

# Board of Scientific Advisors

## Meeting Minutes

November 14, 2005

Building 31C, Conference Room 10  
Bethesda, Maryland

### Quick Links

[Members](#)

[Agenda & Future Meetings](#)

[Meeting Minutes](#)

---

[BSA: Page 1](#)

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for their 32nd meeting on Monday, November 14, 2005, in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Robert Young, President, Fox Chase Cancer Center, presided as Chair.

The meeting was open to the public from 8:00 a.m. until 4:35 p.m. on November 14 for the NCI Director's report and budget overview; a report on NCI/Congressional relations; a status report on the Cancer Research Network; presentations of concepts for Requests for Applications (RFAs) and Requests for Proposals (RFPs), and concepts for RFA re-issuance.

#### **Board Members Present:**

Dr. Robert Young (Chair)  
Dr. Hoda Anton-Culver  
Dr. Kirby I. Bland  
Dr. Susan J. Curry  
Dr. William S. Dalton  
Dr. Raymond N. DuBois, Jr.  
Dr. H. Shelton Earp III  
Dr. Kathleen M. Foley  
Dr. Sanjiv S. Gambhir  
Dr. Joe W. Gray  
Dr. William N. Hait  
Dr. James R. Heath  
Dr. Mary J.C. Hendrix  
Dr. Susan B. Horwitz  
Dr. Hedvig Hricak  
Dr. Erick Hunter

#### **Board Members Present:**

Dr. Christopher J. Logothetis  
Dr. Lynn M. Matrisian  
Dr. Kathleen Mooney  
Dr. Edith Perez  
Dr. John Potter  
Dr. Mack Roach III  
Dr. Richard L. Schilsky  
Dr. Ellen V. Sigal  
Dr. Margaret R. Spitz  
Dr. Jane Weeks

#### **Board Members Absent:**

Dr. Davis S. Alberts  
Dr. Esther H. Chang  
Dr. Patricia A. Ganz  
Dr. Leroy Hood

Ms. Paula Kim

Dr. Kenneth W. Kinzler

Dr. Michael P. Link

**NCAB Liaison:**

TBN

**Others present:** Members of NCI's Executive Committee (EC), NCI staff, members of the extramural community, and press representatives.

## TABLE OF CONTENTS

- I. [Call to Order and Opening Remarks](#); Dr. Robert Young
- II. [Consideration of the June 27-28, 2005, Meeting Minutes](#); Dr. Robert Young
- III. [Report of the Director, NCI](#); Dr. Andrew von Eschenbach
- IV. [NCI and Congress](#); Ms. Susan Erickson
- V. [Status Report: Cancer Research Network](#); Drs. Robert Croyle, Ed Wagner, Mark Hornbrook, Victor Stevens, and Suzanne Fletcher
- VI. [RFA/Cooperative Agreement/RFP Concepts](#); Presented by NCI Program Staff
  - Office of the Director and Division of Cancer Control and Population Sciences
    - [Increasing the Utilization and Impact of the NCI's Cancer Information Service](#)
  - Office of the Director
    - [The Human Cancer Genome Program \(RFA/Cooperative Agreement/RFP\)](#)
- VII. [Working Lunch: National Biospecimen/Biorepositories](#); Drs. Anna Barker and Carolyn Compton
- VIII. [VIII. RFA/Cooperative Agreement/RFP Concepts](#); Presented by NCI Program Staff
  - Division of Biology
    - [Tumor Microenvironment Consortium \(RFA-Coop. Agr.\)](#)
  - Division of Cancer Prevention
    - [Alliance of Glycobiologists for Detection of Cancer and Cancer Risk \(RFA/Coop. Agr.\)](#)
- IX. [RFA Concept Re-issuances](#); Presented by NCI Program Staff
  - Office of the Director

- Minority Institution Cancer Center Partnership (MI/CCP) (RFA/Cooperative Agreement)

X. **Adjournment**; Dr. Robert Young

---

## **I. CALL TO ORDER AND OPENING REMARKS—DR. ROBERT YOUNG**

Dr. Young called to order the 32nd regular meeting of the BSA and welcomed members of the Board, NIH and NCI staff, guests, and members of the public. He welcomed new members: Drs. Susan Curry, Director, Institute for Health Research and Policy, University of Illinois at Chicago; William Dalton, Chief Executive Officer and Center Director, H. Lee Moffitt Cancer Center and Research Institute, University of South Florida; James Heath, Elizabeth W. Gilloon Professor and Professor of Chemistry, California Institute of Technology; and Kathleen Mooney, Professor, University of Utah College of Nursing. He reminded members of the conflict-of-interest guidelines and called attention to confirmed meeting dates through November 2007 and the Joint National Cancer Advisory Board (NCAB), BSA, and Board of Scientific Counselors (BSC), including the chairs of the Presidents Cancer Panel (PCP), and Director's Consumer Liaison Group, Retreat on 10 January 2006. Members of the public were invited to submit to Dr. Paulette Gray, Director, Division of Extramural Activities (DEA), in writing and within 10 days, comments regarding items discussed during the meeting.

[top](#)

---

## **II. CONSIDERATION OF THE JUNE 27-28, 2005 MEETING MINUTES — DR. ROBERT YOUNG**

**Motion:** The minutes of the June 27-28, 2005 meeting were approved unanimously.

[top](#)

---

## **III. REPORT OF THE DIRECTOR, NCI—DR. ANDREW von ESCHENBACH**

Dr. Andrew von Eschenbach, Director, NCI, welcomed members of the Board and thanked them for their commitment and effort. Dr. von Eschenbach informed members that he had been asked by the President to be the Acting Commissioner, FDA, while continuing in the role of Director, NCI. He noted that he had taken a leave of absence from the administrative responsibilities associated with the NCI Directorship and delegated those responsibilities to Dr. John Niederhuber, Deputy Director for Translational and Clinical Sciences, who had been appointed to the position of Chief Operating Officer, NCI, by Secretary Michael Leavitt, Department of Health and Human Services (DHHS). He emphasized that he continues to be responsible for the overall NCI mission, initiatives, goals, and priorities that have been established over time; he noted that there will be no change in them. Dr. von Eschenbach acknowledged and commended the NCI leadership on the integrated and collaborative manner in which they have discharged their individual roles and responsibilities as leaders of the Centers and Divisions and within the Office of the Director (OD). He informed members that NCI's future direction remains unchanged, specifically with regard to the commitment and dedication to eliminating the suffering and death due to cancer by 2015.

