

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
NATIONAL CANCER INSTITUTE  
129<sup>th</sup> NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting  
February 18-19, 2004**

**Building 31C, Conference Room 10  
National Institutes of Health  
Bethesda, Maryland**

**NATIONAL CANCER ADVISORY BOARD  
BETHESDA, MARYLAND  
Summary of Meeting  
February 18-19, 2004**

The National Cancer Advisory Board (NCAB) convened for its 129<sup>th</sup> regular meeting on Wednesday, February 18, 2004, in Conference Room 10 of Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Wednesday, February 18, 2004, from 8:30 a.m. to 4:30 p.m. The meeting was closed to the public from 4:30 p.m. until adjournment at 5:30 p.m. The meeting was reopened to the public on Thursday, February 19, 2004, from 8:30 a.m. until adjournment at 11:35 a.m. NCAB Chair Dr. John E. Niederhuber, Professor, Departments of Oncology and Surgery, University of Wisconsin-Madison, presided during both the open and closed sessions.

**NCAB Members**

Dr. John E. Niederhuber (Chairperson)  
Dr. Samir Abu-Ghazaleh  
Dr. James O. Armitage  
Dr. Moon S. Chen, Jr.  
Dr. Kenneth H. Cowan  
Dr. Jean B. deKernion  
Dr. Stephen C. Duffy  
Dr. Ralph S. Freedman  
Dr. James H. French (absent)  
Dr. Elmer E. Huerta  
Dr. Eric S. Lander (absent)  
Dr. Susan M. Love  
Dr. Arthur W. Nienhuis  
Dr. Larry Norton  
Ms. Marlys Popma  
Dr. Franklyn G. Prendergast (absent)  
Dr. Amelie G. Ramirez  
Ms. Lydia G. Ryan

**President's Cancer Panel**

Dr. LaSalle D. Leffall, Jr. (Chairperson)  
Dr. Margaret Kripke

**Alternate Ex Officio NCAB Members**

Dr. Michael A. Babich, CPSC  
Dr. Raynard Kington, NIH  
Mr. T.G. Patel, VHA  
Dr. Richard Pazdur, FDA  
Dr. John F. Potter, DOD  
Dr. Prem Srivastava, DOE

**Members, Executive Committee, National Cancer Institute, NIH**

Dr. Andrew von Eschenbach, Director, National Cancer Institute  
Dr. Alan Rabson, Deputy Director, National Cancer Institute  
Dr. Anna Barker, Deputy Director, Strategic Scientific Initiatives  
Dr. J. Carl Barrett, Director, Center for Cancer Research  
Ms. Nelvis Castro, Deputy Director, Office of Communications  
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences  
Dr. Ellen Feigal, Acting Director, Division of Cancer Treatment and Diagnosis  
Dr. Joseph Fraumeni, Director, Division of Cancer Epidemiology and Genetics  
Dr. Harold P. Freeman, Director, Center to Reduce Cancer Health Disparities  
Dr. Peter Greenwald, Director, Division of Cancer Prevention  
Dr. Paulette Gray, Acting Director, Division of Extramural Activities  
Ms. Janice Mullaney, Acting Deputy Director for Management, Office of the Director  
Dr. Dinah Singer, Director, Division of Cancer Biology  
Ms. Sandy Koeneman, Executive Secretary, Office of the Director

**Liaison Representatives**

Ms. Roshunnd Drummond, American Society of Therapeutic Radiology and Oncology  
Dr. Margaret Foti, American Association for Cancer Research  
Dr. Robert W. Frelick, Association of Community Cancer Centers  
Ms. Barbara K. LeStage, National Cancer Institute, Director's Liaison Group  
Ms. Judy Lundgren, Oncology Nursing Society  
Ms. Mary Mitchell, American Society of Therapeutic Radiology and Oncology  
Dr. Monica Leibert, American Urologic Association  
Dr. Clare O'Connor, National Science Foundation  
Ms. Nancy O'Reilly, The American College of Obstetricians and Gynecologists  
Ms. Barbara Stewart, Association of American Cancer Institutes  
Ms. Julie Taylor, American Society of Clinical Oncology  
Ms. Marie Zinninger, American College of Radiology

**TABLE OF CONTENTS**

**DAY ONE: WEDNESDAY, FEBRUARY 18, 2004**

I.	Introduction, Welcome, and Approval of December 2003 Minutes—Dr. John E. Niederhuber.....	1
II.	Future Meeting Dates Confirmed Through 2005—Dr. John E. Niederhuber.....	1
III.	NCI Director’s and Joint Board Retreat Reports—Dr. Andrew von Eschenbach .....	1
	Questions and Answers.....	4
IV.	President’s Cancer Panel—Dr. LaSalle Leffall, Jr. ....	4
	Questions and Answers.....	5
V.	Conflict of Interest Issues at NIH—Dr. Maureen Wilson.....	6
VI.	Legislative Update—Ms. Susan Erickson .....	7
	Questions and Answers.....	8
VII.	Special Recognition: 2004 NCAB Members—Drs. Andrew von Eschenbach and John E. Niederhuber .....	8
VIII.	Strategic Leadership To Accelerate the Prevention and Cure of Cancer—The Vital Role and Responsibility of the AACR—Dr. Margaret Foti.....	8
	Questions and Answers.....	11
IX.	Current Imaging Issues, Including CT Colonography—Dr. Daniel Sullivan.....	11
	Questions and Answers.....	14
X.	Sarcoma Progress Review Group Report: A Roadmap for Sarcoma Research— Drs. Lee Helman, Todd Golub, and Karen Antman .....	15
	Questions and Answers.....	16
XI.	Update: Office of Cancer Communications—Ms. Nelvis Castro and Ms. Mary Anne Bright.....	18
	Questions and Answers.....	19
XII.	NCI Annual Report and New Bypass Budget—Dr. Mark Clanton and Ms. Cherie Nichols .....	19
	Introduction .....	19
	Questions and Answers .....	20
	Bypass Budget.....	20
	Questions and Answers .....	21
XIII.	Annual Delegations of Authority—Dr. Paulette Gray.....	21
XIV.	Closed Session .....	22

**TABLE OF CONTENTS (continued)****DAY TWO: THURSDAY, FEBRUARY 19, 2004**

XV.	Tumor Microenvironment—Dr. Joan Brugge .....	22
	Questions and Answers.....	25
XVI.	NCI Energy Balance Priorities: New Initiatives and Research Highlights— Drs. Robert Croyle and Rachel Ballard-Barbash .....	25
XVII.	Update: Center for Strategic Dissemination—Dr. Edward Maibach.....	27
	Questions and Answers.....	28
XVIII.	Subcommittee Reports .....	29
	Subcommittee on Activities and Agenda—Dr. John Niederhuber.....	29
	Subcommittee on Cancer Centers—Dr. Arthur Nienhuis .....	29
	Subcommittee on Clinical Investigations—Dr. John E. Niederhuber .....	29
	Subcommittee on Planning and Budget—Ms. Cherie Nichols .....	29
	<i>Ad Hoc</i> Subcommittee on Communications—Dr. Susan Love.....	29
	<i>Ad Hoc</i> Subcommittee on Confidentiality of Patient Data—Dr. Amelie Ramirez .....	30
XIX.	Future Agenda Items.....	30
XX.	Adjournment—Dr. John Niederhuber .....	30

**DAY ONE: WEDNESDAY, FEBRUARY 18, 2004**

**I. INTRODUCTION, WELCOME, AND APPROVAL OF DECEMBER 2003 MINUTES—  
DR. JOHN E. NIEDERHUBER**

Dr. Niederhuber began by asking for a moment of silence to remember patients with cancer and those who have passed away from cancer. In particular, he noted the death on February 7 of former NCAB member Dr. Alfred Goldson, Professor and Chair, Department of Radiation Oncology, Howard University School of Medicine. Dr. Niederhuber welcomed members and *ex officio* members of the Board; representatives of liaison organizations; members of the President's Cancer Panel (PCP); Dr. Paulette Gray, Acting Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), and Executive Secretary, NCAB; other NCI staff; and members of the public. Dr. Niederhuber introduced and welcomed Dr. Prem Srivastava, *ex officio* member representing the Department of Energy (DOE), and noted the retirement of Dr. Hugh McKinnon, *ex officio* member representing the Environmental Protection Agency (EPA). He invited the public to submit to Dr. Gray, in writing and within 10 days, comments regarding items discussed during the meeting.

Dr. Niederhuber reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

**Motion.** A motion was requested and made to approve the minutes of the December 2003 NCAB meeting. The motion was seconded, and the minutes were unanimously approved by the Board.

**II. FUTURE MEETING DATES CONFIRMED THROUGH 2005—  
DR. JOHN E. NIEDERHUBER**

Dr. Niederhuber called Board members' attention to future meeting dates listed in the Agenda, which had been confirmed through 2005. He asked that members review the tentative dates listed through December 2006 so they can be moved to confirmed status as soon as possible.

