Asia-- particularly in the younger age groups--are evidence of the importance of preventing cancer. Another example is the reduction in breast cancer mortality for women of all ages, which results from earlier and better detection of early stage cancer and improvements in treatments such as adjuvant chemotherapy.

Progress in prevention, diagnosis, and treatment has been possible only because of

the existence of a strong cancer research infrastructure, which is the result of public investment. And because the best treatment results require the close, prospective collaboration of several specialists, progress has also depended on multidisciplinary research efforts in basic, translational, and clinical research. The centerpiece for these efforts is the National Cancer Institute (NCI) supported cancer centers, which continue to be the principal sites where these integrated research activities take place.

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History and Background of the NCI Cancer Centers

There is a long history of national commitment to a system of integrated, multidisciplinary cancer research aimed at rapid translation of research findings into coordinated care for cancer patients. In 1960 the National Institutes of Health established the General Clinical Research Center Grants Program to provide an opportunity for universities to establish clinical research facilities. The purpose of this program was to provide a resource to enhance the quality of clinical investigation in a medical institution apart from general hospital care. A year later, in 1961, NCI announced three new grant programs which were to have a direct bearing on broadening the base of cancer research activity in the United States: the Cancer Research Facilities Grant (CRFG); Program Project Grants (PO1s) for cancer research; and Cancer Clinical Research Center Grants (PO2s or CCRCG). The intent of these funding mechanisms was to provide support for broadly based, multidisciplinary cancer research efforts.

By 1963 there was a fairly well-defined cancer centers program of approximately $6 million at 12 institutions. The activities at these centers were diverse, including research in radiation therapy, medical oncology, and surgery, as well as basic science. Little effort was made to define or organize the cancer centers, except as a category within the NCI budget, until 1968 when the National Cancer Advisory Board provided guidelines and the concept of the planning, or exploratory grant. The Cancer Centers Program of the NCI was formally conceived and established as a result of the National Cancer Act of 1971. The initial model for a cancer center was drawn from several of the older, free standing institutions: Roswell Park, Memorial-Sloan Kettering, M.D. Anderson, and Fox Chase (Institute for Cancer Research). The 1971 Act gave a broad mandate to the centers that includes research, excellence in patient care, training and education, demonstration of technologies, and cancer control.

Congress envisioned a regional focus for the centers program and in 1968 the House Appropriations Committee recommended that geography be considered in the establishment of new cancer centers. This has continued to be an issue of congressional interest over the years.

Because there were already over 60 cancer centers supported by NCI, administrative efforts were required to reconcile existing programs with the intent of the new

legislation. In June of 1973 NCI published information and guidelines for the Cancer Center Support Grant (CCSG), approved in principle by the NCAB, and described two classes of cancer centers: comprehensive and specialized.

Through the CCSG, or "core" grant, a funding mechanism was provided that supported a cancer research program on an "institutional" basis rather than the traditional approach of funding a multiplicity of individual research and project grants. This was intended to force a review of an institution's cancer research program in totality; this integration and promotion of institutional cancer-related activities remains a principal criterion for success of an NCI-designated cancer center.

Since the early 1970s a significant number of cancer centers have formed, and a few have been phased out. Currently, NCI recognizes basic science, clinical and comprehensive cancer centers, the latter including basic, clinical, and cancer prevention research. Some of the centers located within major research universities are organized as a matrix: the cancer center has defined administrative arrangements, space, budget and shared resources, and a system of membership that draws widely from the institution those faculty with a primary interest in cancer research. Basic science centers are characterized by strong and focused cancer research and high scientific productivity. Basic science centers as well as clinical and comprehensive centers provide the fundamental information, or substrate, essential for translation research into clinical trials and practice.

In 1996 there are 55 research centers funded through the NCI Cancer Centers Program, each distinguishable from the other, but with a single purpose of discovery research in the prevention and cure of cancer. Currently funded at an annual amount of $147 million (plus $20 million for the Specialized Program of Research Excellence (SPORE)), the program represents approximately 6 percent of the total NCI budget.

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Goals and Objectives of the Cancer Centers Program

A cancer center is a nationally visible and stabilizing organization. To become an NCI-designated cancer center requires that the institution already has in place a substantial and broad portfolio of peer-reviewed cancer research support and a scientific staff recognized for its cancer research skills in a wide array of scientific areas. The CCSG is intended to facilitate excellence in cancer research and collaboration among scientific and clinical disciplines.

NCI recognizes cancer centers through competitive reviews of applications for a CCSG. The cancer centers supported by CCSGs share specific characteristics. These attributes, in turn, demonstrate the value added by the CCSG to the underlying cancer research capabilities of an institution. An NCI-designated cancer center is more than a collection of good research grants. It is a setting in which shared

resources, multidisciplinary staff, and common research goals synergistically affect cancer investigation and provides a means for drawing in and promoting vestigial cancer activities in an institution.

Cancer centers by definition have a specific cancer focus. This has proven particularly important in the effectiveness of research centers located in major research universities, where NCI support promotes interactions among investigators, often distributed widely throughout the institution, enhances a broadened training base for those entering careers in cancer research, and promotes an interdisciplinary approach to cancer investigation.

Institutions planning an application for a CCSG (or renewing an existing grant) must decide on the importance of their cancer programs and how best to support a cancer research center. This requires strong and effective leadership, space, and resources. Clinical cancer research approvable as part of a CCSG must utilize patient resources effectively through innovative research protocols.

In addition, cancer centers are important community and regional resources. Centers provide information and education about cancer to the public and its representatives and to community leaders. These research centers are valuable sites for attracting and training young investigators in an environment that demonstrates the interrelatedness of different approaches in cancer research and applications in practice.

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Opportunities

Cancer centers already have demonstrated that complex research strategies are feasible, and they are poised to undertake novel multidisciplinary approaches to important new research opportunities. Cancer centers as a group are premier sites for performing peer-reviewed research, as demonstrated by the more than $515 million (52 percent) of investigator-initiated grants (RO1s) and $168 million (63 percent) of program project grants (PO1s) NCI awards to institutions which hold NCI cancer center grants. Despite this history of success, cancer centers are facing a new set of challenges, some posed by the advancement of science, some by a changing health care environment, and some by the administrative structures which govern their operation.

Recent reviews of the program recommended several enhancements, while finding the centers generally in fine condition and meriting the public investment.[1,2] This review represents another opportunity to recommend further improvements. The Cancer Centers Program Review Group believes that the centers program remains a central and significant component of the nation's cancer research investment. The stability and centralized support provided by the CCSG allows an institution to conduct a wide array of investigations into the etiology and treatment of cancers. In a turbulent era when clinical research must adjust to the new realities of managed

care, cancer center support is especially critical in ensuring that there is a place where cutting-edge cancer research can be conducted. And, at a time when advances in the science have enlarged our focus to include asymptomatic as well as symptomatic individuals, and genetic susceptibility and early detection can play a key role in risk reduction, clinical investigations will require an even broader array of researchers and access to greater numbers of research participants. The Review Group strongly believes that the NCI cancer research centers will play a leading role in meeting these diverse challenges.

