# Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future

**Report of the P30/P50 Ad Hoc Working Group**

**February 2003**

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# EXECUTIVE SUMMARY

National Cancer Institute (NCI)-Designated Cancer Centers, funded through the P30 mechanism, play a fundamental role in the nation's cancer research agenda. These centers are unique entities where discovery, development, and delivery come together to make progress in the alleviation of the burden of cancer. As such, they are a model of translational research, unparalleled by any other national effort in any disease area. In an embattled health care system, the NCI Cancer Centers Program provides the nation with an extraordinary opportunity to address one set of diseases in a comprehensive manner, relying on the best science, clinicians, community networks, and patient groups to improve the quality of care.

Members of the 39 comprehensive cancer centers, 14 clinical cancer centers, and 8 basic cancer centers are responsible for more than 50 percent of the entire NCI research portfolio. In addition, NCI-Designated Cancer Centers have facilitated the application of major discoveries in molecular and cellular biology to cancer care through partnerships with NCI and industry. NCI leadership must capitalize on these centers and their institutional prestige to most effectively translate and disseminate methods of improved cancer care and innovation to the American public.

In addition, during the last decade the Specialized Programs of Research Excellence (SPOREs)—funded through the P50 mechanism—have embraced and increased the impact of translational research, a previously under-funded and under-appreciated area. SPOREs in multiple organ sites have advanced translational research, creating a new career path for joint clinical and basic science investigations. As befitted a new program area, the SPORE structure created through peer review self-contained, large research programs with a critical mass at single institutions, typically NCI-Designated Cancer Centers.

Because translational research has now matured and budgets are flattening, NCI is seeking mechanisms for improving the efficiency and integration of its P30 and P50 programs, while at the same time maximizing the number of institutions performing translational research. Under the auspices of its Subcommittee on Cancer Centers, the National Cancer Advisory Board convened an ad hoc P30/P50 Working Group to examine the P30 and P50 award mechanisms in terms of how they might best be positioned to support and facilitate increased discovery and translation of research into the future.

The recommendations of the Working Group are grouped into three overarching themes, as summarized below: 1) understanding the implications of budgetary issues; 2) expanding the roles and expectations of centers and SPOREs; and 3) increasing the efficiency and effectiveness of these funding mechanisms. More elaborate discussion and detailed recommendations can be found in the full report.

**Recommendation 1: The Cancer Centers Program and SPORE program are vital components of NCI's translational research efforts and must be sustained, even in today's challenging financial environment.**

**1.1 The P30 cancer centers are the engine of NCI's extramural research program and are the bases for community outreach and dissemination to the wider**

**research and geographic communities. In the short term, funding can be stretched by limiting growth to slightly above that of RO1s and by suspending the P20 program due to its limited success in leading institutions to an eventual P30 award.**

**1.2 Despite its success, the P50 SPORE program cannot grow at its present rate. It can be sustained by a) slowing its growth to a rate not greater than that of the RO1 mechanism; b) lowering the average cost per award in part by reducing the number of required projects and elements; c) allowing SPOREs to focus on pathway, mechanism, or population research; d) fusing appropriate shared resources with those of the P30 in a given institution; and e) implementing a program requirement for matching NCI funds with other sources of non-federal and philanthropic support.**

**Recommendation 2: NCI should take better advantage of the entrepreneurship and vitality of cancer centers by systematically and routinely engaging them in NCI's strategic planning and budgetary discussions. Furthermore, to leverage the existing strengths of cancer centers, NCI should encourage the development of novel research resources, dissemination techniques, and community collaborations. Specifically, NCI should:**

**2.1 Include cancer center directors on a regular basis in NCI's strategic planning process, providing them the opportunity to offer guidance in developing new NCI initiatives and disseminating research findings.**

**2.2 Look to centers as sites for piloting new research and dissemination programs to assure cost-effective integration with existing resources.**

**2.3 Allow salary support through the P30 award for clinical researchers who actively engage in trials in recognition of the essential role these individuals play in translational research.**

**2.4 Revise the funding of P30 shared resources to provide more appropriate support for critical and underfunded activities, such as tissue banks and data management, and for essential new exigencies such as regulatory compliance.**

**2.5 Encourage geographic distribution by creating a new category of cancer center for academic institutions not able to meet all requirements of P30 applications; these institutions would be associated with and funded through an existing P30 center.**

**2.6 Provide support through the P30 mechanism for cancer centers actively seeking links with state health departments or other state agencies, or with the Centers for Disease Control and Prevention (CDC).**

**2.7 Modify the P30 award to encourage and support centers to develop infrastructure and test novel methods for disseminating new knowledge in clinical, cancer control, and early detection research.**

**Recommendation 3: NCI should make a concerted effort to improve the efficiency, effectiveness, and evaluation of the research processes in centers, SPOREs, and cooperative groups. Specifically, NCI should:**

**3.1 Adopt as a top priority the development of an integrated national clinical research informatics system.**

**3.2 Limit the additional review of clinical trials that are supported by previously peer-reviewed funding mechanisms to safety and regulatory issues.**

**3.3 Work with the federal Office for Human Research Protections to engage cancer center Institutional Review Boards in developing a strategy for centralized review of multi-center trials.**

**3.4 Streamline the review of P30s by eliminating the need for some site visits.**

**3.5 Adjust the P30 review process to consider and accord weight in scoring activities involving collaboration with P50s, cooperative groups, and participation in networks, as well as community service, outreach, and dissemination.**

**3.6 Initiate a planning process to develop quantifiable metrics for determining the size of the P30 award that reflect the broad spectrum of involvement of individual cancer centers in discovery, dissemination, and the delivery of care.**

**3.7 Employ a two-tiered system of review for the P50 SPORE program, with a parent committee empowered to review applications across sites from the perspective of managing the program in its entirety.**

**3.8 Develop a process to describe and quantitate on an annual basis the overall contributions of the P30/P50 programs.**

This report contends that NCI-Designated Cancer Centers and the associated SPORE program are central to discovery and represent the best, most practical national network for testing and disseminating innovations that reduce cancer mortality. The strategic directions listed above and discussed in the full report will further improve the ability to translate and disseminate research advances.

Unfortunately, the next several years are likely to be a period during which overall NCI resources will at best be constrained in terms of growth in constant dollars, and at worst be reduced. Thus, in the short term, implementation of recommendations requiring funding can be accomplished only through 1) ensuring flexibility in the P30 and P50 mechanisms; 2) re-budgeting NCI funds, both within and outside the Cancer Centers Branch to achieve economies of scale; and 3) facilitating and establishing partnerships, such as those with industry for informatics and with CDC for dissemination initiatives.

However, because the opportunities are too great and the task too important to ignore, the Working Group looks to NCI leadership—with the help of cancer centers and SPORE leadership, advocates, and others—to seek substantial increased funding for the P30 and P50 mechanisms over the next three to five years. Full funding should result in an NCI-led, evidence-based outreach and dissemination effort; continuation of the world's finest discovery research infrastructure; a robust, integrated translational, clinical, and prevention trial apparatus that responds rapidly to innovation; increased patient accrual to clinical and prevention trials; new mechanisms for geographic coverage by the Cancer Centers Program; and an increase in the novelty and number of SPORE grants. The benefit to delivery, dissemination, and coordination will be easily demonstrable.

The cancer center and SPORE infrastructures, operating through the nation's leading public and private institutions, offer a critical link to the American people. Implementation and funding of these strategic initiatives will focus this unparalleled resource on discovery and development and demonstrably enhance delivery of the latest prevention, early detection, and therapeutic advances.

# I. INTRODUCTION

Public support of cancer research over the long term ultimately depends on how well the research community translates scientific discoveries into the measurable reduction of cancer risk and burden. Since the early days of the National Institutes of Health (NIH), Congress and the public have shared the strong sense that every effort should be made to close the gap between what can be learned at the laboratory bench and what can be applied at the bedside. Thus, for nearly 50 years, the United States has invested heavily in cancer research and in recent years has made substantial progress toward reaching major goals related to reducing the incidence and burden of cancer:

- A growing understanding of the genetic mechanisms of cancer has created the opportunity for the development of therapeutic agents targeted to specific molecules and pathways.
- The rates of new cancer cases and cancer deaths are falling overall.
- Some prevention behaviors have shown improvement. Adult smoking is down dramatically since the 1960s, although rates fell only slightly in the 1990s. Alcohol and fat consumption is headed down, while fruit and vegetable consumption is up.
- The use of screening tests for breast, cervical, and colorectal cancers is increasing; screening for colorectal cancer, however, remains low.

However, in other important areas that demand attention, we are losing ground:

- Some cancers are rising dramatically, such as cancer of the esophagus and melanoma skin cancer. The rates of lung cancer in women continue to rise, but not as rapidly as before.
- Smoking among youth has been on the rise, although data show that there may be a recent, promising decline.
- People are doing less to protect themselves from exposure to the sun.
- Cancer treatment spending continues to rise along with total health care spending.
- Unexplained cancer-related health disparities remain among population subgroups. For example, African Americans and those with low socioeconomic status have the highest overall rates for both new cancers and deaths.

It is clear that sustained research conducted at all levels—from the molecular to the population—is needed to improve cancer prevention, diagnosis, treatment, and survival. Such critical basic, translational, and clinical research funded by the National Cancer Institute (NCI) is likely to take place in NCI-Designated Cancer Centers or special programs that focus on specific cancers (Specialized Programs of Research Excellence, or SPOREs). The future role of these cancer centers and SPORES in advancing the translation of knowledge to clinical application is the topic of this report.

### The Nation's Cancer Centers Program

For many years, NCI has relied on the Cancer Center Support Grant (P30, or CCSG) to facilitate interdisciplinary science in cancer research programs in the United States. In FY 2002, the NCI Cancer Centers Program budget was nearly $192 million, or 6.6 percent of the total extramural NCI budget. These funds provide partial support for 61 NCI-Designated Cancer Centers in 31 states, as well as P20 Planning Grants. Although this commitment is small in comparison to that for grants to

individual investigators (RO1 grants constituted 34.8 percent of the extramural budget), it represents a critical force in cancer research, treatment, and prevention and is firmly anchored in NCI's commitment to the National Cancer Program.

Of the 61 NCI-Designated Cancer Centers that were funded in 2002, 8 are basic cancer centers, 14 are clinical cancer centers, and 39 are comprehensive cancer centers. Most of the states in which cancer centers are located have only one comprehensive cancer center; however, some highly populated states have several comprehensive cancer centers (e.g., California has five). [1]

These cancer centers, particularly those deemed comprehensive, are expected to combine the forces of basic, translational, and population cancer research to achieve improved cancer prevention, diagnosis, and treatment. Justification for the Cancer Centers Program has been based on the presumption that clinical progress can only be made by teams of clinicians, clinical investigators, and basic scientists working together to translate information gained at the cellular and molecular level into new therapeutics and diagnostics. Moreover, because cancer is not a single disease, each type of cancer presents distinctive scientific and clinical challenges that require the kind of intensive subspecialization that a single oncology division or department working in isolation in one location simply cannot provide.

