

**To Create a Strategic Scientific Vision for
the National Cancer Program and Review Progress of
the National Cancer Institute**

**Report of the National Cancer Advisory Board
Ad Hoc Working Group**

December 2010

December 7, 2010

National Cancer Advisory Board
National Cancer Institute
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Board Members:

On behalf of the National Cancer Advisory Board's Ad Hoc Working Group to Create a Strategic Vision for the National Cancer Program and Review Progress of the National Cancer Institute, we are pleased to submit this report, in which we assess the Institute's accomplishments and priorities in order to support the most promising new programs and research efforts.

After seven months of fact-finding and deliberation, the Working Group is fully convinced that the National Cancer Institute continues to be at the forefront of the Nation's cancer research effort and is at the center of the National Cancer Program. NCI faces many challenges in advancing cancer research in the coming decade. Some of these are described in the report. In regards to specific programs or topics, the Working Group primarily considered those that present opportunities for changes in direction and resource allocation by NCI. Recommendations are made to encourage and help facilitate these changes. We offer this report for review and action by the National Cancer Advisory Board.

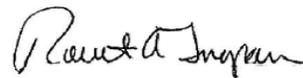
We and our colleagues on the Working Group are grateful for your unfailing support and encouragement throughout the course of our deliberations. In addition, we wish to acknowledge the invaluable assistance given to us by Dr. Paulette Gray and colleagues of the National Cancer Institute staff. We were also fortunate to have had the opportunity to hear from numerous members of the Institute staff through testimony delivered during the course of our discussions, as well as from leaders in the extramural and industrial communities.

We have all been privileged to serve the National Cancer Advisory Board and the National Cancer Institute in this manner, and we stand ready to answer any questions that may arise. We hope that our report will be of value to you, the National Cancer Advisory Board, and the new Director of the National Cancer Institute, in planning and setting priorities for the future.

Sincerely,



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NATIONAL INSTITUTES OF HEALTH
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Executive Summary

In February 2010, the National Cancer Advisory Board (NCAB) of the National Cancer Institute (NCI) established a Working Group to assess the current status of NCI's intramural and extramural research programs and to recommend actions NCI can take to meet future challenges in an era of limited budget expansion and rapid scientific change. NCI leadership and the Board recognize the need to identify and develop practices to revise and/or end programs that produce lower return in order to sustain successful programs, initiate new areas of scientific development, and support the most promising new scientific opportunities.

The Working Group met on three occasions over six months and heard presentations from current NCI leadership; former NCI Directors; leaders from various NCI divisions and programs; basic, clinical, and population scientists; Cancer Center leaders; leaders in academia, government, and industry; authors of the Institute of Medicine (IOM) report on NCI's clinical trials programs entitled *A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program*; and the current National Institutes of Health (NIH) and NCI Directors.

The Working Group focused its efforts on those scientific areas that present particular challenges and opportunities for changes in direction and resource allocation. It did not attempt to evaluate the scientific productivity of investigator-initiated research project grants, which are reviewed individually by study sections and have been the source of great progress over the past decade. It also did not focus on intramural laboratories, which are carefully and regularly reviewed by NCI's Board of Scientific Counselors (BSC). The Working Group did, however, examine NCI's intramural clinical research program in adult oncology as embodied in its Medical Oncology Branch (MOB), which has experienced significant recent changes in leadership and scientific focus, is critical to NCI's translational research mission, and is increasingly constrained by rising Clinical Center costs.

Engagement with the Private Sector

One of NCI's most important advantages is the ability of basic scientists, translational experts, and cancer clinicians to collaborate with industry to most efficiently bring advances in cancer care to society. NCI should also position staff and trainees in ways that encourage and facilitate productive interaction with industry colleagues and allow for information exchange and collaboration that respects the unique roles of both government and industry. The Working Group also encourages NCI to continue to support basic research that produces new knowledge and understanding of cancer. At the same time, in view of current fiscal constraints, NCI must consider its investments in drug discovery and development in regard to those of industry.

Conflict of Interest Policies

During its discussions, the Working Group was disturbed by the recently adopted NIH conflict of interest regulation that prohibits consulting engagements and other collaborative research relationships between NCI scientists and industry. Because such collaborations are essential for fulfilling one of the NCI's core missions, the Working Group considered whether this regulation should be re-assessed and revised.

Recommendation 1: The Department of Health and Human Services should permit NIH scientists to engage in ethically conducted and fully transparent consulting and

collaborative relationships and scientific collaborations with the private sector, including with Substantially Affected Organizations, as part of their official duties, provided that the scientists receive prior review and approval from their Institute Director and from the NIH Office of the Director. Such interactions should be encouraged as an important avenue to progress in cancer research.

Clinical Trials Programs

The Working Group recognizes the historical importance of the cooperative groups in conducting critical Phase 3 trials in children and adults with malignancies and in sharing its extensive databases and tissue banks for translational research. They also noted that there is a potential for the cooperative group trials to serve as a mechanism to: 1) examine the comparative effectiveness of new versus established therapies; 2) determine costs and benefits of new treatments; and, 3) test innovative concepts of targeted therapies in uncommon subsets of tumors.

The Working Group reviewed the Institute of Medicine report, was briefed by IOM committee members at its 7-8 July 2010 meeting, concurs with its findings, and endorses its recommendations.

Recommendation 2: The Working Group strongly encourages NCI to implement the IOM recommendations and recommends that the National Cancer Advisory Board be given regular progress reports.

NCI-Frederick

The NCI-Frederick facility provides NCI with a critical mechanism for responding rapidly to emerging research opportunities and public health needs. However, the Working Group is concerned that oversight of Frederick programs may be insufficient. For example, pilot programs have been established and significantly expanded without external expert review.

Recommendation 3: NCI should carefully review and evaluate its investment in the Frederick facility to ensure that resources are used for the highest priorities. The existing review process does not assure the appropriate transparency for a significant portion of the NCI budget. Thus, NCI should reassess the criteria and procedures that it uses to evaluate and approve new initiatives at NCI-Frederick. Additionally, ongoing NCI-Frederick programs should receive thorough regular review to ensure that they continue to serve the highest priorities of the Institute and make effective use of available resources. In particular, major initiatives such as the cancer Biomedical Information Grid (caBIG) and Cancer Human Biobank (caHUB) may require periodic assessment, reconsideration and review.

Recommendation 4: The NCAB should have the opportunity to offer its advice on proposed new and major expansions of the Frederick program prior to implementation. The Board should receive regular reports on the progress of current, new, or expanded initiatives/activities.

Recommendation 5: The NCI must determine whether the NCI Community Cancer Center Program, if retained, should be a Frederick activity, i.e., a contract supported program, or undergo the same competitive peer review process as Community Clinical Oncology Program (CCOPs), Minority Based-CCOPs, Cooperative Groups Program, and other programs that support clinical research.

Recommendation 6: The NCI should consider establishing a chartered committee to advise and evaluate ongoing activities at the Frederick facility.

Cancer Prevention Programs

The Division of Cancer Prevention (DCP) has conducted large-scale, high-profile, and expensive trials of hormonal interventions to prevent breast and prostate cancer, and its current drug screening and development programs have led to the development of numerous candidates for clinical evaluation. Even so, the Working Group could not determine whether the various DCP programs can effectively prioritize these multiple candidates. Of equal concern, these programs do not seem to connect effectively with basic science laboratories, large-scale genomics programs, nor with the NCI's therapeutic drug development or cancer control programs.

Recommendation 7: Given the clinical significance of cancer prevention and its scientific relationship to other NCI programs (e.g., therapeutic drug development, basic science, population genetics, environmental factors, and cancer control), consideration should be given to restructuring Division of Cancer Prevention to better integrate with other NCI research laboratories, and to achieve scientifically rigorous and productive research goals. A close working relationship with the Division of Cancer Control and Population Sciences (see Recommendation 8), Division of Cancer Biology, and with the Division of Cancer Treatment and Diagnosis would result in enhanced synergies and more effective use of resources.

The Division of Cancer Control and Population Sciences has undertaken significant efforts to forge productive relationships within NCI and NIH, including relationships with other HHS agencies. Examples are collaborations with the Centers for Disease Control and Prevention (CDC) and the American Cancer Society to improve cancer surveillance and with a variety of agencies for tobacco control. The division has supported excellent population and behavioral science research initiatives. Particularly noteworthy is its research portfolio in genome-wide association studies and the impact of genetic variation on human cancer risks.

Recommendation 8: The Division of Cancer Control and Population Sciences has forged important collaborative relationships within and outside NCI. These efforts are essential to an effective cancer control program and should continue. In addition, the division should pursue further efforts to examine synergies and efficiency in resource utilization with the Division of Cancer Prevention and the Division of Cancer Treatment and Diagnosis.

Intramural Research Program

NCI's intramural research programs have a long and remarkable history of research accomplishments, leading the transition from the study of biochemistry of malignancy to the current emphasis on molecular oncology. The Medical Oncology Branch is critical to the coordination of translational research and multidisciplinary clinical investigation in major adult

solid tumors and lymphomas. However, an important concern is the branch's difficulty in attracting senior faculty and talented fellowship candidates. Another issue is the fragmentation of medical oncology interests and staff among multiple NCI branches, particularly in the lymphoma and bone marrow transplantation programs.

Recommendation 9: NCI leadership should encourage the development of new mechanisms for supporting talented young investigators in the field of clinical oncology in order to replenish its ranks. In particular, the Medical Oncology Branch should focus its research programs on questions that utilize the unique intellectual and patient resources of the NIH Clinical Center and the Center for Cancer Research laboratories.

Recommendation 10: NCI leadership should examine administrative solutions that facilitate collaboration with industry within the parameters set by the conflict of interest policy, and if these fail, NCI leadership should petition for modifications of the policy to encourage such ethical and transparent collaborations. Without these changes, the intramural faculty will become increasingly isolated from the mainstream of cancer drug development and will continue to have limited access to interesting compounds.

Recommendation 11: NCI leadership should consolidate medical oncology faculty within a single branch in order to provide a coherent environment for mentoring, training, and translational research.

Recommendation 12: NCI and NIH leadership must resolve the growing financial predicament of the Clinical Center and assure the stability of its intramural clinical research effort.

NCI Training Programs

NCI extramural training programs have focused increasingly on postdoctoral trainees and fellows, apparently because these individuals have shown a higher "return on investment," in that they have pursued cancer research careers and successfully secured investigator-initiated R01 grant support from NCI. Hence, a battery of seven K-type mentored transition award mechanisms, especially those supporting physician scientists, has been emphasized. The NCI T32 program eligibility policy has been skewed strongly toward mentors holding NCI R01 funding and toward postdoctoral trainees pursuing projects that are explicitly cancer related. Simultaneously, predoctoral training has been de-emphasized and the important goal of promoting team research during training is not being pursued effectively.

Recommendation 13: Recognizing that cancer can arise from defects in a broad range of cellular processes, most of which remain poorly understood, NCI should consider rebalancing its training mechanisms to support a more equal blend of cancer-directed and basic, clinical, population-based, and environmental science.

Recommendation 14: NCI should increase its overall expenditure for training programs, especially to increase funding for early training, i.e., funding for medical student research programs (e.g., matching or supplementing institutional or private sources) and particularly for broad-based T32 support of predoctoral trainees. Aside from its positive impact on cancer research, re-establishing NCI predoctoral

T32 support will spur the development of cancer training curricula, stimulating interest and awareness about cancer and ultimately expanding the cancer research workforce.