But to meet these challenges, there must be flexibility in the system. Cancer centers must be able to expediently expand or contract research programs as the need arises and redirect resources to meet new challenges and opportunities. In addition, opportunities must exist for the creation of new types of cancer research centers, which might not be recognizable by today's standards, and phasing out of those centers which are no longer responsive to the demands of research. Finally, to improve the quality of all centers, the criteria by which they are reviewed must be re-evaluated and realigned. This will require a major overhaul of the guidelines, review criteria and review process currently in place. In a view toward the future, the Review Group also proposes an expanded role for cancer centers as regional and national resources.

The Review Group believes that if the National Cancer Institute considers and implements the recommendations outlined in this report, the overall structure and performance of the nation's cancer centers program will be vastly improved, further facilitating progress toward reductions in the morbidity and mortality of cancer.

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COMPREHENSIVENESS AND THE STRUCTURE AND FUNCTION OF CANCER CENTERS

No two cancer centers conduct their research activities in an identical fashion. In fact, the strength of the cancer centers program has always relied on the diversity of cancer centers and their ability to capitalize on unique research strengths and scientific opportunities. Thus, cancer centers have developed in a number of different organizational settings: some are independent, freestanding institutional entities entirely dedicated to cancer research; many have been formed as clearly identifiable entities within academic institutions and promote interactive cancer research programs across departmental and/or college structures (e.g., matrix centers); and others, while having a clear centralized administrative and scientific leadership, involve multiple institutions to enhance overall research capability. The one constant feature of all NCI cancer centers is that they have strong, broad research bases, organized into cancer-focused collaborative research areas or programs, from which to generate new ideas and results that lead to advancements in the detection, diagnosis, treatment, and prevention of cancer.

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Essential Organizational and Administrative Characteristics of a Cancer Center

In addition to excellence in research, the Review Group believes that the general criteria for cancer centers are well defined in the present guidelines. The six essential characteristics of a cancer center, when broadly applied and interpreted, have served the country well in sustaining an effective and strong center program. NCI should continue to use these characteristics but should ensure their broad interpretation.

- The center must have a clearly identifiable overall scientific focus in cancer research. This generally includes basic science and often a broad range of clinical and population-based research as well.
- There must be a strong commitment of the parent institution to the cancer center, as demonstrated by an effective administrative structure and access to resources and space.
- The center must have appropriate and adequate organizational capabilities to conduct research and evaluate and plan center activities.
- The center must have appropriate and adequate facilities dedicated to the conduct of administrative, shared resources, and research activities.
- The qualifications of the cancer center director as a scientist and an administrator with clear leadership experience are critical.
- There should be research activity in a variety of disciplines and there should be a high degree of interdisciplinary coordination and collaboration.
- Emphasis should be placed, however, on the broad definitions of essential characteristics rather than the details currently outlined in the present Cancer Centers Guidelines.

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History of the NCI Cancer Center Designations

In June 1973, NCI published information and guidelines for the Cancer Center Support Grant (CCSG), which had been approved in principle by the National Cancer Advisory Board. At that time, two classes of centers were described: comprehensive and specialized. Comprehensive cancer centers were described as those conducting long-term, multidisciplinary cancer programs in biomedical research, clinical investigation, training, and demonstration, and community-oriented programs in detection, diagnosis, education, epidemiology, rehabilitation, and information exchange. Specialized cancer centers were described as those which have programs in one or more, but not all, of the above areas in which research efforts, specialized study, or a form of patient treatment has resulted in well-defined areas of emphasis. More detailed characteristics for the two types were developed in order to provide guidelines to meet the criteria described in section 408(a) of the National Cancer Act of 1971.

While all cancer centers have unique characteristics, for the purpose of administrative convenience the cancer centers program presently classifies traditional centers as either "basic," "clinical" or "comprehensive." Comprehensive cancer centers formally receive this special designation by NCI after competing successfully for a clinical CCSG because they meet all of the criteria for comprehensiveness, which includes the entire range of research functions from basic research to clinical research to prevention research, as well as community outreach and service activities. Clinical cancer centers conform to many but not all of the criteria for comprehensiveness and sponsor strong basic and clinical cancer research activities. Although basic cancer centers are devoted exclusively to strong, multidisciplinary basic research activities, many are actively involved in the translation process through their collaborative arrangements with other institutions, including comprehensive and clinical cancer centers and/or industry. Currently there are 26 comprehensive centers, 17 clinical centers, and 12 basic centers (including 1 cancer prevention and control center).

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Proposed New Cancer Center Designations

The Review Group recommends that there be two, rather than three center designations: *comprehensive cancer research centers* and *cancer research centers*. The existing terminology of basic and clinical cancer centers does not properly encompass the scope or role of these cancer centers. Clinical centers are not limited to clinical research and all have substantial basic science activities. Basic cancer centers are almost never limited to basic research alone. Thus, all NCI-designated cancer centers which do not fulfill the comprehensive requirements should be called cancer research centers, with no nominal distinctions among them. This also allows the addition of new types of centers without requiring confusing or constricting name changes.

Comprehensive Cancer Research Center

Since the passage of the National Cancer Act in 1971, Congress, the Administration, NCI, and its extramural advisors have found value in designating centers with broad and integrated cancer research activities as comprehensive cancer centers. The Review Group believes that this term should be slightly modified to comprehensive cancer *research* center. Adding "research" to the title reflects the intention of the Review Group that research remain the central emphasis of these centers. Evaluation should be based on peer review of a center's research program, as well as demonstrated coordinated research in each of the major areas considered to be essential for making substantial progress in preventing, diagnosing, and treating cancer (basic, clinical, and population-based research).

The research characteristics required for the comprehensive designation may change over time. Centers applying to renew their comprehensive designation must therefore be capable of responding in a timely manner to nationally recognized and

agreed upon research priorities in the fight against cancer.

In the 1980s the identification by NCI of a research mission in cancer prevention represents an object lesson on the value of changing or expanding the criteria for comprehensive cancer center designation. Before this action was taken, cancer prevention research was limited, and efforts to stimulate activities in these areas at the nation's major cancer research centers were largely unsuccessful, despite scientific evidence of the applicability of prevention research as an appropriate discipline, and a clear mandate from Congress to support more cancer prevention research.

Development of cancer prevention research required the development of an institutional infrastructure suitable for training scientists and providing stable positions for scientists interested in cancer prevention. Because comprehensive cancer research centers can have a major and immediate impact on the academic infrastructure, NCI's addition of a prevention requirement for the designation of comprehensiveness had a salutary impact on progress in these fields of research.

Cancer prevention efforts were also facilitated through the CCSG mechanism by allowing support for a senior leader's salary and providing developmental funds to be expended for cancer prevention pilot programs and faculty recruitment. In this example, requiring prevention activities as a criterion for comprehensiveness was a useful and acceptable approach because new funds were provided for those activities. If additional essential characteristics are to be added to the definition of an NCI-designated comprehensive cancer research center, with them should come the potential for relevant budgeting and funding of the key administrative components needed to support that activity.

Despite the fact that cancer centers have vitalized cancer prevention research, the existing criteria for cancer control activities need to be better defined. The essential criteria regarding community outreach inadequately address the need for population-based research, behavioral research, and a variety of other cancer control activities. In addition, the criteria for information dissemination need revision as they are too constrained around NCI's Cancer Information Service (CIS) systems. All comprehensive cancer research centers need to provide substantive activities in information dissemination, including aspects that reflect the uniqueness of the individual center as well as the population it serves, but the specific form it takes should be the center's prerogative.