Although progress in cancer prevention and early diagnosis is slow, important advances have been made by cancer centers. For example, the nurses' and physicians' study in the Dana-Farber/Harvard Cancer Center is the largest analysis of the incidence of cancer and its links to lifestyle choices, such as diet, in any population worldwide. The M.D. Anderson Cancer Center has been at the forefront of chemoprevention of cancer, and several chemo-preventive agents are now in clinical trials. The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins has been a leader in the clinical application of cancer genetics, particularly in colorectal cancer, which has led to improved genetic testing for individuals with hereditary colorectal cancer syndromes. Bone marrow transplantation to treat leukemia was developed at the Fred Hutchinson Cancer Research Center, and tremendous progress has been made in increasing the survival rate for childhood leukemia at the St. Jude Children's Research Hospital Cancer Center.

In addition to conducting innovative basic and clinical research, cancer centers also are expected to be at the forefront of the continuing development of effective cancer education and prevention methods, with the additional expectation that they actively disseminate these methods to the surrounding community and, in some cases, a wider region. Finally, comprehensive cancer centers are expected to offer the highest quality surgical, radio-therapeutic, and medical treatments for cancer. Thus, cancer centers are vital parts of a national anti-cancer strategy and are widely regarded as centers of excellence—not only by researchers, but also by patients seeking state-of-the-art treatment and access to clinical trials.

[1] Lists of P30 and P50 awardees are available on the NCI website at www3.cancer.gov/cancercenters/centerslist and spores.nci.nih.gov/applicants/index_applicants.)

## Specialized Programs of Research Excellence (SPOREs) (P50s)

In 1992, in response to growing pressures to more effectively and directly apply research knowledge to alleviating the burden of cancer, NCI established the Specialized Programs of Research Excellence (SPOREs) to "promote interdisciplinary research and to speed the bi-directional exchange between basic and clinical science to move basic research findings from the laboratory to applied settings involving patients and populations." The stated goal of the SPORE program, funded through the P50 mechanism, is to bring to clinical care settings novel ideas that have the potential to reduce cancer incidence and mortality, improve survival, and improve the quality of life. Each SPORE grantee develops and maintains specialized resources that are intended to benefit not only SPORE scientists, but all scientists working on a specific organ site. Unlike the Cancer Centers Program, the P50 directly supports research. In 1992, nine SPORE programs covered four organ sites.

In FY 2002, the SPORE budget was half that of the P30 program budget at nearly $95 million—or 3 percent of the total NCI budget—and involved 44 separate organ-specific awards for breast, prostate, lung, gastrointestinal, ovarian, gynecological, genitourinary, brain, skin, and head and neck cancers, and lymphoma. Of the 44 awards, 41 were located at cancer centers. Thus, the emphasis placed on translational research in the majority of P30 centers has been reflected by their success in competing for SPORE grants. The P50 SPORE program, in turn, has extended the capabilities of the cancer centers by providing direct support for translational research projects, specimen banks, and pilot studies on specific disease sites. Over the next several years, NCI plans to extend the P50 SPORE program to 14 site categories, each of which would have one receipt date annually for an overall portfolio of 60-65 awards, however, budget constraints could alter these plans.

## Need for Assessment

The current five-year budget period has allowed accelerated growth of both the P30 centers and P50 SPORE budgets. While creating opportunities for further advances, this growth must be separately considered for each program, as well as framed by the need to anticipate more modest federal budget growth in the future. In addition, despite a 16 percent increase in the FY 2002 budget for these programs, NCI is facing a shortfall in program commitments. This is therefore a critical time, both financially and scientifically, to assess the current status and accomplishments of the cancer center and SPORE programs, plot directions for future growth, evaluate management and budgetary policies, and explore mechanisms for enhancing interactions between NCI, cancer centers, SPOREs, and other critical partners in cancer research.

Such an evaluation must recognize that the missions of cancer centers and SPOREs extend well beyond the NCI grant base, as many other sources of research support, health care delivery activities, and services are provided that extend into the communities and populations that are being served. Ideally, these awards allow institutions to adapt fluidly to the exponential growth in knowledge of the genetic, molecular, cellular, and environmental processes responsible for the development of cancer and assure the rapid development of state-of-the-art interventions and clinical trials based on this knowledge. The current challenge is determining how to meet these goals more efficiently and effectively.

### Charge to the Working Group

Under the auspices of its Subcommittee on Cancer Centers, the National Cancer Advisory Board convened an ad hoc P30/P50 Working Group to examine how the P30 and P50 award mechanisms might best be positioned to support and facilitate increased discovery and translation of research. NCI Director Andrew C. von Eschenbach charged the Working Group with accomplishing the following:

1) explore how these awards can be used to maximize translation of research discoveries into interventions;
2) set clear priorities for goals in view of the likelihood of more moderate growth expectations for NCI award mechanisms;
3) explore possible incentives to coordinate and lead activities that leverage NCI support with other governmental, private, philanthropic, and industrial partners in order to meet high-priority national needs and objectives and to catalyze greater community and regional involvement with cancer centers;
4) consider how P30 and P50 awards may play a greater role in developing the objectives of a national agenda that is focused on reducing cancer risk and burden, as defined by the NCI Progress Review Group reports; and
5) suggest goals for these specific centers programs over the next five years and measures that could be applied to evaluate progress.

### Functioning of the Working Group

The Working Group met six times over a six-month period. It requested and received detailed data on the history, budget, and operations of the cancer center and SPORE programs and heard testimony from a variety of NCI and federal agency personnel, cancer center directors, and representatives of state, professional, and scientific organizations (see appendix for list of speakers). In addition, in order to better define and describe the capabilities of the cancer centers, NCI conducted a survey of P30 cancer center directors designed with input from the Association of American Cancer Institutes (AACI). Respondents were asked to answer questions about patient populations, staffing, budget, research, training, technology transfer, and community and regional partnerships. Of 61 potential responses, 50 were received.

## II. PROGRESS IN CANCER RESEARCH OVER THE PAST 50 YEARS

Until just a century ago, cancer was visible only in its outward manifestations. It took the development of advanced microscopy to reveal the cancer cell itself, and over the past 25 years complex biotechnologies have enabled scientists to pursue, at the molecular level, knowledge of the mechanisms that trigger cancer's uncontrolled and deadly cell growth. Using the tools of molecular biology and molecular genetics, scientists are making great leaps in discovery and are mapping out the links between chromosomes, genes, and cancer.

From the turn of the century to World War II, the standard treatments for cancer were either surgery or radiation therapy, as the drugs and chemicals that had proved so effective against other diseases, for example, infectious disease, were found to be powerless against cancer. Discoveries

made in the 1940s, however, demonstrated that cancer also was vulnerable to drug and chemical compounds, and by the early 1990s, more than 40 chemoprevention trials tested the power of assorted vitamins, minerals, and drugs against cancer.

While chemotherapies were being tested and magic bullets to eliminate cancer pursued, advances also were being made in the older methods of surgery and radiation therapy, which, often with the addition of chemotherapy, remained the major treatments for all but a small proportion of cancer patients. At the same time, advances were occurring in cancer detection, with the goal of achieving early diagnosis, as evidence from many studies demonstrated that screening for cancer before symptoms appear increases the chances of successful treatment.

In addition, over the past 25 years numerous links have been established between lifestyle and cancer, with epidemiological research indicating that fully a third of cancer deaths are at some level influenced by diet. Studies also suggest that regular exercise offers at least modest protection from some kinds of cancer. Strategies targeted at keeping cancer from occurring, progressing, or recurring remain invaluable weapons in the cancer-fighting arsenal.

In the 1980s, the discovery of oncogenes, proto-oncogenes, and tumor suppressor genes led to new efforts aimed at understanding the genetic basis of cancer. The ability to sequence DNA produced a wide range of inventions: DNA probes that seek out genes of known sequences; DNA atlases that list sequences of different genes; and gene banks—central computerized repositories for storing known sequences that can be used in clinical investigations**.** In addition, the development of hybridomas and advances in immunology spawned the field of biologicals, and the role of viruses in causing some types of cancer was elucidated. Another technique, immunodiagnosis, uses antibodies linked to radioactive isotopes, which seek out and identify cancerous growths. These antibodies can be used to study cancer growth in the laboratory or can be injected into the body as markers for tracking cancer cells.

Advances in computer technology in the 1980s transformed diagnostic imaging, making it possible to visualize organs and soft tissues at a level of detail that had been available previously only through anatomical dissections. Imaging techniques such as computed tomography imaging, positron emission tomography, magnetic resonance imaging, and ultrasound provide additional windows into the body, allowing the detection of tumors or other abnormalities in areas that are not accessible through physical examination or x-ray alone.

As we enter the new millennium, the Human Genome Project and the Cancer Genome Anatomy Project have underscored the basis of cancer at the molecular level, as an accumulation of genetic changes that alter the behavior of the cell. Understanding how these changes define cancer will lead to earlier detection, better diagnostic classification, and the development of new targets for therapy.

# III: BACKGROUND, ACCOMPLISHMENTS, AND FUTURE CHALLENGES OF THE P30 AND P50 PROGRAMS

## The Cancer Centers Program

A review of the history of NCI's efforts in clinical and translational research can help further an appreciation of the current status of programs in this area and the rationale behind their development. NCI has a 40-year history of committing resources to the development of a system of integrated, multidisciplinary cancer research aimed at more rapid translation of research findings into coordinated care. In 1961, NCI announced three grant programs that broadened the base of cancer research activity in the United States: the Cancer Research Facilities Grant (CRFG); the Program Project Grants (PO1s) for cancer research; and the Cancer Clinical Research Center Grants (PO2s, or CCRCG). CRFGs permitted construction of buildings solely devoted to cancer research, while CCRCGs provided funds for collaborative research and the construction of clinical cancer research units similar to those in the General Clinical Research Centers program. These funding mechanisms were intended to provide support for broadly based multidisciplinary cancer research efforts.