Recommendation 15: NCI should create an Integrative Cancer Research Training Award, which would bring together two or more trainees (at any training level) with different disciplinary foci, especially those linking basic and clinical approaches, to establish a collaborative research and training plan. This new training mechanism would commonly present basic research in a direct cancer context, making explicit the cancer relevance of the basic studies. Importantly, this mechanism would also help to establish, at the level of training, a culture of collaboration and teamwork that would then extend into the independent careers of the trainees.

Cancer Centers Program

NCI-supported Cancer Centers have become the dominant contributor of new knowledge in laboratory, clinical, and population sciences related to cancer. New models of funding research programs, particularly the Specialized Programs of Research Excellence (SPORE) program, have contributed valuable support to cancer center activities. The original model of funding, in which the Center grant aimed at providing a fixed percentage of total NCI grant dollars, is no longer workable, because funding for the Cancer Center Support Grants (CCSGs) as a percentage of total NCI grant dollars varies enormously among cancer centers. One shortcoming of the current system is that the existing model of CCSG funding provides few flexible dollars to support innovative early research. Cancer center directors interviewed by the Working Group believed that there is an inordinate focus during review on administrative processes and on fulfilling complex guidelines and not on research productivity. Moreover, the current model lacks strong incentives to conduct team research involving multiple centers and facilities and across NCI funding mechanisms, as well as establish public-private research partnerships.

Recommendation 16: NCI should increase the emphasis of Cancer Center Support Grant review on programmatic accomplishments, scientific innovation, and productivity. The funding model should be merit based. There should be less emphasis on adhering to rigid comprehensiveness and administrative compliance guidelines. It is expected that focusing, as indicated, will decrease the size of CCSG applications.

Recommendation 17: NCI should encourage and reward innovative trans-disciplinary partnerships established between basic, translational, clinical and population-based cancer centers or between cancer centers and other NCI-sponsored activities such as cooperative groups and Specialize Programs of Research Excellence (SPOREs).

Specialized Programs of Research Excellence

The Specialized Programs of Research Excellence program has been an important instrument for supporting disease-specific translational research. Through this mechanism, admirable progress has been made in lung, breast, and prostate cancers and in other diseases. The program provides funding for multidisciplinary projects, for team science, and developmental projects that might otherwise have difficulty in peer review. In most instances, the SPORE award complements the CCSG cores and administration funding, although programmatic reviews of CCSGs and

individual SPOREs are not coordinated, i.e., when they are conducted or through a single site visit process.

Recommendation 18: The scope of SPOREs should move beyond disease-specific programs to include unique tumor biology research programs, e.g., oncogene driven tumors (such as *k-ras*, *c-myc*, etc), which include multiple tumor types, or tumors driven by defects in deoxyribonucleic acid (DNA) repair or apoptosis.

Recommendation 19: Consideration should be given to coordinating the review of cancer centers and SPOREs, since the vast majority of SPOREs (more than 95 percent) are held by cancer centers, and represent the scientific engine that justifies the clinical component of the core grant.

NCI and Comparative Effectiveness Research

Given recent and ongoing changes in the comparative effectiveness research (CER) enterprise in the US, NCI has several opportunities provide leadership. The Working Group encourages NCI's continued involvement in developing the data infrastructure and methods to support CER, through collaborative efforts within NIH as well as other government and non-government agencies. NCI also can help to ensure that CER is used to promote more personalized cancer care, with careful attention to the needs of priority populations. To address a current knowledge gap, the Working Group would support NCI's investment in a broader form of CER that examines the effectiveness of different delivery, organization, and financing systems for cancer care. Finally, NCI should ensure that training programs plan for the next generation of cancer-related comparative effectiveness researchers.

Conclusions

Given the current budget constraints, it is critical that NCI promote a prudent, sustained investment in the full spectrum of cancer research. NCI must identify and focus on its core strengths in research (basic, clinical, and population) and avoid duplicating successful programs, such as drug development by industry. NCI is strongly encouraged to significantly modify or end programs that are no longer highly productive or unique. As the scientific and fiscal environment changes, the objectives of key NCI infrastructure programs, such as the cooperative groups and the Frederick facility, also should change, as will organizational structures and staffing. The Working Group supports the NCI Director in making significant changes in structure and leadership to meet evolving needs and is enthusiastic about opportunities for progress in the next decade, given the tremendous advances in science that are occurring and the presence of a new NCI Director.

Report of the NCAB Ad Hoc Working Group

Charge to the Ad Hoc Working Group

At its February 2010 meeting, the National Cancer Advisory Board (NCAB) of the National Cancer Institute (NCI) voted to create an ad hoc Working Group (WG) —

. . . to look back over how the NCI has evolved over the last 40 years since the passage of the National Cancer Act of 1971 as well as, even more importantly, project what the NCI needs to do during the next decade. The working group is charged to review the NCI current operating structure and strategic vision - to assess the effectiveness of the scientific programs and business management structure of the NCI, in order to determine the gaps and opportunities for delivering scientific progress in understanding, diagnosing, treating, and preventing cancer.

Introduction

Congress established NCI through the National Cancer Institute Act of 1937 (P.L. 244, 75th Congress). The Institute was created to “conduct and support research with respect to the cause, diagnosis, prevention, and treatment of cancer, rehabilitation from cancer, and the continuing care of cancer patients and also the families of cancer patients.”

For the past 73 years, NCI has been the Federal Government’s lead agency for conducting cancer research. NCI has made steady progress in understanding the biological and molecular changes underlying cancer and in demonstrating the ability of cytotoxic chemotherapy to cure selected tumors (e.g., childhood leukemia, adult lymphomas, choriocarcinoma, and testicular cancer) and prevent recurrence after primary surgery of breast cancer, colon cancer, and other types of cancer.

NCI’s intramural laboratories and clinical branches have been the training ground for generations of basic and physician scientists who have built outstanding cancer research careers both nationally and internationally. The flexibility and resources of NCI’s intramural research program and its Frederick, Maryland, facility have played a pivotal role in defining curative treatments for advanced Hodgkin’s disease, choriocarcinoma, testicular cancer and various forms of leukemia. In addition to its contributions to cancer, NCI’s intramural program has made significant investments in understanding the Acquired Immunodeficiency Syndrome (AIDS) virus. Specifically, in the 1980s, NCI scientists identified the AIDS virus, developed the first test kit for detecting antibodies to the virus, and developed the first effective drugs for this disease. Additionally, NCI’s population and prevention scientists have: 1) identified several inherited cancer syndromes; 2) provided insights into the genetics and environmental factors associated with cancer susceptibility; and, 3) shown that cancer mortality can be reduced through a variety of diagnostic, behavioral, and environmental interventions.

The National Cancer Advisory Board, the principal advisory group that provides oversight of NCI programs and activities, recognizes that a confluence of transformative forces (scientific, demographic, and fiscal) has created the need to evaluate NCI’s progress over the past decade and to define its forward path. When considering the scientific force, it is clear that the past two decades have witnessed unprecedented progress in: 1) understanding the biological basis of cancer; and, 2) developing prevention, detection, and treatment strategies based on that knowledge. In fact, the year 2000 marked a major inflection point in the fight against cancer.

Significant scientific cancer biology advancements during the prior decade provided a broader knowledge of malignant transformation, metastasis, and drug resistance processes. Compelling new treatment and prevention targets were identified for chronic myelogenous leukemia, lymphomas, breast, lung, and colon cancers. Successful outcomes from these research efforts have resulted in industry's development of additional targeted agents. The pace of targeted drug development has quickened, resulting in the identification of effective new treatments for melanoma, subsets of lung, ovarian, and many other cancers. Major successes in cancer prevention include the development of a vaccine against the hepatitis B virus that prevents primary liver cancer, and a vaccine against human papilloma virus (HPV) that prevents cervical cancer.

A related major development has been the rapid growth of a broad commitment of the pharmaceutical and biotechnology sectors to the development of new cancer treatments. This interest has resulted in large measure from the growth of scientific knowledge about cancer. Although initially successful in its attempts to find new cancer drugs, industry remains heavily dependent on NCI-supported science for identification of targets, and on NCI's cooperative groups and cancer centers for collaboration on future drug development.

With the molecular oncology revolution, a second transformative force, i.e., the increase in global concern about cancer has emerged. Major changes in cancer demography and the resulting worldwide interest in cancer research have occurred because of public health improvements, the aging of populations globally, increased environmental awareness, and the associated increase in cancer incidence. From both a demographic and economic standpoint, cancer has become a growing health threat. By 2030, the number of individuals newly diagnosed with cancer in the United States is expected to grow to 2.3 million cases per year, with approximately 12 million survivors. Worldwide, cancer is projected to cause the death of 10.3 million people each year by 2020. In fact, since 2002, deaths from cancer have increased more than 50 percent in most of the world (the Americas, Africa, Middle East, Asia, and the South Pacific). Of all cancer deaths in 2005, more than 70 percent occurred in low- and middle-income countries.

Disparities persist regarding the burden of cancer among underserved populations, both nationally and internationally, resulting from delays in cancer diagnosis and limited access to treatments, and subsequent poor survival rates. Additionally, uncurbed tobacco use, alcohol consumption, obesity, poor diet, sedentary lifestyles, and many cancer causing viruses (e.g., human immunodeficiency virus (HIV), hepatitis B and C, and HPV) are critical factors that have contributed to the increasing global incidence of cancer over the past decade.

Financial considerations also have contributed to the global concerns about cancer. Increasing cancer incidence and the simultaneous development of new drugs have contributed to a sharp rise in the costs of cancer care in the United States and abroad. Cancer care expenditures in the United States increased from \$104 billion in 2006 to \$120 billion in 2009 (not including indirect costs). Drug costs alone are expected to reach \$100 billion globally in the next few years. Additionally, total global costs of cancer care exceeded \$228 billion in 2009. Providing state of the art early detection, diagnosis, and treatment will require a monumental investment for most countries.

With improvements in public health in the developing world, cancer is an increasingly significant health issue. Since it is now recognized as an important global target for research

investment, there is increased interest and demand for trans-national efforts in cancer prevention, diagnosis, and treatment. Cancer research in Europe and Asia has grown rapidly over the past two decades and has contributed new treatments and new insights into the viral, environmental, and genetic causes of cancer. Partnerships in research between the U.S. and foreign scientists have become increasingly important for progress to be made in controlling this disease. Even though NCI has long supported collaborative research between laboratories and clinics, both nationally and internationally, the Institute can now influence cancer research that addresses unique populations and/or conditions. In other words, NCI must now be prepared to initiate, support, and take full advantage of global collaborative research opportunities on a larger scale than ever before.

The third important force is the poor fiscal climate affecting economies worldwide, with negative effects on government and industry research budgets. New technologies and research offer unique and unprecedented opportunities for individualizing risk assessment, informing strategies for cancer prevention and control, and personalizing treatment approaches. These dramatic changes and opportunities have occurred at a time when the NCI has had no meaningful increase in its budget for the past seven years. Since it is unlikely that NCI will receive significant budget increases in the short term, the Institute must realign its priorities to support the best opportunities for progress.

The confluence of these forces—the rapid growth of molecular oncology as an enterprise and as the underpinning of all aspects of cancer research and industrial investment in cancer drug development; rising incidence of cancer and globalization of cancer research; and severe fiscal restraints facing the Federal Government and global economies—must be given full consideration going forward. NCI and its advisors must reassess the Institute’s accomplishments and priorities in order to support the most promising new programs and research efforts.