The criteria for a comprehensive designation will depend upon demonstrated excellence in peer-review funded research across a broad range of basic science, clinical research, and population-based science. Population-based science includes not only the cancer prevention research activities described in the previous comprehensiveness designation but is expanded to include disciplines such as psychosocial, behavioral, outcomes, and cost-effectiveness research. A center can fulfill the population-based science criteria by developing substantial peer-reviewed

funded grant research in any one or more of these areas.

The Review Group recommends the following criteria for comprehensiveness:

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Basic Laboratory Research

There should be a reasonable breadth and depth of integrated personnel, laboratory facilities, and financial support dedicated to basic research. The primary portion of that support should be from sources that utilize NIH peer review or that employ review procedures that are equivalent to NIH peer review. The centers should use this base of support to promote multidisciplinary interactions between scientists engaged in basic cancer research and to stimulate collaborations among basic investigators, clinical investigators, and population-based science investigators.

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Clinical Research

A comprehensive cancer research center fosters a strong clinical research program(s) which derives significant research support from external sources that are peer-reviewed by the NIH standard. Clinical studies should involve relevant basic cancer center laboratories whenever applicable. A center should be a major source of innovative clinical studies that can later be exported--for example, to clinical cooperative groups or into general medical practice. The cancer research center should provide mechanisms for the transfer of technology involving the development of innovative clinical protocols, participation in the development of effective new drugs, and the timely dissemination of information on new basic and clinical advances in cancer medicine.

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Population-Based Research

A major program in one or more facets of population-based science is necessary for a center to be comprehensive. This is a broad area-- including research on cancer risk, prevention, early detection, quality of life, and outcomes--that is directed to reduction of cancer incidence and mortality and improvement in the experience of cancer patients. Such research efforts may involve epidemiologists, psychosocial or behavioral scientists, outcomes researchers, individuals with expertise in the design of intervention trials, or others, as appropriate. Regardless of the area of population-based science selected, comprehensive cancer research centers are required to have a peer-reviewed research base that meets the standard of a program under CCSG guidelines. It is important to emphasize that this criterion requires one or more funded *research* programs. Although community outreach and public education are laudable service activities which should be encouraged, they are insufficient to

fulfill the population-based research requirement for comprehensive designation.

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Interactions Between Basic, Clinical, and Population-based Research

> A comprehensive cancer research center should demonstrate interactions between basic, clinical, and population-based research. It should facilitate the rapid transfer of promising laboratory discoveries to innovative clinical applications involving patients and populations, including clinical treatment and prevention, as well as facilitate the movement of unique observations in patients and populations into relevant laboratory investigations. Further, once a unique opportunity is identified, a distinguishing feature of comprehensive cancer research centers is the ability to sustain productive interactions either as basic/clinical collaborative research within the center and/or as collaborative research between elements of the center and other organizations, such as research institutions or the biotechnology industry.

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Desirable, but Not Required, Activities of a Comprehensive Cancer Center

Many other activities of a properly functioning comprehensive cancer center will enhance the productivity, impact, and contribution of the center to the region and the nation. While these are desirable and important, they are not solely sufficient for the comprehensiveness designation. They include education and training of biomedical researchers and health care professionals, public information services, and community service and outreach.

It is the strong belief of the Review Group that many of these important service and community activities have evolved into NCI requirements for the comprehensive designation without the provision of sufficient financial support or quality review to guarantee their success. Any programs felt to be critical by NCI to the success of the cancer centers program should include a mechanism for funding such activities. All mandated activities should be funded. Stated another way, there should be no unfunded mandates by NCI.

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Cancer Research Centers

Previously the centers program recognized several different categories of cancer centers in addition to the comprehensive centers, including clinical cancer centers, basic science centers, and specialized cancer centers, such as cancer prevention centers. All of these designations were found by the Review Group to be flawed to some extent. Clinical cancer centers are a misnomer as they include both clinical and basic science activities. Basic science centers often involve some aspects of population-based research and conduct some translational research in collaboration with other institutions. As a result the Review Group felt that it was appropriate to

consider all of these entities as NCI-designated cancer research centers, with a more expanded interpretation of what constitutes this designation.

It is the view of the Review Group that the growth of other scientific disciplines, such as psychological, behavioral, outcomes, and cost-effectiveness research, is sufficient that they might now be a focus of a cancer research center.

In order for any cancer center to be so designated, however, it would have to demonstrate all of the essential organizational and administrative characteristics of a cancer center as well as an integrated and interactive research program of proven peer-reviewed excellence. The Review Group strongly believes that institutions where substantial clinical, basic, or population-based cancer research exist should engage these programs in cancer center activities. The failure to develop a broad-based and fully integrated research program at an institution where that potential exists should be considered a serious deficiency.

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Review of the Two Cancer Center Designations

Review of a comprehensive cancer research center is broader than review required for other cancer centers. This is necessarily so because of the greater breadth of research activities, shared research resources, and mechanisms by which the center responds to research priorities. The review of comprehensive cancer research centers must be an integrated process, but may require more site visit time than that of a typical cancer research center. It also requires inclusion of reviewers who are familiar with the meaning of the term comprehensiveness. As with the review of any center, value must be placed on excellence in discovery, the integrated cancer focus, and the research value added by the influence of the center. The focus of the review should be on substance rather than process. However, there should be only one review for comprehensive cancer research centers, and the issue of comprehensiveness should not be separated from CCSG review.

This can be accomplished by reviewing each of the three separate research aspects--basic science, clinical, and population-based research--separately, and by providing a descriptive priority rating for each along with an overall numerical score for the center. Centers with insufficient research excellence in population-based research would not be designated as comprehensive. It should be recognized that a center seeking the comprehensive designation and presenting insufficient strength in all research areas could potentially receive a significantly lower priority score, which might endanger approval even as an NCI-designated cancer research center, or result in a significantly lower level of funding. In addition, the Review Group believes that the review process would be strengthened, as would the National Cancer Program, by reviewing all centers of similar designation in one cycle, i.e., all comprehensive centers or all cancer research centers.

In comparison, review criteria for the cancer research centers would include many of

the same requirements outlined for comprehensive cancer research centers but would focus on the particular areas of research excellence unique to that center. Central to this review would be evidence of excellence in discovery, an integrated cancer focus, and the value added to institutional cancer research resulting from the cancer center. As with the comprehensive cancer centers, the focus of the review should be on substance rather than process.

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Recommendations

- **Two types of cancer centers should be designated by NCI: comprehensive cancer research centers and cancer research centers.** The existing terminology of basic and clinical cancer centers does not properly encompass the scope or role of these cancer centers. Clinical centers are not limited to clinical research and all have substantial basic science activities. Basic cancer centers are almost never limited to basic research alone. Thus, all NCI-designated cancer centers which do not fulfill the comprehensive requirements should be called cancer research centers, with no nominal distinctions among them.
- **These designations should include the word "research" to more accurately describe the activities supported by NCI.**
- **Centers with significant and meritorious clinical and population-based programs are expected to engage these activities within the center.** The failure to develop a broad-based and fully integrated research program at an institution where that potential exists should be considered a serious deficiency.
- **Despite the fact that cancer centers have vitalized cancer prevention research, the existing criteria for cancer control activities need to be better defined.** The essential criteria regarding community outreach inadequately address the need for population-based research, behavioral research, and a variety of other cancer control activities.
- **There should be no separate review of comprehensiveness, and the issue of comprehensiveness should not be separated from CCSG review.** A center that fulfills the criteria of excellence in and integration of basic, clinical, and population-based research shall automatically receive the comprehensive designation.
- **There should be no unfunded mandates.** NCI should provide a mechanism for funding any activities felt to be critical to the success of the cancer centers program.