By 1963, a reasonably well-defined but informal Cancer Centers Program was in place with a budget of approximately $6 million across 12 institutions. The activities at these centers were diverse, including research in radiation therapy, medical oncology, and surgery, as well as basic science. However, 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 (NCAB) provided guidelines for cancer centers and introduced the concept of the planning, or exploratory, grant. The 1971 National Cancer Act provided a broad mandate to the centers that included 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, which has continued to be an issue of congressional interest over the years. Because there were already more than 60 cancer centers supported by NCI, administrative efforts were required to reconcile existing programs with the intent of the new legislation. In June 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 through the traditional approach of funding a multiplicity of individual research and project grants. This was intended to force a review of an institution's total cancer research program. The model for this concept was a single large grant made to the Memorial Sloan-Kettering Cancer Center in 1966, which was intended to provide partial support for the total research program, replacing more than 40 smaller, individual grants. This allowed NCI to review Sloan Kettering's entire program in a single site visit and allowed Sloan Kettering to provide infrastructure support to an integrated program of clinical, population, and basic cancer research in a more coordinated manner. Similar grants were soon awarded to the M.D. Anderson and Roswell Park Cancer Centers.

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, which together provide the fundamental information, or substrate, essential for the translation of research into clinical trials and practice. Cancer centers that are located within major research universities are organized as a matrix, with defined administrative arrangements, space, budget, shared resources, and a system of membership that draws widely from the institution faculty who have a primary interest in cancer research.

### *The CCSG P30 Award Mechanism*

Requests from institutions eligible for cancer center support are subjected to a competitive peer review process that evaluates and ranks applications according to scientific merit. Successful applicants are awarded a CCSG to fund the scientific infrastructure of the cancer center, including elements such as scientific leadership and administration; research resources that provide ready access to state-of-the art technologies; and flexible funds that help the center pursue its objectives and take immediate advantage of new research opportunities. The CCSG does not support individual research projects; rather, such projects are funded through individual RO1s and PO1s as well as other competitive, externally peer-reviewed grants that are awarded to cancer center investigators.

Each institution receiving a CCSG award is recognized as an NCI-Designated Cancer Center, of which there are three types, based on the degree of specialization of research activities. Generic cancer centers have a narrow research agenda that may focus, for example, on basic sciences; clinical cancer centers usually integrate strong basic with strong clinical science; and comprehensive cancer centers integrate strong basic, clinical and prevention, control, and population sciences. Although the CCSG is mainly limited to support of research infrastructure, all clinical and comprehensive cancer centers also provide clinical care and service for cancer patients. In addition, comprehensive and clinical cancer centers have extensive ancillary cancer-related activities such as outreach, education, and information dissemination, none of which currently is supported by the CCSG mechanism.

Some institutions start to organize a cancer research effort with an eye toward applying for a CCSG sometime in the future. NCI offers assistance to institutions in this early phase of development through a P20 Cancer Center Planning Grant (CCPG), a mechanism that offers support for the development of the scientific leadership, scientific excellence, and integrated scientific approaches needed to focus on cancer problems. Many centers have foregone the P20 step and successfully applied directly for a P30 grant.

### *Current Status of Cancer Centers as Institutions: Results of a Survey*

The results of a survey conducted by NCI on behalf of the Working Group show that, as intended, the P30 CCSG has formed a solid base of support for the 61 active NCI-sponsored cancer center award sites, allowing these institutions and their leaders to build and leverage truly impressive programs. Each of the 61 cancer centers in 31 states serves millions of people. Many of these centers reach an area encompassing three dozen or more counties within the regions that they serve. The administrative, research, clinical, training, and outreach functions conducted by each center through the P30 grant leverages many times the total amount of such activities conducted in these

centers. The 50 survey responses help illustrate the profound effect the centers have had on the regions they serve as well as the national cancer effort as a whole.

- **The P30 mechanism leverages other sources of income**

In terms of gross research and operational support, the 50 reporting cancer centers represent 89% percent of the total P30 budget in FY 2001, the base year for the data collected. The total amount of research support and operating budgets that are leveraged through each center is striking (table 1). For example, among the basic science centers, the total annual award averaged $2.6 million, which provided a base for another $6.5 million in NCI funding and $12.4 million from other granting sources and industrial agreements. Among the clinical matrix centers, the P30 award averaged $1.8 million, the base for an additional average of $13.2 million from other NCI sources and $23.5 million from other granting and industrial sources. Comprehensive matrix centers average somewhat larger P30 awards ($3.3 million), which are leveraged by an average of $20.6 million in other NCI support and $41.8 million in other support. The benefits of specialization are evident in the free-standing cancer centers and those located in independent institutions, which have P30 awards averaging $5.6 million annually, while their overall NCI support averages $44.4 million and other grant and industrial support averages nearly $52 million annually.

**Table 1: Cancer Center Annual Income**
**(Average per Reporting Center[1])**

| | Basic Science | Clinical Matrix | Comprehensive Matrix | Free Standing/ Autonomous |
|---|---|---|---|---|
| CCSG (P30)[2] | $2,607,369 | $1,821,340 | $3,349,014 | $5,630,540 |
| NCI-Sponsored Research[3] | $6,465,993 | $13,166,383 | $20,564,739 | $44,443,091 |
| Total Sponsored Research | $20,429,204 | $36,966,788 | $62,399,085 | $96,143,464 |
| Institutional Support | $1,544,857 | $1,769,354 | $1,471,073 | $38,086,763 |
| State/Local Support | $48,429 | $944,444 | $373,174 | $14,558,943 |
| Gift Support | $1,546,143 | $4,272,629 | $2,144,871 | $6,790,766 |

[1]Basic [7 reporting], Clinical Matrix [9 reporting], Comprehensive Matrix [26 reporting]) and Free Standing/independent [8 reporting]. Here, the term "free-standing/independent" refers to a broader set of well established, well funded institutions than that term typically is used, and either are entities unto themselves or are largely administratively independent units within another entity (Memorial Sloan Kettering Institute, M.D. Anderson, Fred Hutchinson, Fox Chase, Dana Farber, St. Jude, Roswell Park, Beckman Research Institute).
[2]Direct and Indirect
[3]Direct

The total non-P30 research support in these centers is well in excess of $1.5 billion annually, more than 10 times the amount of support generated by the P30 awards themselves. Additional income is derived from institutional sources, state and local support, endowment income, and gifts. Many centers raise additional funds from general philanthropy. The ability to attract, concentrate and focus financial support from such diverse sources is central to the overall progress achieved through the Cancer Centers Program.

- **P30 awardees are centers of clinical care and clinical research**

Equally impressive has been the impact of the centers on direct patient care (table 2). Over the last five years, the reporting centers with clinical activities collectively have seen more than 830,000 newly diagnosed patients with cancer, which represents an estimated 23 percent of the newly diagnosed patients in the collective regions they serve, in addition to approximately 341,000 cases that were referred from greater distances. These estimates suggest that the centers evaluate approximately 15 percent of all patients with cancer in the United States and that the majority of these patients receive care in one of the reporting cancer centers.

**Table 2: Patient Care in Cancer Centers**
**(Total in All Reporting Centers over the Past Five Years)**

| | Clinical Matrix | Comprehensive Matrix | Free Standing |
|---|---|---|---|
| Number of Newly Diagnosed Patients from Region | 95,927 | 384,783 | 348,931 |
| New Patients from Outside Region | 62,667 | 98,338 | 179,755 |

In the most recent reporting year, centers enrolled nearly 30,000 subjects in clinical trials (6,700 patients total in Phase I trials, 12,600 in Phase II trials, and more than 11,000 in Phase III trials). In addition, more than 650,000 subjects are being followed in epidemiological and prevention studies conducted by these centers. These activities are accomplished through affiliations with more than 260 hospitals and well over 300 satellite practice sites.

- **Cancer centers provide training in diverse cancer-related professions**

In addition to patient contact, the centers as institutions represent major venues for training (table 3). In the most recent five-year reporting period, the centers collectively trained more than 9,000 basic scientists, more than 3,800 clinical fellows, and nearly 3,000 oncology nurses.

**Table 3: Fellowship Training**
**(Total Individuals Trained over the Past Five Years)**

| | Basic Science | Clinical Matrix | Comprehensive Matrix | Free Standing |
|---|---|---|---|---|
| Laboratory Fellows | 1,411 | 1,271 | 3,336 | 3,093 |
| Clinical Fellows | 39 | 639 | 1,320 | 1,850 |
| Oncology Nurses | - | 290 | 1,198 | 1,477 |

- **Summary**

The information collected by the survey indicates that the CCSG (P30) provides infrastructure support and flexible funding that catalyzes the coordination and integration of the many discovery, development, and delivery activities encompassed within each cancer center. The P30 mechanism has been a highly effective means of facilitating the complex elements needed for a national cancer effort. The survey also documented the numerous prestigious awards received by faculty and staff at these institutions, including the Nobel prize and Lasker awards, the issuance of more than 2,500 patents in the last five years, and center participation in more than 400 clinical studies that led to Food and Drug Administration (FDA) approval of a new treatment or diagnostic indication.

### *Future Challenges*

Among the challenges facing cancer centers are the expanded opportunities to understand disease pathogenesis, improve diagnoses, and advance treatment in the context of static or potentially shrinking fiscal resources. The ability to capitalize on the explosion of knowledge relevant to cancer biology will require a growing and costly infrastructure to support increasingly complex and expensive biotechnology and bioinformatics. The expansion in the NCI budget over the past several years has fostered the growth of an increasingly productive research enterprise, the potential of which is significantly threatened by a looming fiscal crisis.

Another resource increasingly in short supply is clinician scientists available to organize and conduct clinical trials. Unfortunately, there is a decline in the number of new physician/scientists, especially those with the scientific training needed to bridge the laboratory and clinical science and who can create and execute original clinical trials. Academic physicians are under considerable pressure to engage in patient care activities in support of their salaries, thus, the dearth of physician/scientists is exacerbated by a reduction in time available for research.

A third significant challenge facing cancer centers is compliance with the regulations relevant to conducting clinical trials. The combined regulatory requirements of the Food and Drug Administration and the Office of Human Research Protections have evolved to create a highly inflexible environment for the evaluation and testing of novel therapeutic agents for the treatment of cancer. Physician/scientists who might be inclined by temperament and training to engage in clinical trials might feel more drawn to a career in laboratory-based research because of the absence of hurdles and complexities involved in conducting clinical trials. These pressures are occurring in the context of the need to rapidly move many new therapeutic agents through clinical trials in order to capitalize on targeted therapeutics directed at specific molecules or essential cellular pathways. Because of cancer centers' key and essential roles in conducting clinical trials, these regulatory hurdles represent a serious burden and major challenge for NCI-supported cancer centers.

## The P50 SPORE Program

Institutions receiving SPORE grants are expected to conduct the highest quality, balanced, translational research on the prevention, etiology, screening, diagnosis, and treatment of a specific organ site cancer. SPORE applicants are judged on their current and potential ability to move basic research findings into a clinical or population setting or, conversely, to take a finding from the clinic/population and expand upon it in the laboratory. A SPORE must develop and maintain

human cancer tissue resources for the particular organ site that will benefit translational research; foster extended collaborations in critical areas of research need with laboratory and clinical scientists within the institution, as well as in other institutions; and participate with other SPOREs regularly in sharing positive and negative findings, assessing scientific progress in the field, identifying new research opportunities, and promoting inter-SPORE collaborations.