The National Cancer Program

The 1971 National Cancer Act recognized NCI’s leading role in the National Cancer Program (NCP), a broader national effort to control cancer. While NCI is widely viewed as the cornerstone of the NCP, it is but one of several governmental, private, and philanthropic entities contributing to the broader national effort to control cancer, i.e., the advancement of cancer diagnosis, prevention, and treatment. These efforts include a broad array of volunteer organizations as well as research and medical communities. In terms of yearly expenditures, the National Cancer Program includes NCI at \$5 billion, other Federal agencies (including the National Institutes of Health (NIH) Institutes and Centers (ICs), Centers for Disease Control and Prevention (CDC) the Department of Defense at \$3 billion, private industry at \$9.2 billion, state agencies at \$376 million, and foundations and nonprofit organizations at \$667 million, for a total of approximately \$18 billion. These figures do not include the important contributions of private philanthropy, primarily to cancer centers and academic institutions. Federal regulatory agencies such as the Food and Drug Administration (FDA) and the U.S. Environmental Protection Agency (EPA) are also critical components of the National Cancer Program.

The Origins of This Report

The National Cancer Advisory Board is a presidentially-appointed panel established by the National Cancer Act of 1971. It is granted statutory responsibility to advise the Secretary of Health and Human Services (HHS) and the NCI Director “with respect to the activities carried out by and through the Institute.” The Act required that NCAB members be “leading scientific or

medical authorities outstanding in the study, diagnosis, or treatment of cancer or in fields related thereto.” The NCAB meets regularly to approve grants and advise NCI’s leadership regarding major Institute initiatives and changes in policy and programs. Congress intended the NCAB to conduct regular reviews of NCI’s intramural and extramural research programs and the National Cancer Program, and to offer its advice on a regular basis to the NCI Director regarding its evaluation of the nation’s efforts to fight cancer.

In February of 2010, the Board approved establishment of this Working Group to assess the current status of NCI’s intramural and extramural research programs and to recommend actions NCI can take to meet future challenges in an era of limited budget expansion and rapid scientific change. NCI leadership and the Board recognize the need to identify and develop practices to revise and/or terminate programs that produce lower return in order to sustain successful programs, initiate new areas of scientific development, and support the most promising new scientific opportunities.

This Working Group was formed in April 2010 and includes 25 leaders from the scientific community, industry, and advocacy groups, as well as 4 NCAB members (see appendix). Four co-chairpersons were designated. Three (Goodwin, Ingram, and Chabner) are NCAB members, and the fourth (Sharp) is a Nobel Prize-winning scientist and former NCAB member and chairperson. The Working Group met on three occasions (5-6 May, 7-8 July, and 25-26 August 2010) to hear presentations from current NCI leadership; former NCI directors; basic, clinical, and population scientists; leaders in cancer centers, academia, government, and industry; authors of an Institute of Medicine report on NCI’s clinical trials programs; leaders from various NCI divisions and programs; and the current NIH and NCI Directors.

The WG focused its efforts on those scientific areas that present particular challenges and opportunities for change in direction and resource allocation. It did not attempt to evaluate the scientific productivity of investigator-initiated research project grants, which are reviewed individually by study sections and have been the source of great progress over the past decade. Nor did it focus on intramural laboratories since those are carefully and regularly reviewed by NCI’s Board of Scientific Counselors (BSC). It did, however, examine NCI’s intramural clinical research program in adult oncology within the Medical Oncology Branch (MOB), which has experienced significant recent changes in leadership and scientific focus, and is increasingly constrained by Clinical Center costs.

The Working Group was particularly interested in scientific accomplishments over the past decade of select NCI extramural programs and the current allocation of resources to the Frederick Contract Research Facility, Cancer Centers Program, Specialized Programs of Research Excellence (SPOREs), and Clinical Trials Cooperative Groups Program. The Working Group’s intent was to identify areas for new or increased investment as well as programs that merit decreased investment or reorganization. The Working Group evaluated the following:

- NCI’s relationships with the private sector;
- NCI’s role in comparative effectiveness research;
- extramural clinical trials programs, including the Clinical Trials Cooperative Groups, the affiliated Community Clinical Oncology Program (CCOP), and the NCI Community Cancer Centers Program (NCCCCP);
- cancer prevention, control, and population sciences programs;
- the Frederick Cancer Research Facility, including drug development activities;

- the intramural research program, specifically the Medical Oncology Branch;
- the Cancer Centers program;
- the SPORE program; and
- NCI training programs.

The Working Group's findings and recommendations in these broad categories are presented below.

NCI and the Private Sector

The private sector plays an increasingly important role in the National Cancer Program. In a field formerly dominated by NCI efforts, large pharmaceutical companies and the biotechnology industry, including more than 1500 individual companies, have: 1) emerged as major contributors to cancer therapeutics in the past two decades, 2) invested heavily in cancer drug discovery; and 3) brought to the clinic more than 200 new compounds annually in recent years. Development and refinement of these new drugs are often complex undertakings that require collaboration of industry with the NCI-supported Cancer Centers, NCI's intramural program, and clinical trials groups. These NCI-supported entities participate in early evaluation (Phase 1 and Phase 2 in grant and contract-supported efforts) and later stages of development (late Phase 2 and Phase 3) in the Cooperative Groups. In addition, NCI has become an important mediator of collaborative efforts between companies by arranging for the evaluation of combinations of products coming from competitive companies and for directly comparing competitors' drugs. NCI and its grantees have been important innovators in developing new trial designs and novel approaches to biomarker development related to industrial products.

In addition to participating in NCI-supported clinical trials, along with NCI-designated Cancer Centers, many hospital-based and private oncologists participate in a vast array of industry-sponsored trials without direct government support. The scope of these efforts is international, and their costs greatly exceed NCI's investment in clinical trials.

Despite the importance of NCI and industry relations, barriers to this collaboration exist. The relationship between intramural NCI investigators and the private sector is encumbered by tightly constraining conflict of interest regulations that limit collaboration and consulting and informal exchanges of information and collaboration, in contrast to the relatively more flexible ties between industry and academic researchers. In some cases, these rules negatively impact the ability of NCI and NIH ICs to recruit and retain top level scientists from the private sector.

At the same time, NCI must address the priority of its long standing effort in drug discovery and development. Investments in programs that may duplicate and compete with industry efforts must be avoided.

In addition, NCI cooperative groups conduct clinical trials that represent investment in studies on marketed products that already are yielding large profits to companies. Clinical trials to gain additional indications of such marketed drugs should not be supported by public funds unless these are aimed at special populations that would not be supported by companies. There clearly are trials of comparative efficacy that industry will not undertake, and that NCI can support, to the benefit of the clinical oncology community and its patients. Although the relationship of NCI to industry is critical to the overall success of cancer drug discovery and development, these

interactions require careful attention to avoid overlapping, unnecessary, and counterproductive activities while also encouraging collaboration when appropriate.

In summary, given the tremendous advances in science, the Working Group is enthusiastic about opportunities for future progress in cancer. One of NCI's most important advantages is the ability of basic scientists, translational experts, and cancer clinicians in both its intramural and extramural programs to collaborate effectively with private industry to bring advances in cancer care to society.

The Working Group encourages NCI to establish or enhance current processes to:

- revitalize and maximize transparent collaboration with industry;
- position NCI as the “honest broker” between industry and academia to tackle technically challenging problems, most importantly, developing biomarkers, understanding resistance, and developing combination therapies (which is particularly challenging when those therapies are under development by more than one company);
- leverage NCI's potential role as a “neutral scientific convener” or supporter of a public-private collaboration that can encourage and facilitate pre-competitive collaboration among members of the industry to develop disease models and biomarkers;
- promote development of common terminology and consistent clinical data standards in cancer research, and create incentives for their adoption; with a common language, research can be more collaborative and impactful;
- enable NCI to assume leadership roles in advancing methodology in comparative effectiveness research, as well as in understanding long-term safety issues with new targeted therapies; and,
- provide NCI trainees the opportunity to experience and prepare for careers that span academia, industry, and government.

The Working Group also encourages NCI to: 1) position staff and trainees to interact in productive ways with industry colleagues; 2) allow for information exchange and collaboration that respects the unique roles of each; and, 3) continue support of basic research that produces new knowledge and understanding of cancer. In view of existing fiscal constraints, NCI must balance its investments in drug discovery and development with those of industry.

Conflict of Interest Policies

During the Working Group's discussions, concern was raised repeatedly about the recently adopted NIH Conflict of Interest guidelines, published 31 August 2005¹, prohibiting consulting engagements and other collaborative research relationships between NCI scientists and biopharmaceutical companies. Because such collaborations are essential for fulfilling one of the NCI's core missions, which is to promote the efficient translation of NCI scientists' discoveries into commercially available diagnostic, therapeutic, and preventive products that improve the health of the public, the Working Group considered whether this regulation should be revised.

In reviewing the regulatory language, the WG realized that the current NIH regulation is 1) intended to be considerably more stringent and restrictive than its predecessor; and 2) was

¹ *Federal Register Notice*, Volume 70, No. 168, Pages 51559-51574; 5 CFR Parts 5501 and 5502. Available at: <http://www.nih.gov/about/ethics/08252005supplementalfinancialdisclosure.pdf>

imposed on NIH by the U.S. Office of Government Ethics in the wake of widely publicized revelations involving undisclosed and unapproved relationships between some very senior NIH intramural scientists and pharmaceutical companies. The incidents attracted departmental, Congressional, as well as national media attention and elicited calls ranging from complete prohibition of intramural scientists' interactions with the commercial sector to tighter agency control and more robust staff oversight. In response to these concerns, new and significantly more severe guidelines were imposed on NIH scientists in 2005.

Careful reading of the regulation reveals that *consulting with industry*, for compensation or without compensation, is not mentioned explicitly, neither among the activities prohibited (Section 5501.109, (c)(1)) nor among the activities permitted (Section 5501.109, (c)(2)). However, the regulation explicitly and broadly prohibits employees from teaching, speaking, writing, or editing *for compensation* or from engaging in any employment or self-employment business activity that involves the sale or promotion of products or services of a Substantially Affected Organization (SAO), a Supported Research Institution, or a health care provider or insurer.

SAOs are biotechnology, pharmaceutical, medical device manufacturers, or other entities that are significantly involved in the research, development, or manufacture of biotechnology, biostatistical, pharmaceutical, or medical device equipment, preparations, treatments, or products. Permitted activities, often with limiting conditions, include teaching a university course, authorship and editing, service on Data Safety and Monitoring Committees or Scientific Review Committees that are not created by SAOs, and presenting in Grand Rounds that are not sponsored by SAOs.

The Working Group agrees that the regulatory language clearly bars NCI scientists from consulting *for compensation* with SAOs, but notes that the regulatory language does not even address the possibility of consultation with SAOs without compensation. The Working Group reaffirms that ethical and transparent consulting relationships between NIH scientists and the private sector, and especially with SAOs, are essential in expediting the translation of publicly funded research discoveries into diverse health products that bring great benefit to the public.

Working Group Recommendations Regarding Engagement with the Private Sector

Recommendation 1: The Department of Health and Human Services should permit NIH scientists to engage in ethically conducted and fully transparent consulting and collaborative relationships with the private sector, including with Substantially Affected Organizations, as part of their official duties, provided that the scientists receive prior review and approval from their Institute Director and from the NIH Office of the Director. Such interactions should be encouraged as an important avenue to progress in cancer research.