Dr. von Eschenbach then discussed scientific opportunities that have emerged that make the 2015 goal more realistic and the obstacles that could impede the pace of progress needed to achieve that goal. Opportunities include the exponential growth in the understanding of cancer at the genetic and molecular level and of the person with the disease. He stated that emerging obstacles and barriers are related to the fact that the financial and human capital required to continue to expand these initiatives is becoming more constrained and will require greater responsibility with regard to stewardship. To address both the opportunities and potential barriers, core requirements will be cooperation and integration. Scientific priorities will be assessed across the spectrum of discovery, development, and delivery, and decisions as to the allocation of personnel or budgetary resources will rest ultimately with the senior NCI leadership. Input will be welcomed from a variety of sources in helping to define specific opportunities, but the investments and the balance among them must be carried out in the context of the larger picture within the NCI. Dr. von Eschenbach reminded members that, since the Fiscal Year (FY) 2006 budget has not yet been enacted, final decisions are pending

with regard to the allocation of the budget across the various parts of the portfolio.

Dr. von Eschenbach also discussed the movement of cancer research into the era he described as the molecular metamorphosis, which opened the way to a different understanding of cancer and different ways of addressing and managing the disease, bringing new hope and opportunities for achieving the 2015 goal. Members were told that the role for the NCI is to continue its leadership, which began in 1971 with the passage of the National Cancer Act. At that time, the NCI took the bold step of moving science from an era that was primarily dependent on grant mechanisms for generating new ideas to one that included contract mechanisms for focused, outcome-oriented research. Dr. von Eschenbach stated that, by virtue of this NCI-led cultural transformation, the NCI has been responsible for the molecular metamorphosis. Data from the National Library of Medicine showing the impact of the National Cancer Program (NCP) on medical and scientific literature was presented. He noted that cancer research has led or driven the evolution of knowledge in genetics and disease, and has had a significant impact on application to patients through cancer clinical trials. Dr. von Eschenbach emphasized the importance of continued bold, visionary leadership from the NCI and that support from the BSA that will be required to make the difficult choices in this new era where research must be conducted in a collaborative, cooperative, and interdependent fashion.

When queried about potential conflicts of interest between the roles and functions of the NCI and FDA, the steps being established to make this dual management as viable as possible, how two huge jobs could be done by one person, and how long the dual function would last, Dr. von Eschenbach explained that the two roles are clearly defined in relation to his responsibility and activity and that the duration of the dual function would be decided ultimately by the President. Potential conflicts of interest had been remedied legally, i.e., specific recusals and proscriptions are in place regarding decisions at the FDA that are relevant or related to specific matters that come before the FDA vis-à-vis the NCI. He noted that a conflict of commitment does not exist because his portfolio at the NCI is clearly defined and a strong leadership team is in place.

Dr. Niederhuber welcomed new Board members and thanked them

for their commitment. He informed members of recent personnel announcements: (1) Dr. Harold Freeman, formerly Director, Center to Reduce Cancer Health Disparities (CRCHD), OD, is the Senior Advisor on strategies to achieve the 2015 goal in minority and underserved communities; (2) Dr. Sanya Springfield, Chief, Comprehensive Minority Biomedical Branch, Office of Centers, Training and Resources, (OCTR), is the Acting Director, CRCHD; (3) Dr. Jerry Collins has accepted the position of Associate Director, Developmental Therapeutics Program (DTP), Division of Cancer Treatment and Diagnostics (DCTD); (4) Dr. Carolyn Compton joined the NCI in June as Director, Office of Biorepositories and Biospecimen Research (OBBR); (5) Dr. Piotr Grodzinski, formerly of Los Alamos National Laboratory, is the new Program Director for Cancer Nanotechnology, OD; (6) Mr. John Hartinger, Associate Director, Office of Budget and Financial Management, OD, is also the Acting Deputy Director for Management, OD, replacing Mr. David Elizalde who has accepted a position in the Office of the Surgeon General; (7) Dr. Kenneth Buetow has been named Associate Director for Bioinformatics and Information Technology, OD. Dr. Niederhuber concluded by announcing that: 1) recruitment is actively underway for a person to lead the effort in both anatomic and clinical pathology at the Center for Clinical Research (CCR); and 2) Dr. Steven Rosenberg, Chief, Surgery Branch, CCR, is leading the recruitment effort for a new Chief, Medical Oncology Clinical Research Branch, CCR. He expressed his commitment to the intramural program and the hope that two or three mid- to senior-level researchers would be recruited within the next year.

**NCI Publications.** Dr. Niederhuber informed members that the NCI now has three publications to communicate with the extramural community and the public: 1) the Bypass Budget, which focuses on what can be done with resources, even when those resources are limited; 2) a Strategic Plan, which highlights eight strategic priorities in the current draft; and 3) an Annual Progress Report which will focus on scientific accomplishments in both the intramural program and extramural community.

**NCI Response to Hurricane Katrina.** Dr. Niederhuber characterized NCI's response in meeting the needs of cancer patients and investigators as dramatic and comprehensive. Members were told that with Dr. Mark Clanton leading the NCI effort, an NIH field hospital was established nearby with the help

of volunteers from the Clinical Center. He noted that thousands of patients on clinical trials in that area were moved to care facilities in other states with the help of some BSA members and physicians from other institutions. NCI's Cancer Information Service (CIS) played a major role in establishing a communications network. The acute phase of the disaster response effort focused on patients and physicians' needs. Since then efforts have been directed towards helping investigators on a case-by-case basis. Dr. Niederhuber noted that he has charged a small NCI task force to begin thinking proactively about a strategic plan for action in the event of another crises, such as a flu pandemic.

