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Review Of Cancer Center Support Grants Needs Refocus On Science, Advisors Say

NCI needs to overhaul the review process for the Cancer Center Support Grants to encourage quality research and assure flexibility for pursuing scientific opportunities, an advisory group said.

The recent report of the Cancer Centers Program Review Group made 24 recommendations for revising the criteria for awarding grants that provide funding for "core" resources at the NCI-designated cancer centers.

The group's report to the NCI director and members of the National Cancer Advisory Board and the NCI Board of Scientific Advisors was released last week.

"What the recommendations attempt to do is refocus the whole process on scientific excellence, and to instill greater flexibility in the

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In Brief

Schwarzkopf In NCCS TV Spot; AACI Elects Officers; Nobel Prize In Medicine Awarded

GEN. H. NORMAN SCHWARZKOPF and the National Coalition for Cancer Survivorship have launched a campaign to encourage people diagnosed with cancer to seek support and information from other cancer survivors. The retired general, who led U.S. forces in the Persian Gulf conflict, is featured in a 30-second television public service announcement that urges people with cancer not to face the disease alone, but to link with other survivors by calling the NCCS at its new, 24-hour, toll-free number, 1-888-YES-NCCS (1-888-937-6227). . . . **ASSOCIATION OF AMERICAN CANCER INSTITUTES** has elected the following officers for 1996-97: **Joseph Pagano**, president; **Max Wicha**, vice-president and president-elect; **Edwin Mirand**, secretary-treasurer. Newly elected board members are: **Judith Gasson**, **Ronald Herberman** and **Jerome Yates**. . . . **NOBEL PRIZE** in physiology or medicine was awarded to two scientists who discovered how the immune system recognizes infected cells. Australian **Peter Doherty**, now working at St. Jude Children's Research Hospital, and **Rolf Zinkernagel** of Switzerland will share the $1.12 million prize for their research in the early 1970s at the John Curtin School of Medical Research in Canberra, Australia. The work "fundamentally changed our understanding of the development and normal function of the immune system," said the citation from Sweden's Karolinska Institute.

Center Grants Review Rewards Paperwork, Report Finds

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system, since we can't predict the scientific opportunities down the road," said Joseph Simone, chairman of the committee and executive director of the Huntsman Cancer Care Program at University of Utah.

"There is nothing fundamentally wrong with the Cancer Centers Program, but the boat has been moving slower in the water than it might," Simone said to **The Cancer Letter**. "Every once in a while you have to take the boat out of the water and scrape the barnacles off."

The report was particularly critical of the NCI process for reviewing the support grants.

The existing process involves "redundant and oppressive paperwork requirements" that, at times, are tangential to the value of research at the centers, the review group said in its 36-page report.

"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," the report said.

The report recommended that centers should be primarily reviewed for the quality of science. "Such a shift in focus will result in a more productive cancer centers program with a greater impact on cancer research," the report said.

Other recommendations include:

—Two types of cancer centers should be designated by NCI--comprehensive cancer research centers and cancer research centers--rather than the current basic, clinical and comprehensive designations.

—NCI should give centers increased flexibility in the percent of funds that can be applied to different categories.

—Excessive and rigid record keeping in the application for a center grant, the letter of intent, and in noncompeting renewals should be dramatically reduced.

—NCI program administration should be further separated from the review process.

—NCI should consider an alternative approach to funding cancer center grant renewals that would provide a capped funding increase regardless of the size of the center's existing grant.

—Funding for the lowest-ranked centers should be phased out.

—NCI should develop an informatics program to facilitate the exchange of information between NCI and centers, among centers, and between centers and the public.

"The report will be reinvigorating for the centers program, because it moves the focus from form to science, and will result in a streamlined, more scientifically-oriented review," said Robert Young, a member of the committee and president of Fox Chase Cancer Center.

"The report calls for serious review of centers on the basis of quality, and proposes strategies for funding those highest quality centers fully, and funding those of not as high quality at lesser levels or not at all," Young said to **The Cancer Letter**. "The report backs away from the concept of the centers program as an entitlement program."

NCI has been reluctant to cut funding to centers that were not competitive, Young said.

"We felt the centers program is a more mature program than it was 10 years ago, so the criteria for reviewing centers in 1996 should be different than it was in the mid-1970s when the program was under development," he said.

The centers grant mechanism, formally established in 1971, continues to play an important role in the National Cancer Program, the report said.

"The stability and centralized support provided

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by the program allows an institution to conduct a wide array of investigations into the etiology and treatment of cancers," the report said. "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."

The cancer centers panel was the first of the committees convened by NCI Director Richard Klausner to evaluate the Institute's major programs.

The review group, comprised of 19 scientists and physicians and one patient advocate, was asked to study all aspects of the Institute's $147 million Cancer Centers Program, as well as the $20 million Specialized Programs of Research Excellence.

The centers program accounts for about 6 percent of the NCI's $2.25 billion budget. The program funds 55 Cancer Center Support Grants, ranging in size from $650,000 to $6.5 million, and 12 SPORE grants, which average $2.1 million.

The excerpted text of the committee's report follows:

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.

Essential Organizational and Administrative Characteristics of a Cancer Center

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.
- 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.

History of 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.

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).

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 Centers

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:

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.

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.

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.

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.

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.

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.

Review of 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.

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.

Guidelines, Review Criteria

●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 judgment 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.

Distribution and Use of Cancer Center Funds

●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.

Centers as Regional and National Resources

● 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.