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GUIDELINES, REVIEW CRITERIA, AND THE REVIEW PROCESS

The purpose of the Cancer Center Support Grant (CCSG) is to promote excellent and effective research toward the goal of reducing cancer incidence, morbidity, and mortality. As a funding mechanism, the CCSG provides a focus and stimulus within an environment for cancer research and should be evaluated on the basis of its

impact on fulfilling this objective. An important attribute of a CCSG grant is support for the research infrastructure, such as program leaders, administration, core facilities, and new initiatives. Some of the common characteristics of such centers include multidisciplinary research and interaction of clinical and basic research. Whenever feasible the CCSG should encourage the development of strong research programs in population-based science, such as cancer prevention, as well as interactions with basic and clinical research.

The challenge of demonstrating to reviewers the value of a CCSG in aiding discovery should be given to the center directors. Although a CCSG directly supports only a small portion of the research conducted in a cancer research center, reviews should focus on the difference that the grant has made in cooperative interactions and new initiatives within the center. Because the primary uses of the CCSG are related to sustaining or developing infrastructure for cancer research, review efforts should concentrate on the extent to which the infrastructure improved the research efforts of the center.

Because cancer research centers conduct numerous and varied activities in cancer research, it is particularly challenging to devise a review strategy which encourages flexibility yet retains accountability, and fosters diversity without breeding inequities. It is the view of the Review Group that NCI has responded to this challenge by creating a burdensome and costly review process which often overlooks the value of the science being produced. There is too much focus on the administrative aspects of the CCSG, filling out forms, keeping extensive and unnecessary records, and complying with redundant and oppressive paperwork requirements. This emphasis is not only unnecessary, it consumes valuable time and human resources.

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Reward Excellence

As much as possible, the relative level of funds granted to a cancer center should reflect the relative importance and excellence of the research being conducted at that facility. Importance and excellence are evaluated by peer review and considered within the context of the programmatic needs of the nation's cancer research efforts. It is recognized that the total center budget is finite and that not all centers can be funded. Thus, in distribution of total funds to each center, it is crucial that the effectiveness of the center in fulfilling the purposes of cancer research be the driving factor in making awards.

Currently the review process is unduly focused on evaluation of the details of the infrastructure supported by the CCSG. Thus, an inordinate amount of time is spent by reviewers analyzing budgets and core facilities, the percent efforts of program leaders in the core facilities, and whether the facilities are used for purposes beyond those of the center. The focus on evaluation of process has fossilized the centers program to the extent that center directors are unnecessarily more concerned about record keeping in core facilities than actually accomplishing innovative cancer

research. Review should focus on the quality of research underway in the center. Such a shift in focus will result in a more productive cancer centers program with a greater impact on cancer research. It is important to remember, however, that although great science is absolutely necessary to receive support under the centers program, it is not sufficient. Reviews should focus on the value added by receipt of the CCSG.

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Flexibility in Use of Cancer Grants

The Review Group believes that more flexibility in the use of center grant support would allow the center director to rebudget between categories in response to research needs (see Section IV). Arbitrary caps on use of funds for senior leadership, program leaders, and staff investigators salaries should be removed. There should be more flexibility in the use of funds for developmental purposes, particularly for the recruitment of new investigators, implementation of new shared resources, and fostering of new research initiatives. The Review Group recommends that new guidelines allow the center director to redirect funds from other categories to the developmental and shared resources categories so that each may increase by up to 25 percent, without the approval of NCI, as long as the funds are not moved into areas which were rated less than outstanding or excellent during the review process. Of course, the center director may rebudget other funds with the approval of NCI. Justification for such reallocations should be documented and reviewed at the time of renewal. Although this flexibility would appear to complicate the review process, it should be the responsibility of the center director to justify these decisions in terms of the center's performance in achieving its research objectives. The wisdom of peer review will determine whether the decisions were in the best interest of cancer research.

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Revision of the Guidelines for Cancer Resarch Center Support

The guidelines for a cancer center grant have evolved in the bureaucracy from general principles to a detailed recipe. This has stifled creativity and innovation. The guidelines should be revised to allow more flexibility in both the conceptual basis and operation of centers. The overriding principle of review should be the determination of the extent to which the CCSG has had a synergistic effect on the research program of the center and added value to the overall achievements of its scientific programs. (A draft of the Review Group's template for revised guidelines shall be provided to the Director of NCI.)

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Paperwork Reduction

The inordinate paperwork required by the current administrative structure is hindering the creativity and effectiveness of the centers. For example, many centers are forced to hire individuals to keep extensive records of uses of core facilities in order to provide reviewers with the required details as to how the shared facilities

are being used. The administrative record keeping is excessive, expensive, and should be dramatically reduced. Requirements for supporting documentation should be re-examined and eliminated. For example, for core facility usage, number of users broken down by percent of cancer center members and percent with peer-reviewed grants is informative and relatively easy to provide. Linkage to specific grants is unnecessary. The cost of accounting for each item used from a core facility is frequently excessive.

Whenever possible the cost of record keeping should be considered relative to the value of the information collected. Use of facilities should be evaluated on the basis of how it serves the research program of the center. If review is conducted on this basis, it is likely to result in improved use of the facilities.

Another example of the excessive paperwork required in the review of a center is the current use of the "letter of intent." This document can be greater than 50 pages in length, in essence a "shadow grant." The current practice of requesting a "shadow grant" with budgets should be discontinued. In the future the letter of intent for a competitive renewal should be one or two pages in length.

A center grant is not a contract. The director of the center has the responsibility to lead and supervise the grant over the years between reviews. In general, the responsibility for constructing the organizational format of a center should be left with the center director, not with NCI administration. At the moment, the amount of detail expected in a noncompetitive application is excessive. Thus, the amount of narrative detail required in a noncompeting renewal should be reasonable. For example, the director should outline any major changes in direction, loss or gain of significant personnel, or important advances. However, it is not necessary to repeat the information available in the overall, initial grant. Along these same lines, the administrative burden can be eased by encouraging a more concise narrative section of the grant proposal for a competitive review of a center. This limitation would encourage a focused presentation and make easier conceptual review of the application.

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Constitution of Review Panels

The refocusing of the review process on science as contrasted to process should make the work of the review panel more interesting and challenging. The panel will be required to make critical judgements as to the importance of the centers in promoting cancer research. Panels also will be required to evaluate the leadership and direction of the center as it confronts future challenges. These more abstract judgements cannot be codified and therefore require that the panel be constituted with people of broad vision with experience in leadership across multiple component programs. The challenge to meet the needs of high quality review should attract these individuals to participate.

Currently a poorly used resource for reviewers are cancer research center directors

and their senior faculty. NCI should encourage, not discourage, these individuals to participate as reviewers. Experienced, senior cancer center administrators could be useful in administrative aspects of the review process just as cancer center scientists could contribute to scientific review.