Review of Programmatic Areas

NCI Clinical Trials Programs

NCI supports clinical research in its extramural programs through the Cancer Therapy Evaluation Program (CTEP), which is conducted and supported by grant, contract, or cooperative agreement. The Working Group devoted its primary attention to the Clinical Trials Cooperative Groups, which are supported as U10 cooperative agreements to large,

multispecialty, multi-institutional groups that conduct a portfolio of trials reviewed and approved by NCI staff. These trials have had an enormous impact on cancer treatment, establishing standard therapies for most of the childhood malignancies as well as for many of the common adult malignancies, such as breast, colon, and lung cancer. In addition, the groups actively collaborate with industry and basic science laboratories to test new drugs and develop insights into determinants of response or toxicity. Intergroup, interdisciplinary disease-specific steering committees have been instituted to prioritize trials. Cooperative Group databases and tissue banks have become increasingly important tools for translational research. Their data and tissues have become a national resource used by academic and industrial laboratories.

The Clinical Trials Cooperative Group Program, created in 1955 to address opportunities for treating childhood leukemia, now consists of 10 groups (9 adult and 1 pediatric). Six of the groups have a narrowly defined portfolio of trials aimed at a particular disease, patient population, or treatment modality (e.g., radiation therapy, surgery). Four groups have a broader, multimodality, and multi-disease focus, conducting clinical trials through networks of cancer centers and community oncology practices across the United States (approximately 2,000 sites). More than 25,000 patients are recruited into trials annually by an estimated 14,000 investigators. The groups interact closely with NCI in all phases of protocol development, deployment, performance monitoring, and collaborative activities.

Cooperative groups receive funding through three separate budget allocations. The major funding stream, which represented approximately 2.9 percent of the total NCI budget in fiscal year (FY) 2009 (\$143.8 million in base support) comes from the Division of Cancer Treatment and Diagnosis (DCTD) and provides support for trials directed at the evaluation of new treatments for cancer. This basic support is enhanced by a second allocation of \$90 million from the Division of Cancer Prevention (DCP) for the Community Clinical Oncology Program sites, which includes \$8.1 million for the Minority-Based CCOP (MB-CCOP) effort. CCOP participants come from community-based private and hospital-centered practices. CCOPs participate in a portfolio of cancer prevention trials, but they also accrue patients into NCI-sponsored therapeutic trials and contribute approximately one-third of all NCI group accruals. Currently, there are 47 CCOPs in 29 states.

The MB-CCOP membership consists of 16 sites in 10 states, the District of Columbia, and Puerto Rico, and it contributes patients to both prevention and treatment trials. The program was launched in 1990 as part of the efforts of the CCOPs to improve access of underserved populations to NCI trials. At least 40 percent of the local populations served by the MB-CCOP are minorities.

In addition to the regular cooperative group membership and the CCOPs, NCI created in 2007 a new entity, the NCI Community Cancer Center Program, a partnership of NCI and hospitals in underserved communities. The NCCCCP was established to create a community-based cancer center network to support cancer clinical trials (including cooperative group trials), enhance access of underserved populations, collect biological specimens for research purposes, and increase the quality of care at community hospitals. In many instances, it funds institutions and practices that are also supported by the CCOP program. A concern is that in contrast to the competitively reviewed cooperative agreement mechanism used to fund the cooperative groups and CCOPs, the NCCCCP program is reviewed, administered and funded through a Frederick contract. (The NCCCCP is considered further in the assessment of the NCI Frederick operations.)

Significant concerns have been raised in recent years regarding the efficiency, scientific productivity, and potential duplication of the cooperative groups. In response the NCI Director requested that the IOM conduct a detailed study of NCI's Cooperative Groups, which culminated in a 2010 report entitled *A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program* (National Academies Press, 2010). In its review of the organization and operation of the NCI Clinical Trials Cooperative Group Program, the IOM committee identified significant problems and recommended improvements. Key study findings included the following:

1. Duplicative and overlapping organizational structures for developing, implementing, and conducting trials among the 10 groups.
2. Unacceptable delays in initiating new trials, averaging 2.5 years from concept to accrual of first patient. Delays appear to result from administrative inefficiencies and multiple levels of review within the groups and NCI compounded, in some cases, by protracted negotiations for industry support or drug supply.
3. Underfunding of trials in that member institutions receive an average of \$2,000 per accrual, at a cost to the local site of approximately \$6,000 per case.
4. Failure to complete trials; 40 percent never reach accrual goals.

In summary, the IOM committee reaffirmed the critical need for publicly funded cancer clinical trials to identify cancer patient treatment options, for conducting translational research, and recommended that NCI:

1. Improve the speed and efficiency of the design, launch, and conduct of clinical trials, including a disengagement of NCI review of trials for which it is not the sponsor.
2. Improve the prioritization, selection, support, and completion of cancer clinical trials.
3. Examine possible consolidation of common functions such as "up-front" and "out-back" protocol development and trial conduct among the groups.
4. Consider consolidating key functions of the multiple adult oncology groups.
5. Incorporate innovative science and trial design into cancer clinical trials.
6. Financially incentivize participation of patients and physicians in clinical trials and address the underfunding of accrual.
7. Stop supporting clinical trials of marketed products that are already yielding large profits to companies.

The Working Group recognizes the historical importance of the cooperative groups in conducting critical Phase 3 trials in children and adults with malignancy and in sharing their databases and tissue banks for translational research. They also noted that there is a potential for the cooperative group trials to serve as a mechanism to 1) examine the comparative effectiveness of new versus established therapies; 2) determine relative costs and benefits of new treatments; and, 3) test innovative concepts of targeted therapies in uncommon subsets of tumors.

The Working Group reviewed the Institute of Medicine report, was briefed by IOM committee members at its 7-8 July 2010 meeting, concurs with its findings, and endorses its recommendations.

Working Group Recommendation Regarding NCI's Clinical Trials Programs

Recommendation 2: The Working Group strongly encourages NCI to implement the IOM recommendations and recommends that the National Cancer Advisory Board be given regular progress reports.

NCI-Frederick

NCI's facilities in Frederick, Maryland, were established in 1972 as a government-owned, contractor-operated facility (the only such HHS facility in existence). It was established as a Federally Funded Research and Development Center (FFRDC) to provide NCI with a high degree of flexibility and a rapid response capability. Currently, it is supported by an Operations and Technical Support contract, which is re-competed every five years and was last competed in 2005 and funded at \$373 million in 2009. Since 2005, NCI-Frederick has provided scientific support for 25 of the 27 NIH Institutes and Centers. Extramural scientists also have access to its services, reagents, and facilities. In 2009, NCI-Frederick provided \$34.2 million in services to 100 NCI-supported and 209 National Institute of Allergy and Infectious Diseases (NIAID)-supported extramural clinical trials to test cancer and AIDS treatments in national and international locations.

The Frederick facility and its portfolio of support functions are competitively reviewed via the contract mechanism every five years. Oversight of Frederick is provided by the NCI Scientific Program Leadership (formerly Executive Committee), although there is no formal advisory committee.

Proposals for new research projects at Frederick are submitted by the NCI Director and by NCI divisions, offices, and centers. In addition, the FFRDC has supported vaccine and drug development for other NIH Institutes and Centers and may become an important contributor in an NIH wide drug discovery initiative proposed by NIH leadership last year.

Initial approval of project concepts at this FFRDC has been provided by the NCI Scientific Program Leadership. Concepts may be brought to the NCI extramural advisory boards (i.e., NCAB, BSC, and Board of Scientific Advisors (BSA)) for advice, but pilot projects may be initiated without formal concept approval. Once initiated, a project may be expanded or altered according to the needs and priorities of NCI senior leadership without formal external review. Current programs include the following:

- AIDS and Cancer Virus Program
- Advanced Technology Program
- Biopharmaceutical Development Program (cancer drug development activities)
- Support of the NIAID Vaccine Clinical Materials Program
- NCI Community Cancer Center Program
- The Cancer Genome Atlas
- Core Genotyping Facility
- Nanotechnology Characterization Laboratory
- caBIG Support
- Small Animal Imaging Program
- caHUB (Human tumor biobanking)

The Frederick facility supports a significant percentage of NCI's drug discovery and development activities through its collaborative activities with the Division of Cancer Treatment and Diagnosis (DCTD), which contributed \$48.8 million in contract funding in FY 2009. These activities include drug discovery screening, candidate selection, preclinical evaluation, and optimization of its own drug candidates. NCI cooperates extensively with private industry and academic laboratories in evaluating new compounds, some of which originate in industry. The newly implemented NCI Experimental Therapeutics (NExT) program is designed to serve the preclinical drug development needs for candidate molecules proposed by extramural scientists from academic laboratories, and offers services ranging from lead discovery through preclinical pharmacology and toxicology.

A particular concern, as previously stated, is that the newly established NCCCP is reviewed, administered, and funded through the Science Applications International Corporation (SAIC) contract, which is the Frederick Cancer Research Facility contractor. The original NCCCP program initially funded 10 sites at 16 community hospitals. NCI's initial investment in the 10 pilot sites was \$500,000 per site per year for a total of \$5 million annually and a total commitment of \$15 million over a three-year period, i.e., from 2007 to 2010. In 2010, using American Recovery and Reinvestment Act funds, NCI significantly expanded the NCCCP yearly funding to \$80 million. These funds were allocated to the original pilot sites and to new sites. Significant reservations regarding NCCCP accomplishments were expressed by the NCAB during a 2009 board presentation. Specifically, the board noted that there was a lack of information on clinical trials accrual, a lack of progress in accruing minorities to clinical trials, and expressed concerns about its overlap with the CCOP and MB-CCOP programs. Similar concerns were raised at a presentation to the NCI Board of Scientific Advisors.

A new Frederick program, the Advanced Technology Partnerships Initiative, with an annual budget of approximately \$760 thousand, was established in 2009 to accelerate the delivery of new products to cancer patients through the strategic application of advanced technologies and by facilitating translational research partnerships. Its creation was in response to a 2006 Government Accountability Office report, which cited an urgent need to improve the drug development process through increased collaboration among government, academic, and industry partners.

A new facility, with 330,000 square feet of laboratory space (replacing 200,000 square feet of decommissioned space and adding 130,000 square feet of new space) has been built at Frederick by a private developer, and will be leased by NCI. It will house additional drug development laboratories and will include incubator space for companies that want to collaborate with the NCI drug development program.

Working Group Findings Regarding NCI-Frederick

- NCI-Frederick provides NCI with a critical mechanism for responding rapidly to emerging research opportunities and public health needs. A particularly cogent example was its role in response to the national AIDS epidemic over the past 25 years. Another major contribution has been its primary support for NCI's cancer drug development efforts over the past 40 years. This support was particularly important in the era of cytotoxic drug development, when it aided the production and clinical development of a number of new agents, including paclitaxel and cisplatin. More recently, the Frederick contract has been used to fund a variety of major new investments in information technology, clinical outreach (NCCCP), drug development, and tissue banking, but in

some instances these programs have been established and expanded without any oversight from any of NCI's advisory boards, such as the NCAB and BSA.

- Over the last 10 years, the FFRDC has contributed significant support to the development of industry-owned drugs, such as bortezomib, cetuximab, depsipeptide, and pralatrexate. While these activities have undoubtedly benefited drug development, the recent expansion of its infrastructure and establishment of new programs, should be carefully assessed to determine the potential overlap with private industry interests.
- Review of programs at Frederick occurs by processes that were not fully transparent to the Working Group, especially the relationship of the Frederick contract activities to other NCI initiatives and mechanisms or to other parts of the National Cancer Program. For example, NCCCP appears to overlap and duplicate the CCOP and MB-CCOP programs in significant ways. Additionally, it does not appear that the NCAB or any NCI advisory group reviews requests for new or significant expansion of Frederick programs.
- Major new initiatives of the Frederick program, such as NCI's NExT, caBIG, and NCCCP, should receive regular review and oversight to ensure that they are meeting their goals and continue to be of the highest priority.