**Update: Translational Research Working Group (TRWG).** Dr. Niederhuber presented an update on the status of the TRWG, which is being organized under the direction of Dr. Ernest Hawk, Office of Centers, Training, and Resources (OCTR), OD. The TRWG is a follow-up to, and modeled after, the Clinical Trials Working Group (CTWG). Several elements of the TRWG strategic plan have been completed. Drs. Lynn Matrisian and William Nelson have been engaged as senior TRWG leadership, and the membership roster has been developed. The TRWG will produce a report similar to that produced by the CTWG. A Web-based communication platform has been developed, and the site will be used for public comment sessions. Two roundtables are planned that will be convened for broader input. To allay concerns expressed in the cancer community, Dr. Niederhuber emphasized that all NCI-sponsored translation research programs will be evaluated, not just the Special Programs of Research Excellence (SPOREs).

**Update: NCI Budget.** Dr. Niederhuber reminded members that although the FY 2005 NCI budget increased by 3 percent over FY 2004, taps and adjustments reduced the total significantly, creating an essentially flat budget. Dr. Niederhuber noted that meetings at all levels within the NCI and with NIH Institute and Center (IC) Directors have been held to address budgetary issues. These issues include the prospect of a 2 percent reduction across the board in the discretionary part of the federal budget and possible taps by the NIH or HHS to deal with expenses such as those associated with the Katrina response and improvements to the security system. Members were informed that NCI planning has been predicated on a 2 percent decrease in the FY 2006 budget. Dr. Niederhuber emphasized, however, that the NCI is committed to maintaining: (1) momentum by reallocating resources within the budget; (2) the

number of competing grants at the same level as it was in FY 2004 and FY 2005; and (3) an adequate level of support for young investigators to ensure that the pipeline of investigators coming into research programs at the universities is not broken.

[top](#)

---

#### **IV. NCI AND CONGRESS - MS. SUSAN ERICKSON**

Ms. Susan Erickson, Director, Office of Policy Analysis and Response, began by reviewing the status of FY 2006 appropriations. Ms. Erickson also reported that NCI staff had participated in two Congressional hearings and that Dr. Elias Zerhouni, Director, NIH, testified before the House Energy and Commerce Committee at a July 17 hearing during which the first draft of the NIH Reauthorization Bill was introduced. She summarized key points of the draft.

Ms. Erickson concluded with a status report on other legislation of interest to the NCI, such as the Patient Navigator Outreach and Chronic Disease Prevention and the Postage Stamp for Breast Cancer Research bills. She also called attention to a number of other resolutions that give the members of Congress an opportunity to spotlight specific diseases of interest, usually by designating a week or month to raise awareness. In this Congress, resolutions were passed on pancreatic cancer, childhood cancer, and sun safety in addition to long-standing breast and prostate cancer resolutions.

#### **In discussion, the following point was made:**

- NCI senior staff are working proactively with NIH leadership to address the cancer community's concern about provisions in the NIH reauthorization draft legislation that relate to changes in the funding stream, NCI's authorizations, and adequate scientific oversight of the proposed common fund.

[top](#)

---

#### **V. STATUS REPORT: CANCER RESEARCH NETWORK -**

**DRS. ROBERT CROYLE, ED WAGNER, MARK HORN BROOK, VICTOR STEVENS, AND SUZANNE FLETCHER**

Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences (DCCPS), reminded members of extensive discussions among health care leaders about ways to integrate the worlds of biomedical research and health care delivery, in terms of payment and management. Key themes that emerged from the discussions were: (1) the importance of context and of understanding what makes clinical care efficient and effective; (2) the need to monitor and improve the quality of care, not just focus on the quantity of care; (3) the need to utilize modern information technology more efficiently; (4) the need to expand the delivery of early detection and preventive care; and (5) the need to use and leverage health care systems and their infrastructures as platforms for biomedical research. He stated that the CRN was established 6 years ago to support the implementation of collaborative research across several of the Nation's largest managed care systems. The RFA funded a single cooperative agreement grant to support coordination of this effort and research projects that were later leveraged to obtain additional R01 funding from the NIH and other sources. Dr. Croyle stated that consideration of the re-issuance of this initiative is scheduled for the February BSA meeting. He called attention to the new Journal of the National Cancer Institute (JNCI) Monograph that describes the CRN and the first wave of scientific projects that have emerged from the Network. He then introduced the presenters: Dr. Ed Wagner, Principal Investigator (PI), Group Health Cooperative, Seattle, WA; Dr. Mark Hornbrook, Leader, CRN Scientific and Data Resources Core, Kaiser Permanente Northwest, Portland, OR; Dr. Victor Stevens, PI, HIT I and HIT II Core Projects, Kaiser Permanente Northwest; and Dr. Suzanne Fletcher, PI, PROTECTS Core Project, Harvard Pilgrim Health Care, Harvard Medical School.

**Overview of the CRN.** Dr. Wagner explained that the original RFA sought delivery systems with research capacity that could generate information on large numbers of people, both their cancer experience and the totality of their health care experience. The goals of that RFA and the renewal were: research, capacity building, data standardization, evaluation, and collaboration. CRN sites include six regions of Kaiser Permanente from Hawaii to Georgia and six integrated health systems in other parts of the

country. Dr. Wagner noted that two new centers added as a result of the renewal are Kaiser Permanente of Georgia, which provides access to the Southeast and a large African American population; and Lovelace Clinic Foundation in New Mexico, which serves a large Latino population. Key features of the CRN are: 10 million enrollees (4 percent of the U.S. population) across 12 sites; racial and ethnic diversity; provision of comprehensive care (primary care to hospice); mature research centers; and high cancer patient retention. The CRN is funded through an NCI cooperative agreement that is co-sponsored by the Agency for Healthcare Research and Quality (AHRQ) and has the goal of developing partnerships with academic and cancer centers, as well as other consortia.

Dr. Wagner reminded BSA members of research resources that Health Maintenance Organizations (HMOs) can bring to bear in addressing research questions: defined populations; comprehensive automated data; electronic medical records (EMRs), from the same vendor in most cases; patient Web sites for two-way communication; standardized tumor registries linked with NCI's Surveillance, Epidemiology, and End Results (SEER) or SEER-styled state registries; formal QI programs and HEDIS reporting; and a history of innovation, especially around prevention and screening. Key CRN accomplishments to date are its 35 funded projects; publications in an extensive number of professional journals in addition to the JNCI Monograph; capacity building that includes the two new centers, an Investigators Workshop to introduce CRN resources to investigators without previous major collaboration with the Network, 15 trainees, and six pilot projects. Collaborations include a formal affiliation with the Dana-Farber Cancer Institute and ongoing negotiations with other Cancer Centers. Dr. Wagner concluded with a brief summary of participation in CRN's six core projects to highlight the CRN's strong research advantage inherent in its ability to mount huge sample sizes because of its large, defined populations.