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Separation of Review and Program Administration

It has long been NIH-wide policy to separate grant review from program administration. Consistent with this broad policy the peer review of centers should be a distinct process from the administrative aspects of NCI's cancer centers program. The NCI cancer centers program staff originally facilitated the process and performed a liaison role for the cancer research centers within the various branches and divisions of NCI and NIH. Recently, however, the relationship between program staff and the cancer research centers has become more rigid and controlling, and has created a perception of impeding the process through detailed task management rather than streamlining. The Review Group firmly believes that it is necessary to re-establish a healthy dialog between NCI staff and centers. One way this may be accomplished is to re-establish the primacy of the function of NCI program staff to help each cancer research center become successful by assisting them strategically rather than micro-managing their processes.

Program staff should not interact with the review process other than to provide the guidelines for the center's grant. The NCI review process should direct the site visit and inform the panelists of their charge for the review. The process should be as objective and fundamental as possible. In the current guidelines for review, the seven pages of instructions to reviewers concerning the programmatic aspects of the CCSG mechanism is extreme and should be modified. The focus of review should be on scientific excellence, the extent of scientific interaction occurring, the research value added by the CCSG, and the strength and vigor of the leadership.

The site visit and peer review evaluation should be a critical component in judging centers for funding. In addition, the programmatic needs as articulated by NCI leaders also should be considered. However, separation of these two forces in shaping the future of the centers grants is important. Only if independently valid can these two inputs be trusted in directing the NCI centers program.

It also would be helpful for NCI to facilitate, not mandate, information exchange and collaboration among the various clinical programs run through NCI. Currently, cancer centers implement their own trials, be they pharmaceutical, NCI-endorsed, with cooperative groups, or prevention. There is little coordination or interaction among the divisions within NCI responsible for trials, which causes additional complexity for cancer research centers. Collaboration among NCI divisions and cancer research centers should be made easier through information technology and coordination by NCI.

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Recommendations

- **Centers should be primarily reviewed for the quality of science, and the value added by the CCSG to the advancement of excellence in all appropriate areas of cancer research.** To receive a center grant the organization must fulfill the six essential characteristics of a cancer center. The review process should consider if this is the case. One of these characteristics is a focus on cancer. If the center is part of an institution or university which has clinical activities in cancer, this focus is interpreted to depend on inclusion of both clinical and other research activities. Although a large part of a center grant supports infrastructure, these facilities are not the primary basis of review. Rather, the cancer research which they facilitate should be the primary basis for evaluation.
- **The review process and guidelines should be consistent with an increased flexibility in the percent of funds that can be applied to different categories.** Evaluation should focus on how the director used this flexibility to promote cancer research. Among other things the review process should judge whether a director has wisely and responsibly used the ability to rebudget 25 percent of any category to support new, innovative, and important cancer research.
- **The excessive and rigid record keeping expected in the application for a CCSG, in the letter of intent, and in the noncompeting renewals should be dramatically reduced.** A new and less confining set of guidelines should be developed and the review process should be more focused on novel concepts, opportunities, and proven accomplishments, and less on detailed records of facility use and budgets. In general, one of the consequences of revision of the guidelines should be a reduction in the paperwork necessary for a CCSG.
- **The NCI program administration should be further separated from the review process.** Program staff should be advocates and guides for cancer centers. An established set of guidelines should be the basis of the review process and the site visit should be directed by the NCI Division of Extramural Activities. Cancer center program administration should support site visit teams and serve as a resource but should not prepare the reviewers with specific questions about the nature of the CCSG application. At all times program staff should avoid comments to reviewers which could be construed as prejudicial.
- **Each peer review committee should be constituted with the best available people, among whom should be individuals who are knowledgeable in the nature of cancer centers and the CCSG mechanism.** A greater emphasis in the evaluation of CCSG on potential future and past contributions to cancer research will increase the demands on the review committee. Thus the site visit group will have to be staffed with individuals of mature judgement and wisdom in regard to the CCSG program and its objectives.
- **To reduce administrative burdens, there should be no separate review of comprehensiveness.**

- **To facilitate better relative review, all grants of a particular designation (comprehensive cancer research center or cancer research center) should be reviewed at a single meeting of the parent review committee each cycle.** There are on average 5 to 6 comprehensive and 5 to 6 other types of CCSGs funded in any one year. Even though these are small numbers, the review process can better judge their relative merit if each subgroup is evaluated at a single meeting.

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DISTRIBUTION AND USE OF CANCER CENTER FUNDS

The public and Congress have demonstrated a desire to fund cancer research. Currently the total cancer centers budget is $147 million (plus $20 million for the SPORE program), or approximately 6 percent of the $2.25 billion NCI budget. Cancer research centers are increasingly visible mechanisms through which to provide public support; they serve as foci for funding all types of cancer research from fundamental to applied. In addition, centers are successful in leveraging federal dollars through independent fundraising efforts with private giving, corporate liaisons, and state funding.

The Cancer Center Support Grants (CCSG), which average $2.4 million and range in size from $650,000 to $6.5 million, is the single most important source of funding for cancer research centers not because of the amount--which is greatly exceeded by other funding sources--but because of the central contribution it makes to the national infrastructure for cancer research. The CCSG nurtures an interdisciplinary environment with a focus on cancer research, lends institutional and public credibility to the center's efforts, facilitates success in raising funds from other sources, and provides flexibility, which fosters initiatives and new developments in cancer research.

The ability to support such initiatives at early stages represents one of the most valuable aspects of the CCSG. The resources provided by this support mechanism allow center directors to recognize, foster, and support novel research directions, collaborations, and interdisciplinary and translational efforts. At their early stages, such initiatives are often not eligible for competitive funding.

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Access to the Cancer Research Centers Program and Levels of Funding

The cancer centers program budget is likely to require some expansion judging from the interest of a number of high quality institutions, some of which have exploratory, or planning, grants. If it is in the best interest of the national cancer effort to fund more centers, it may be necessary to:

- redefine types of centers so that diverse institutions are encouraged to enter the program;
- continue to fund the best centers (although durable funding is essential for

centers, it should not be an entitlement);
- fund only the highest rated components of a center's research program; and/or
- relate the level of CCSG support to the quantity and quality of the research supported by that grant.

The current size of CCSG budgets varies by an order of magnitude and according to designation. Under the existing designation system, on average, comprehensive centers receive larger awards than do clinical or specialized centers. Without some method which results in the redistribution of funds, calculations show that a flat cancer centers budget (allowing for inflation, cost-of-living increases, and increases in existing CCSG renewals) will result in a reduction in the number of cancer research centers.

Therefore new mechanisms must be found that ensure that: 1) excellent centers continue to be funded at appropriate levels; 2) meritorious new centers can be funded; and 3) less competitive centers receive reduced support or are phased out in a sensible fashion. Additionally, attention must be paid to the equitable distribution of funds among centers based on scientific merit and productivity rather than history. While these goals are simple in principle, they are not easily implemented. At present, funding for centers is only rarely discontinued.

The current practice of awarding CCSG renewal applications--intended to result in a more equitable distribution of funds--imposes a cap of 50 percent increase over the existing CCSG. It is the perception of the Review Group that this system has resulted in an award structure which is based on the status quo rather than excellence in scientific programming. Theoretically, centers with large core grants can request (and may get) large increases in any category (up to 50 percent). In practice, this rarely occurs. This means that historical discrepancies in size, whether or not justified, are difficult to change. In addition, centers differ markedly in structure and research portfolio, with some emphasizing clinical research and others basic science. Because their funding needs are so varied, absolute dollar caps based on existing CCSG size do not appear to make sense. And, although ratios of CCSG funds to total NCI support is one useful metric on which to base funding decisions, it is imperfect. Many centers receive support for cancer research from sources other than NCI, which may be discounted in the review process. Furthermore, some institutions report NCI peer-reviewed research in their application which is loosely, if at all, related to its center program, resulting in a ratio system which does not apply to all centers equally.