Each SPORE and the network of SPOREs are expected to conduct research that will have the most immediate impact possible on reducing the incidence and mortality of human cancer. A SPORE should support a mix of basic and clinical researchers whose formal interactive and collaborative research efforts will result in new approaches for early detection, diagnosis, therapy, prevention, and control of human cancer. The SPORE mechanism is not intended to support basic research to the exclusion of clinical research.

The success of the SPORE P50 mechanism has been to legitimize, popularize, and advance translational cancer research. The program has galvanized the formation of basic/clinical teams focused on particular disease sites at many institutions, resulting in novel and effective approaches to cancer prevention, diagnosis, and treatment, and producing better understanding of the biology of cancer from different sites at the clinical, cellular, and molecular levels.

In addition, the P50 mechanism has supported enhanced infrastructure for informatics, biostatistics, and tissue procurement at a time when these cores were decidedly under-funded through the CCSG and by the cancer centers. Moreover, SPORE programs encourage collaboration within and between P50s, P30s, and cooperative groups in the development of bio-repositories (e.g., tissue, serum, plasma); the writing of protocols; the evaluation of common data elements; and the advancement of the use of genomics and expression arrays. Additionally, SPOREs have created and supported career development pathways in translational research that were not previously available.

***Current Status***

The first P50s were awarded in 1992 in breast and prostate cancer. Today, there are 44 active awards covering 11 organ sites. Recent advances attributed, in part, to SPORE-conducted research include the following:

- The discovery that smokers who carry certain gene types are less likely than others to successfully quit. This finding raises the possibility that specially tailored cessation programs may help these smokers.

- A better approach to detecting the early signs of lung cancer. Investigators found that the use of fluorescent light in bronchoscopy dramatically improved physicians' ability to identify the early signs of lung cancer.

- Further evidence that family clusters of pancreatic cancer have a genetic basis. After tracking relatives of pancreatic cancer patients since 1994, researchers recently confirmed that those with two or more relatives with pancreatic cancer are at higher risk for the disease. This finding provides important information for these relatives and their physicians and supplies scientists with a vital first step toward identifying the responsible genes.

- Promising results in an initial clinical trial of a treatment vaccine that stimulates the immune system of pancreatic cancer patients to take action against the tumors. Investigators have now expanded testing of this new treatment to a larger number of patients.

- Additional evidence that variations in the molecular profiles of different types of breast tumors can yield important clues about the prospects for relapse and long-term patient survival. Other SPORE investigators studying breast cancer reported encouraging results from their studies of ductal lavage, a new approach to early breast cancer detection.

***Future Challenges***

The SPORE program has been growing at a rapid rate, but one that is not sustainable in the future because of overall NCI and NIH budget constraints. With a level budget starting in FY 2004, it is anticipated that the SPORE portfolio will plateau at approximately 60 awards total, with varying target numbers of awards for different organ sites. The ability to make awards in FY 2004 and beyond will depend almost entirely on funds "turning over" from expiring grants. With an average grant period of five years, approximately 12 awards could be made per year consistently in the future.

Traditionally, NCI tries to maintain a minimum success rate for applications in the range of 20 to 25 percent. However, under the current plans, the SPORE success rate for 2004 and 2005 could be as low as 10 percent. Receipt of a large number of applications for only a few awards will also lead to large numbers of amended applications, which will increase the proportion of SPORE funds needed for interim funding and lead to significant applicant and reviewer burnout.

With the current cap and requirements for SPORE components, individual projects stay below $200,000, which will not fund many serious efforts in epidemiology, prevention, and detection or clinical Phase I or Phase III trials. Moreover, the timeframe for translation is protracted and depends on the consistent support of NCI and industrial partners

**Relationship of Centers and SPOREs**

Of the 41 P50 awards made to P30 institutions, 39 went to comprehensive cancer centers, while 2 were awarded to non-comprehensive centers. Eighteen of the SPORES are awarded to centers with P30 budgets below $5 million total annual costs, but six of those went to centers whose budgets are slated to rise above that level during the next funding year. This leaves only 12 of 41 P50s deriving from "smaller" cancer centers. Three additional SPORES were awarded to institutions with no cancer centers.

There are two sources of growing imbalance in the P30-P50 relationship in the NCI portfolio that could be troublesome in the future. Of the 61 active P30 centers, 38 have no P50s and therefore do not directly benefit from the program. Putting the distribution another way, 5 centers have 19 P50s, and 10 centers have 29 of 44 SPORES. It is also important to point out the monetary size distribution of P30 awards versus P50s. The FY 2002 average total annual P50 award (direct plus indirect) is $2.55 million including supplements. In contrast, 29 of the P30s (nearly half), have annual total awards that are less than the average award for a single P50 grant. Only 12 of 61 P30s have FY 2001 total costs in excess of $5 million annually (in other words, greater than or equal to 2 average

P50s). If this trend were to continue, there is a risk of less integration and competition of P30s and P50s, rather than more collaboration and integration.

### Administrative Challenges to Translational and Clinical Research

Compliance with federal regulations, particularly those related to human subjects protections and new drug approvals, if done correctly, is a labor-intensive activity. Protocol submission and review, data collection, management and monitoring of clinical trials, preparation for audits, and reporting as required to government agencies are real costs of clinical research and are increasing over time. Multi-site trials often require multiple reviews by Institutional Review Boards (IRBs), a practice that is cumbersome and one does not necessarily lead to greater protection of research subjects. Although these administrative challenges face all who are conducting clinical research, at a time when so many cancer interventions are ready for clinical testing, it is especially critical that administrative procedures be streamlined while high levels of regulatory and ethical compliance are maintained.

## IV. ANALYSIS AND RECOMMENDATIONS

The P30/P50 Working Group believes that the P30 centers program should be a centerpiece of the nation's cancer research investment. The stability and centralized support provided through this funding mechanism allow institutions to conduct a wide array of investigations into the etiology and treatment of cancers. At a time when clinical research is increasingly expensive and difficult to conduct, cancer center support is especially critical in ensuring that there are places where cutting-edge basic, clinical, prevention and control, as well as translational cancer research can be conducted. Cancer centers serve as an essential setting for clinical investigations by providing the critical links between the bench and the bedside. The SPORE program has been an important new addition to NCI's efforts in translational research and has served as a complement to the Cancer Centers Program. These intensive research programs have served as a focus for disease-specific activities—including education, detection, and prevention—and by involving patients and advocates in these activities, they have raised the level of cancer care.

Progress in cancer biology, genetics, immunology, and molecular biology has accelerated, creating new prospects for clinical investigation. A greater number of candidate drugs, vaccines, and other biologics exist now than at any other time, demanding careful selection of agents for study of clinical benefit and requiring significant increases in patient accrual to clinical trials. In addition, advances in informatics and electronic communication offer an entirely new approach to interaction and data transfer and analysis in the clinical research setting. At the same time, powerful forces to contain medical costs and limit NCI resources may prove to be rate-limiting factors in the application of new knowledge.

The recommendations of the Working Group are grouped into three overarching themes: 1) understanding the implications of budgetary issues; 2) expanding the roles and expectations of centers and SPOREs; and 3) increasing the efficiency and effectiveness of these funding mechanisms. In addition, the Working Group provides its vision of the ideal cancer center of the future as well as its view of the components and mission of the ideal P50 program of the future.

## P30s and P50s as Essential Elements of NCI's Research Portfolio: Budget Implications

Cancer centers play a fundamental role in the nation's cancer research agenda. Cancer centers are unique entities where discovery, development, and delivery come together to help to alleviate the burden of cancer in humans. As such, they are a model of translational research, unparalleled by any other national effort in any other disease area. In an embattled health care system, the Cancer Centers Program provides the nation with a singular opportunity to address one set of diseases in a comprehensive manner, relying on the best science, clinicians, community networks, and patient groups to improve the quality of care.

Institutional members of the 39 comprehensive, 14 clinical, and 8 basic cancer centers conduct more than 50 percent of the research in NCI's portfolio. Moreover, NCI-Designated Cancer Centers have facilitated the application of major discoveries in molecular and cellular biology to cancer care through partnerships with NCI and industry. NCI leadership must capitalize on the resources of these centers and their institutional prestige to more effectively translate and disseminate better cancer care and innovation to the American public.

During the last decade, the SPORE program dramatically increased the impact of translational research. SPOREs in multiple organ sites have legitimized and advanced translational research, creating a new career path for joint clinical and basic science investigations. As befitted a new program area, the SPORE structure created self-contained, large research programs with a critical mass at single institutions (often cancer centers) and provided for career development, core resources, and pilot projects.

### *Realign the Rates of Growth of the P30 and P50 Programs*

The Working Group was charged with setting clear priorities to accommodate goals in view of prospects for more moderate growth in the NCI budget in future years. Indeed, as outlined earlier in this report, there is now an expectation that funding may be limited for the next few years, requiring critical funding priority decisions. The Working Group recognizes the need to consider these programs in light of budget constraints, but emphasized that both programs are outstanding and could benefit from significant funding expansion. Both programs are vital components of NCI's translational research efforts and must be sustained, even in today's challenging financial environment.

> **Over the next five years the SPORE budget should grow at a rate no greater than that of the RO1 budget, and the rate of growth of the Cancer Centers Program budget should be slightly above that of the RO1 budget.**

Cancer centers in particular provide the research infrastructure needed for an increasingly complex array of discovery-oriented translational and clinical research objectives. Given the growing need for infrastructure support and the expanded mandate that is implicit in subsequent recommendations, disproportionate growth of the Cancer Centers Program budget over and above that of the R01 pool is a high priority.

In contrast to the slow growth of the Cancer Centers Program budget in recent years, the SPORE program budget has grown exponentially and now is nearly 50 percent of that of the Cancer Centers Program. Although the Working Group believes that the impact of this program on translating research from bedside to clinic has been substantial, it also believes that program growth should be slowed and only grown at a rate that is feasible in the context of NCI's budget. Subsequent recommendations in this report offer mechanisms to create greater flexibility in the program that will allow additional projects to be funded and current competitive SPORES to remain funded.[2]

### *Phase Out the P20 Awards*

Since 1992, NCI has funded 25 P20 planning grant awards, with 2 institutions receiving 2 each. Six of the 25 awards are still active as P20s; two of these are second P20s for the institutions involved. Of the remaining 19, 7 made a successful transition to a P30. An additional institution has applied for a P30 and is awaiting a final summary statement from the parent committee. Eleven P20 applicants failed to make the transition to a P30—in some instances because they chose not to apply, in others because the score was not in a fundable range. Included in the 11 applicants are the first applications for the institutions that have been funded twice (a three-year gap between applications is required).