**CRN Informatics Resources.** Dr. Hornbrook presented a schematic of the various CRN informatics resources and how they are interconnected. He pointed out that health plan information technology (IT) systems are the essential building blocks of the CRN in that they facilitate the study of cancer and cancer care from a population perspective. These include the HMOs' automated clinical, financial, and administrative data systems, the patient-

oriented Web site, and the EMRs. These comprehensive systems provide complete pictures of patients' cancer care and expenses, including prevention and diagnostic services. Virtual data warehouses (VDWs) at each locality substantially reduce programmer effort to build data files for research purposes because they contain standardized data extracted from that HMO's administrative data systems. Dr. Hornbrook noted that, by storing standardized data locally, Health Insurance Portability and Accountability Act (HIPAA) compliance is achieved inasmuch as only de-identified data leave the covered HIPAA entities. HMO administrative data systems are augmented by the patient-oriented Web site, which features secure portals through which patients can confer with their doctors. In addition, the CRN is currently testing Web-based interventions in two studies, which, if successful, could be scaled up and integrated across the CRN. With regard to the EMR systems, the CRN is developing strategies to extract data to make better use of all health care encounters, both real and virtual.

Dr. Hornbrook emphasized that the first priority is placed on standardizing data from cancer registries operated by, or accessible to, CRN health plans. These include SEER, state tumor, hospital-based, and HMO-operated registries that document cancers diagnosed among health plan members during their active enrollment periods. Standardization efforts will focus on laboratory test results, including cancer screening. He expressed an interest, as a health economist, in developing the CRN virtual data warehouse to complement the SEER-Medicare link.

Members were told that the CRN is participating in the NIH Clinical Trials Roadmap, working to adapt all of the CRN informatics tools to support an efficient clinical trials network. He noted that NCI's Cancer Bioinformatics Grid (caBIG) is a major collaborator with the CRN in population science by providing the conduit between informatics innovations at Cancer Centers and the dissemination of these innovations in real-world systems.

In closing, members were reminded that a recent NCI-sponsored summit on health care delivery systems and research platforms identified six gaps pertaining to cancer research and cancer patient care. He discussed each with respect to the CRN.

**CRN and Tobacco Control: HMOs Investigating Tobacco (HIT).** Dr. Stevens began by reminding members of the rationale

for tobacco interventions in routine medical care. Research on the effectiveness of such intervention led to the development of national treatment guidelines (PHS 2000) for providing tobacco cessation services in primary care settings. The guideline strategies (the 5As) are: **Ask** about tobacco use at every visit; **Advise** tobacco users to quit; **Assess** willingness to make a quit attempt; **Assist** the smoker in quitting; and **Arrange** follow-up contact. Dr. Stevens noted that, when followed, these guidelines are effective and probably provide the best evidence base for any of the available cancer prevention efforts. Further support for this intervention is provided by data from a clinical trial in which smokers were asked whether clinicians and nurses should encourage them to quit and offer assistance to those who quit. The data showed that patients expect help from their health care providers. Data from another prospective clinical trial revealed that patients want help, are receptive to help, and express a greater degree of satisfaction with their medical care when they receive assistance to quit. Dr. Stevens noted, however, that HMOs and other health care systems have not been as aggressive about implementing tobacco services as might be desirable. The CRN's first attempt to address the problem was HIT I, a survey of more than 5,000 smokers in nine HMOs. HIT I findings were presented.

The CRN is currently conducting HIT II with the goal of describing the primary care tobacco cessation practice patterns in four diverse HMOs with about 25 percent minority enrollment. Specific aims are to measure adherence to the national treatment guidelines (5As) and test the effectiveness of focused feedback on the tobacco treatment practice patterns of primary care physicians. HIT II methods include developing a natural language processing (NLP) coding program for free-text notes (which had been found to contain about one-half of the useful information on tobacco cessation treatment services); assessing adherence to tobacco treatment guidelines; and providing practice pattern feedback to randomly selected primary care physicians over 18 months. The challenge of hard-coding free text was addressed by the development of a NLP technique called MediClass, which goes beyond word recognition to look at grammar and word context, thereby allowing a more sophisticated analysis of free text. MediClass has undergone validity testing at four HMOs. HIT II is now providing feedback to physicians with the goal of achieving the 90th percentile of improvement in implementing each of the 5As. Data from the feedback are expected to be available in mid-

2006.

Looking forward, Dr. Stevens expressed the CRN belief that the proportion of health plans with EMRs will increase from the current 10 percent to 50 percent or more during the next 10 years, and that EMRs will be ubiquitous within 15 years. EMR-based measures may then be practical for assessing primary prevention services for whole populations.

**Progress in Breast Cancer Research.** Dr. Fletcher briefly reviewed the seven different breast cancer studies conducted by the CRN since 1999: efficacy of prophylactic mastectomy (PM); satisfaction and psychosocial outcomes after PM; efficacy of breast cancer screening in women at increased risk; participation by Asian women in breast cancer trials; diffusion of aromatase inhibitors into community practice; breast cancer treatment effectiveness in older women; and clinical and pathologic predictors of ductal carcinoma in situ (DCIS) progression. In a detailed review of three of the studies, she noted that the study to assess the efficacy of prophylactic mastectomy was conducted at the time of increasing interest in that procedure as an option for high-risk women and few published studies from community practices. Six health systems across the country participated, representing about 7.5 million people. Using the CRN automated systems, records from 1979 to 1999 were examined. This study is ongoing.

Next, Members were informed that CRN's computerized databases are used to answer some questions relatively quickly, in this case, the diffusion of new therapies into practice. Five months ago, two of the CRN health plans with automated pharmacy databases and computerized tumor registries developed a program to study the diffusion of aromatase inhibitors as therapy for women with estrogen receptor (ER)-positive breast cancer. This study is scheduled to be expanded to 10 sites soon.