Working Group Recommendations Regarding NCI Frederick

Recommendation 3: NCI should carefully review and evaluate its investment in the Frederick facility to ensure that resources are used for the highest priorities. The existing review process does not assure the appropriate transparency for a significant portion of the NCI budget. Thus, NCI should reassess the criteria and procedures that it uses to evaluate and approve new initiatives at NCI-Frederick. Additionally, ongoing NCI-Frederick programs should receive thorough regular review to ensure that they continue to serve the highest priorities of the Institute and make effective use of available resources. In particular, major initiatives such as the cancer Biomedical Information Grid (caBIG) and Cancer Human Biobank (caHUB) may require periodic assessment, reconsideration and review.

Recommendation 4: The NCAB should have the opportunity to offer its advice on proposed new and major expansions of the Frederick program prior to implementation. The Board should receive regular reports on the progress of current, new or expanded initiatives/activities.

Recommendation 5: The NCI must determine whether the NCI Community Cancer Center Program, if retained, should be a Frederick activity, i.e., a contract supported program, or undergo the same competitive peer review process as Community Clinical Oncology Program (CCOPs), Minority Based-CCOPs, Cooperative Groups Program, and other programs that support clinical research.

Recommendation 6: The NCI should consider establishing a chartered committee to advise and evaluate ongoing activities at the Frederick facility.

Cancer Prevention Program

NCI formally included cancer prevention in its research portfolio after it was congressionally mandated in the 1971 Act. Cancer prevention research has had different names and has resided in different NCI divisions since then. The current NCI Division of Cancer Prevention originated in October 1997 when the Division of Cancer Prevention and Control was divided into two programs (DCP and Division of Cancer Control and Population Sciences (DCCPS)), despite some overlap in their missions. Research fostered by DCP focuses on the primary prevention of disease, using chemopreventive strategies, and spans the disease process, including: risk assessment; early interventions to detect and prevent cancer; symptom management during treatment; and supportive care at the end of life. The division is organized into research efforts that aim to develop new cancer prevention strategies and compounds, biomarkers for early detection, clinical trials that test new interventions, and basic nutritional science. The division's budget was \$178.8 million in FY 2009.

Working Group Findings Regarding NCI's Cancer Prevention Program

- DCP has conducted large-scale, high profile trials of hormonal interventions to prevent breast and prostate cancer. These trials have demonstrated reductions in the incidence of both breast (with tamoxifen or raloxifene) and prostate cancer (with finasteride), although significant side effects and the costs of the drugs have limited widespread adoption of these strategies.
- Even though DCP's current drug screening and development programs have led to the development of numerous candidates for clinical evaluation, the Working Group could not ascertain whether the various programs can effectively prioritize these candidates and implement their development. The division's drug development program does not seem to connect effectively with basic science laboratories and programs, large-scale genomics programs, or the NCI therapeutic drug development program.

Working Group Recommendation Regarding Cancer Prevention Programs

Recommendation 7: Given the clinical significance of cancer prevention and its scientific relationship to other NCI programs (e.g., therapeutic drug development, basic science, population genetics, environmental factors, and cancer control), consideration should be given to restructuring the Division of Cancer Prevention to better integrate with other NCI research laboratories, and to achieve scientifically rigorous and productive research goals. A close working relationship with the Division of Cancer Control and Population Sciences (see Recommendation 8), the Division of Cancer Biology, and with the Division of Cancer Treatment and Diagnosis would result in enhanced synergies and more effective use of resources.

Cancer Control and Population Sciences Program

The Division of Cancer Control and Population Sciences was created in 1997 to advance basic and applied research in the behavioral, social, population, and environmental sciences to enhance interventions that independently, or in combination with other approaches, reduce cancer risk, incidence, morbidity, and mortality and improve quality of life. In recent years, DCCPS has enhanced the Nation's cancer surveillance infrastructure, scope, and usability (i.e., Surveillance Epidemiology and End Results (SEER)); created a highly productive epidemiology consortium;

developed behavioral interventions at each stage of the cancer continuum; and created a growing focus on cancer survivorship research. Its results include a coordinated national tobacco control research program; the identification of numerous environmental, lifestyle, and inherited risk factors for cancer; new models for transdisciplinary research, advances in cancer modeling and dissemination of more than 100 efficacious cancer control strategies to federal, state, and local governments as well as to non-governmental organizations.

The division also operates the Cancer Intervention and Surveillance Modeling Network and is developing new strategies for leveraging the SEER database with Medicare and CDC databases. The Cohort Consortium involves investigators from 41 cohort studies, including more than 4 million research participants internationally. Other efforts are focused on linking epidemiology databases with genome-wide association studies, providing leadership in measuring food intake and physical activity, supporting centers for population health and health disparities, leveraging large health care systems for research purposes, advancing statistical techniques for analysis of a range of data, using modeling to predict changes in cancer incidence and mortality and conducting cancer survivorship, informatics, and comparative effectiveness research (collaborating with the Agency for Healthcare Research and Quality (AHRQ)). The DCCPS budget in FY 2009 was \$623 million.

Working Group Findings Regarding NCI's Cancer Control and Population Sciences Program

- DCCPS has undertaken significant efforts to forge productive relationships with other HHS agencies, such as CDC, AHRQ, EPA, FDA, and the Centers for Medicare & Medicaid Services, as well as with other NIH Institutes and Centers and with the American Cancer Society and Robert Wood Johnson Foundation, among others. The Working Group commends these activities and encourages other divisions to pursue similar partnerships when appropriate.
- DCCPS has supported outstanding population, behavioral, and environmental science initiatives. Particularly noteworthy is its research portfolio in genome wide association studies and the impact of genetic variation on risk for human cancers.

Working Group Recommendation Regarding NCI's Cancer Control and Population Sciences Program

Recommendation 8: The Division of Cancer Control and Population Sciences has forged important collaborative relationships within and outside NCI. These efforts are essential to an effective cancer control program and should continue. In addition, the division should pursue further efforts to examine synergies and efficiency in resource utilization with the Division of Cancer Prevention and the Division of Cancer Treatment and Diagnosis.

Intramural Research Program

NCI's intramural research programs have a long and remarkable history of research accomplishments, leading the transition from the study of biochemistry of malignancy to the current emphasis on molecular oncology. In the area of cancer treatment, these programs provided the first evidence for cure of a solid tumor (choriocarcinoma) and the first use of combination chemotherapy for the cure of a malignancy (MOPP (mechlorethamine, vincristine sulfate (Oncovin), procarbazine, prednisone) in Hodgkin's disease and related chemotherapy on

non-Hodgkin's lymphoma, and trained several generations of basic and physician scientists during the post-World War II era, a time of explosive growth in the biomedical sciences as applied to cancer.

The Center for Cancer Research (CCR) was created in 2001 to oversee and coordinate NCI intramural basic, translational, and clinical research. With a FY 2009 budget of \$416 million, CCR provides flexible funding and resources to support bench-to-bedside research on NIH's Bethesda campus. Across the entire NIH intramural clinical research program, CCR represents 15 percent of the overall effort, and it conducts 40 percent of all the research at NIH's Clinical Research Center. Similarly, CCR accounts for approximately 50 percent of all technology transfer and intellectual property activity on the NIH campus. CCR has conducted a rigorous review of its intramural research laboratories and branches and, to its great credit, has reduced its number of principal investigators by 20 percent over the past eight years. Some examples of high-profile CCR research emphasis include a focus on early phases of clinical drug development; understanding the biology and genetics of cancer and HIV; immunology and immunotherapy of cancer; antiviral vaccines (HPV); and innovative imaging technologies. The CCR continues to support high profile leaders in many fields related to cancer biology and immunology.

The Working Group focused its attention on the NCI Medical Oncology Branch as a critical unit in conducting translational studies in adult oncology within the intramural NCI. The Medical Oncology Branch, and its predecessor, the Medicine Branch, has had an enviable record of accomplishments in therapeutic research, and has been the training site for many of the current leaders in cancer research. With outstanding programs in lymphoma, ovarian, and breast cancer, from 1950 to 1990, the MOB attracted outstanding young talent. The NCI's intramural program was the premier site for training cancer research physician scientists.

Over the past two decades, a number of factors have significantly challenged the MOB's ability to attract similar talent and carry out its research mission. Specifically, the rise of regional cancer centers; the loss of key investigators in breast, lung, and gastrointestinal cancer; rigid conflict of interest rules limiting opportunities for collaboration with universities and industry; and a noncompetitive salary scale have resulted in the inability to recruit senior expertise and talented trainees. Even though the Medical Oncology Branch remains NCI's leading research enterprise for adult oncology, other CCR branches are also devoted to bone marrow transplantation, immunology, and cancer biology and support adult oncology investigators and research that are not part of MOB. Their use of MOB's patient resources and fellows has increased. This splintering of responsibilities within the medical oncology program has created competition for resources and a lack of coordinated leadership.

These problems are compounded by the rising cost of care within the Clinical Center (CC) at a time when overall NCI budgets are flat. The financial burden for NCI is also compounded by the diminishing contribution of other NIH Institutes as they seek alternatives to the increasingly expensive costs of doing research in the Clinical Center. As the largest single user of intramural clinical services in the Clinical Center, MOB is particularly vulnerable to these financial constraints since NCI currently is responsible for approximately 40 percent of the Clinical Center's research activity. Specifically, the NCI accounted for 36 percent of inpatient days and 37 percent of outpatient visits to the CC last year. Its contribution to the Clinical Center is approximately \$97 million of CCR's annual budget of approximately \$770 million.

The major recent and outstanding research accomplishments of the Medical Oncology Branch have come from studies of cutaneous T-cell lymphoma and histone deacetylase inhibitors, the development of new regimens for treating lymphomas, collaborative studies of lymphoma biology, and Phase 0 studies of Poly (ADP-ribose) polymerase (PARP) inhibitors. Proposed trials in non-small cell lung cancer, gastrointestinal cancer, ovarian cancer, and prostate cancer have been slow to evolve, because new faculty have only recently come on board. These trials have not yet produced notable results. There is a strong clinical pharmacology group, but with limited access to new high-priority industry compounds.

Because of multiple changes in leadership, the loss of prominent faculty, and the rise of highly competitive programs in academia over the past two decades, the NCI MOB fellowship program, formerly a leader in the academic community, has had difficulty attracting top notch, research applicants. It has also been unable to replenish its faculty ranks from within its own training program. While a number of recent MOB recruits may strengthen specific disease programs, it is too soon to evaluate their impact on the field since most are early in their research careers.

Working Group Findings Regarding NCI's Intramural Medical Oncology Branch

- MOB plays a critical role in coordinating translational research and multidisciplinary clinical investigation of major adult solid tumors and lymphomas. Strong research contributions continue to be evident, particularly in the development of the new histone deacetylase inhibitor, rombedepsin, and outstanding research in lymphoma biology and in armed monoclonals. The biomarker Phase 0 studies represent another notable contribution to demonstrating the feasibility of the PARP concept.
- A major concern for the branch has been its inability to attract both senior faculty and talented fellowship candidates. The latter group is particularly important as traditionally it has provided a pool of talented individuals who have become future national and international scientific leaders.
- Many factors, such as salary levels, rigid conflict of interest regulations, competition from academic programs, barriers to working with industry, and loss of prominent senior faculty, contribute to MOB's recruiting difficulties.
- The fragmentation of medical oncology interests and staff among multiple NCI branches, particularly in the lymphoma and bone marrow transplantation programs, has negatively impacted MOB's overall effectiveness.