**III. NCI DIRECTOR'S AND JOINT BOARD RETREAT REPORTS—  
DR. ANDREW von ESCHENBACH**

Dr. von Eschenbach began by thanking NCAB members and the cancer community for their support of the NCI. He acknowledged the contributions of Dr. Alan Rabson, Deputy Director, NCI, and the leadership infrastructure within the Institute in providing support to the benefit of all in the cancer arena. He noted that the support also enabled him to focus during his first years on the future of the Institute, building on the successes and progress in its past and present. He reminded members that the challenge goal of eliminating suffering and death due to cancer by 2015 was announced the previous year and stated that the rationale and strategy for addressing the goal have been amplified over the past year. The strategy is based on understanding cancer as a disease process that can be preempted to detect, predict, and eliminate some cancers and modulate the behavior of others such that people can live with and not die from, cancer.

Dr. von Eschenbach stated that the past year has been spent building on mission vision and goals and developing strategy in two areas: organizational structure and management of resources. In regard to organization, he noted that a "shared governance" model is being created within the Office of the Director (OD) in which the executive function is shared with key members to broaden and increase the sphere of management of the entire enterprise. Four Deputy Director positions have been created to work directly with the Director to manage and integrate the NCI portfolio of discovery, development, and delivery across the Institute. Dr. von Eschenbach noted that the Divisions and Centers remain the operational units

for the portfolio. Through the Executive Committee (EC), Division Heads and Center Directors will continue to play a role in the senior leadership of the NCI for planning strategy and tactics and in defining programs.

Dr. von Eschenbach listed the four new deputy positions and recruitment information. The first is the Deputy Director for Integrative Biology and Molecular Oncology, with responsibility for discovery; recruitment is in its final stages. The second is Deputy Director for Advanced Technologies and Strategic Partnerships, which is positioned at the intersection of discovery and development; this position is to be filled by Dr. Anna Barker. The third is the Deputy Director for Translational and Clinical Sciences, at the intersection of development and delivery; recruitment is underway. The fourth is the Deputy Director for Cancer Care and Delivery Systems; Dr. Mark Clanton has been appointed to fill this position. Dr. von Eschenbach acknowledged the work of Dr. Karen Antman, who served as an advisory consultant to address the area of translational research and clinical science. He noted that Dr. Rabson will continue to focus specifically on patient and professional relationships in the OD. Dr. Rabson has inaugurated a process whereby professional organizations and patient advocacy groups meet on a formal basis for dialogue and discussion on setting future strategic priorities for the Institute.

Dr. von Eschenbach reported that the position of Deputy Director, Office of Management, is in the process of being filled. He thanked Ms. Janice Mullaney, who has been acting in that capacity. He also thanked Ms. Mullaney, Mr. John Hartinger, Associate Director, Office of Budget and Financial Management, and the entire budget office for their ongoing service and able management of the Institute's human and fiscal resources. He reminded members of the inauguration of an annual "All Hands" Meeting last year on the theme of Progress with a Purpose. He noted that the focus of this year's meeting is on the human endeavor within the Institute and throughout the cancer enterprise that makes it reasonable to envision a country and world in which no one suffers and dies due to cancer. Dr. von Eschenbach stated, therefore, that creating an atmosphere and organization that appropriately addresses the needs of the workforce and workforce development will be an important focus for NCI leadership in the coming year. Challenges to be addressed exist in the area of budget and fiscal resource management, as well as opportunities for leadership and career development programs. In that regard, according to Dr. von Eschenbach, a process has been instituted in which the Director's Gold Star is awarded for exemplary service. The program of compensation and rewards also is being reexamined to ensure that exceptional performance and contributions are recognized. In addition, the mandate for the NCI Office of Diversity and Employment Programs, headed by Ms. Christina Bruce, will be broadened to become the NCI Office of Workforce Development. This is being done to ensure that an atmosphere is being developed that reflects, respects the value of, and promotes diversity in every possible context.

Dr. von Eschenbach concluded his review of NCI organizational structure, function, and leadership endeavors with the announcement that Dr. James Dorshow will formally join the NCI as Director, Division of Cancer Treatment and Diagnosis (DCTD). Other key recruitments are underway.

Next, Dr. von Eschenbach reported that a pilot strategy called the *NCI Cancer Bulletin* has been launched to address the need for mechanisms and opportunities to communicate more effectively with the community of cancer stakeholders. The *NCI Cancer Bulletin* is a Web-based, weekly publication and a means to disseminate useful, authoritative cancer information on a timely basis, as well as provide a forum for two-way communication between the NCI and the community. One feature of the publication is the Director's Update, a weekly opportunity for the Director to provide his perspective on issues and to notify the community of available opportunities. Another feature is guest editorials from key people and key organizations in the community, for example, Drs. Mark McClellan and Lee Hartwell. Dr. von Eschenbach invited feedback and input from the Board on the pilot program.

One recent example of the type of real-time communication and dissemination that is possible through the *NCI Cancer Bulletin* was information published on the outbreak of mouse hepatitis virus at the NCI-Frederick Cancer Research and Development Center (FCRDC). Another was the press conference announcement by the Secretary of Health and Human Services (HHS), the Surgeon General, Centers for Disease Control and Prevention (CDC) Director, and Dr. von Eschenbach of the joint program to create and expand a national network of Quit Lines for smoking cessation. Quit Lines is a joint effort of the CDC, the NCI, and organizations like the American Cancer Society (ACS), Tobacco-Free Kids, and American Legacy Foundation to create opportunities for evidence-based intervention. Another recent story announced the successful end to patient recruitment for the National Lung Screening Trial, which was launched in September 2002, with a goal of recruiting 50,000 individuals.

Dr. von Eschenbach announced that the Cancer Bioinformatics Grid (caBIG) will be launched formally on Thursday, February 19, when the NCI will be hosting 200 Cancer Center investigators who will be participating in this pilot project. He commended the work of Dr. Kenneth Buetow, Director, Center for Bioinformatics, and his staff in creating the bioinformatics platform that will enable the integration and coordination of many activities across the spectrum of the cancer research discovery, development, and delivery enterprise. Dr. von Eschenbach noted that one important aspect of caBIG is the infrastructure it will provide for horizontal integration among the Cancer Centers and for vertical integration of the Centers with the communities they serve and with the NCI.

Dr. von Eschenbach noted that the annual Cancer Center Directors Retreat will be convened on March 8 to examine strategic opportunities that are available. This retreat, together with the recently completed budget retreat that brought together the NCAB, Board of Scientific Advisors (BSA), and Board of Scientific Counselors (BSC), provided opportunities to focus on the future from different perspectives.

Next, Dr. von Eschenbach reviewed the ramifications of reductions that will be taken from NCI's Fiscal Year (FY) 2004 appropriation of about \$4.7 B that was signed into law on January 23, a 3.9 percent or \$178 M increase over 2003. These include the across-the-board reduction of 0.5 percent and another administrative decision that reduces the NCI increase from \$178 M to \$137 M. Further assessments within the NIH for everything from centralized activities to NCI's \$16 M commitment to the NIH Roadmap Initiatives and outyear commitments related to noncompeting renewals of investigator-initiated grants have the net effect of beginning the year in a \$2 M deficit. Dr. von Eschenbach stated that there will be essentially no money for new strategic initiatives, and that it will be necessary to redeploy resources already within the NCI base to be able to act on strategic opportunities like caBIG and the Integrative Cancer Biology Initiative. He emphasized that aggressive, long-range financial planning will be needed to lay out the strategies and map the plans to financial and human resources if the initiatives are to be carried out. Dr. von Eschenbach noted that NCI's senior leadership, including the EC, Division Heads, and Center Directors, are committed to careful thought and deliberation in this process and are committed to protecting the investigator-initiated research portfolio. However, they also are working across a strategy that guides and directs the entire enterprise and will be deploying resources at times from one part of the organization to another to be able to meet strategic opportunities and strategic priorities. Dr. von Eschenbach noted that a few guiding principles have been established to protect investigator-initiated research as a high priority as work begins on the President's FY 2005 budget request. He expressed gratitude for NCAB support in the process of addressing the human and fiscal resource challenges in a time of unbelievable scientific opportunity. He stated that the NCI is committed to focus on that opportunity and use the greater-than-ever human and fiscal resources to ensure the end of suffering and death from cancer by 2015.



## Questions and Answers

Dr. Larry Norton, Deputy Physician-in-Chief for Breast Cancer Program, Memorial Sloan-Kettering Cancer Center, asked for more information on strategic partnerships with industries related to cancer. Dr. von Eschenbach listed collaborations already undertaken in trans-NIH activities, with other HHS agencies including the CDC and Center for Medicare and Medicaid Services (CMS), with major cancer professional organizations, and with the pharmaceutical and biotechnology industries. These collaborations will continue to be pursued within the context of appropriate interactions and relationships that advance the mission.