Members were told that a new CRN study to develop a model for predicting DCIS recurrence or progression to invasive breast cancer, was described. Dr. Fletcher noted that more than 3,100 women diagnosed with DCIS between 1991 and 2001 comprise the study population.

Dr. Fletcher noted that these studies illustrate three types of breast

cancer research: (1) health care delivery; (2) treatment efficacy in the community; and (3) predictors of good and bad outcomes after cancer diagnosis. She expressed the view that the third type, if successful, is an important future path for the CRN and will demonstrate the potential of combining the CRN's strength in population science with the power of bench science that is the strength of academic medical and cancer centers. She concluded by summarizing the future directions for the CRN.

**In discussion, the following points were made:**

- Preliminary studies, as reported in the JNCI Monograph, are attempting to predict whether disparities in African American populations are related to poverty versus race. The CRN is developing those studies as a P01 program project grant.
- The CRN should explore the possibility for synergy that could result from collaborating in some way with the American Cancer Society and American College of Surgeons and their work with the National Cancer Database, which has DCIS as a major patient-care evaluation site.
- Young investigators are being encouraged to participate in the CRN with the help of minority supplements to increase the number of ethnically diverse investigators and the participation by women of Asian descent in breast cancer trials. Greater involvement by the Cancer Centers with the CRN would provide another conduit for young investigators to participate in population science.
- The CRN initiative can be used as a model for raising the level of care received in the average community practice where the health care systems are less well organized.

[top](#)

---

**VI. RFA/COOPERATIVE AGREEMENT AND RFP  
CONCEPTS—PRESENTED BY NCI PROGRAM STAFF**

**Office of the Director and Division of Cancer Control and**

## Population Sciences (DCCPS)

**Increasing the Utilization and Impact of the NCI's Cancer Information Service (CIS) (RFA).** Dr. Linda Squiers, Office of Communication, CIS, stated that the purpose of the proposed project is to stimulate research that explores effective national, regional, or community-based interventions that increase the use and impact of the CIS by underserved populations. The project is intended to address the problem that, although cancer information seeking is widespread and access to cancer information is greater than ever before, the American public is facing challenges to finding credible cancer information that meets their needs. This was indicated in the findings of the Health Information National Trends Study (HINTS). The NCI is equipped to meet these challenges through its Web site ([www.cancer.gov](http://www.cancer.gov)) and through the CIS, which provides access to information specialists through a toll-free telephone number (1-800-4-CANCER), instant messaging service (LiveHelp), and e-mail. It is critical for the NCI to understand the environmental or psychosocial factors related to the public's use of the CIS. Identifying specific barriers to utilization, as well as discovering and testing effective strategies to overcome barriers identified in research, is vital to the CIS mission of providing accurate and up-to-date cancer information to all segments of the U.S. population. Research funded through this RFA would be conducted in collaboration with CIS regional offices, including the Contact Centers, Partnership Program, and the Research Program.

A budget of \$1.3M per year is estimated to fund 6-7 grants (R21s), for a total of \$2.6M for the 2-year project period.

### **In discussion, the following points were made:**

- Research funded by this RFA should identify the specific barriers that exist among the medically underserved and non-information seeking populations, as well as specific strategies for stimulating information-seeking behavior in those populations.
- The RFA should contain specific language with respect to outreach to advocacy groups, inasmuch as advocates circulate in the various patient communities and can carry

the message.

- Concept language in the background section document should be strengthened regarding the need to base the research on current theory and concepts.
- A presentation on how the CIS does or does not reach certain populations should be considered. A survey of available cancer information services other than the CIS should be included.

**Motion:** A motion to approve the OD/DCCPS RFA concept entitled “Increasing the Utilization and Impact of the NCI’s Cancer Information Service” was 19 yeas, 3 nays, and no abstentions.

### **Office of the Director (OD)**

**The Human Cancer Genome Project (RFA/Cooperative Agreement and RFP)**. Dr. Gregory Downing, Director, Office of Technology and Industrial Relations, OD, stated that the mission of this proposed initiative is to develop a systematic approach to identifying genetic alterations of cancer that have meaningful clinical impact on a few rationally selected cancer types. This pilot project would be carried out in collaboration with the National Human Genome Research Institute (NHGRI). Objective and overarching goals of the pilot are to systematically develop and apply current genomic analysis technologies to identify genes in regions of potential importance to cancer, and tie that capability to the NHGRI’s ability and infrastructure for resequencing of these particular candidates. Key components of the pilot would be: (1) human cancer biospecimen core resource; (2) NCI-supported Cancer Genomic Characterization Centers (CGCCs); (3) NHGRI-supported Medical Genome Sequencing Centers (MGSCs); and (4) data management, bioinformatics, and computational analysis.

The proposed pilot project would be conducted using 1-3 organ-site-specific tumor biospecimens from approximately 500 patients. The NCI would support a system for the collection, processing, and distribution of high-quality controlled biospecimens to the CGCCs and NHGRI’s high throughput MGSCs. The CGCCs would use an

array of technologies to identify new genomic regions of interest from these specimens to be sequenced at the MGSCs, which would focus also on technology improvement or new sequencing technology development. The data management resources and analytical tools would be supported by NCI's caBIG, thereby enabling access to sequence data and genomic analyses by the entire cancer research community. Initiatives that would be supported by RFA funding are the CGCCs (3-4 awards, \$12M/year) and technology development for medium-high throughput cancer cell analysis (5-7 awards, \$1M/year), plus an additional \$2M/year for Small Business Innovation Research (SBIR) awards from the designated SBIR funding pool. Initiatives that would be supported by RFP funding are the biospecimen sample collection core (1 award, \$2M/year for contracts) and the bioinformatics core through the caBIG (4-6 awards, \$2M/year for contracts).

Estimated cost per year for 13-18 grant and contract awards is \$17M, for an estimated cost of \$50M (excluding the SBIR component) for the 3-year project period.