NCI has just issued a 2003 P20 solicitation for a center planning grant competition that will permit any institution currently poised to begin development an opportunity to compete for planning funding. Two of the 11 that failed to win a P20 in 2002 are reapplying in the 2003 round. Beyond this juncture, however, a moratorium has been recommended, because there are few institutions remaining with a sufficient NCI research award base that have expressed interest in becoming NCI-Designated Cancer Centers, but that lack the resources to submit directly a P30 application. In the meantime, several cancer centers have successfully competed for a P30 grant without first obtaining a P20 award.

**The P20 planning grant should be phased out after the next cycle.**

### *Create Flexibility in the SPORE Program and Integrate with the P30 Program*

During the last decade, the SPORE program dramatically increased the impact of translational research, an under-funded and under-appreciated area. Because translational research has now matured and budgets are flattening, NCI should seek integration, efficiency, and economies of scale between translational R01s, P01s, networks (such as Early Detection Research Networks [EDRN]), SPOREs, and cancer centers, and at the same time maximize the number of institutions performing translational research. To this end, some modifications of the current SPORE guidelines are needed.

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[2] A subsequent recommendation made in this report would result in a net transfer of funding from the SPORE to the Cancer Centers Program as more dollars are allocated to support shared resources within centers rather than SPORES. The funding levels recommended below are independent of those transfers. In other words, the centers budget should be allowed to grow as recommended, in addition to the transfers, while the residual budget for the SPORE Program should grow as recommended, without expectation that there will be compensatory growth to reflect the transfer of shared resource funding to the centers.

The current P50 mechanism provides funding for a broad range of research and developmental activities, from basic to human intervention studies. These grants are intended to promote multidisciplinary research focused on a specific cancer (or related cancer) site(s). SPORE grants differ from traditional Program Project (P01) grants in that they also provide support for pilot research projects and a career development program, as well as provide investigators with greater flexibility for modifying their research activities when new opportunities arise. The grants may be funded for up to five years.

SPORE grants have specific requirements that are fairly rigid: There must be at least four major research projects; there must be at least four investigators with peer-reviewed funding applicable to the organ site being investigated; there must be at least one project on cancer early detection or cancer prevention that is population-based; and there must be a tissue core with solid pathologic support to collect and store tissues and other biological specimens for study. Currently, the SPORE must be focused on a single disease site or related disease sites; grantees are not allowed to examine pathways of disease that may be common among different organ sites. The requirement for a population study also has budgetary ramifications, because these projects are usually more expensive than laboratory-based studies. This can lead to difficulty in proposing a minimum of four projects, along with career development and developmental research, with a total budget that must fall below the $1.7 million annual direct cost capitation. If NCI were to minimize the required components, the average size of a P50 grant could be reduced, which would permit more SPOREs to be funded.

Additionally, the present ad hoc structure for the review of SPOREs does not promote uniform review standards and does not allow one committee to evaluate balance in the SPORE program. The creation of a SPORE parent committee similar to the cancer centers parent committee would facilitate the assessment of the science (translation and clinical impact) more evenly than do ad hoc committees, and could realistically set budgets that are consistent with what is needed to perform research across the SPORE program. If the requirement for a set number of projects were omitted, a rigorous two-stage review would also allow funding for only the most meritorious components of an application. In addition, if SPOREs were allowed to focus on cancer control and population science as stand-alone research projects, including research across organ sites, these changes should result in the funding of more SPOREs with a lower average cost. SPOREs should also be encouraged to do work in under-developed research areas, including organ sites not currently funded. This could be accomplished by eliminating the current structure of a set number of SPOREs for designated disease sites.

**The SPORE program should be modified to allow greater flexibility (e.g., non-organ specific concentration), fewer projects (e.g., two versus the required four), and greater integration with the P30.**

**The SPORE program should employ a two-tiered system of review, with a parent committee managing the program in its entirety.**

### *Facilitate Collaboration and Sharing Among Centers and SPORES*

The SPORE program has grown extremely rapidly over the past decade. By the end of FY 2003, the P50 program budget will represent at least 50 percent of the budget of the P30 program. The

average P50 award is relatively large compared to the average award for individual cancer centers. Specifically, nearly half of cancer centers (29) have annual awards that are less than the average award for one SPORE grant. The vast majority of P50 awards (41 of 44) are made to institutions with an NCI-funded cancer center. To a large extent, the SPORE program has evolved as a mechanism for funding translational research within cancer centers without a formal linkage between the two programs.

Although the Working Group is supportive of continued growth of the SPORE program, it offers several recommendations that will, if implemented, expand the scope of the centers program funding mechanisms. Although both the cancer centers and the SPORE programs are models of success, perceived differences in their missions have impeded collaboration between them. Even though there is no programmatic conflict between the P30s, which are primarily infrastructure grants, and P50s, which fund research as well as infrastructure, the sharing of resources is not always planned or implemented through either. And, although many SPOREs are housed within cancer centers and often are an integral part of the Cancer Centers Program, such relationships are the product of individual and institutional leadership and are not necessarily a result of any formal arrangement or conditions imposed by NCI. In some cases, a disconnect between the two programs at the same site can be found because the center directors have no authority or budget to impose on SPOREs to do collaborative translational research, and there is no NCI mandate to combine shared resources, where appropriate, for greater efficiency.

The Working Group believes that core components of each program, such as databases, informatics, clinical trial support, gene expression and proteomics databases, and tissue banks, could be shared or consolidated. Wherever possible, these cores should be pooled and shared to reduce duplication and to create synergy. It is the opinion of the Working Group that when a SPORE is located at a cancer center it should function as a component of the center, as experience has shown that SPOREs can be effectively managed in this way. During the proposed review of the SPORE program, NCI should carefully review the core components to assess how well they are integrated with those of the cancer center.

If policies were imposed to minimize duplication and fragmentation across the P30 and P50 programs, the resulting cost savings could be used to fund more research and improve the geographic distribution of awards**.** In addition, NCI could act to strengthen the network of centers in the same way it has facilitated networking of SPOREs. For example, NCI could bring the center directors together to discuss science, not process, and explore ways to encourage inter-center consortia.

As noted earlier, overlap occurs in funding mechanisms for support of shared resources. The Working Group acknowledges that a single source of grant funding may not be sufficient to fully support a shared resource, but believes that efforts should be made to encourage institutions to focus their funding from multiple sources into individual shared resources rather than create multiple entities that are dedicated to the same technology but funded through different mechanisms. These considerations led to the following recommendation:

> **Integration among centers and SPOREs should be facilitated by NCI and included in the guidelines for each program so that such efforts can be considered and rewarded through the CCSG review process. In addition, NCI should harmonize the guidelines for P30s, SPOREs, CCOP, and cooperative groups to create more explicit**

**and encompassing language to describe shared resources that can be included in the grant. NCI should organize initiatives to consolidate some cores (e.g., informatics, tissue banks) across these research entities if such centralization will improve the quality of the science, increase access to material and information, and boost administrative efficiency.**

### Enhancing and Expanding Cancer Center Resources

The Working Group concludes that, despite its unique role in bridging scientific knowledge and improved health, the centers program in particular has not been allowed to evolve as freely as have other aspects of the National Cancer Program. Rather than creating flexibility that promotes innovation within the centers program, NCI has created new programs. The Working Group recommends that, instead of establishing separate structures, NCI should look first to the centers as a mechanism to implement new programs. Overall, NCI leadership should view the cancer centers as a critical resource for policy and planning and as an agent of change in a national strategy to combat cancer.

**NCI should take better advantage of the entrepreneurship and vitality of cancer centers. Center directors should become a regular part of the NCI strategic planning process and should be provided the opportunity to offer guidance in developing new NCI initiatives and disseminating research findings.**

**As recommended by the 1996 Cancer Centers Review Group, cancer centers should be given more latitude to experiment with novel structures and program portfolios. NCI should look to the centers for piloting specific research solicitations, not only to support research in the cancer environment, but also to build an integrated cancer research system.**

#### *Address Geographic Distribution by Creating Hubs with Collaborating Organizations*

Over the years, considerable effort has gone into ensuring that the cancer centers are distributed widely so that most or all patients in the United States, at least in principle, have access to an NCI-Designated Cancer Center. Further, a broad regional distribution is thought to enhance the ability of centers to influence the quality of care throughout the country by setting standards and reaching out to their communities through the dissemination of knowledge. The planning grant mechanism (P20) was established to facilitate the establishment of centers throughout the country; however, other mechanisms should be sought to broaden the geographical impact of existing centers.

The deliberations and recommendations of the Working Group represented an evolution and extension of the deliberations of the last centers program review. The 1996 committee recommended the formation of a cancer centers forum to share information, especially population-specific information. According to the 1996 committee's report:

> 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 them.

A pressing unmet need remains for extending NCI programs into areas that currently are not served by an NCI P30-supported cancer center, although a number of such geographically under-represented areas do have institutions that have near-term potential for significant, but more limited, specialized activities of the kind that would be encompassed by a full cancer center.

**To improve the geographic reach of cancer center activities, the P30 should include new mechanisms for promoting formal relationships with other academic institutions that do not have P30 support.**

The Working Group envisions the development of formal relationships with other academic institutions as a strategy for extending geographic distribution, rather than continuing to attempt to cultivate free-standing cancer centers in smaller academic institutions in currently underserved areas of the country. Ideally, each center could establish a formal relationship with an organization from two or more of the following categories:

- Regional academic institutions that cannot qualify for a P30 grant, but that have substantial research activities in the clinical, basic, or population sciences.
- Community medical centers or oncology practice groups with a substantial commitment to clinical and/or translational cancer research.
- State agencies, health departments, or community service organizations that can participate in research or demonstration projects with the center.
- Another NCI-Designated Cancer Center for collaboration on projects that leverage the strengths of each.

These collaborating centers should be able to apply for infrastructure support through a mechanism similar to that used to support cancer centers at minority-serving medical schools (U54 awards) or as a P30 supplement for time-limited projects. In this context, the P30 center would provide leadership, coordination, and integration of activities and might also provide services such as data management, access to shared resources, or a clinical trials office. Any of these activities might be funded through the P30 mechanism, included in the budget of the new collaborating centers as a pass-through to the P30 centers, or included in a grant supplement.