In response to questions from Dr. Ralph Freedman, Professor, Department of Gynecologic Oncology, The University of Texas M.D. Anderson Cancer Center, Dr. von Eschenbach explained the lines of reporting from Division Heads to the new Deputy Directors. He noted that the intent is to flatten and decentralize the administrative structure, giving more opportunities for direct input into executive function.

### **IV. PRESIDENT'S CANCER PANEL—DR. LaSALLE LEFFALL, JR.**

Dr. LaSalle Leffall, Jr., Charles R. Drew Professor of Surgery, Howard University College of Medicine, reminded NCAB members that the President's Cancer Panel (PCP or Panel) has been examining issues and challenges associated with cancer survivorship. Five meetings on this topic held between May 2003 and January 2004 in various venues nationwide and abroad focused on the European perspective of cancer survivorship, challenges faced by pediatric cancer survivors, survivorship among adolescents and young adults, the needs of adult survivors, and concerns of older adult cancer survivors, those diagnosed after the age of 60.

Dr. Leffall presented an update on testimony from older adult cancer survivors at a recent meeting in Philadelphia, where the Panel heard from both invited speakers and members of the local community. Older adults share common survivorship issues with other age groups, but face very specific survivorship concerns. Much remains to be learned about the long-term physical and psychological effects of cancer and its treatment in this population, including: (1) the effect of comorbid conditions that mask disease symptoms and complicate treatment regimens, and (2) the influence of age and genetics on drug metabolism. Adequate surveillance data on this population are needed. A public awareness program also is needed with tailored messages and materials about the need for cancer screening and early detection. Challenges with respect to supportive services to maintain quality of life are: (1) the inability of some on fixed incomes to afford such services; (2) access to effective, well-informed support networks; and (3) the burden on caregivers of older survivors who also may be the same age and having health problems. Moreover, it was observed that members of the medical profession may not be adequately trained in meeting the informational and psychosocial needs of these older patients, and that guidelines for long-term, followup care for older adults should be established.

Dr. Leffall noted that a number of older survivors strongly supported a concept of a survivorship team to plan the transition from treatment to daily living and to coordinate followup care, a virtual medical home for each survivor. A key member of the team would be a navigator or case manager to assist older patients in advocating for themselves in a complex medical system. Testimony also supported development of a standardized electronic health record that can be accessed and updated by all members of the survivorship team. This would be a valuable tool for the survivors themselves who might not understand or remember everything they have experienced. A theme that surfaced repeatedly in the testimony was a sense of obligation to give something back by sharing their knowledge and experience with others, for example, through support groups, established foundations to fund research and education, and speaking ministries.

In addition to testimony from survivors, the Philadelphia meeting featured remarks by cancer care professionals and representatives of the insurance industry, including the CMS. Data presented indicated that by the year 2030, 70 million Americans, or one in five, will be over the age of 60, double the current size of this age group. Because 59 percent of cancer diagnoses occur among those over 60, a critical issue raised by both physicians and insurers was how to meet the costs of the impending health care burden, as well as the needs of cancer survivors. Insurance industry representatives expressed support for efforts to increase participation in clinical trials and for the development of evidence-based guidelines to standardize reimbursement of cancer care costs. Other priorities cited were the need for advances in prevention and early detection, as well as development of more effective, less toxic treatments.

Dr. Leffall stated that the Panel's next task is to consider the testimony and written remarks received in conjunction with the series of meetings and prepare a report to the President, Congress, and the Nation. In addition to providing an overview of the challenges faced by cancer survivors as a whole, the report will spell out the Panel's recommendations for short- and long-range steps that should be taken by the health care system, policymakers, and the research community in response to what has been learned.

Dr. Leffall reported that the next set of meetings will focus on translating research into clinical practice. Four meetings will address barriers to progress in the translational process, to include the role of academic medical centers, NCI-designated Cancer Centers, and the community cancer centers and how they fit into their larger communities. Topics that may be covered include the peer-review process, issues related to infrastructure, workforce sustainability, financing of clinical research, and the potential for forging effective partnerships among the various sectors involved in translating research into application.

Dates and locations for the 2004-2005 meetings are: August 30, San Francisco, CA; September 27, Columbus, OH; November 1, Houston, TX; and January 4, New York, NY.

In added remarks, Dr. Margaret Kripke, Executive Vice President and Chief Academic Officer, University of Texas M.D. Anderson Cancer Center and member of the Panel, emphasized the enormous challenge cancer in the older population will present to health care systems, cancer centers, and cancer treatment communities. She expressed concern that neither cancer centers nor the National Cancer Program is prepared for what will be a deluge of cancer cases and health care needs in this population.

### **Questions and Answers**

Dr. Niederhuber asked whether the Panel would be exploring how the large number of community-based centers scattered across the Nation can be networked without additional resources, in light of the fact that the country can support only a finite number of comprehensive or clinical delivery systems. Dr. Leffall replied that the Panel plans to address the problem of connecting or reconnecting those community-based centers with the rest of the cancer enterprise. Dr. Kripke noted that the role of the academic medical centers in helping to translate research at every step and what are the best mechanisms for moving research out into the communities were questions the Panel hopes to address over the next year. Dr. von Eschenbach summarized the response that the NCI has already begun to make: (1) the work of Drs. Julia Rowland and Mark Clanton and the Office of Cancer Survivorship in the collaborations with the CMS and the Food and Drug Administration (FDA), and (2) the work of Drs. Rabson and Antman with outside groups and the P30/P50 Working Group to revise the cancer center guidelines. He emphasized that the NCI will continue to work on the horizontal integration of the cancer centers and their vertical integration with the community to address issues raised by the Panel.

## V. CONFLICT OF INTEREST ISSUES AT NIH—DR. MAUREEN WILSON

In an introduction to this presentation, Dr. von Eschenbach reported that Dr. Maureen Wilson, Assistant Director, Ethics Office, OD, was one of the most recent recipients of the Gold Star Award for her work in guiding the NCI in its response to stewardship issues having to do with ethics and conflict of interest. Dr. Wilson then presented the Board with an update of ethics issues at the NIH and what is being done to address concerns seen recently in the public press. She stated that she would concentrate on the areas of the use of Title 42 as a personnel appointment mechanism, lecture awards, and the consulting relationships between the NIH and employees.

Dr. Wilson reminded members that appointment under Title 42 versus previous appointments under the Senior Executive Service, Senior Scientific Service, or Commissioned Corps had appeared in the press as a mechanism to avoid public financial disclosure. She presented the findings of the Office of Government Ethics (OGE) 1995 audit of the NIH to determine how financial disclosure was being enforced. At the time, the NIH and the NCI determined public financial disclosure by mechanism and by salary range, and the NCI had 77 appointees who filed. Of those, 50 were experts serving under the Public Health Service Act and were not included in the required public financial disclosure system. Those experts were removed from filing on the advice of the OGE because they were not covered under the implementing regulations for public financial disclosure. Dr. Wilson noted that as a result of acting on OGE advice, the NCI now has 15 people who file public financial disclosures. She added that there has been a recent review, and a number of other positions are going to be added to NCI's list of those required to file, including the NCI Clinical Director and Scientific Directors. The extramural programs also are being examined to determine which of those individuals should be added. Dr. Wilson noted, however, that 1,423 of the approximately 3,000 NCI employees do disclose their holdings and activities to the NCI Ethics Office, and the Ethics Office is working with the scientists and Office of General Counsel Ethics Division to assure rigor in safeguarding the interests of the NIH and protecting the interests of the individual in these cases.

In the area of lecture awards, concerns raised in the press were that individuals were receiving money to deliver lectures that would otherwise be considered part of their official duties. Dr. Wilson explained the opinion handed down by the DHHS Office of Government Ethics that such an award should be treated as an award for meritorious public service if it met the criteria for an award; i.e., it was funded to ensure perpetuity and the awardees were chosen by a committee or pursuant to written criteria. It also was the opinion of the Office of Government Ethics that individuals such as institute directors should not be excluded from being so recognized. A ruling was made in 1998 that institute directors and other highly placed individuals across the NIH could accept such awards from grantees provided it were possible at the time to disqualify the individual from activities affecting the awarding institution from the time the award was offered until all activities associated with the award were completed. Dr. Wilson concluded, therefore, that the activities portrayed in the press have been consistent with the advice of counsel and with DHHS procedures. A review of this matter is ongoing both at the NIH and throughout the DHHS.