It is the belief of the Review Group that centers whose budgets are proportionately low but which have excellent proposals for expansion of their research portfolio should be permitted to make their best case for increased funding. Distribution of funds should be based on quality and quantity of cancer-related research, with special emphasis on the research value added by the presence of the CCSG. The level of funding of the CCSG should relate proportionately to the overall grant

activity, extent of institutional subsidization of the center, and level of excellence at the center.

The Review Group proposes that an alternative approach to increased funding be considered. If all centers, regardless of existing CCSG size, were able to request an increase in their level of funding by $500,000 at competitive renewal, there would be greater equity in the distribution of funds. From a programmatic aspect it is unlikely that any center is going to achieve more than a $500,000 increase in any given grant cycle. This system would allow for proportionately large increases for small centers, but would not preclude the possibility of increases, which would be proportionately smaller, for large centers. New centers, however, should continue to have an initial cap of $850,000 over three years. All decisions should be reviewed by and be the formal responsibility of the cancer research centers parent review committee.

In order to make funds available for such increases, and in particular, to allow admittance of new centers to the program, it will be necessary to change the current practice of continued funding for virtually all centers. The Review Group proposes that funding for the lowest ranked centers in each cycle be discontinued through a phasing out mechanism. One possible approach would be three years of probationary funding at a level of 80 percent of the current amount in the first year, 60 percent in the second year, and 40 percent in the third year. During this period the center could reapply for increased funding. This probationary/phase out decision recognizes that part of the CCSG funds support infrastructure, the rapid loss of which would reduce the ability of many research programs to advance. This status is not intended to support weak or noncompetitive science. Rather, it should be used to support centers which have a number of excellent programs but have developed weaknesses in other important programs or in one or more of the six essential characteristics of a center. For example, these could include loss of leadership, decrease in institutional commitment, or an inappropriate use of center resources. An anticipated consequence of this probationary status is an increase in the number of current centers which will not be funded in the future and the opportunity to fund excellent new centers.

Implementation of this type of quality-based review should result in significant turnover (perhaps as high as 20 percent) in CCSGs that are funded over a five-year period and should refocus the emphasis of the entire centers program on research excellence.

Another mechanism for making available funds for new centers and augmentation of developing centers is through use of the so-called "sliding scale" approach. That is, centers with outstanding priority scores should receive 100 percent of the recommended amounts, whereas centers with lesser priority scores should receive lesser percentages of the recommended amounts. It will be important for the parent committee to review the entire portfolio of CCSG priority scores if this method is to

be applied.

The Review Group feels strongly that a merit-based funding mechanism should be implemented though there was no strong preference for which mechanism should be employed, i.e., phase-out of the lowest ranked grants each cycle, a sliding scale approach, a combination of the two, or another alternative. Phase-out and a sliding scale are listed in the recommendations provided at the end of this section.

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Use of Funds Within a CCSG

At present, the majority (57 percent) of a CCSG supports shared (or core) facilities. On average, developmental funds constitute 14 percent of a grant; administration receives 11 percent; senior leaders 7 percent; staff investigators 6 percent, and program directors 5 percent. Increased flexibility, support for staff investigators, and use of developmental funds are aspects of the CCSG that could be expanded if they are critical to the center director in fulfilling the mission of the cancer research center. In addition, there should be greater flexibility in the types of categories considered fundable. Program staff should not predefine what is fundable in absolute terms because the centers are agents of discovery, change, and innovation. It is the director's responsibility to demonstrate how a more flexible use of funds, if necessary for new categories, enhances discovery.

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Increased Flexibility

The Review Group believes that increased flexibility to move funds among categories in core grants will help to ensure the best use of funds. It recommends that funds may be moved from any category to developmental activities or shared resources, so those categories may increase by up to 25 percent, without prior NCI approval, as long as the funds are not being routed to areas which were rated less than outstanding or excellent during the initial review process. The center director, obviously, may rebudget other funds with the approval of NCI. Such flexibility should serve a clear research purpose, preferably innovative, rather than substitute for routine institution support. Increased flexibility calls for added accountability, evidence of discovery, a clear demonstration of value added-particularly interdisciplinary-and therefore poses an added challenge for review (see Section III).

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Staff Investigators

In recent years funding for the staff investigator category has been discouraged because in earlier years it consumed substantial dollars of the centers program, was said to be difficult to review for quality, and tended to be handled as an entitlement. The Review Group believes that the staff investigator category can be a useful one especially for short-term or startup support directed toward new research initiatives. The possibility of partial salary support of high quality investigators should continue to be available. The level of support should relate to individual peer-reviewed

research support; staff investigator salary support should not be used to replace lost grant funding, as short-term funding for this purpose is available through another CCSG category.

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Developmental Funds

Developmental funds are a vital aspect of CCSGs. Such funds make new initiatives possible and support new faculty. The Review Group recommends that up to 25 percent of a year-one CCSG budget may be devoted to the developmental category.

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Training

Cancer research centers are dynamic foci for training the next generation of cancer researchers. They are particularly well suited for capitalizing on interdisciplinary and translational approaches. In general, training should continue to be reviewed and funded by the specialized training mechanisms which have historically worked well. The director should be able to use developmental funds to provide short-term support for training in special situations justified by a new research initiative (e.g., physician-investigators, staff investigators, molecular epidemiologists). In no case should center funds be used as an escape valve to meet routine training needs. Use of funds for training purposes should be evaluated on the basis of research productivity.

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Renovation, Remodeling, and New Equipment

Over the history of the cancer centers program, budgetary allotments for remodeling, and major equipment purchases have been included. These are important objects of expenditure and should be allowable within guidelines that permit considerable flexibility. Reasons for allowing renovation, as well as equipment costs, include the changing environment for research, the types of cancer research conducted in the centers, the need to recognize the importance of the facilities in which this research is conducted, and the essential requirement that these facilities and equipment be up-to-date for the type of research practiced. In addition, it is not possible to depreciate equipment through indirect cost recovery that is purchased on federal grants, including the CCSG. Thus, equipment that is provided as part of the grant or other federal support, and must be replaced, cannot be done so with the usual depreciation recovery procedures. Allowances should be made in the core grants for replacement of major equipment purchased with federal funds on a reasonable schedule of useful life of such equipment. In general, a center grant can include a request for replacement of equipment, renovation, and remodeling in the grant request.

Construction is essential if centers are to be real entities. The leveraging of supplemental NCI funding for construction of research facilities is a particularly effective use of NCI funds because it facilitates obtaining the remaining dollars

needed for construction. Such funding should be continued and expanded. It should not compete with CCSG funding, but review of construction grants should be recoupled with CCSG review to insure excellence and congruence with the program.

Supplemental funding has been sporadically available for other purposes as well. The Review Group encourages the continuation of this mechanism because it provides the opportunity to pursue new research challenges between the usual five-year renewal cycle.