Working Group Recommendations Regarding NCI's Intramural Research Program

Recommendation 9: NCI leadership should encourage the development of new mechanisms for supporting talented young investigators in the field of clinical oncology in order to replenish its ranks. In particular, the Medical Oncology Branch should also focus its research programs on questions that utilize the unique intellectual and patient resources of the NIH Clinical Center and the Center for Cancer Research laboratories.

Recommendation 10: NCI leadership should examine administrative solutions that facilitate collaboration with industry within the parameters set by the conflict of

interest policy, and if these fail, NCI leadership should petition for modifications of the policy to encourage such ethical and transparent collaborations. Without these changes, the intramural faculty will become increasingly isolated from the mainstream of cancer drug development and will continue to have limited access to interesting compounds.

Recommendation 11: NCI leadership should consolidate medical oncology faculty within a single branch in order to provide a cohesive environment for mentoring, training, and translational research.

Recommendation 12: NCI and NIH leadership must resolve the growing financial predicament of the Clinical Center and ensure the stability of its intramural clinical research effort.

NCI Training Programs

The 1998 NCI Strategic Plan for Research Training and Career Development presented four goals: 1) strengthen support for clinical and population scientists; 2) facilitate multidisciplinary, team science and translational research; 3) attract new scientific disciplines into cancer research; and, 4) engage underserved populations more effectively. Since then, numerous strategies have been defined and pursued by NCI extramural and intramural training programs to achieve these goals. A Training Commission was created in 2005 to determine outcomes of various training and career development mechanisms, and in both 2005 and 2008, NCI's training programs were reorganized to better coordinate and integrate the overall endeavor.

NCI's investment in training has been more or less flat at approximately \$160 million annually since completion of the NIH budget doubling in 2003; total trainees have declined slightly during that period, with support currently provided to approximately 1700 individuals.

Working Group Findings Regarding NCI's Training Programs

- Perhaps as a result of the Strategic Plan and the Training Commission, NCI extramural training programs have increasingly focused on postdoctoral trainees and fellows, apparently because these individuals have shown a higher "return on investment," in that they have pursued cancer research careers and successfully secured investigator-initiated R01 grant support from NCI. Hence, a battery of seven K-type mentored transition award mechanisms, especially those supporting physician scientists, has been emphasized. The NCI T32 program eligibility policy has become skewed strongly toward mentors holding NCI R01 funding and toward postdoctoral trainees pursuing projects that are explicitly cancer related; predoctoral training has been de-emphasized. NCI suggested that the R25 Cancer Education Grants Program mechanism instills in trainees the value of multidisciplinary team science and translational research. Based on data presented by staff, there is little evidence that this mechanism is either appropriate or is being used effectively toward these ends. Thus, the important goal of promoting team research during training is not effectively being pursued at this time at NCI (or at other Institutes and Centers).
- In parallel with these NCI extramural activities, the NCI intramural training programs have established the Cancer Prevention Fellowship Program and the NCI Summer Cancer Research Internship Program to enhance diversity. NCI is exploring development (with

NIH and FDA) of a fellowship in research-related regulatory review. NCI hosts a post-baccalaureate program that brings more than 200 trainees annually to the campus.

Working Group Recommendations Regarding NCI's Training Programs

Recommendation 13: Recognizing that cancer can arise from defects in a broad range of cellular processes, most of which remain poorly understood, NCI should consider rebalancing its training mechanisms to support a more equal blend of cancer-directed and basic, clinical, population-based, and environmental science.

Recommendation 14: NCI should increase its overall expenditure for training programs, especially to increase funding for early training, i.e., funding for medical student research programs (e.g., matching or supplementing institutional or private sources) and particularly for broad-based T32 support of predoctoral trainees. Aside from its positive impact on cancer research, re-establishing NCI predoctoral T32 support will spur the development of cancer training curricula by stimulating interest and awareness about cancer and ultimately expanding the cancer research workforce.

Recommendation 15: NCI should create an Integrative Cancer Research Training Award, which would bring together two or more trainees (at any training level) with different disciplinary foci, especially those linking basic and clinical approaches, to establish a collaborative research and training plan. This new training mechanism would commonly present basic research in a direct cancer context, making explicit the cancer relevance of the basic studies. Importantly, this mechanism would also help to establish, at the level of training, a culture of collaboration and teamwork that would then extend into the independent careers of the trainees.

Cancer Centers Program

The NCI Cancer Centers Program was formally established through the 1971 Act. The existing 12 Centers were grandfathered into the program. All NCI-designated Cancer Centers are expected to capitalize on their institutional cancer research capabilities by integrating research programs across intra-institutional boundaries into a single transdisciplinary research center. NCI recognizes two general categories of centers: 1) Specialized Cancer Centers, which focus on a particular aspect of cancer research, such as laboratory, clinical, or population science; and, 2) Comprehensive Cancer Centers, which include a broader array of research components (laboratory, clinical, and population sciences) as well as programs concerned with community service, outreach, dissemination, and education and training; of which, there are 25 Specialized and 40 Comprehensive Centers.

NCI Cancer Centers are significant participants in the clinical evaluation and care of cancer patients in the United States. An estimated 16 percent of U.S. cancer patients are initially diagnosed in NCI-designated Cancer Centers. It is likely that a larger percentage of patients are ultimately treated because of their status as referral centers for rare cancers and for those that have not responded to standard treatment. In 2008, approximately 39,000 patients were newly enrolled in therapeutic trials at NCI-designated Cancer Centers.

Cancer center grants are funded on a five-year cycle and range in direct costs from approximately \$700,000 to \$8.8 million. Most funding is applied to support research cores,

including a clinical trials core, where applicable, with modest and variable funding available for the development or support of research programs. Comprehensive Cancer Center reviews are focused on accomplishments and proposed translational research efforts, i.e., coordinated research activities between laboratories and clinical researchers.

Since cancer centers were established, there have been several evaluative reviews with subsequent changes in program and review processes. For instance, in response to a 2003 NCAB ad hoc Working Group review, major changes included streamlining the application, modifying the review process, and enhancing communication among center directors and NCI.

Working Group Findings Regarding Cancer Centers

- NCI-supported Cancer Centers have become the dominant contributor of new cancer knowledge in laboratory, clinical, and population sciences. Over the past 20 years, their translational research programs have defined the molecular lesions of major cancers and have developed therapies for specific subsets of human cancers, such as lung, breast and colorectal. Cancer centers work effectively with NCI, pharmaceutical, and biotechnology companies in testing new drugs and conducting translational studies that define pathways of drug resistance. Increasingly, Cancer centers have dominated the competition for basic and translational research funding. NCI cancer center grants are amplified 10 fold or more by training grants, investigator-initiated R01s, program project and SPORE grants, and foundation and philanthropic dollars.
- New models of funding research programs, particularly the SPORE program (see below) have contributed valuable support to cancer center activities. The original model of funding, a fixed percentage of total NCI grant dollars, is no longer workable because funding for the Cancer Center Support Grants (CCSGs) as a percentage of total NCI grant dollars, varies enormously among cancer centers. One shortcoming of the current system is that the existing CCSG funding model provides minimal flexible dollars to support innovative research.
- There is an inordinate focus during review on administrative processes and on fulfilling complex guideline requirements, rather than on emphasizing research productivity.
- The existing cancer center model lacks a strong incentive to conduct “team” research involving multiple centers and facilities or collaboration with other NCI programs such as cooperative groups. This type of multicenter research is essential for bringing together the talents and resources of multiple institutions to focus on a specific problem or patient population, and has proven valuable in understanding and studying subsets of human malignancies driven by uncommon mutations. Collaborative projects between comprehensive or clinical cancer centers and basic research centers have the potential to create synergies in addressing research needs and priorities. Unfortunately, collaborative efforts are not encouraged under the current model of cancer center funding.

Working Group Recommendations Regarding Cancer Centers

Recommendation 16: NCI should increase the emphasis of Cancer Center Support Grant review on programmatic accomplishments, scientific innovation, and productivity. The funding model should be merit based. There should be less

emphasis on adhering to rigid comprehensiveness and administrative compliance guidelines. It is expected that focusing, as indicated, will decrease the size of CCSG applications.

Recommendation 17: NCI should encourage and reward innovative trans-disciplinary partnerships established between basic, translational, clinical and population-based cancer centers or between cancer centers and other NCI-sponsored activities such as cooperative groups and Specialize Programs of Research Excellence (SPOREs).

Specialized Programs of Research Excellence

The Specialized Programs of Research Excellence, a successor to the original Organ Systems Program, was created in 1991 to promote interactions between basic and applied scientists for the development of new cancer interventions for specific organ sites (e.g., breast, prostate, lung, gastrointestinal, etc.). The SPORE program supports a broad range of translational research, which is aimed at improving the detection, treatment, and prevention of specific cancers, and requires collaborations across medical and research disciplines. Most, but not all, SPORE awards are held by Cancer Centers even though other entities, such as community cancer centers, may compete for SPORE funds. These applications 1) are reviewed in a cycle that is independent of the cancer center reviews; 2) provide an average of \$2.5 million in direct funding per year for projects and related cores; and, 3) support four to five research projects, developmental projects and career development awards for young investigators. To improve coordination among NCI's complex system of programs and resources for translational research, in 2008, the SPORE program was moved from the Office of the NCI Director into the Division of Cancer Treatment and Diagnosis. In FY 2009, the SPORE program budget was \$131.4 million.

Working Group Findings Regarding the SPORE Program

- The SPORE program, as reflected in the testimony of investigators, has been an important instrument for supporting disease-specific translational research, with admirable progress in lung, breast, and prostate cancer, as well as other diseases. This program provides funding for multidisciplinary projects, team science, and developmental projects that might otherwise have difficulty in peer review. In most instances, a funded SPORE grant complements CCSG funding of cores and administration. However, the review of the CCSGs and SPORES is not coordinated.

Working Group Recommendations Regarding the SPORE Program

Recommendation 18: The scope of the SPORE should move beyond disease-specific programs to include unique tumor biology research programs, e.g., oncogene driven tumors (such as *k-ras* and *c-myc*), which include multiple tumor types, or tumors driven by defects in deoxyribonucleic acid (DNA) repair or apoptosis.

Recommendation 19: Consideration should be given to coordinating the review of cancer centers and SPOREs, since the vast majority of SPOREs (more than 95 percent) are held by cancer centers, and represent the scientific engine that justifies the clinical component of the core grant.

NCI and Comparative Effectiveness Research

The NCAB Working Group perceives this to be a time of tremendous opportunity for NCI's involvement in comparative effectiveness research (CER). Recent investment of funds through the American Recovery and Reinvestment Act and the establishment of the Patient-Centered Outcomes Research Institute (PCORI) are changing the face of the CER enterprise in the United States. As the new CER enterprise takes shape, the NCAB Working Group recognizes NCI's substantial investments in CER to date and supports NCI's continued involvement in the following types of efforts:

- Developing data infrastructure for CER. Cancer CER requires improved capacity for learning from the routine delivery of care (i.e, claims and electronic health records) and conducting CER trials more efficiently. NCI can strengthen and enhance the information technology infrastructure, with the goal of enabling collaboration through distributed data networks and adoption of clinical data standards to facilitate data integration.
- Facilitating the development and refinement of methods for CER. Given the large volume of CER research sponsored by the NCI, the Institute may play a pivotal role in shaping new methods for CER in collaboration with broader NIH, other government, and non-government efforts.
- Using CER to promote more personalized cancer care. By encouraging investigators to study relevant subgroup effects in CER, NCI can support the development of evidence used to make cancer care more patient-centered.
- Ensuring that priority populations are not left behind in cancer CER. Across the spectrum of cancer research there are opportunities to better account for the specific needs and challenges of priority populations, including the elderly, children, racial/ethnic minorities, individuals with disabilities, and the poor. NCI can help deliver on the promise of CER by promoting research and other initiatives to address knowledge gaps regarding cancer control in these populations.
- Training future generations of researchers to carry out cancer-related CER. The Mentored Career Development grants awarded by NIH are one mechanism for fostering the development of a skilled future workforce.