Finally, Dr. Wilson addressed the information in the press about consulting relationships between NIH employees and industry, particularly in the area of biotechnology and pharmaceuticals, and the amounts of money involved. She noted that the NCI has an extensive process for reviewing requests for extramural personal activities, whether for compensation or not. It is the responsibility of the supervisors to review requests from employees they supervise, analyze them for relatedness to the science and with respect to administrative considerations, and decide which requests should go forward to the NCI Ethics Office for further action. Dr. Wilson noted that not all requests are approved. A review of a 5-year sample of activities that were submitted indicated that approximately 22 percent of the requests were turned down. Dr. Wilson noted that, to address these concerns at the NIH level, Dr. Elias Zerhouni,

Director, NIH, has designated Dr. Bernard Kington, Deputy Director, NIH, as NIH Deputy Ethics Counselor. Dr. Kington has been so delegated the authority from the DHHS. He will be responsible for reviewing financial disclosure and advice not only for individuals within the OD, NIH, but also for a number of appointments at the NCI. Dr. Wilson stated that she would be involved in the process for NCI personnel, including deputy directors, scientific and clinical directors, and a number of extramural program officials. She noted further that an NIH Ethics Advisory Committee has been established to act as a peer-review committee for many of these activities. The co-chairs are Dr. Kington and Dr. Michael Gottesman, Deputy Director for Intramural Research, NIH. NCI's representative is Dr. Joseph Fraumeni, Director, Division of Cancer Epidemiology and Genetics (DCEG). This committee will monitor activities involving the biotech and pharmaceutical industries as well as activities involving future income streams, income of more than \$10,000, or stock or stock options. This committee also will review award approval requests for more than \$2,500. In addition, a blue ribbon committee has been established as a subcommittee of the Advisory Committee to the Director, to be chaired by Drs. Bruce Alberts and Norman Augustine. The subcommittee will examine NIH review processes to determine disclosure obligations and management practices to advise on possible improvements. Dr. Wilson noted, in conclusion, that the NCI undergoes an ongoing review by the Inspector General and an OGE review every fourth year.

## **VI. LEGISLATIVE UPDATE—MS. SUSAN ERICKSON**

Ms. Susan Erickson, Acting Director, Office of Policy Analysis and Response, NCI, began with a brief review of the chronology of the FY 2004 Appropriations Omnibus Bill, which was signed into law on January 23, 2004, as Public Law 108-109. She noted that the FY 2005 appropriation cycle began with the presentation of the President's Budget in February, in which the NIH receives \$28.757 B (a 2.6% increase) and NCI \$4.87 B (a 2.8% increase). Senate and House hearings on the NIH budget have tentatively been scheduled for March and April, respectively. The formats for the respective hearings have not been disclosed, nor have any of the theme hearings been identified.

Ms. Erickson reported the enactment of Public Laws of significance to the NCI. The first is entitled "The 21<sup>st</sup> Century Nanotechnology Research and Development R&D Act," which established a National Nanotechnology Research Program. Ms. Erickson noted that funds were authorized, but not appropriated, to fund the program in several Federal agencies; however, an amendment late in the process deleted authorization of appropriations for the NIH and three other agencies. The second Public Law of particular relevance to the NCI was the Medicare Reform Act. A section of the Act established a Health Care Infrastructure Improvement Program, which provides loans to qualified hospitals to make capital improvements and allows loan forgiveness under criteria to be established by the Secretary, HHS. Authorized appropriations of \$200 B for this program become available in July and extend through September 2008. The NCI is participating in the HHS implementation of this law. The loan program will cover capital costs of projects to improve health care infrastructure, including construction, renovation, and other capital improvements. A qualifying hospital is defined as one engaged in research in the causes, prevention, and treatment of cancer. The institution also must be either an NCI-designated Cancer Center or the designated official Cancer Center of a particular state.

Ms. Erickson then called attention to the Cooperative Research and Technology Act (CREATE), which was introduced in June 2003, that was approved by the House Judiciary Committee in January 2004, and will now come up for the full vote of the House. The Act addresses a key loophole in intellectual property law in that it promotes research collaboration among universities, the public sector, and private enterprise, and discourages challenges of the validity of a patent achieved through collaboration.

Finally, Ms. Erickson gave an update of the briefing for staff of the Health, Education, Labor, and Pensions (HELP) Committee on the Surveillance, Epidemiology and End Results (SEER) Program. Division of Cancer Control and Population Sciences (DCCPS) Program staff presented information about the types of data collected by the SEER Program and its uniqueness as a resource for analysis and prediction. The collaborative interaction of the NCI SEER Program and the CDC National Program of Cancer Registries also was highlighted. Committee staff indicated that the information provided in the briefing would be useful as they consider working on new cancer legislation.

### **Questions and Answers**

In discussion, Dr. Niederhuber asked that Ms. Erickson keep the Board informed of scheduled hearings on the Institute of Medicine (IOM) Report and of any additional information that is received on the specific types of projects that would be covered by the loan program for health care infrastructure improvement. Dr. Norton emphasized the potential impact of nanotechnology on cancer research activities and expressed concern that the NIH, and by extension the NCI, was deleted from the authorization for appropriations.

### **VII. SPECIAL RECOGNITION: 2004 NCAB MEMBERS— DRS. ANDREW von ESCHENBACH AND JOHN E. NIEDERHUBER**

Dr. von Eschenbach joined Dr. Niederhuber to recognize and thank five retiring members for their years of service on the NCAB: Dr. Stephen Duffy, Executive Vice President, American Academy of Facial Plastic and Reconstructive Surgery and the International Federation of Facial Plastic Surgery Society; Dr. Elmer Huerta, Director, Cancer Preventorium, Washington Cancer Institute, Washington Hospital Center; Dr. Susan Love, Clinical Professor of Surgery, David Geffen School of Medicine, University of California at Los Angeles; Dr. Larry Norton, Deputy Physician-in-Chief for Breast Cancer Program, Memorial Sloan-Kettering Cancer Center; and Dr. Amelie Ramirez, Associate Professor, Department of Medicine and Deputy Director, Chronic Disease Prevention and Control Research Center, Baylor College of Medicine.

### **VIII. STRATEGIC LEADERSHIP TO ACCELERATE THE PREVENTION AND CURE OF CANCER—THE VITAL ROLE AND RESPONSIBILITY OF THE AACR— DR. MARGARET FOTI**

Dr. Margaret Foti, Chief Executive Officer, American Association for Cancer Research (AACR), stated that she would describe the mission, characteristics, and foci of the AACR of today, explain how the AACR carries out its role of accelerating progress; and discuss the need for strategic leadership to meet the 2015 challenge goal. She reminded members that the AACR is the oldest and largest cancer research organization in the world, with 22,000 members from more than 60 countries and nonmember constituencies of more than 80,000 scientists worldwide. As a result, the AACR is the world's collective brain trust in cancer research and in all cancer-related fields, which maximizes the opportunities for crossdisciplinary research. Dr. Foti noted that the AACR has a consistent focus on cutting-edge science and has been focusing on how to be more proactive in these areas. In addition, AACR's many annual meetings and journals, as well as its international scope, size, and diversity, make the organization an authoritative source of the latest cancer research findings, providing many opportunities for networking, mentorship, and crossdisciplinary interactions.

Dr. Foti noted that AACR's overarching strategies for accelerating progress against cancer begin with its leadership in science and technology. In that regard, AACR strategic planning sessions of the board and task forces have been identifying promising new research areas and intervention opportunities: (1) new collaborations have been recommended; (2) strategies for integrating science and discovery with

translation to the clinic have been considered, including the development of better animal models, accelerating new compound testing, identifying tools needed to facilitate technology transfer and the next wave of targets; and (4) new constructs to speed cancer drug discovery and development are being considered. Representative mechanisms for maximizing scientific impact include: (1) annual meetings, special conferences, educational workshops, and print and online media; (2) scientific retreats and think tanks; (3) scientific committees, task forces, and working groups; (4) programs in association with other organizations and with cancer survivors and advocates; and (5) representation on NCI scientific advisory boards and program review groups (PRGs).

Dr. Foti briefly reviewed growth areas in basic science, translational research, clinical research, and epidemiology and prevention that have been identified in strategic planning sessions. AACR has acted to address these areas through its many mechanisms for action. For example, crossdisciplinary task forces currently working on high-priority basic science areas include those on aging and cancer, pediatric oncology, tumor immunology, behavioral science, and prevention. A task force on hematological malignancies is planned. In the area of translational research, Dr. Foti highlighted the NCI-funded workshop on molecular biology and clinical oncology, a synergistic collaboration with the NCI on a molecular target series to advance translational research. Another highlight was the increasing collaborations with the FDA to advance translational research. In the area of clinical research, Dr. Foti highlighted: (1) the AACR-American Society for Clinical Oncology (ASCO) Workshops in Clinical Cancer Research, which were started in 1986 and are a mechanism for training young physician scientists in clinical trial design; and (2) collaborations on panels with the FDA and ASCO on the topic of surrogate endpoints for therapy. In the area of epidemiology and prevention, Dr. Foti noted that AACR interest in chemoprevention, which dates back to the 1960s, is now being exercised in the annual AACR international prevention meeting. She stated that this focus will be further strengthened as the AACR goes forward with a number of task forces addressing prevention and behavioral research, and a strong molecular epidemiology working group.