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SPORES

An example of an experiment to encourage cancer centers and other institutions to focus on research critical to the National Cancer Program is the Specialized Program of Research Excellence (SPORE), initiated by NCI in 1991. SPORE funds are investigator-initiated, competitively awarded grants focused on translational research involving specific cancer organ sites. This support is part of the cancer centers allocation within each annual NCI budget (currently $20 million) with current grants for breast, lung, prostate, and gastrointestinal cancer. The grants are intended to assemble a critical mass of laboratory, clinical, and population-based scientists in the study of selected solid tumor types. With very few exceptions, SPORES are awarded to cancer centers.

There are currently 12 SPORE grants, ranging from $1.6 million to $2.41 million, and averaging $2.1 million. SPORES respond to national priorities for cancer research, and a case can be made that a focussed approach to a given disease has merit. The Review Group believes that it is premature to review the value of the SPORE program, but recommends that the NCI Director in the future call for an independent review of the SPORE program for evidence of innovative contributions to translational research. In the meantime, there should be no mandate for a specific number of SPORES targeted to a particular disease, nor should there be a requirement to have SPORES for specific diseases. The basis for funding should be, as always, a requirement for meritorious discovery research. All support mechanisms, including SPORES, should encompass a large enough area of discovery so that there are enough competing proposals and they can be ranked effectively and competitively.

A major concern of the Review Group is that SPORES have the potential for redundant funding. One response to this concern may be a requirement for clearly innovative content in SPORES compared with existing research funded in a given institution, instead of a re-aggregation of existing and well-funded programs.

An alternative mechanism for SPORES may be large disease-targeted PO1s. In any case, SPORES provide a complementary approach to basic cancer research. Institutions without CCSGs as well as existing NCI cancer centers should be encouraged to apply for SPORES. Finally, the SPORES program is experimental. It should be reviewed for duplication, evidence of competitive funding, and quality

and innovation. The Review Group believes that there is merit to the SPORES mechanism but does not believe that SPORES should compete with CCSGs for the funding pool.

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The Planning Grant

Planning grants currently cost $250,000 each per year. That is, the 16 grants currently funded cost at least as much as one or two CCSGs. The number of planning grants which are converted to CCSGs is very low. In recent years, most of the new CCSG awards have gone to institutions which did not receive a planning grant. Although a planning grant may have merit for some institutions seeking to become a cancer center, it is not clear from any systematic evaluation that this is so.

The Review Group is concerned that, as currently configured, planning grants can unduly raise expectations of eligibility or the likelihood of receiving a CCSG. Therefore, the standards by which planning grant applications are reviewed and awarded must be changed. In order to receive a planning grant an institution must provide evidence that it has made efforts to measure up to the essential characteristics of a cancer center, i.e., it must demonstrate institutional commitment, authority of a director, and appropriate minimal funding. As a demonstration of its commitment and organization, it should be the applicant institution which is the source of planning funds, not NCI.

It is hoped that the recommendations of Group concerning NCI designations and the review process will encourage different kinds of cancer centers to apply and be funded. Current planning grants should be phased out and a low priority assigned to this use of funds. Should the program be continued, a more rigorous process for reviewing and awarding planning grants might change the dynamic of new entrants into the cancer center community.

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Recommendations

- **The Review Group proposes an alternative approach to funding competitive grant renewals of cancer centers: all centers, regardless of existing CCSG size, may apply to increase their level of funding by a capped amount ($500,000, for example) and all cancer centers would have the potential to expand their research support and excellent smaller centers would potentially be able to grow more rapidly.** For many Review Group members, CCSG funding as a ratio of peer-reviewed cancer research funding has great appeal for its symmetry, objectivity, and apparent fairness. However, after reviewing the considerable efforts of NCI staff to develop this approach, its fairness was sufficiently uncertain that the Review Group is reluctant to recommend it unless a fair and reasonably simple formula--not subject to inappropriate inclusions of cancer-related grants that are not an integral part of the cancer center--can be devised.
- **Funding for the lowest ranked centers should be discontinued through a**

phasing out mechanism. One such mechanism would be three years of probationary funding at a level of 80 percent in the first year, 60 percent in the second year, and 40 percent in the third year.

- **Centers with outstanding priority scores should receive 100 percent of the recommended amounts, whereas centers with lesser priority scores should receive lesser percentages of the recommended amounts.** This option currently is an alternative but is rarely, if ever, used.
- **To improve flexibility and innovation, funds may be moved from other categories into developmental activities or shared resources without prior NCI approval, so that each may increase by up to 25 percent, as long as the funds are not being routed to areas which were rated less than outstanding or excellent during the initial review process.**
- **The staff investigator category can be a useful one especially for retention of outstanding investigators or for interim or startup support directed towards new research initiatives.**
- **Up to 25 percent of a year-one CCSG budget may be devoted to the developmental category.**
- **The center should be able to use developmental funds for interim support for training in special situations justified by a new research initiative.** In no case should center funds be used as an escape valve to meet routine training needs.
- **Funds for the SPORE program should not compete with CCSG funds, but should appear as a separate line item in the NCI budget.**
- **If the planning grant mechanism used by prospective centers to prepare an application for a center grant is to be continued, despite the low rate of success, its use for that purpose should be formally reviewed and the standards for initial grant review should be raised.**

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CANCER CENTERS AS REGIONAL AND NATIONAL RESOURCES

By their nature, cancer centers serve as regional and national resources. They are agents of discovery and sources of information that should be shared with the scientific community and the public. In particular, centers with clinical or population-based research programs can advance public awareness of scientific advances, such as new prevention and early detection methods (e.g., genetic testing), or progress in cancer treatment. In addition centers can promote excellence in cancer care by promulgating guidelines, standards, and benchmarks based on scientific evidence.

The wide diversity of types of cancer centers and their regional environments has led to a variety of approaches to serving as regional and national resources. This diversity is an efficient means of doing what is appropriate and no attempt should be made to force every center to march in lockstep in exercising its regional and national reach. Furthermore, unfunded mandates of specific activities place an unacceptable burden on centers, forcing them to divert funds from other non-CCSG

sources.

With these caveats, there are opportunities for multiplying the reach and effectiveness of cancer centers regionally and nationally and of rationing resources and skills for the benefit of a wider population. Many efficient mechanisms already exist for the exchange of information among cancer scientists--such as national meetings, workshops, symposia, cooperative ventures, and multiple publications--but more can be done. The key to enhancing these efforts is the development of a robust, interactive informatics program. Such a network would facilitate information exchange between NCI and the cancer centers, among centers, and among centers and regional organizations.

A cancer centers web site, for example, could provide such diverse data as:

- open institutional clinical trials
- cancer care guidelines
- a library of cancer information for doctors and nurses in the region, as well as a listing of stored tissue, DNA, or special reagents for scientific investigations
- real-time collection of data from clinical trials, e.g., outcome analysis, population studies, and pharmaceutical information, such as the status of development of new chemotherapeutics and biologicals
- cancer center administrative information such as CCSG guidelines, schedules for review, deadlines, and a help desk at NCI
- a formal e-mail system with bookmarks for easy access to NCI center program staff, review staff, and CCSG members in all centers
- a telemedicine capability to facilitate rapid expert review of pathology and diagnostic images
- a visual teleconferencing capability not only for clinical consultation, but for scientific exchange, and to be used for some committee meetings to reduce the need for travel.