Following Dr. Downing's presentation of the concept, Dr. Francis Collins, Director, NHGRI, spoke in favor of proceeding with the proposed pilot project at this time. Dr. Collins noted that 1) this is a unique and historic opportunity to discover the complete atlas of genetic alterations in cancer; 2) this initiative is not just about sequencing; it is an integrated effort that puts together sequence data with multiple other types of data, and the sum will be greater than the parts; 3) by partnering with the NHGRI, the NCI is effectively doubling the impact of the initiative and the return on investment; 4) the complete and accurate characterization of cancer cannot be efficiently conducted as a cottage industry; 5) a critical mass of funding is needed to ensure success—for the biospecimen core resource, CGCCs, MGSCs, technology development, and data management/bioinformatics/computational core; and 6) objections to the Human Cancer Genome Project are similar to those lodged against the Human Genome Project (HGP) 20 years ago, and the HGP has proven to be transforming in terms of scientific progress. In conclusion, Dr. Collins emphasized that the proposed project is a pilot and that scale up would be predicated on providing evidence that the data justify doing that. All options are open for the future.

**In discussion, the following points were made:**

- BSA subcommittee discussions focused on (1) whether looking for somatic mutations in primary cancers would be the best and most appropriate scientific approach at this time; (2) technical feasibility; and (3) timing, in regard to making this a priority at this time. The subcommittee recommended that if the proposed pilot project were to go forward, it should do so with a clear definition of milestones, goals, and stopping rules. A concern was that, given the heterogeneity of tumors, the pilot might not produce meaningful answers.
- Areas of concern are: 1) skepticism about whether a single platform sequencing would be informative; 2) the need to look at linked data in the sense of linking sequencing data to human disease, providing evidence of benefit early on; 3) how to balance the issues between collecting tissue of sufficient quality for technology development and collecting tissue related to specific disease types where important questions could be framed; and 4) the availability of such tissue banks.
- Metrics for evaluation should be clearly defined.
- The natural user communities (e.g., SPOREs, integrated cancer biology program) that would be consumers of the sequencing that the proposed project will generate should be engaged in thinking about this project, to evaluate the utility of the sequence and help ensure the project's success.
- Although the pilot project will focus on only two tumors, it will establish systems needed to deal with issues like heterogeneity and whole genome amplification as well as the evaluation of these genomic technologies.

**Motion:** A motion to approve the OD RFA/Cooperative Agreement and RFP concept entitled “The Cancer Genome Program (TCGP)” with recommendations for an increase in funding for the Technology Development RFA, including the defined clinical outcome metrics in the RFA, and greater clarity with regard to choice, acquisition, and disposition of the biospecimens was approved unanimously.

---

## **VII. WORKING LUNCH - UPDATE: NATIONAL BIOSPECIMEN/BIOREPOSITORIES - DRS. ANNA BARKER AND CAROLYN COMPTON**

Dr. Anna Barker reviewed the history of NCI's efforts during the past 3.5 years to bring some harmonization to the NCI-supported biorepositories and develop guidelines and approaches for the NCI community. Dr. Barker reported briefly on a meeting chaired by the NCI the previous week during which representatives from 20 different nations discussed their national biospecimen activities. One finding was that some countries with national health care systems are moving quite strategically to build their bases for personalized medicine and for specific aspects of disease. Dr. Barker then introduced Dr. Carolyn Compton, Director, Office of Biorepositories and Biospecimen Research (OBBR), OD.

Dr. Compton noted that what is happening at the national level with biospecimens and NCI's leadership role can be compared to what is happening in the cancer genome realm. In the area of biorepositories, there are many different and valid approaches, but they have never been harmonized on a broad scale and with enough scientific depth. That is the goal of NCI's efforts to harmonize processes and policies for NCI-supported biorepositories. Board members were reminded of future NCI investments in terms of the pathway to personalized medicine, the key role of biospecimens in the future of molecular medicine, and NCI's biospecimen issues to be addressed. Dr. Compton described the highlights of NCI's multi-year analysis of biospecimens and biorepositories. She told members that inventory results revealed widespread heterogeneity in practices among NCI-supported programs, leading to the conclusions that NCI-supported biorepositories are not optimized for molecular medicine and that the return on NCI's \$50M investment can be improved. Dr. Compton noted that the Biorepository Coordinating Committee (BCC), composed of representatives from all NCI divisions that fund or are involved with research dependent on human biorepositories and has the mission of defining best practices for NCI-supported biorepositories, was formed to consolidate all NCI efforts in this area. As a first step, the BCC initiated a review of the literature from authoritative sources and sought extensive input from the

scientific community toward developing guidelines for NCI biorepositories.

Dr. Compton reported that the BCC is in the process of generating the first generation guidelines. They will include recommendations for: (1) common best practices for research biorepositories; (2) quality assurance/quality control (QA/QC) programs; (3) implementation of enabling informatics systems; (4) addressing ethical, legal and policy (ELP) issues; (5) establishing reporting mechanisms; and (6) providing administration and management structures. Dr. Compton noted that second generation guidelines will be based on the premise that the best practices for preserving the physical quality of the biospecimen and biomolecules within it do not fit in a single category. SOPs to ensure the highest quality specimens will depend on specimen type, the analytical method to approach the biomolecule, and the research question and will take a form analogous to an ice cube tray. She reported that a research network is being established through the OBBR to address the second generation guidelines on a scientific basis. Existing data will be collected to fill the ice cube tray with what is already known, and the unknowns will be divided up in the investigator network to produce the additional data that are needed. The assumption is that each cube will have SOPs that are unique and will have scientific data based on biospecimen research and the variables that could occur in the processing, storage, handling, and acquisition of that particular type of specimen. The goal is to move from empirical SOPs for biorepository operations to purely data-driven SOPs. Dr. Compton concluded that this can occur if best practices can be standardized across biorepositories and continually informed with data from the research network.

**In discussion, the following points were made:**

- The special and unique characteristics of molecular epidemiology biorepositories and their needs should be considered in future discussions and writing, inasmuch as they may have serial samples from subjects without cancer and be a very valuable control source.
- Biorepositories formed from consortia or shared agreements will require special consideration and handling in the areas of management and data sharing.