A second AACR strategic focus has been on the education and training of scientists and on related workforce issues. Dr. Foti noted that AACR conducts workshops in the pathobiology of neoplasia, clinical cancer research, and molecular biology in clinical oncology, and that other workshops are in planning stages. A task force to discuss workforce issues is considering new scientific disciplines needed in cancer research, the retooling of senior scientists in new areas of emphasis, and how to address the physician-scientist crisis. Dr. Foti applauded Dr. von Eschenbach's statement that workforce issues would be a focus for the NCI in the coming year, and she welcomed discussions on that topic.

Dr. Foti noted that a third AACR strategy for accelerating progress lay in the communication of science to a myriad of constituencies through AACR journals and meetings. She pointed out that *Cancer Research* has been in existence since 1917, and AACR's five journals have experienced a 15 percent increase in submissions over the past year. In addition, online access to the journals has doubled in that same timeframe (from 4 million to 8 million hits). AACR's fourth strategy for accelerating progress has to do with acting as a catalyst for advances in the prevention and cure of cancer through partnerships with other sectors and organizations, including academia, government, the lay public, industry, survivors and advocates, and the philanthropic community. In addition, the AACR maintains research partnerships worldwide to address cancer as an international problem.

Dr. Foti noted that education of the public was the fifth strategic area of focus for the AACR in response to increasing expectations of the public in the areas of cancer prevention and cure; quality health care and quality of life; the availability of current scientific, medical, clinical trials access, and science policy information; and progress and a return on the investment in cancer research. She stated that the advice would be sought from the NCI as to how AACR could make a difference in this area. Currently, a concentrated effort is being made through the annual public forum conducted in conjunction with the

AACR's annual meeting. The latest advances in cancer prevention, detection, and treatment are highlighted for more than 1,000 participants, for example, in Ask-the-Experts Sessions, which allow one-on-one interactions between the public and leading scientists.

The AACR's sixth strategy for accelerating progress against cancer was to promote the education of survivors and advocates. Dr. Foti called attention to the Scientist-Survivor Program spearheaded several years ago by Dr. Barker, which brings together scientists and survivors to address ways to better educate their larger constituencies. The fifth iteration of this program was held recently in Orlando, FL. Dr. Foti emphasized the power of survivors and organizations working together. As examples of this, she cited a program called "Making Cancer a National Priority" developed in conjunction with Mr. Hamilton Jordan, a three-time survivor, and cyclist Lance Armstrong, member of the President's Cancer Panel and a survivor, and presented by them at the National Press Club in Washington, DC. The objective of the program was to describe the current views of the public on cancer. Dr. Foti called attention to a campaign launched in December 2003 as a joint venture with the Lance Armstrong Foundation (LAF) to increase public awareness about cancer; gather data on public views on cancer, progress, and funding; and encourage private-sector investment in cancer research. An AACR-LAF National Poll was conducted as the kickoff event to discern public views on cancer, the rationality of their fears, what the Nation is doing to address the problem, the costs of cancer, and the benefits of a dramatic reduction in cancer and cancer deaths. Findings were: (1) getting cancer was the public's greatest fear; (2) cancer ranked above Alzheimer's disease, heart disease, HIV/AIDS and diabetes as diseases or medical conditions of the greatest concern; (3) about 80% of the responders favored a substantial increase in Federal spending; and (4) the public believed that not enough was being done to fund cancer research.

Dr. Foti briefly described AACR's actions in accord with the implementation of its seventh strategy for accelerating progress against cancer, namely, through science policy, government relations, and advocacy. These include: (1) advocacy for increased appropriations; (2) communication with the Administration about opportunities in cancer research; (3) education of legislators and policymakers about the value of cancer research and the economic and human cost of cancer; (4) provision of expert advice on science policy issues; and (5) collaboration with colleagues in the cancer community to ensure that cancer remains a national priority.

Next, Dr. Foti discussed the strategic leadership needed to meet the 2015 challenge goal, noting at the outset that the AACR believes strongly that the NCI has raised the bar for the entire cancer community and has made possible the progress achieved thus far. She stated that the AACR believes a historic crossroads has been reached in the evolution of cancer and cancer research, and that many challenges and opportunities lay ahead. There is concern, however, that although cancer incidence and death rates have decreased, the number of incidences is increasing due to the aging population and advances in detection. Dr. Foti stated that the AACR stands ready to address these challenges with the expert guidance of its multidisciplinary membership and proactive strategies for meeting the scientific needs. Moreover, the AACR is interested in further collaborations with the NCI to build areas that are synergistic and to address the public's concern for greater and faster progress. This will involve determining what is needed to reduce incidence, mortality, and suffering due to cancer; building the necessary systems and structures; and leading these efforts. Dr. Foti noted that the AACR believes that much progress has been achieved from the Nation's investment in cancer research, but that new strategies and approaches are needed as indicated by Dr. von Eschenbach in his opening letter to the FY 2005 Bypass Budget.

Dr. Foti identified Recommendation #12 in the IOM Report on NIH Organizational Structure as an area of concern to the AACR. She noted that the recommendation, which asks for a reassessment of provisions of the National Cancer Act of 1971, fails to recognize the progress made since 1971 because of the national emphasis given to cancer in this country. She expressed the AACR view that this

recommendation has the potential to undermine future advances and erode the facilitative authorities of the NCI Director. She stated that the AACR is taking the stance that the National Cancer Act must be retained and further strengthened to meet the demands of the public that cancer be addressed in a coordinative way. Dr. Foti noted, however, that if a new cancer act is developed, it would be helpful to update and strengthen the 1971 provisions, define contemporary goals for the National Cancer Program, place continued emphasis on cancer as a major health threat to the Nation, and give the NCI a leadership role in major parts of the NIH Roadmap Initiatives, as well as what it needs in funding, flexibility, and authorities to conquer cancer. She stated that the AACR would continue its roll in all of the areas discussed, work to strengthen AACR-NCI partnerships, and advocate for adequate funding for the National Cancer Program.

In conclusion, Dr. Foti noted that the AACR looks to and learns from the past as it contemplates the future and believes that it is poised to engage in “breakthrough thinking” about the next wave of progress in the prevention and cure of cancer. The AACR will work tirelessly with the NCI to lead the way in this endeavor.

### **Questions and Answers**

Dr. Ramirez asked about special efforts to bring training to individuals from underserved populations to ease the current shortage. Dr. Foti replied that the AACR roster of demographic councils includes a Minorities in Cancer Research Council that is developing a strategic plan to increase the number of minorities in cancer research and to address cancer and disparities in minorities. Dr. Kenneth Cowan, Director, University of Nebraska Medical Center, asked about AACR plans in the area of training for physician scientists. Dr. Foti described a physician scientist initiative that is in the planning stages and will provide funding for physician scientists, particularly at the career development award level. The program is expected to begin in the next year. Dr. Norton commented on the success of the AACR’s small, focused meetings as vehicles for information dissemination, networking, and integration. He asked if thought had been given as to how the NCI could relate to that activity to address challenges that exist in the area of communication between experts, for example, between basic and clinical scientists for today’s clinical trials. Dr. Foti replied that the AACR is increasing and strengthening its small meetings initiative by increasing the number of organ-site meetings, but had as yet no official interactions with the NCI on the meetings. She expressed the view that new kinds of meetings are needed, for example, smaller and more focused and with specific outcomes. She noted, however, that smaller meetings would be more expensive but may present opportunities for collaboration with the NCI and possible publication of outcome, if goals in terms of the NCI’s scientific objectives are met. Dr. von Eschenbach commented that the AACR presentation underscores a strong platform of partnership and opportunities for integrating the strengths and achievements of the AACR, and that the NCI is committed to a continuing relationship and collaborations.

### **IX. CURRENT IMAGING ISSUES, INCLUDING CT COLONOGRAPHY— DR. DANIEL SULLIVAN**

Dr. Daniel Sullivan, Associate Director, Cancer Imaging Program, DCTD, began by attributing the interest in this topic to the recent article in the *New England Journal of Medicine (NEJM)* showing that virtual colonoscopy (computed tomographic [CT] colonography) was equivalent to optical endoscopy. He noted that his presentation would explore the implications of virtual colonoscopy research for the NCI agenda, beginning with background information and then addressing related issues. Imaging issues raised by CT colonography (CTC) or screening relate to standards, reader variability, computer-assisted diagnostics (CAD), screen-detected lesions, clinical trials methodology, molecular imaging, and optical imaging.