The opportunities for exchange are limited only by imagination and funding. Some ideas will die on the vine because they turn out to be of little use, but once an informatics infrastructure is in place, efficiency will effect the appropriate and useful changes.

It is apparent that the system must be able to operate at a variety of levels geared for the laboratory, clinical, and population scientist, practicing oncologists and support staff, and the public. The development and activation of such a system poses an enormous challenge, but the opportunities for further leveraging the strengths and resources of cancer centers for the public good are immense. The time is right, the technology is available, and the purpose is noble.

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Inter-center Communications

The ability to share the collective wisdom of cancer centers should be an important priority of the cancer centers program. The program should facilitate rather than mandate collaboration, possibly by providing supplemental funds to encourage specific, highly desirable collaborative studies. NCI should consider establishing a cancer centers forum on a web site, accessible only to those involved in the cancer centers program. Certain centralized information would be shared among centers. Some of this information could be linked with other web sites that distribute information and interact with the general research community, regional medical communities, patients, and the general public. The logical home for this web site is within NCI, although much of the information would come directly from the cancer centers.

A cancer centers forum could be designed to exchange ideas and share work in progress. A pool of common information resources could be created through the forum, categorized by research topic and disease type. The forum could also be used to identify centers which might participate in pilot or Phase 1 clinical trials. Some structure is necessary, but flexibility to expand in multiple directions is essential.

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Regional Responsibilities

There are many services that the cancer centers program has been expected to provide from its inception: basic, clinical, and population-based research; education and training of new medical professionals; and public education. These expectations have existed within Congress, the medical community, and the public. In the past, the comprehensiveness designation made these service functions a requirement, even though no supplemental funding supported these efforts. This has sometimes led to criticism of the entire cancer centers program.

While the Review Group recommends that these service functions be removed from the comprehensive requirements, it believes that all NCI-designated cancer research centers (not just comprehensive cancer research centers) should endeavor to meet the needs of their communities. It also believes that no cancer research center should be expected to develop these programs without commensurate funding available to develop and/or sustain services of excellence equivalent to their excellent research programs.

It is the Review Group's opinion that NCI's Cancer Information System provides a valuable service to consumers. Evaluation of this program is proceeding and should include input from cancer centers to ensure a coordinated effort which retains the strengths of the program and improves its ability to disseminate information.

However, current restrictions on information dissemination should be relaxed. While it was never the intent of the Cancer Information Systems to dictate the information a cancer center can provide, this does happen in certain areas. A cancer centers forum could establish a separate site that allows general information to be centralized and accessible to all cancer centers, not just those that currently house a

regional Cancer Information System node. Each cancer center could describe its unique program and the value it offers the community. NCI's International Cancer Information Center could facilitate the logistics and provide centralized information, and each cancer center could generate its program information.

This would provide another mechanism to help evaluate a center's effectiveness in "meeting the special needs of their community." Supplemental funding should be considered to allow cancer centers to widely disseminate pertinent information in additional formats (print, electronic media) to their regional communities.

Each cancer center is expected to provide resources and insights for populations in its geographical area which have not been adequately studied. While it is unlikely that a cancer center can accomplish this task on its own, centers are uniquely qualified to serve as a regional catalyst for this purpose. Cancer centers can initiate the dialog needed to define perceived needs, create a sharing of scientific expertise, and help reduce duplication and conflict within their communities. Discoveries made from community projects also could be distributed through the cancer centers forum.

Multiple cancer centers in the same metropolitan area face a unique challenge. Close geographic proximity among centers can create friction as they try to interact with the same communities and recruit patients to clinical trials. This may create confusion and can result in the delivery of mixed messages to the public. It also can breed competition where collaboration should be encouraged. Because of this unique situation, centers within a region should be encouraged to create synergy among themselves.

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Recommendations

- **A robust informatics program should be developed by NCI to facilitate the exchange of information between NCI and cancer centers, among NCI cancer centers, and between cancer centers and the public.** This would allow the exchange of such diverse information as tissue bank libraries, cancer care guidelines, up-to-date information on open clinical trials, and cancer center administrative information. One aspect of this program could be a cancer centers forum, established as a web site, for sharing of information among cancer centers.
- **Non-research service functions are important for all cancer research centers (not just comprehensive centers) and a separate funding mechanism outside the CCSG should be available for these services.**

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Conclusions

Despite notable progress in understanding and treating cancer, it remains a formidable group of diseases that require an aggressive, sustained commitment to

research. A central component of NCI's research efforts is the Cancer Centers Program, which supports a unique network of integrated, highly productive, and publicly visible cancer research efforts.

All programs of such scope and complexity eventually need renewal; the Cancer Centers Program is now ripe for such a process. The Review Group believes that, with implementation of the changes suggested in this report, centers can better respond to the broadening opportunities in biology, cancer care, and their practical applications. Further, the Review Group believes that the management efficiency of the program can be significantly improved; the review process should refocus on scientific excellence and the productive integration of disciplines; the process should tangibly reward excellence; and new center structures should be considered.

The Program Review Group believes that if NCI considers and implements the recommendations outlined in this report, the overall structure and performance of the nation's cancer centers will be vastly improved, further facilitating progress toward reductions in the morbidity and mortality of cancer.

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APPENDIX: PROGRAM REVIEW GROUP PROCESS

The Cancer Centers Program Review Group met seven times over a seven-month period. The meeting dates were:

- January 24, 1996
- February 21, 1996
- March 12, 1996
- April 24, 1996
- May 24, 1996
- June 27-29, 1996
- July 22, 1996

The Review Group requested and received detailed data on the history, budget, and operations of the Cancer Centers Program; heard testimony from a variety of NCI personnel and cancer center directors; and solicited and received comments in writing from the cancer centers community. Testimony was heard from the following individuals:

- Andrew Chiarodo
- John Glick
- Brian Kimes
- Richard Klausner
- Margaret Holmes
- David Irwin
- David Livingston
- David Maslow
- Harold Moses

- Alan Rabson
- Edward Sondik
- Robert Wittes
- Ernst Wynder

The Review Group formed five subcommittees, each of which took primary responsibility for a set of issues identified by the full Review Group. Issues addressed by the subcommittee were discussed by the entire Review Group at each meeting. The subcommittee chairs met in Salt Lake City, Utah in June 1996 to refine the third draft of the report, which was then submitted to the full Group for its review in July 1996. After the July meeting, additional comments were taken by the chair for final revisions. Simultaneously, the template for the guidelines was developed by three committee members for review by the entire Review Group. Throughout the process, the Chair provided periodic updates on the progress of the Review Group at meetings of the Board of Scientific Advisors and the National Cancer Advisory Board. In addition, the Chair met with the Prevention Program Review Group and the Clinical Trials Program Review Group.

Prior to soliciting final comments from the Cancer Centers Program Review Group, the Chair met with the NCI Director to report the Review Group's findings and recommendations and to check for the clarity of the report. The draft was then sent to the Review Group members for its concurrence and identification of errors or omissions. Final comments on the draft were conveyed to the Chair and a final report was submitted to the NCI Director.

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[1] Centers Subcommittee of the National Cancer Advisory Board, chaired by Dr. John Durant, 1998. (Back)

[2] Institute of Medicine Report of a Study: A Stronger Cancer Centers Program (Washington, DC: National Academy Press, 1989). (Back)

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