This model builds on an existing program, funds new centers, and permits the established P30 awardee funding to provide access to core facilities and programs that can support and complement the specialized but narrower range of activities at the partner institution. As such relationships grow and prosper, they will "help fill in the map" to bring outreach and research to more areas of the country. The program will benefit both the parent P30, by strengthening its own capabilities in specific areas of collaboration, and the new specialized center, by providing access to a much broader range of discovery, development, and delivery vehicles. Ultimately, specialized centers over time may maintain a stable partnership or they may choose to evolve a broader range of activities that would permit their eventual development into a fully independent P30 applicant.

***Facilitate the Roles of Centers in Dissemination and Delivery***

Efforts to improve the care of patients with cancer occur along a continuum that ranges from the discovery and dissemination of new knowledge to the delivery of care. In general, centers have been and should continue to be the engines of discovery, centers where new knowledge is generated that has broad impact on the care of patients whether they are treated in an NCI-Designated Cancer Center or in a community oncology practice. Effective dissemination of new knowledge and the successful application of new findings are critical to achieving the benefits of research. For example, cancer patients and the advocacy community see cancer centers as not only focal points of cutting edge research, but also as hubs of evidence-based care, where the latest research findings are being applied to the benefit of patients. As such, cancer centers are important community and regional resources that provide information and education about cancer to the public and to community leaders.

The Working Group believes that all NCI-Designated Cancer Centers (not just comprehensive cancer research centers) should make an effort to meet the needs of their communities. However, no cancer center should be expected to develop these programs without commensurate funding to develop and/or sustain quality services. Supplemental funding should be considered to allow cancer centers to widely disseminate pertinent information in numerous formats (e.g., print, electronic media) to their regional communities.

Without directed funding, passive dissemination of information is more likely to occur, which can be slow, taking as long as 17 years from original concept to wide application through the published literature**.** If cancer centers are to take the lead in translational and innovative clinical research, a proactive process must be in place for rapidly moving interventions into the hands of practitioners.

Because cancer centers are community based, they can achieve what NCI cannot by making essential connections with grassroots groups (e.g., advocates, physicians, educators). Cancer centers, because of their stature and visibility, also can reach out to other academic institutions, community hospitals, oncology practices, and public institutions (such as state health departments). In particular, with adequate funding and rewards for doing so, centers can reach regions that are currently not served by an NCI-Designated Cancer Center.

In addition to modifying P30 and P50 reviews to include assessments of outreach and dissemination, research is needed regarding effective dissemination methods. Most cancer center control-related funds are not being spent on diffusion and dissemination, but rather on epidemiology and

behavioral research. Only nine centers mentioned dissemination in mission statements or other documents—and four of these were associated with schools of public health.

The Working Group's survey of cancer centers has shown that the P30 funds are highly leveraged by funds provided by the institution through state support, endowment income, or philanthropy. These funds undoubtedly support knowledge dissemination and community outreach efforts. However, the Working Group concludes that identifying these areas as priorities through the P30 funding mechanism can enhance the centers' roles in dissemination of new knowledge and community outreach. For example, funds could be requested to establish an office of dissemination and outreach with dollars allocated to support leadership and staff. Revision of the guidelines would be necessary to identify this component of a center as a potential use of cancer center funding, with the development of appropriate review criteria to evaluate effectiveness.

> **The P30 award should be modified to encourage and support centers to develop infrastructure and test novel methods for disseminating new knowledge in clinical, cancer control, and early detection research. Appropriate review criteria should be developed to evaluate the effectiveness of centers that elect to make use of this funding mechanism.**

Centers must also develop ways to find funding for dissemination and outreach through partnerships. For example, the American Cancer Society and the Centers for Disease Control and Prevention (CDC) have programs already in place for outreach and dissemination, including important registries and cancer screening programs at CDC. NCI can play an important role in enhancing interactions between centers, SPOREs, and state cancer programs by including funding for dissemination and outreach in the CCSG. Although there is no expectation that the cancer center support grant would fully fund such efforts, monies allocated through grants for these activities should be highly leveraged by local support. Indeed, centers should be encouraged to seek funding from CDC to support their dissemination and outreach efforts.

> **Cancer centers should actively seek links, where appropriate, with state health departments, CDC, and other agencies in their state. Funding through the P30 should provide staff support for these activities. Centers should be rewarded in the review process for proactively pursuing involvement, where applicable, in developing state cancer plans.**

### *Support Clinical Investigators*

Funding for the staff investigator category of the P30 award has diminished since the origins of the program because it was believed to be costly and difficult to review for quality and was seen as an entitlement that basic scientists did not receive. In 1996, the Cancer Centers Review Group emphasized the importance of the staff investigator category, especially for short-term or startup support directed toward new research initiatives. This Working Group concurs with that recommendation.

There has been ample description of the steady decline in the number of physicians who are willing or able to spend the time needed to learn, develop, and sustain a career as a clinician seeing a

substantial number of patients and who also participate in clinical trials and translational research. This decline has occurred in part because the economic barriers of medical school debt and declining professional and hospital reimbursement force clinicians to care for patients to the exclusion of time for research. These clinician-investigators should be viewed as a critical resource in a cancer center and should be supported through the P30 mechanism for their research time.

> **Physicians with major clinical responsibilities and who play important roles in clinical trials development and execution should be eligible for partial salary support through the CCSG. Such individuals should be considered an essential resource of the clinical trials enterprise.**

### *Streamline Review of Clinical Trials and Strive for Better Coordination*

Stunning advances in our understanding of basic cancer biology have occurred during the past two decades. Our growing understanding of genetic instability, the mechanisms of apoptosis, self-sufficiency in growth signals and insensitivity to anti-growth signals, sustained angiogenesis, tissue invasion and metastases, the strategies by which cancer cells develop immune tolerance, and the mechanisms of limitless replicative potential have uncovered many potential therapeutic targets. Clinical research is a wide-ranging and complex endeavor that applies fundamental knowledge about disease processes to the development and testing of new diagnostic and therapeutic advances and that, conversely, relies on clinical observations to pose research questions for the laboratory. Clinical trials are the mechanism for the testing of new approaches to cancer prevention, diagnosis, and treatment. As such they are a critical component of the National Cancer Program and NCI's research program.

Comprehensive and clinical cancer centers and SPOREs can be major sources of innovative clinical studies that can later be exported to cooperative groups or into general medical practice. In addition, basic science cancer centers can serve as the source of new approaches and as a location for reverse translation—that is, exploration at the basic level of observations made in the clinic. Thus, cancer centers are in a unique position to 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. SPOREs have been particularly focused on transition from the laboratory to the clinic and have already developed drugs and markers that are changing clinical practice.

However, the systems for conducting NCI-supported clinical trials, regulatory requirements imposed by FDA and IRBs through the Common Rule (45 CFR 46) have created a highly inflexible environment for the evaluation and testing of novel therapeutic agents for the treatment of cancer. Moreover, NCI's systems of clinical trials review and support are highly complex and are often unable to respond quickly to new therapeutic opportunities, as witnessed by the evolution of a separate clinical trials network in the context of the SPORE program.

NCI clinical trials are supported through a number of mechanisms, including the Cancer Therapy Evaluation Program (CTEP), which includes the Cooperative Groups Program, the Community Clinical Oncology Program (CCOP) of the Division of Cancer Prevention, and through the Cancer Centers Program. Hundreds of clinical trials, especially in their earliest stages, are supported through

these and other research mechanisms, such as individual research grants, program project grants, cooperative agreements, and contracts.

In FY 2002, the Division of Cancer Treatment and Diagnosis CTEP had 3,300 clinical trials sites involving 11,000 investigators. There are nine cooperative groups with thousands of members, some of which are located at cancer centers and involved in SPOREs. Most cancer centers participate in at least one cooperative group, and some participate in as many as six or seven.

CCOP is an NCI mechanism managed within the Division of Cancer Prevention that links community cancer specialists and primary care physicians with clinical cooperative groups and NCI-Designated Cancer Centers to conduct cancer treatment, prevention, and control clinical trials. There are 50 CCOPs and 11 Minority-Based CCOPs in 35 states, the District of Columbia, and Puerto Rico, with approximately 400 participating hospitals in which approximately 4,000 physicians enter patients into trials. In FY 2002, CCOPs entered approximately 7,000 patients into cancer treatment clinical trials, accounting for about one-third of all patients in NCI Phase III treatment efficacy trials. The groups rely on cancer center members for scientific leadership, core resources, and patient accrual

Cancer centers are involved a wide variety of clinical trials supported through NCI or other NIH institutes, industry, or internally. In 2001, the cancer centers reported more than 30,000 individuals enrolled in Phase 1-3 clinical or epidemiological trials, playing a vital role in the clinical research enterprise. Centers can exploit scientific opportunities to develop ideas, fund opportunities, mentor young investigators, provide access to special populations and core resources, connect with the community, interface with advocates, coordinate regulatory oversight, and train research staff from groups.

In addition, new anti-cancer agents are being studied in patients for the first time in Phase I and II clinical trials under NCI Investigational New Drug (IND) sponsorship in institutions funded by NCI cooperative agreements. NCI's Developmental Therapeutics Program has numerous drug development initiatives located at cancer centers and SPOREs. In addition, many of the approved applications in the RAID program come from center and SPORE investigators.

Thus, there are many overlapping relationships in NCI's clinical trials program. The cancer clinical trials system is complex and involves many collaborators, including investigators, physicians, industry, academia, and NCI. Interactions between these groups range from formal, to ad hoc, to nonexistent. Moreover, the methodologies used by the various groups are often different and therefore not interoperable. In 1997, the NCI Clinical Trials Review Group described the clinical trials methodologies used by the then 11 cooperative groups and 51 cancer centers as a "Tower of Babel," in which protocol format, clinical endpoints, data collection forms, informed consent, toxicity criteria, and computerization of data differed among groups. Only NCI is in a position to improve uniformity and communication among these disparate groups that are all seeking the same goal. Yet, all of these programs are managed by different components within the organization.

NCI's challenge is to improve collaboration in order to leverage the resources that flow into all of these research structures. For example, CCOP's rules prevent them from conducting Phase I and II trials with cancer centers. In addition, collaborations with industry, for example for tissue banking, are encouraged in cancer centers but discouraged for SPOREs. NCI should harmonize the guidelines for each structure and resist the temptation to build new structures that divert resources

from research. Before initiating another program, NCI should first assess whether it can best be conducted through or in collaboration with the center or SPORE programs.

In addition, NCI review of clinical trials is sometimes slow and redundant with other peer reviews. To move translational research findings more quickly into trials requires improved efficiencies.