Dr. Sullivan briefly reviewed what virtual colonoscopy is and why it is important. The procedure is done on multidetector scanners that scan the entire abdomen in about 1 minute each for the patient's front and back. The computer then reconstructs the two-dimensional (2-D) images that are produced into a 3-D volume of the entire abdomen, calculating the center line of the colon and subtracting all other information. The radiologist reads the 3-D construct to identify areas of polyps. One shortcoming of the procedure is that patients identified as having polyps would have to undergo regular colonoscopy for their removal. Dr. Sullivan listed reasons why CTC is potentially important: (1) colon cancer is very common, causing 60,000 deaths annually—second leading cause of cancer-related deaths in the United States; and (2) although screening is recommended for adults at average risk, compliance is very low because recommended tests are fecal occult blood test (FOBT), flexible sigmoidoscopy, double-contrast barium enema, or colonoscopy. Less than one-half of the average-risk U.S. population has been screened. Dr. Sullivan pointed out that endoscopic (optical) colonoscopy (OC) may not be practical for population screening because of the backlog (estimated 80M eligible adults, 8,000 gastroenterologists), clinic and procedure time (about 2 hours), the need for intravenous sedation or anesthesia; the false negative rate, cost (\$2,000), and risk associated with the procedure for a low yield (85 percent are negative). Dr. Sullivan noted, therefore, that CTC could serve as a more acceptable, less time-consuming and costly alternative.

Dr. Sullivan noted that several clinical trials over the past 5 years have compared CTC with OC for colon screening with varied results. In general, CTC was found in those trials to be inferior to OC. He pointed out, however, that CTC technology has been progressing significantly with the advent of multidetector scanners, 3-D versus 2-D views, and improved image processing. Dr. Sullivan noted that a recent Department of Defense (DOD) trial based primarily at the Bethesda Naval Hospital, Walter Reed Army Hospital, and San Diego Naval Hospital, which accrued 1,200 military retirees and their dependents over age 50, concluded with the finding that CTC was equivalent to OC. Reasons for this were: use of the multidetector versus single-detector CT scanners; vigorous bowel prep (laxatives, clear liquid diet, oral barium, oral iodine solution), and the use of 3-D “fly-through” evaluation as the primary evaluation for all studies. Dr. Sullivan pointed out that the vigorous bowel prep was an issue in terms of generalizability of the test to obtain these kinds of results in a less compliant and cooperative population. He then gave a video demonstration of the procedure. He noted that commentary in the various newspapers and journals could be summarized as pointing out the need for additional data before widespread use of CTC could be advocated because of the special population and controlled situation in the DOD trial.

Dr. Sullivan reported that the NCI-sponsored American College of Radiology Imaging Network (ACRIN) has completed a retrospective study of reader variability, and a prospective protocol is in progress. In addition, Dr. Carl Jaffe, Cancer Imaging Program (CIP), has been monitoring the evolution of the technology and has consulted with other NCI staff about identifying the NCI approach. The outcome of their consultation was a December meeting of stakeholders that included eight extramural researchers with expertise in radiology, gastroenterology, biostatistics, and epidemiology; seven NCI staff members representing the Division of Cancer Prevention (DCP), DCCPS, and DCTD; seven CMS staff members to address coverage and reimbursement issues; and two FDA staff members interested in CAD and radiation exposure. Recommendations from the meeting were: (1) a multisite trial is needed with close collaboration between radiologists and gastroenterologists to see if the DOD results could be reproduced in the general community; (2) the trial should be limited to the best technology, and the prep issue should be addressed; (3) trial size should be 2,000 to 4,000 subjects; (4) the trial should be powered to look at inter-site variability; (5) comparing CTC with other screening tests would be desirable to help with future modeling exercises; (6) accurate cost data should be collected for cost-effectiveness analysis; and (7) tissue and blood specimens should be collected for the biorepository. Dr. Sullivan noted that the trial team is addressing these recommendations and will be bringing a proposal forward to the NCI EC.

Next, Dr. Sullivan commented on CIP work to address some of the issues raised by CT colonography or screening, beginning with reader variability. He reminded members that accurate diagnosis depends on quality of both image acquisition and image interpretation, the latter requiring a combination of perception and cognition skills. In this regard, Dr. Sullivan summarized the findings from his and a colleague's 1996 study looking at the variability of interpretation of mammograms. The same set of 80 mammograms was sent for interpretation to a random sample of radiologists across the country. Significant variability was found. Publication of the results evoked considerable reaction, but confirmatory data has evolved since then, and it has been generally accepted that the reasons for the variability are not understood and solutions are not yet known.

Dr. Sullivan characterized the ideal outcome of efforts to improve analytic accuracy among radiologists, noting that findings in the study using mammograms would be applicable to the identification of lung nodules on a chest x-ray or finding polyps on a CT colonogram. He illustrated the factors that confound the radiologic analysis, including the presence of distracting information. Questions pertinent to solving analysis variability are why some individuals are better and faster, and what can be done to solve the problem. Dr. Sullivan suggested that the NCI could help by developing computer detection schemes similar to those commercially available for mammography. He pointed out that although the computer will not replace the decisionmaking role of radiologists, better programs need to be developed to assist them. CAD algorithms can assist with "data deluge," reduce false negatives and false positives, reduce inter- and intra-observer variation, assist with quantification and change analysis, and integrate multiple sources of data. Given the fact that 10 companies are now developing CAD algorithms for CTC, it will be necessary to compare one CAD algorithm versus another and compare radiologists' performance in practice with and without a CAD system. Important questions to be answered include: (1) how can CAD performance be determined, given the different databases, methods of scoring, and "truths" that are involved; and (2) how can consumers evaluate the algorithms. Dr. Sullivan called attention to an article in the *Journal of the National Cancer Institute (JNCI)*, which suggests that, to address these questions, there is a need for large national databases to expedite CAD development and that "protected" databases are needed for testing algorithms against each other.

Dr. Sullivan noted that one CIP initiative, the Lung Image Database Consortium (LIDC), has the goal of collecting a large number of spiral CT images to develop a Web-accessible image database for the comparison of CAD methods, and to encourage standards for software assessment. The Consortium is in the process of working with the Foundation of the NIH to establish a partnership with industry, academia, and government to develop multiple, large image databases. The objective is the development and validation of application-specific software, such as CAD methods and therapy-response metrics. Dr. Sullivan noted that initial responses from industry have been positive, and General Electric has volunteered to develop a demonstration project that would be put forward for the industry in general to consider, with specific timelines and amounts of money that might be requested.

Dr. Sullivan discussed the issue of detecting false positives or unsuspected lesions on screening tests, noting that this problem will surface in CTC because the scan involves the entire abdomen. He expressed the view that improved methods are needed to deal with all screen-detected lesions, and that more effort and more resources should be put into the development of minimally invasive or noninvasive image-guided ablative techniques. As an example of the variety of available image-guided interventions (IGIs), he described a case in which an abdominal CT scan revealed a small renal cell carcinoma. The malignancy was subjected to a needle biopsy for confirmation and ablated using radio frequency ablation; the patient is disease-free at 2 years. Another example was magnetic resonance imaging (MRI)-guided focused ultrasound therapy, which is ideal because it is done from outside the patient and is entirely computer controlled. Dr. Sullivan informed members that an IGI Methodology Workshop was convened earlier in February to discuss theoretical and practical issues involved in conducting clinical trials and to

identify future plans. Participating in the discussion of the significant hurdles involved were investigators, biostatisticians, NCI staff, FDA staff, and industry representatives.

As a final issue raised by CTC or screening, Dr. Sullivan discussed the need to develop methods to improve optical endoscopy and to provide more specificity to the task of sorting out the identified lesions, in as much as only about one-half are of major concern. He briefly described tumor detection studies in a mouse model of colon polyposis using an optically fluorescent agent that is activated only in the presence of a certain enzyme, for these studies cathepsin B. The agent was discovered in one of the NCI-sponsored molecular imaging centers and has been licensed for commercial development to VisEn Medical, a small company in Boston. The company plans to initiate clinical trials of this agent in about 2 years. Dr. Sullivan expressed the CIP view that the developmental gap in the molecular imaging area is the need for technologies for high-throughput screening of potential imaging agents. These would include the development of: (1) combinatorial libraries and libraries of chemical diversity biased toward imaging-agent chemistry; and (2) assays constructed to identify signaling properties as opposed to perturbing properties. Dr. Sullivan stated further that there is a need for the establishment of standards in conjunction with this emerging area of optical techniques, optical scopes, and optical agents, including the so-called optical biopsy, which uses spectroscopy. These would be similar to a reference standard for a laboratory *in vitro* method. Toward that end, according to Dr. Sullivan, the NCI CIP has developed a Network for Translational Research and Optical Imaging (NTROI) to foster complex, multi-institutional collaboration on the task. Key challenges for the Network are to: (1) standardize technology and analysis platforms; (2) develop reference standards; (3) demonstrate the value that would be added to conventional imaging; and (4) define the clinical role for optical techniques.

### Questions and Answers

Dr. James Armitage, Dean, University of Nebraska College of Medicine, asked about training for the human component of analysis to ensure accuracy and reproducibility of the results. Dr. Sullivan agreed that attention should be given to developing training for the kinds of skills needed and appropriate materials for interactive learning. Dr. T.G. Patel, Program Chief, Veterans Health Administration, asked whether studies were planned for using alternative providers for CTC screening in light of the estimates that there are only about 8,000 gastroenterologists for the 80 million potential consumers. Dr. Sullivan pointed out, first of all, that annual screening probably is not needed, but appropriate screening intervals need to be evaluated. He stated that because of manpower work issues, paraprofessionals are beginning to be considered for screening mammography and may be considered for other types of studies. Dr. Patel observed that it has not yet been defined who will benefit from screening for colorectal cancer and which test would be most appropriate. Dr. Sullivan noted that the DOD has committed significant research funding to military hospitals to explore those types of issues because of the success of the CTC trial. NCI DCP and CIP staff have been contacted by the head of gastroenterology at the Bethesda Naval Hospital to be involved in designing studies.