- It will be necessary to anticipate technologic developments and applications such as noninvasive surgical procedures and begin to incorporate early removal of the specimen into surgical plans, and consider the use of sensors within the specimen to record the quality of the specimen.

[top](#)

---

## **VIII. RFA/COOPERATIVE AGREEMENT/RFP CONCEPTS - PRESENTED BY NCI PROGRAM STAFF**

### **Division of Cancer Biology (DCB)**

**Tumor Microenvironment Consortium (RFA/Cooperative Agreement)**. Dr. Dinah Singer provided a history of meetings that led to the Tumor Microenvironment Consortium RFA, which represents a synthesis of recommendations that were developed during 10 think-tank sessions sponsored by the DCB in 2004. DCB staff reviewed and summarized the sessions and compiled the information into overarching themes. A summary of the recommendations was published in the Cancer Research.

Dr. Suresh Mohla stated that the intent of the RFA is to establish a Tumor Microenvironment Consortium (TMEC), whose major objective would be to delineate the mechanism of tumor host interactions in cancer by understanding stromal composition, the role of stroma in normal tissues, and the role of stroma initiation, progression, and metastases. Dr. Mohla informed members that the scientific goals of the individual research programs will be to pursue defined biology driven projects, with an emphasis on delineating the mechanistic aspects grown in the tumor microenvironment interaction. The consortium goals, in contrast, are to take all the expertise available in the research programs and develop resources for the research community at large. The investigators who are funded through this program are expected to collaborate with other consortium members to develop resources by leveraging expertise that might be concentrated in a single research program, generate novel reagents and technologies, and ensure that these technologies are disseminated through the NCI-managed bioinformatics resource. Whereas, the scientific goals of the consortium will be to develop models, whether they are novel

in vitro three-dimensional models, organotypic models, or animal models. Specifically, the focus will be to develop efficient techniques to isolate and purify stromal cells from normal and tumor tissues; identify and characterize stromal markers as well as develop tools to identify such markers; and develop dynamic and real time in vivo imaging techniques suitable for visualizing molecules, cells, and tumors.

The estimated first year cost will be approximately \$1.8M each, at approximately \$1.2M in direct costs, for a total cost of \$12M per year for six research programs over 5 years. Intramural programs would be eligible to apply and, if approved, would be supported by intramural funds.

**In discussion, the following points were made:**

- In response to questions about the proposed consortium and the appropriateness of using the R01 mechanism, staff noted that, if established correctly, this kind of initiative could help to energize the R01 community.
- Concern was expressed about the types of outreach programs that will be needed to involve the larger community.

**Motion:** A motion to approve the DCB RFA/Cooperative Agreement concept entitled “Tumor Microenvironment Consortium” was unanimously approved with the request that language be included in the RFA that would incorporate a pilot- or planning-type mechanism.

**Division of Cancer Prevention (DCP)**

**Alliance of Glycobiologists for Detection of Cancer and Cancer Risk (RFA/Cooperative Agreement).** Dr. Sudhir Srivastava introduced the Alliance of Glycobiologists for Detection of Cancer and Cancer Risk RFA/Cooperative Agreement. Dr. Srivastava stated that humans are believed to synthesize tens of thousands glycan structures. Glycomics, which is the study of glycans, is a new frontier using extraordinary technology to detect complex

carbohydrates for clinical application. He noted that the concept addresses what is known about glycans and their use in cancer and adds rigor to existing approaches in the quest for biomarkers for clinical applications in genomics and proteomics. It is consistent with NCI's comprehensive approaches to augment pre-emption, prediction, and prevention. Many other institutes are involved in this consortium, thus upholding the NIH Roadmap on trans-institutes collaboration to accelerate discovery and clinical application.

Dr. Karl Krueger stated that the RFA proposes to promote translational research to identify, develop, and validate cancer biomarkers based on glycan (complex carbohydrates) structures and introduce a new cadre of leaders in glycomic chemistry to apply their expertise to novel approaches for cancer detection and diagnostics. The initiative is based on altered carbohydrate expression that appears to be common to oncogenic transformation, often contributing to the invasive and malignant properties of the neoplastic cells, and glycomic biomarkers or glycan structures that represent a largely untapped arena relevant to cancer detection and diagnosis. The alliance's scientific goals include 1) elucidating glycan structures that would contribute toward cancer biomarkers, 2) exploiting glycan arrays for cancer biomarker discovery and possibly adapting for cancer screening or cancer detection tests, and 3) developing tools and reagents to facilitate high throughput glycomic screening technology. An important component of this alliance is the Consortium for Functional Glycomics, which is funded by the National Institute of General Medical Sciences (NIGMS) with additional support from the National Center for Research Resources and recently portrayed in an issue of Chemical and Engineering News. The tumor glycome laboratories would be funded by U01 funds, which would be openly competed.

Dr. Krueger noted that this initiative would contribute to NCI's 2015 goal by helping to develop glycomic biomarkers to enable early detection of cancer through a simplified and cost-effective means. It also complements NCI's clinical proteomics technology initiative. Regarding NCI's areas of strategic focus, this initiative specifically addresses early detection, prevention, and prediction. It is proposed to use the U01 mechanism to fund the tumor glycome laboratories, as substantial programmatic involvement will be necessary to operate this alliance.

The estimated cost is \$3.2M annually over 5 years, with \$2.5M funding between four to six tumor glycome laboratories. In addition, \$500,000 annually would be allocated for reagents and services supplied by the Consortium for Functional Glycomics. From Year 2 onward, an additional \$200,000 would be earmarked for data management and analysis as performed in collaboration with EDRN's data management and coordinating center

**In discussion, the following points were made:**

- Questions were raised regarding the operation of the tumor glycome laboratories, the structure of the coordinating unit, the involvement of R01 investigators or other members of the scientific community, and the access to specimens.
- The study of glycoproteins is related closely to proteomics and that duplication of work might occur, as a consortium involving proteomics already exists.
- The proposed project should have a formal structure to link it with the Early Detection Research Network and clear linkages with the Clinical Proteomic Technologies Consortia.

**Motion:** A motion to approve the DCP RFA/Cooperative Agreement concept entitled “Alliance of Glycobiologists for Detection of Cancer and Cancer Risk” was approved by a vote of 13 in favor, 9 against, and no abstentions, and with the recommendation that the proposed project have a formal structure to link it with the Early Detection Research Network and clear linkages with the Clinical Proteomic Technologies Consortia.