**NCI review of clinical trials that are supported by peer-reviewed funding mechanisms should be limited to safety and regulatory issues and should focus on facilitating rapid implementation of trials. Specifically:**

**a. NCI immediately should implement the following:**

1) **eliminate CTEP review of grants or Phase I and II studies unless CTEP holds the IND;**
2) **impose a 30-day turnaround on those studies requiring review.**

**b. Over the next year, NCI should:**

1) **develop a plan for improved coordination of all clinical research mechanisms, including cooperative groups, phase 1 and 2 contracts, SPORES, and centers;**
2) **convert the funding mechanism for cooperative groups and Phase I and II studies from a contract to an assistance mechanism.**

### *Improve Compliance with Regulatory Requirements while Increasing Efficiency*

The anticipated evolution of cancer therapeutics toward the development of agents targeted to specific molecules and pathways within cancer cells requires a capacity to rapidly move such agents into clinical trials in combination and to include drugs in combinations that are inactive when tested singly. A major regulatory barrier to effective clinical investigation is the need for the review of a single protocol by more than one IRB. The long-standing focus on local review has necessitated the consideration of cooperative group protocols and collaborative studies by multiple IRBs, often leading to disagreements in protocol design and disparities in the development of informed consent documents. Despite recommendations by the National Bioethics Advisory Commission (2001)[3] and the Institute of Medicine (2002)[4] for the adoption of "central IRBs," movement in this area has been slow because local IRBs have a strong sense of responsibility and legal liability for the research conducted within their center. The Office for Human Research Protections (OHRP) has yet to exhibit significant leadership in resolving this impasse.

**NCI should work with OHRP to engage cancer center IRBs in developing a strategy for centralized review of multi-center trials.**

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[3] National Bioethics Advisory Commission. 2001. Ethical and Policy Issues in Research Involving Human Participants (Washington, DC: US Government Printing Office).

[4] Institute of Medicine. 2002. Responsible Research: A Systems Approach to Protecting Research Participants (Washington, DC: National Academy Press).

***Support Clinical Bioinformatics***

Bioinformatics, particularly in support of clinical research, remains a major concern of the Working Group. The 1996 Cancer Centers Review Group emphasized the need to facilitate information exchange as outlined below:

> 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.

The Working Group perceives that relatively little progress has been made in responding to these recommendations and reiterates the importance of the 1996 Review Group's recommendations in this area.

The Working Group concludes that there is a compelling need to create rapidly a national clinical trials research and informatics system using common data elements and open source programming that could be locally expanded or modified. This effort should involve the cancer centers, AACI, the pharmaceutical industry, and various components of NCI, including cooperative groups. The goal is to achieve seamless data exchange across NCI, cancer centers, SPOREs, cooperative groups, the

pharmaceutical industry, and FDA. The Working Group estimated that a $100 million investment would be required, and a suggestion was made that at least 50 percent of this be sought from the pharmaceutical industry.

**NCI should make the creation of a national clinical research and informatics system a priority and ensure that its efforts are appropriately integrated with those of the centers, AACI, industry, and other interested parties.**

### *Support Clinical Trials Infrastructure*

NCI-supported clinical trials can have a tremendous impact on standard of care, which has a major impact on the way oncology is practiced in the United States. However, the process of moving basic laboratory discoveries to accepted and proven therapies for cancer patients is a long, arduous, and expensive one that must be made more efficient in order to improve the quality of the cancer clinical trials system. There are several key players in the clinical trial process including the scientific community, primary care providers and their patients, NCI through its various funding mechanisms, OHRP, IRBs, industry, and FDA. Those conducting clinical trials must be knowledgeable about and sufficiently staffed to work with all of these parties. Without proper resources, the clinical trials system is likely to remain inefficient, unresponsive, and unduly expensive.

Funding for core support of clinical trials is sorely needed. Accruing patients, maintaining databases, and ensuring compliance with regulatory and legal requirements are real costs of conducting clinical research. In addition, major intellectual property and confidentiality issues exist in working with the private sector. If NCI would like the centers programs to be more active in translational research, then it must ensure that P30 funds are used, as appropriate, for the services that support translational and clinical trials infrastructure, including, for example, clinical trials offices; biostatistics; database development and clinical informatics; and protocol review and monitoring committees.

Historically, the P30 has been focused on providing funding for the infrastructure required to conduct a broad range of research activities. Particular emphasis has been placed on the support of laboratory-based research, although over the past decade progressive emphasis has been placed on providing appropriate infrastructure for clinical research as well. Although this is encouraging, shared resources to support cancer prevention and control research have remained limited to a few centers. The Working Group supports a continued effort to distribute the infrastructure support provided by the P30 over a broad spectrum of shared resources.

**The shared resources mechanism of the P30 should be revised to provide more appropriate funding for critical and under-funded activities, such as tissue banks and data management, and for essential new exigencies, such as regulatory compliance.**

**To further support infrastructure, NCI should explore mechanisms by which funds could be provided on a matching basis with funds raised by cancer centers from private and philanthropic sources.**

***Streamline the P30 Review Process***

The purpose of the P30 is to promote excellent research toward the goal of reducing cancer incidence, morbidity, and mortality. The funds are intended to provide a focus and a stimulus for cancer research and should be evaluated on this basis. In 1996, the Cancer Centers Review Group recommended that centers should be primarily reviewed for the quality of science, and such review should be based on the "value added by the center grant to the advancement of excellence in all appropriate areas of cancer research." This Working Group reiterates the importance of that recommendation and encourages NCI to explore ways to implement it. Although a P30 directly supports only a small portion of the research conducted in a cancer center, reviews should focus on the difference that the funds have made in promoting research, enhancing cooperative interactions, and developing new initiatives. Review efforts should concentrate on the extent to which the infrastructure support has been used to improve the research efforts of the center.

The Working Group believes that despite recommendations by the 1996 Review Group that the review process be streamlined and made more efficient, a burdensome and costly review process in still in place that often overlooks the value of the science being produced. Too much focus remains on the administrative aspects of the P30, with an inordinate amount of time being spent by reviewers analyzing budgets and core facilities. Centers spend far too much time preparing review materials that do not necessarily reflect the true culture and accomplishments of the center. In addition, the focus on administrative issues rather than scientific and clinical programs is a disincentive for senior scientists to serve as reviewers. In particular, the review process for P30s does not reward centers for translational research or for dissemination and communication activities. P30 dollars constitute a small percentage of what cancer centers do, and because the grant supports only infrastructure, that is all that is reviewed, with research and care activities, which are supported from separate sources, remaining unaddressed. Such a division is at odds with any effort to assess the overall impact a center has on cancer research or care.

In the future, cancer centers are likely to evolve into more diverse and complex organizations, and the peer-review system will need to adapt in order to focus on research accomplishments, while NCI staff conducts administrative review largely through electronic means, with input from cancer center administrators. This would be facilitated through the development of a universal software program that could be used by all centers to collate and submit required information. Clinical trials data should be uniform and plastic so they can be used for a variety of purposes. Site visits should be carried out to address substantive issues that cannot be resolved in other ways, for example, new centers, a change of center director, or a dramatic change in research productivity.

**The review process should undergo a major modification to increase efficiency. As recommended by the last Cancer Centers Review Group, the primary review should address the quality of the science and the synergism of the center. Examples of time- and cost-saving modifications that should be made to the review process include the following:**

- **Initial review of competitive renewals should be conducted by a parent committee.**
- **NCI staff should review the administrative and procedural aspects of the grant necessary for fiscal accountability.**

- **Site visit review of administrative issues should be restricted to issues of concern uncovered by the initial parent committee review or found by NCI staff.**
- **Site visit review should be reserved for new applicants and for centers seeking more than a 10 percent increase in the amount of their grant.**

The P30 review process offers little reward for activities that are central to the mission of NCI, which is not only to make discoveries, but also to disseminate the new information to the public and the broader research community. The P30 Guidelines and review process should expand the review guidelines to include and reward clinical care and local, regional, and national cancer leadership. Overall, the review process should focus on what cancer centers really do and the value added by the P30 award.

### *Improve Metrics and Processes for the Awards Process and Program Evaluation*

The funding ratio used in making awards originally was intended to control expenditures and allow for growth in the program. Thus, it was originally intended to serve as a cap rather than a benchmark or "moving target," which is what it has become. In addition, using NCI funding (in particular, RO1s) as a measure against which to award funds is likely to penalize centers conducting more clinical and translational research. The Working Group concludes that the NCI-funded research base as a parameter on which to base budgetary calculations for individual centers is too restricted and that methods should be found within the guidelines to recognize and reward outstanding efforts of individual cancer centers across a broad spectrum of effort, including dissemination and outreach.

**NCI should initiate a planning process to develop quantifiable metrics for determining the size of the P30 award that reflects the broad spectrum of involvement of individual cancer centers in scientific discovery, dissemination of information, and delivery of care.**

The evaluation and documentation of the progress and success of the P30 and P50 programs would be of enormous value by allowing for the identification of flawed and successful strategies and thus helping to direct future efforts. The documentation of achievements would be useful in communicating to the external community the results of investment in the nation's P30 and P50 programs. Based on experience, Working Group members recognize the extraordinary difficulty of developing specific measures of achievement for programs that are as broad and diverse as these are, but they believe nonetheless that efforts in this area are required.

The Working Group recommends that, at a minimum, an annual survey of cancer centers should be conducted documenting their major achievements in developing new approaches to cancer prevention, detection, and treatment, as well as their role in disseminating these advances to the broader community. Identification of barriers to advances, as well as novel approaches to overcome such barriers, should also be identified. Similarly, leaders of P50 grants should provide brief annual summaries of their achievements in developing novel and effective approaches to cancer prevention, detection, and treatment. The earlier recommendation made in this report to establish a parent committee for the SPORE program and a two-tiered level of review will provide new means by which to assess the overall impact of the SPORE program.

Although it is questionable whether it is possible to establish a meaningful list of five-year goals for the P30 and P50 programs, the Working Group would be deeply disappointed if, in five years, the combined programs had failed to identify new leads to cancer prevention, new tests proven capable of early detection, and a series of FDA-approved new cancer treatments. Most importantly, one would hope to observe a continued downward trend in age-specific cancer incidence and mortality and substantial diminution of disparities between populations based on race or ethnicity.

# V. SUMMARY: "IDEAL" FEATURES OF NCI-DESIGNATED CANCER CENTERS AND SPORES BY THE YEAR 2012

One of the charges to the Working Group was to envision what the cancer centers and SPORE program should look like in 2012. The Working Group vision for each program follows.

### Characteristics of the Cancer Center of the Future

The characteristics of an ideal cancer center of a decade from now will vary because of differences in type (comprehensive, clinical, basic, population), location (large metropolitan area with several centers or more sparsely-populated areas), structure (free-standing or matrix), and resources. However, some features will apply to virtually all centers.