Dr. Norton pointed out that flat lesions, which do not form polyps, may actually be premalignant or malignant; therefore, a trial designed to identify 1 centimeter polyps would miss lesions that could lead to morbidity and mortality from colon cancer. He asked about the potential for alternating virtual and optical colonoscopy in a trial. Dr. Sullivan agreed that other strategies would be needed to deal with slow-growing, flat lesions, and that is the type of issue being discussed for the DOD trial. Dr. Love asked if there was a way to screen for cognitive skills, for example, in potential residents. Dr. Sullivan noted that it might be possible to define tests that identify the desirable skills. Dr. Freedman commended the CIP for considering the array of issues raised by virtual colonoscopy and screening, and attempting to establish the validity of a test that could address a great need.

**X. SARCOMA PROGRESS REVIEW GROUP REPORT: A ROADMAP FOR SARCOMA RESEARCH—DRS. LEE HELMAN, TODD GOLUB, AND KAREN ANTMAN**

Dr. Lee Helman, Chief, Pediatric Oncology Branch (POB), Center for Cancer Research (CCR), NCI, presented a brief orientation to the Sarcoma Progress Review Group (PRG) Report by outlining problems associated with trying systematically to approach sarcoma research. Sarcomas are difficult to diagnose because they comprise a group of heterogeneous diseases, making clinical studies difficult to do in even smaller defined categories. Moreover, diagnosis is often delayed as patients with the lumps and bumps, which are characteristics of sarcoma as well as minor injuries, often are referred to general surgeons. A final difficulty is that categorization is confounded by the current diagnostic coding systems, which are characterized by location; sarcomas are not site-specific.

Using ACS estimates of bone and soft-tissue sarcoma, Dr. Helman pointed out that sarcoma is a rare disease compared with lung, colorectal, and breast cancers, but almost twice as prevalent as either Hodgkin's disease or testis cancer, yet causes more deaths than the combined totals of the latter two diseases. Next, Dr. Helman summarized the status of sarcoma funding using NCI extramural funding estimates for FY 2001-FY 2002 by PRG-focused sites. Funding for sarcoma was relatively modest compared with that for other sites; moreover, a substantial proportion of the funding was for AIDS-associated Kaposi's sarcoma (KS), which is becoming less of an issue with the advent of active antiretroviral therapies.

Dr. Helman referred next to advances in knowledge about the genetics of sarcoma over the past decade and implications for clinical trials. Sarcomas segregate into two major categories: (1) those with tumor-specific recurrent chromosomal translocations and simple karyotypes; and (2) those without specific chromosomal alterations and complex karyotypes (chromosomal instability). Patient numbers may increase when the diseases are defined by specific genetic characteristics, and clinical studies could be better and easier to perform. The development of an effective structure to accelerate the pace of progress in the treatment of sarcomas could serve as a model for many other rare diseases and would integrate into some of the NIH Roadmap Initiatives.

Dr. Todd Golub, Associate Professor, Pediatric Oncology, Dana-Farber Cancer Institute, continued the presentation on the Sarcoma PRG report with a discussion of scientific issues. First of all, he emphasized the point made by Dr. Helman that molecular understanding of sarcomas, as in the cases of KS and gastrointestinal stromal tumors (GIST), can lead to identifying effective therapies that do not require a *de novo* drug development effort. With molecular understanding, drugs developed for other indications can be used for rare cancers or orphan diseases in general.

Dr. Golub described the Sarcoma PRG as bringing together the majority of leaders in sarcoma research (laboratory, clinical, and public health investigators), sarcoma patient advocacy groups, representatives from the pharmaceutical industry, as well as experts outside the sarcoma research field. This group of investigators agreed that current sarcoma research is fragmented across the country, making clinical trials difficult, not only because of the limited number of patients but also because the limited number of patients is further divided by the multiple organizations for clinical research. The major recommendation of the Sarcoma PRG was to create a dedicated sarcoma-specific organizational structure, provisionally called the Sarcoma Research Consortium (SRC), to serve as a focal point for sarcoma clinical trials and related clinical- and laboratory-based research. The SRC would facilitate networking of investigators and centers committed to sarcoma research.

Dr. Golub explained that the recommendation is to establish 10-20 designated sarcoma centers of excellence (SCEs) across the country where patients, when possible, would be treated. The leadership body of the SRC would include clinical investigators, biologists, and advocates from the SCEs and from

other institutions. The leadership group would develop a national research agenda for sarcoma, prioritize the trials for maximum enrollment, and organize key cores to facilitate basic biology research to enable everyone working in the field. Patients, when possible, would be seen at an SCE, but practice guidelines would be developed to facilitate state-of-the-art treatment of patients where access to an SCE was not practical. Infrastructure for biostatistical analysis, molecular reference laboratories, and a centralized tissue bank also would be part of the clinical trials structure. Dr. Golub noted the strong consensus of the PRG regarding the need for an overall organizational structure that transcended existing cooperative groups to bring together all sarcoma researchers to form a cohesive group with authority and resources to make decisions that were important for sarcoma as a high priority. Dr. Golub noted that the output of much of this work would be in the form of a sarcoma information resource for researchers, patients, and physicians.

Dr. Golub then listed specific scientific recommendations of the Sarcoma PRG: (1) fund and foster focused research on key areas of sarcoma biology; and (2) develop sarcoma-specific animal models. He briefly discussed the types of research envisioned in the first recommendation and the types of animal models to be developed in the second.

Dr. Karen Antman, NCI Deputy Director for Translational and Clinical Science, described the Sarcoma PRG recommendations related to providing an infrastructure for translational research: (1) fund and foster comprehensive approaches to sarcoma profiling and target discovery; and (2) develop a centrally available sarcoma research toolkit of core reagents (including cell lines, model systems, annotated tissue banks, biomarkers, and imaging) and the means of accessing technology platforms. She pointed out that these recommendations also are part of both NCI's strategic plan and the NIH Roadmap Initiatives, which has implications for obtaining resources from both sources.

A final recommendation of the Sarcoma PRG was to design prospective clinical trials whose principal objective is to compare early surrogate (intermediate) markers to conventional endpoints. The clinical trials would be tightly linked to appropriate tissue banking and would incorporate novel statistical methodologies appropriate to sarcomas. They would be conducted concurrently with a series of innovative therapeutic trials, and would develop, validate, and then use approved surrogate markers as endpoints to shorten the time necessary for conducting clinical trials, an NCI objective in its strategic priorities for 2015 and highlighted in the NIH Roadmap.

Finally, Dr. Antman presented the results of a MEDLINE search of clinical research studies to illustrate the trend toward decreasing numbers of published sarcoma clinical studies from the United States compared with continued numbers of publications from Europe. She noted that the Sarcoma PRG recommendations would focus on sarcoma as a model for uncommon tumors. Taken together, rare tumors account for one-half of all cancer deaths, an issue to be addressed if the 2015 challenge goal is to be met.

### **Questions and Answers**

Ms. Lydia Ryan, Service Line Clinical Director, Children's Healthcare of Atlanta, AFLAC Cancer Center, asked whether the Sarcoma PRG discussed the issues of: (1) closing the mortality gap in this population, particularly around adolescents and young adults; (2) promoting collaboration and cross talk between pediatric and adult oncologists; and (3) addressing the social, economic, and clinical trials access issues this population faces. Dr. Helman replied that one of the discussions in setting up the SRC was that it would promote integration between medical and pediatric oncologists and begin to address the problem of getting adolescents and young adults into clinical trials. Ms. Ryan recommended an amendment to the SRC organizational structure to include both pediatric and adult focuses. Dr. Armitage suggested that the proposed organizational structure be more like that of the Rhabdomyosarcoma Study

Group to achieve the same extraordinary results. Dr. Helman cited the need to achieve faster progress in determining the differences of the disease in adults versus children now that the genetic distinctions are known. Dr. Golub agreed with Dr. Armitage's concern in the long term, but pointed out that the current understanding of sarcomas is so rudimentary that a focused effort to elucidate the biology would be enabling.