In summary, the NCAB Working Group believes that continued or enhanced prioritization of these types of activities will help NCI maintain its position as a leader in cancer-related CER.

Conclusions

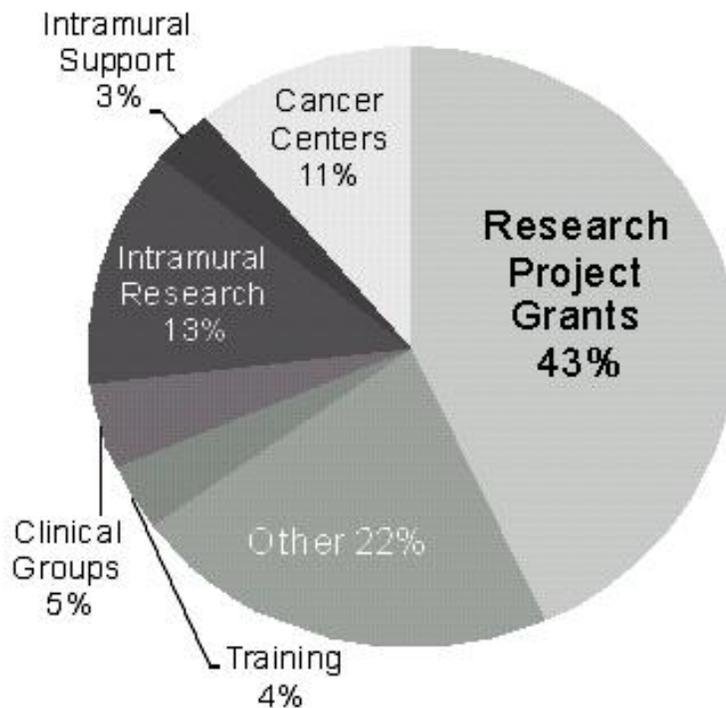
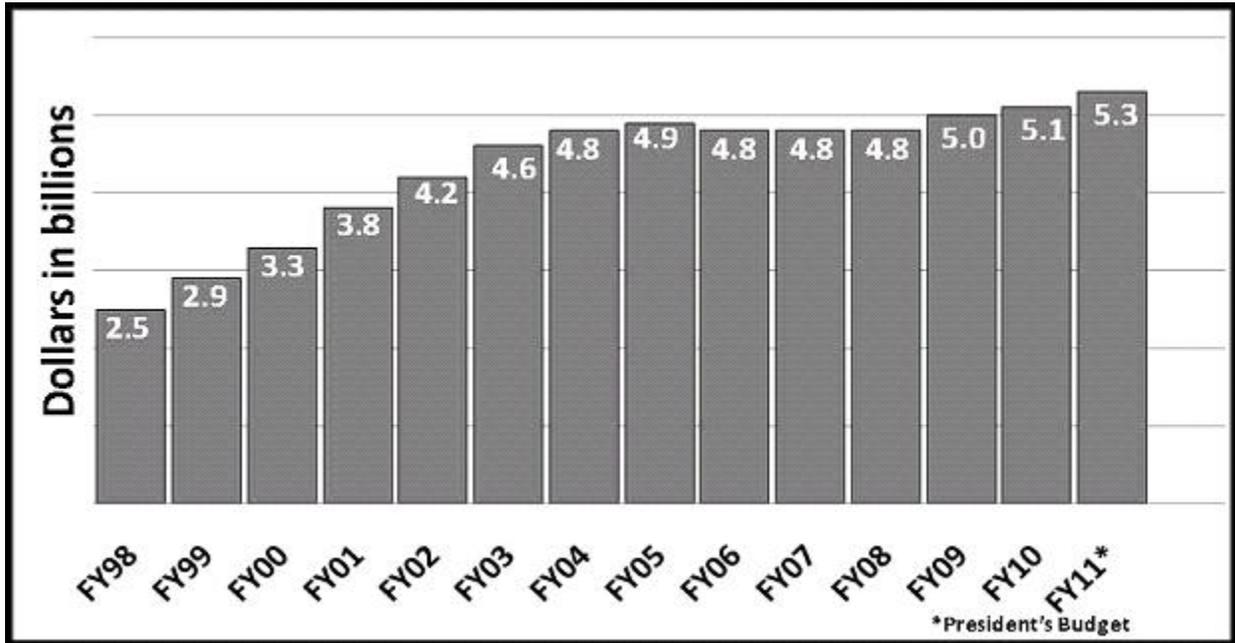
Given the current budget constraints, it is critical that NCI promote a prudent, sustained investment in the full spectrum of cancer research. NCI must identify and focus on its core strengths in research (basic, clinical, and population) and avoid duplicating successful programs, such as drug development by industry. NCI is strongly encouraged to significantly modify or end programs that are no longer highly productive or unique. As the scientific and fiscal environment changes, the objectives of key NCI infrastructure programs, such as the Cooperative Groups and the Frederick facility, will also need to undergo change, as will organizational structures and

staffing. The Working Group supports the NCI Director in making significant changes in structure and leadership to meet evolving needs.

Likewise, NCI must continue to be at the forefront of the Nation's cancer research effort. Given the scientific resources that exist in other NIH Institutes and Centers, and in industry and academia, and in view of the probability of constrained fiscal resources in the short term, NCI must use its leadership authority to aggressively seek collaborations across NIH and in the academic, nonprofit, and industrial sectors whenever feasible and appropriate. This viewpoint will require close collaboration with the pharmaceutical and biotechnology industries to take full advantage of the progress in understanding cancer biology and to bring effective new preventive, diagnostic, and therapeutic advances to cancer patients as quickly as possible.

APPENDIX A Budget Information

NCI's budget for Fiscal Year (FY) 2009 was \$5 billion. Not included in these figures are \$1.256 billion in American Recovery and Reinvestment Act (ARRA) funds allocated to NCI as one-time funding for FY 2009 and 2010. After witnessing a doubling of its budget from 1998 to 2003, and not counting ARRA funds, budgetary growth has been flat for the past seven years. NCI is now increasingly constrained by erosion in real dollars.



APPENDIX B Invited Speakers

May 4-6, 2010

Samuel Broder, M.D.

Vice President and Chief Medical Officer
Celera Genomics
Rockville, MD

Kenneth H. Buetow, Ph.D.

Director
Center for Bioinformatics and Information
Technology
National Cancer Institute, NIH
Bethesda, MD

Ronald A. DePinho, M.D.

Professor of Medicine
Departments of Medical Oncology/Molecular
and Cellular
Harvard Medical School
Dana-Farber Cancer Institute
Boston, MA

James H. Doroshow, M.D.

Director
Division of Cancer Treatment and Diagnosis
National Cancer Institute, NIH
Bethesda, MD

William H. Goodwin, Jr., M.B.A.

Chairman and President
CCA Industries, Inc.
Richmond, VA

Joe W. Gray, Ph.D.

Director
Division of Life Sciences
Associate Director of Biosciences
Lawrence Berkeley National Laboratory
Berkeley, CA

William N. Hait, M.D., Ph.D.

Senior Vice President
Worldwide Head of Hematology and Oncology
Johnson & Johnson Pharmaceuticals Group
Raritan, NJ

William R. Sellers, M.D.

Vice President and Global Head
Oncology
Novartis Institutes for BioMedical
Research, Inc.
Cambridge, MA

Richard L. Schilsky, M.D.

Professor of Medicine
Section of Hematology/Oncology
Biological Sciences Division
University of Chicago
Pritzker School of Medicine
Chicago, IL

Deborah Schrag, M.D., MPH

Attending Physician/Oncologist
Associate Professor of Medicine
Harvard Medical School
Dana-Farber Cancer Institute
Boston, MA

Phillip A. Sharp, Ph.D.

Institute Professor
Koch Institute for Integrative Cancer Research
Massachusetts Institute of Technology
Cambridge, MA

Ellen V. Sigal, Ph.D.

Chair and Founder
Friends of Cancer Research
Arlington, VA

Leland H. Hartwell, Ph.D.

President and Director
Fred Hutchinson Cancer Research Center
Seattle, WA

Ernest T. Hawk, M.D., MPH

Vice President for Cancer Prevention
Head, Division of Cancer Prevention Population
Sciences
Boone Pickens Distinguished Chair for Early
Prevention of Cancer
The University of Texas M.D. Anderson Cancer
Center
Houston, TX

Richard D. Klausner, M.D.

Managing Partner
The Column Group
San Francisco, CA

John E. Niederhuber, M.D.

Director
National Cancer Institute, NIH
Bethesda, MD

Richard Pazdur, M.D.

Director
Division of Oncology Drugs
Food and Drug Administration
Silver Spring, MD

J. James Rohack, M.D.

President
American Medical Association
Chicago, IL

Carolyn D. Runowicz, M.D.

Director
The Carole and Ray Neag Comprehensive
Cancer Center
Northeast Utilities Chair in Experimental Oncology
Professor of Obstetrics and Gynecology
Division of Gynecologic Oncology
University of Connecticut Health Center
Farmington, CT

Ann M. Vickery, J.D.

Partner
Hogan Lovells
Washington, DC

Bert Vogelstein, M.D.

Investigator, HHMI
Clayton Professor of Oncology and Pathology
Johns Hopkins University
Baltimore, MD

Andrew C. von Eschenbach, M.D.

Senior Director for Strategic Initiatives
Center for Health Transformation
Washington, DC

Ralph Weissleder, M.D., Ph.D.

Professor
Harvard Medical School
Director, Center for Systems Biology
Massachusetts General Hospital
Boston, MA

Robert H. Wiltrout, Ph.D.

Director
Center for Cancer Research
National Cancer Institute, NIH
Frederick, MD

Speakers July 7-8, 2010

Laurence H. Baker, D.O.

Professor, Department of Internal Medicine
Professor of Pharmacology, Department of
Pharmacology
Chairman, Southwest Oncology Group
Chairman, SARC
University of Michigan
Ann Arbor, MI

Bruce A. Chabner, M.D.

Clinical Director
Massachusetts General Hospital Cancer Center
Chief of Hematology/Oncology
Massachusetts General Hospital
Boston, MA

Francis Collins, M.D., Ph.D.

Director
National Institutes of Health
Bethesda, MD

Robert L. Comis, M.D.

Professor of Medicine and Director of
Drexel University College of Medicine
Clinical Trials Research Center
President and Chairman of the Coalition of Cancer
Cooperative Groups
Chair of the Eastern Cooperative Oncology Group
Philadelphia, PA

Robert T. Croyle, Ph.D.

Director
Division of Cancer Control and Population
Sciences
National Cancer Institute, NIH
Bethesda, MD

Charles L. Sawyers, M.D.

Investigator, Howard Hughes Medical Institute
Chairman, Human Oncology and
Pathogenesis Program
Memorial Sloan-Kettering Cancer Center
New York, NY

Phillip A. Sharp, Ph.D.

Institute Professor
Koch Institute for Integrative Cancer Research
Massachusetts Institute of Technology
Cambridge, MA

James H. Doroshow, M. D.

Director
Division of Cancer Treatment and Diagnosis
National Cancer Institute, NIH
Bethesda, MD

Peter Greenwald, M.D., Ph.D.