[top](#)

---

**IX. RFA CONCEPT RE-ISSUANCES - PRESENTED BY  
NCI PROGRAM STAFF**

**Office of the Director (OD)**

**Minority Institution Cancer Center Partnership (MI/CCP) (RFA/Cooperative Agreement).** Dr. Nelson Aguila informed members that the Minority Institution Cancer Center Partnership program was started in 1999 following a portfolio analysis of the NCI and meetings within the NCI and with other NIH institutes. The intent of the program was to provide minority-serving institutions and cancer centers the opportunity to collaborate through beneficial partnerships. The primary objectives include 1) establishing a competitive cancer program in a minority-serving institution, 2) building long-term collaboration, 3) improving the effectiveness of the cancer center with its program to benefit minority underserved populations, and 4) increasing the number of cancer health disparities research in cancer centers. MI/CCP addresses four areas in cancer: research, training, outreach, and education. The program has three levels of funding: feasibility studies via the P20, a cooperative planning grant; U56, a unique mechanism that applies only to the MI/CCP program; and U54, a comprehensive partnership. The program was approved unanimously in 2000 by the Executive Committee and the BSA as a 3-year strategic pilot program. Fifty-four awards have been made during that time.

Regarding program evaluation, there are immediate, intermediate, and long-term metrics of success. An immediate success is that 18 new faculty members have been hired as a result of the MI/CCP in minority-serving institutions, which is important because increasing the number of faculty or researchers conducting cancer studies helps achieve the program's objective to create stable and competitive cancer research in minority institutions. Long-term success metrics include increased competitive grant funding in minority-serving institutions and increased grant funding in cancer health disparities in cancer centers. Matching and leveraging funds is a key element to establishing long-term collaborations. Additionally, The MI/CCP program has 66 training and outreach pilot programs. The partnership has worked to create a seamless transition for students at minority-serving institutions to train at cancer centers. Other programs also are underway.

Within the intermediate metrics of success, there have been some qualitative assessments and improvements to research infrastructure, some newly created and others enhanced by the partnership. The program has achieved results in terms of institutional commitment. For example, the San Francisco State

University's committed \$1M for a new psycho-oncology program created as a result of a U56 collaboration with UCSF Cancer Center. Leveraged funding and resources include a bill enacted by Puerto Rico legislation that provided \$120M for 10 years to the Puerto Rico Cancer Center; the bill was a direct consequence of the U54 between the Puerto Rico Cancer Center and the M.D. Anderson Cancer Center.

Funding/mechanism: The P20 mechanism is a 4-year nonrenewable grant with a total cost of \$400,000 per year per partnership; U56 is a 5-year nonrenewable grant that provides up to \$800,000 total costs per year per partnership; and the U54 is a 5-year renewable mechanism (the only renewal mechanism in this program) that provides up to \$3.5 million per year for each partnership. In the developmental costs, the U54 also provides funding up to \$275,000 per year for direct costs for a fourth project.

In 2006, plans are to issue six awards, specifically three partnerships from the P20 mechanisms, two awards for one partnership via the U56 mechanism, and two awards and one partnership using the U54 vehicle. Plans are to convert the P20 mechanism into a program announcement in 2006. The estimated total costs over 5 years is \$26.3M.

**In discussion, the following points were made:**

- Questions were asked about the RFA's funding mechanism and whether the RFA would need to be re-issued each year. A Board member expressed concern about the number of U54s and U56s that are funded, and whether increasing the number of U56 awards would cause a cessation in U54 funding.

**Motion:** A motion to concur in the re-issuance of the OD RFAs/ Cooperative Agreement concept entitled "Minority Institution Cancer Center Partnership (MI/CCP)" was unanimously approved.

**Division of Cancer Treatment and Diagnosis (DCTD)**

**Supplements for Image-Guided Interventions in Centers and**

**SPOREs (RFA).** Dr. Sam Gambhir explained that this re-issuance of the Supplements for Image-Guided Interventions in Specialized Programs of Research Excellence (SPOREs) and Centers RFA is for \$1M per year for 2 years for a total of \$2 million as a supplement to P50s and P30s for SPOREs and Cancer Centers. It is estimated that four awards will be made, each for 2 years. In June 2005, 53 submissions were received for this particular solicitation, 37 of those (70 percent) were deemed responsive to the original RFA, and 4 were funded. A large number of high-quality submissions were unable to be funded.

The long-range goal is to see systemic therapies succeed. In the intermediate term, many evolving image-guided interventions can be used. Examples of these include magnetic resonance imaging (MRI) based interventions, positron emission tomography (PET CT) using instrumentation to allow an interventional radiologist to use image guidance to target a tumor, focused ultrasound to treat tumors, nanoparticles that are injected at the site of tumors to identify tumor boundaries, as well as software for image fusion to better guide the interventionalist or surgeon. It is a rapidly evolving area, and the review committee was enthusiastic and unanimous in its vote to approve the funding.

Issues were raised about the performance of the four previously funded projects or grants. All have made good progress to date. Following encouragement from the review committee, the re-issuance calls for more interaction with industry and academics, as well as more language on interactions with the nano centers to take advantage of new emerging nanotechnologies. There were discussions about whether \$1M per year was too little funding for such an important area. Finally, for future consideration it was suggested that synergies between the NCI and the National Institute of Biomedical Imaging and Bioengineering (NIBIB) might help leverage additional funding in this area.

In discussion, the following points were made:

- One Board member commented that image guided intervention is a new specialty that is not limited to radiologists but has expanded rapidly into other therapies.
- A Board member agreed that the field of image-guided

interventions is under funded.

**Motion:** A motion to concur with the re-issuance of the DCTD RFA concept entitled “Supplements for Image-Guided Interventions in SPOREs” was unanimously approved.

[top](#)

---

## **X. ADJOURNMENT—DR. ROBERT YOUNG**

There being no further business, the 32nd regular meeting of the Board of Scientific Advisors was adjourned at 4:35 p.m. on Monday, November 14, 2005.

[top](#)