- **A Hub with Several Collaborating Regional Organizations**

Each center will have a formal relationship with two or more institutions, including regional academic institutions that cannot qualify for a P30 grant; community medical centers or oncology practice groups with a substantial commitment to clinical and/or translational cancer research; state agencies, health departments, or community service organizations that can participate in research or demonstration projects with the center; or another NCI-Designated Cancer Center for collaboration on projects that leverage strengths in each—for example, on a large-scale science project. The P30 center would provide leadership, coordination, and integration of activities and might also provide services such as data management, access to shared resources, or a clinical trials office. Any of these activities might be funded through the P30 mechanism, included in the budget of the new collaborating centers as a pass-through to the P30 centers, or included in the grant supplement.

- **Preferred Testing or Launching Sites for Novel NCI Programs**

The NCI cancer centers are uniquely suited with their existing infrastructure to test or launch new programs. For example, large-scale science initiatives and the development of informatics systems for clinical or basic research, perhaps in collaboration with other NCI-Designated Cancer Centers, would be relatively easy to launch from an existing center, and, just as important, would be easier to phase out because the cancer center infrastructure would continue its traditional activities. The center directors should be engaged regularly by top NCI leaders to suggest and consider such novel programs.

- **Clinician-Investigators Supported as Essential Resources in the Clinical Trials Enterprise**

The numbers of physicians willing or able to spend the time needed to learn, develop, and sustain a career as a clinician who sees a substantial number of patients and who also participates in clinical trials and translational research has suffered a steady decline. These clinician-investigators will be viewed as a critical resource in a cancer center and will be supported through the P30 mechanism for their research time.

- **Incubator for High-Risk, High-Reward Initiatives**

Some centers will be able to undertake projects that would be supported and reviewed differently than their traditional activities. Centers would be the ideal places to take chances with novel structures and projects that would be difficult or impossible to fund in the traditional and conservative peer-review climate. Qualified centers could support a micro version of Bell Labs for cancer research that would pursue directions that are promising but not conventionally fundable. Only senior, experienced reviewers could be used for the peer review of such projects.

- **Review and Data Submission by a Sophisticated New System**

Cancer centers will have evolved into more diverse and complex organizations, and the peer-review system will have adapted to focus on research accomplishments, while administrative review will be conducted by NCI staff largely electronically, with input from cancer center administrators. The process will be facilitated by the new universal software program used by all centers to collate and submit the required information. Clinical trials data will be uniform and plastic so they can be used for a variety of purposes. Site visits will be carried out to resolve substantive issues such as new centers, a change of center director, requests for large increases in budgets, or a dramatic change in research productivity.

## Characteristics of the SPORE of the Future

- **A distinct research program with its own identity that produces respected translational research**

The SPORE program will flexibly fund diverse types of innovative translational research, including both organ-site specific research and thematic research that uses information about common cancer pathways to make clinically useful discoveries for cancer detection, diagnosis, and treatment. Population science will continue to be an important and encouraged component, but not every SPORE will be required to undertake population research. Population studies also can be submitted as stand-alone translational research projects. SPOREs can have as few as two projects, with budgets set in proportion to the work to be undertaken, and flexibility is retained within the grant for rebudgeting as priorities change or new discoveries are made. The $1.75 million budget cap is maintained to accommodate large projects when they are merited. The SPORE program identity is maintained through an annual meeting, separate administration and program office, career research opportunities, and separate peer review.

- **A grant mechanism that functions like a program project grant for translational research that is fully integrated into the cancer centers**

There is a formal requirement for institutional support that includes funds for developmental research, career development, and programmatic support for the SPORE. The responsibility for core infrastructure is shifted to the cancer centers or comparable institutions, and SPOREs take advantage of the core resources present in cancer centers that support tissue acquisition, bioinformatics, biostatistics, and grants administration. Cancer centers participate fully in developing shared structures for organ-specific resources that are used in common by SPOREs, such as tissue and serum banks, custom microarrays, common data elements, and shared protocols for pilot studies.

- **A dynamic program that encourages and supports collaboration and innovation**

Novel approaches developed within P50s are piloted by inter-SPORE collaborations and adopted by the cooperative groups for Phase III trials. SPOREs work with the EDRN, Director's Challenge, and other NCI-supported entities to maximize translational impact. Sharing of resources and research involving more than one SPORE are encouraged and rewarded.

- **Review by a two-tiered system that includes a parent committee to maximize uniform standards and balance with in the SPORE network**

Review of SPORE applications is carried out by a dedicated and experienced parent committee bolstered by ad hoc reviewers with the needed expertise. The parent committee sets a consistent policy in defining translation with more flexibility in both organ-specific and pathway-specific research. Translational excellence is the overarching criterion for funding, encompassing the following elements: novel and effective approaches to prevention, detection, and treatment; better understanding of the biology of cancer from different sites at the clinical, cellular, and molecular levels; publication of studies that define disease site biology; design and implementation of hypothesis driven clinical trials; logical plans for drug and biomarker development for clinical use; and deliberate progress toward translational achievements. The review system also understands and allows well-designed hypothesis-generating studies as well as hypothesis-testing studies. Consistent value is placed on collaboration with other SPOREs and networks.

- **A program that serves as a focus for disease site activities in the community**

Advocacy groups are actively involved in SPORE activities, and SPOREs assist advocacy groups in educating the public and promoting the prevention and early detection of cancer. The level of care is raised by successful treatments that are developed through translational research.

- **A program that has a high impact on cancer prevention and treatment**

An evaluation after at least 25 SPORE grants had been funded for 10 years shows that the ability to detect and treat cancer of specific organs has substantially improved. In addition, discoveries from the SPORE program have demonstrated the efficacy of drugs for cancer prevention that will reduce the incidence of cancer in the future.

# VI. CONCLUSIONS

This report contends that NCI-Designated Cancer Centers and the associated SPORE program are central to discovery and represent the best, most practical national network for testing and disseminating innovations that reduce cancer mortality. The strategic directions discussed in this report will further improve the ability of cancer centers and SPOREs to translate and disseminate research advances.

Unfortunately, over the next several years overall NCI resources will at best be constrained and at worst be reduced. Thus, in the short term, implementation of recommendations that require funding can be accomplished only through 1) ensuring flexibility in the P30 and P50 mechanisms; 2) re-budgeting NCI funds, both within and outside the Cancer Centers Branch to achieve economies of scale; and 3) facilitating and establishing partnerships, such as those with industry for informatics and with CDC for dissemination initiatives.

However, because the opportunities are too great and the task too important to ignore, the Working Group looks to NCI leadership—with the help of cancer centers and SPORE leadership, advocates, and others—to seek substantial increases in funding for the P30 and P50 programs over the next three to five years. The benefits to delivery, dissemination, and coordination will be easily demonstrable. Full funding should result in an NCI-led, evidence-based outreach and dissemination effort; continuation of the world's finest discovery research infrastructure; a robust, integrated translational, clinical, and prevention trial apparatus that responds rapidly to innovation; increased patient accrual to clinical and prevention trials; new mechanisms for geographic coverage by the Cancer Centers Program; and an increase in the novelty and number of SPORE grants.

The cancer center and SPORE infrastructures, operating through the nation's leading public and private institutions, offer a critical link to the American people. Implementation and funding of these strategic initiatives will focus this unparalleled resource on discovery and development and will demonstrably enhance the delivery of the latest cancer prevention, early detection, and therapeutic advances.

**APPENDIX**
**INVITED SPEAKERS**

**July 17-18, 2002**

**Andrew C. von Eschenbach, M.D.**
Director
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**Robert C. Bast, Jr. , M.D.**
Vice President for Translational Research
University of Texas
M.D. Anderson Cancer Center
Houston, Texas

**H. Shelton Earp, M.D.**
Lineberger Professor of Cancer Research
Director
UNC Lineberger Comprehensive Cancer Center
University of North Carolina, Chapel Hill
Chapel Hill, North Carolina

**Jorge Gomez, Ph.D., M.D.**
Chief
Organ Systems Branch
Office of Centers, Training and Resources
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**John Hartinger**
Acting Deputy Director for Management
Office of the Director
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**Brian Kimes, Ph.D.**
Director
Office of Centers, Training and Resources
Office of the Deputy Director for Extramural Services
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**Arthur W. Nienhuis, M.D**.
Director
St. Jude Children's Research Hospital
Memphis, Tennessee

**Steven Rosen, M.D.**
Director
Robert H. Lurie Cancer Center
Northwestern University
Chicago, Illinois

**Joseph V. Simone, M.D.**
President
Simone Consulting
Dunwoody, Georgia

**Linda K. Weiss, Ph.D.**
Chief
Cancer Centers Branch
Office of Centers, Training and Resources
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**Max Wicha, M.D.**
Professor of Internal Medicine
Director
University of Michigan Comprehensive Cancer Center
University of Michigan
Ann Arbor, Michigan

**July 29-30, 2002**

**Joseph S. Bailes, M.D.**
US Oncology Inc.
Houston, Texas

**Olivia Preble-Bartlett, Ph.D.**
Chief
Grants Review Branch
Division of Extramural Activities
National Cancer Institute
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**Ellen Feigal, M.D.**
Acting Director
Division of Cancer Treatment and Diagnosis
National Cancer Institute
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Bethesda, Maryland

**Judith C. Gasson, Ph.D.**
Professor of Medicine and Biological Chemistry
Director
Jonsson Comprehensive Cancer Center
University of California, Los Angeles
Los Angeles, California

**Ronald B. Herberman, M.D.**
Director
University of Pittsburgh Cancer Institute
Pittsburgh, Pennsylvania

**Jon Kerner, Ph.D.**
Assistant Deputy Director for Research Dissemination and Diffusion
Division of Cancer Control and Population Sciences
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**Brian Kimes, Ph.D.**
Director
Office of Centers, Training and Resources
Office of the Deputy Director for Extramural Services
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**David E. Maslow, Ph.D.**
Section Chief
Research Resources Review Branch
Division of Extramural Activities
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**Joyce Niland, Ph.D.**
Chair, Division of Information Sciences
Director, Department of Biostatistics
Professor, Beckman Research Institute
City of Hope National Medical Center
Duarte, California

**Barbara Rimer, D.Sc.**
Director
Division of Cancer Control and Population Sciences
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

**Joseph V. Simone, M.D.**
President
Simone Consulting
Dunwoody, Georgia

**Dennis J. Slamon, M.D., Ph.D.**
Chief
Division of Hematology-Oncology
Department of Medicine
University of California, Los Angeles School of Medicine
Los Angeles, California

**Russ Toal**
President
Georgia Cancer Coalition
Atlanta, Georgia

**Linda Weiss, Ph.D.**
Chief
Cancer Centers Branch
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**August 14-15, 2002**

**Mary J. Hendrix, Ph.D.**
Kate Daum Research Professor
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