Director
Division of Cancer Prevention
National Cancer Institute, NIH
Bethesda, MD

William H. Goodwin, Jr., M.B.A.

Chairman and President
CCA Industries, Inc.
Richmond, VA

Maureen R. Johnson, Ph.D.

Project Officer
NCI Community Cancer Centers Program
National Cancer Institute, NIH
Bethesda, MD

Harold L. Moses, M.D.

Hortense B. Ingram Professor of Molecular
Oncology
Professor of Cancer Biology, Medicine and
Pathology
Director Emeritus
Vanderbilt-Ingram Cancer Center
Nashville, TN

Craig W. Reynolds, Ph.D.

Associate Director
National Cancer Institute at Frederick
Frederick, MD

Speakers
August 25-26, 2010

Edward J. Benz Jr., M.D.
President and CEO
Dana Farber Cancer Institute
Boston, MA

Bruce A. Chabner, M.D.
Clinical Director
Massachusetts General Hospital Cancer Center
Chief of Hematology/Oncology
Massachusetts General Hospital
Boston, MA

James H. Doroshow, M. D.
Director
Division of Cancer Treatment and Diagnosis
National Cancer Institute
National Institutes of Health
Bethesda, MD

H. Shelton Earp III, M.D.
Director and Lineberger Professor
UNC Lineberger Cancer Center
Chapel Hill, NC

Louis V. Gerstner, Jr.
Senior Advisor
The Carlyle Group
New York, NY

Giuseppe Giaccone, M.D., Ph.D.
Head, Thoracic Oncology Section,
Medical Oncology Branch
and Affiliates
National Cancer Institute
National Institutes of Health
Bethesda, MD

William H. Goodwin, Jr., M.B.A.
Chairman and President
CCA Industries, Inc.
Richmond, VA

Harold E. Varmus, M.D.
Director
National Cancer Institute
National Institutes of Health
Bethesda, MD

Linda K. Weiss, Ph.D.
Chief, Cancer Center Branch
National Cancer Institute
National Institutes of Health
Bethesda, MD

Jonathan S. Wiest, Ph.D.
Adjunct Investigator
Laboratory of Cancer Biology and Genetics
National Cancer Institute
National Institutes of Health
Bethesda, MD

Keith Yamamoto, Ph.D.
Executive Vice-Dean
Professor of Cellular and Molecular
Pharmacology
University of California, San Francisco
San Francisco, CA

Lee J. Helman, M.D.
Head, Molecular Oncology Section
Pediatric Oncology Branch
National Cancer Institute
National Institutes of Health
Bethesda, MD

Robert A. Ingram, M.B.A.
General Partner
Hatteras Venture Partners
Durham, NC

Bruce E. Johnson, M.D.
Professor of Medicine
Harvard Medical School
Professor of Medicine
Adult Oncology
Dana-Farber Cancer Institute
Boston, MA

William G. Nelson, M.D., Ph.D.
Marion I. Knott Director and Professor
Department of Oncology
Professor
Departments of Urology, Pharmacology,
Medicine, Pathology, and Radiation Oncology
Johns Hopkins Medicine
Director
The Sidney Kimmel Comprehensive Cancer Center
at Johns Hopkins
Baltimore, MD

Phillip A. Sharp, Ph.D.
Institute Professor
Koch Institute for Integrative Cancer Research
Massachusetts Institute of Technology
Cambridge, MA

**APPENDIX C
Meeting Agendas**

**National Cancer Institute
National Cancer Advisory Board**

**Ad Hoc Working Group to
Create a Strategic Scientific Vision for the National Cancer Program
and Review Progress of the National Cancer Institute**

**Bethesda North Marriott Hotel & Conference Center
5701 Marinelli Road
Bethesda, Maryland**

May 4-6, 2010

Tuesday, May 4 – Forest Glen Room

7:30 p.m. Dinner

Wednesday, May 5 – Salon F & G

7:00 a.m. Continental Breakfast

8:00 a.m. Welcome and Charge to the Working Group

Dr. Carolyn D. Runowicz
Mr. Robert Mittman

8:45 a.m. Establishing the Context-1:
The National Cancer Program

Dr. Phillip A. Sharp

9:00 a.m. Establishing the Context-2:
The National Cancer Act and Beyond

Ms. Ann M. Vickery
Mr. William H. Goodwin

9:30 a.m. Group Discussion

10:00 a.m. Break

10:20 a.m. Establishing the Context-3:
The State of the NCI

Dr. John E. Niederhuber
Dr. Kenneth H. Buetow
Dr. James H. Doroshow
Dr. Robert H. Wilttrout

11:50 a.m. Group Discussion

12:30 p.m. Lunch

1:30 p.m. Former NCI Directors: A Conversation

Dr. Samuel Broder
Dr. Richard D. Klausner
Dr. Andrew C. von Eschenbach

3:00 p.m. Break

3:20 p.m. NCI's Role Catalyzing the Discovery and
Development Continuum

Dr. William N. Hait
Dr. Richard Pazdur
Dr. Ellen V. Sigal

4:50 p.m. Wrap-up

5:00 p.m. Adjourn

5:30 p.m. Dinner – Glen Echo Room

6:30 p.m. Working Group Members' Meeting Only – Linden Oak Room

Thursday, May 6 – Salon F & G

7:00 a.m. Continental Breakfast

8:00 a.m. Recap and Plan

Mr. Robert Mittman

8:10 a.m. A Scientific Vision for 21st Century Cancer Research
Basic Science Panel 1

Dr. Ronald A. DePinho
Dr. Joe W. Gray
Dr. Lee H. Hartwell
Dr. Bert Vogelstein
Dr. Ralph Weissleder

9:30 a.m. Break

9:50 a.m. A Scientific Vision for 21st Century Cancer Research
Clinical and Population Sciences Panel 2

Dr. Ernest T. Hawk
Dr. J. James Rohack
Dr. Richard L. Schilsky
Dr. Deborah Schrag
Dr. William R. Sellers

11:20 a.m. Lunch Discussion for Working Group

1:15 p.m. Adjourn

**National Cancer Institute
National Cancer Advisory Board**

**2nd Meeting of the Ad Hoc Working Group to
Create a Strategic Scientific Vision for the National Cancer Program
and Review Progress of the National Cancer Institute**

**The Ritz-Carlton, Tysons Corner
1700 Tysons Boulevard
McLean, VA 22102**

July 7-8, 2010

Wednesday, July 7 – Salon 1

7:00 a.m.	Continental Breakfast	
8:00 a.m.	Recap from May Meeting	Dr. Bruce Chabner
8:15 a.m.	Clinical Trials and Cooperative Groups – IOM Report - Overview and Introductions - Summary of IOM Report - Perspective of Recommendations	Dr. James Doroshow Dr. Harold Moses Dr. Charles Sawyers Dr. Larry Baker Dr. Robert Comis
9:45 a.m.	Discussion: Clinical Trials & Cooperative Groups	Working Group
10:30 a.m.	Break	
10:45 a.m.	History and Activities of NCI Frederick - Drug Development at Frederick - NCI Community Cancer Centers Program	Dr. Craig Reynolds Dr. James Doroshow Dr. Maureen Johnson
12:15 p.m.	Lunch	
1:15 p.m.	Discussion: NCI Frederick Operations & Contracts	Working Group
2:00 p.m.	NIH Director	Dr. Collins
2:45 p.m.	Discussion	Working Group
3:15 p.m.	Break	
3:30 p.m.	Cancer Prevention Program	Dr. Peter Greenwald
4:30 p.m.	Discussion: Cancer Prevention	Working Group

5:30 p.m. Adjourn

6:00 p.m. Dinner

Thursday, July 8 – Salon 1

7:00 a.m. Continental Breakfast

8:00 a.m. Recap Dr. Bruce Chabner

8:15 a.m. Cancer Control and Population Sciences Program Dr. Robert Croyle

9:15 a.m. Discussion: Cancer Control & Population Sciences Working Group

10:15 a.m. Break

10:30 a.m. Discussion of Draft Report Dr. Phillip Sharp

- Introduction
- NCAB's Role
- Clinical Trials and Cooperative Groups – IOM report
 - Infrastructure
 - Program Assessment
- Intramural
- Frederick
- Prevention & Cancer Control
- Other Issues
- Recommendations

11:45 a.m. Discussion of Unresolved Issues and Other Business Co-Chairs

12:15 p.m. Initial Plans for August Working Group Meeting Co-Chairs

12:30 p.m. Adjournment

**National Cancer Institute
National Cancer Advisory Board**

**3rd Meeting of the Ad Hoc Working Group to
Create a Strategic Scientific Vision for the National Cancer Program
and Review Progress of the National Cancer Institute**

**The Ritz-Carlton, Tysons Corner
1700 Tysons Boulevard
McLean, VA 22102**

August 25-26, 2010

Wednesday, August 25

9:00 a.m.	Coffee/Tea – Meet and Greet	
10:00 a.m.	Welcome & Recap from July 2010 Meeting	Dr. Bruce Chabner
10:05 a.m.	Introductions & Agenda Review	Mr. Robert Mittman
10:15 a.m.	Cancer Centers Program	Dr. Linda Weiss Dr. Edward Benz Dr. William Nelson
11:00 a.m.	Discussion: Cancer Centers Program	Working Group
11:30 a.m.	SPORE Program	Dr. James Doroshow Dr. H. Shelton Earp Dr. Bruce Johnson
12:15 p.m.	Discussion: SPORE Program	Working Group
12:45 p.m.	Lunch	
1:30 p.m.	Intramural: Medical Oncology	Dr. Lee Helman Dr. Giuseppe Dr. Giaccone
2:15 p.m.	Discussion: Intramural—Medical Oncology	Working Group
2:45 p.m.	Cancer Training Program	Dr. Jonathan Wiest Dr. Keith Yamamoto
3:30 p.m.	Discussion: Training Program	Working Group

4:00 p.m.	Break	
4:30 p.m.	NCI Director	Dr. Harold Varmus
5:30 p.m.	The Capacity for Change	Mr. Lou Gerstner
6:30 p.m.	Working Dinner (<i>General discussion of report with co-chairs</i>)	

Thursday, August 26

7:00 a.m.	Continental Breakfast	
8:00 a.m.	Recap & Timeline	Dr. Bruce Chabner

Discussion of Draft Report

8:15 a.m.	Introduction, Charge, Background, & Capacity to Change	Dr. Phillip Sharp
8:45 a.m.	NCI Authorities, the Role of the NCAB & NCI/NIH Relationships	Mr. William Goodwin
9:15 a.m.	NCI Clinical Trials Program	Dr. Bruce Chabner
9:45 a.m.	NCI – Frederick	Dr. Bruce Chabner Dr. Phillip Sharp

10:15 a.m.	Break	
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Continued Discussion of Draft Report

10:30 a.m.	NCI's Cancer Prevention Program	Dr. Phillip Sharp
11:00 a.m.	NCI's Cancer Control and Population Sciences Program	Dr. Phillip Sharp
11:30 a.m.	Intramural: Medical Oncology	Dr. Bruce Chabner

12:00 p.m.	Lunch	
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Continued Discussion of Draft Report

1:00 p.m.	NCI Training Program	Dr. Phillip Sharp
1:30 p.m.	Cancer Centers and SPORE Programs	Dr. Bruce Chabner
2:00 p.m.	NCI and Industry Relationships	Mr. Robert Ingram
2:30p.m.	Review Overall Recommendations	Dr. Phillip Sharp
3:00 p.m.	Other Issues & Adjournment	Working Group