Dr. Norton emphasized the importance of developing animal models with a better understanding of biologies to inform clinical trial design and suggested that working toward integration between the mouse modeling and clinical investigation worlds would be more cost efficient in the current funding climate and promote efficiency in clinical trial design. Dr. Golub agreed that funding will be a challenge, but the intent was that an important first step would be to organize leaders in the field to make the collective decisions about the disease site and develop a coherent plan for clinical trials that would have a catalytic effect. Dr. Helman pointed out the small size of the field and the relative ease with which all pertinent investigators could be brought together. He noted that the proposed initiative would provide patients either standard of care or clinical research trials while reagents, animal models, and hypotheses for further therapeutic tests are being generated. The SRC leadership would not be exclusive of any one group. Dr. Antman noted that the Sarcoma PRG was aware of the current fiscal restrictions and had considered how to accomplish this initiative in a modular fashion using existing resources.

Dr. Cowan observed that the common themes of animal models, tissue banks, proteomics, genomics, imaging, immunotherapeutics, and target validation appear in all of the PRG reports issued. He asked about integration of these themes across NCI-sponsored initiatives, particularly as research is entering an era where the focus is more on targets than on specific diseases histologically, as well as on delivery of patient care. Dr. von Eschenbach responded, noting that Dr. Cowan's question goes back to his earlier presentation regarding leadership to work across the continuum of discovery, development, and delivery to identify trans-NCI integrations. He pointed out that the proposed sarcoma initiative would lend itself to following the Mouse Models for Human Cancer Consortium (MMHCC) model and would create a Special Consortia of Research Excellence (SCOREs) mechanism that is interinstitutional in that the proposed SCEs would be wedded together in a tightly integrated, multidisciplinary approach. Another example is the blueprint for biorepositories, which was created collaboratively with the cancer community and will enable the integration of and access to specimen data by all in a decentralized way because common standards and a common platform were applied. Another potential advantage is the leveraging of funds and resources in initiatives such as the Prostate Biorepository, which is being co-funded and co-resourced by the NCI, DOD, and a private foundation. Dr. von Eschenbach emphasized that the NCI is facilitating these collaborations across the cancer enterprise so that infrastructure is not recreated and duplicated. To illustrate the type of structure envisioned for the SRC, Dr. Dinah Singer, Director, Division of Cancer Biology (DCB) briefly explained how the MMHCC is organized and operates. Dr. Freedman suggested that the Phase I Clinical Trials Group might be a resource for bringing drug strategies to the SRC. He added that interactions with the Cancer Therapy Evaluation Program, DCTD, might facilitate contact with pharmaceutical companies.

After a brief discussion of possible funding strategies, Dr. Niederhuber stated that the NCAB had accepted the report during a recent conference call and no other action or vote was necessary at this time.

Dr. von Eschenbach pointed out that implementation planning is the next step in response to the Sarcoma PRG report, and that Ms. Cherie Nichols, Director, Office of Science Planning and Assessment, OD, would be leading the implementation response.

**XI. UPDATE: OFFICE OF CANCER COMMUNICATIONS—MS. NELVIS CASTRO AND MS. MARY ANNE BRIGHT**

Ms. Nelvis Castro, Acting Director, Office of Communications (OC), OD, reminded members that a broad overview of the OC and its priorities for FY 2004 was presented at the December meeting. This presentation would focus on four initiatives of particular importance because of their strategic value and broad reach. The first was the weekly electronic publication, *NCI Cancer Bulletin*, which was launched on January 6 via an e-mail to more than 8,000 members of the cancer community, including NCI employees. Ms. Castro listed four goals in publishing the *Bulletin*: (1) carry out NCI's congressionally mandated responsibility to disseminate information to the public; (2) meet an increasing demand for useful information about NCI's programs and initiatives; (3) provide a venue for the Director and NCI leadership to articulate their perspectives on issues relevant to the community and staff; and (4) create a forum that encourages and responds to input from the community. Since its launching, an additional 1,200 have subscribed to the weekly e-mail distribution via the cancer.gov Web site. Regular features include a lead news story that reports on topical issues of concern, the Director's Update, Cancer Research Highlights, Special Report, Funding Opportunities, NCI Notes, and Future Meetings. On a periodic basis, the *Bulletin* will provide updates on legislation affecting the NCI and on the NCI budget. Ms. Castro noted that plans are underway to evaluate the usefulness and value of the *Bulletin* in the coming months, the results of which will guide further development of the publication.

Next, Ms. Castro informed members that the NCI Annual Progress Report is tentatively scheduled for release in April and will serve as a companion piece to the NCI Bypass Budget. The purpose of this new publication is to explain to a broader audience that progress has been made towards eliminating suffering and death due to cancer. It will look back over the year's accomplishments, and the Bypass Budget will look forward, outlining NCI's priorities and directions. The publication will be available in print and on cancer.gov.

Ms. Mary Anne Bright, Acting Deputy Director, OC, OD, reported that, after extensive research into usage patterns over the past 2 years, the OC has initiated a redesign of cancer.gov. The objective of the redesign was to simplify access by users to information being sought. As a result, sites most often accessed will be easier to find overall, and improved navigation for all users is planned. Ms. Bright noted that the home page and portal pages are now available on an intranet site for a preliminary review by stakeholders and NCI staff, and the OC is working with the Center for Strategic Dissemination to test usability. The site will be modified based on input from stakeholder and NCI staff and will be available for a 2-week period in March for review and comment by the broader cancer community. Rollout of the redesigned site is tentatively planned for June.

Ms. Bright then gave an update on a new HHS initiative to establish a National Network of Smoking Cessation Quit Lines, which was announced recently by the Secretary, HHS. Implemented jointly by the CDC and NCI, the network will provide all U.S. smokers with one easy-to-recall phone number to access important quit-smoking services and the latest information on smoking cessation. Ms. Bright noted that 38 states currently provide this service and other states are queued up to implement the Quit Lines pending funding availability. The HHS initiative has three components. In the first component, states with existing Quit Lines will receive supplemental funding to enhance their state line services through cooperative agreements with the CDC. Enhancements might include expanded hours of operation, implementation of bilingual services, or links between local health care communities and the Quit Lines. In the second component, states without Quit Lines will be funded through a CDC grant mechanism to establish them. In the third component of the initiative, the Cancer Information Service (CIS) will provide assistance to smokers in states without Quit Lines through the single national phone number. When a national promotion occurs using the national number, the CIS telecommunications infrastructure will be used to forward calls that come in on that number to the states that offer Quit Line

services. The intention is that the states will continue to provide these services, and CIS will assist only those states without a Quit Line service on an interim basis. She pointed out that the challenge will be in the allocation of funds to support these efforts, which will require \$25 M to be successful, according to Secretary Thompson. A coordinated effort and effective communications also will be needed.

### Questions and Answers

Dr. Freedman asked how the success of the Quit Lines would be evaluated over the long haul. Dr. Croyle replied that the NCI recommended a Quit Line counseling protocol for which there is a strong evidence base. Having been tested in a controlled research setting, the challenge now is how to support and disseminate it broadly. Evaluation will continue as an element in the CIS component of the initiative. Dr. Niederhuber observed that the NCI appears to have a portfolio of communication devices in place to disseminate the message, and there appear to have been changes in the processes. Ms. Castro briefly reviewed some priorities planned for this year, including the proactive media outreach particularly with the minority media, the *NCI Cancer Bulletin*, the redesigned Web site. Dr. Niederhuber relayed an observation from a high school teen that messages directed at changing behavior will miss the mark if they do not have the buy-in of young people. Dr. Croyle noted that a number of activities related to that issue have been going on independently of each other, and a future agenda item might be in order to link the research and programmatic activities more effectively and map out more appropriately what NCI's role is vis-a-vis its various partners. He cited partners like the American Legacy Foundation, which has a powerful media campaign targeted to teens; and the Legacy Center for Tobacco Free Kids, which has mastered the art of using youth to advise them on the content and planning of activities, and grantees developing and testing community interventions. Ms. Ryan observed that the strategies successfully employed in this population would have application in the prevention arena also. Dr. Croyle pointed out that many issues related to youth were raised in the President's Cancer Panel series on survivorship. In addition, a national survey monitoring process—the Health Information Trends Survey—has been initiated to determine where people are getting their information about cancer, what is useful, what is credible, and what are the barriers. Data from all of those sources will feed back into planning for OC activities and will become a public-use dataset for the research community.

## **XII. NCI ANNUAL REPORT AND NEW BYPASS BUDGET—DR. MARK CLANTON AND MS. CHERIE NICHOLS**

### **Introduction**

As background, Dr. Mark Clanton, Deputy Director for Cancer Care Delivery and Systems, OD, stated that the NCI has had such robust capacity to plan around research and cancer control-related activities that an integrated strategic plan is needed that brings all planning efforts together to realize the 2015 challenge goal and fulfill NCI's mission. He demonstrated how all of the planning processes are brought together across the discovery-development-delivery continuum and gave examples of how the disease-specific priorities fit in those specific areas. Platform and infrastructure that serve the entire continuum are bioinformatics, communication, and cancer imaging and molecular sensing. Bioinformatics provides enabling technologies and tools. Communication (and dissemination) enable movement of knowledge forward and backward along the continuum. Cancer imaging and molecular sensing provide technologies and tools across all of the priority areas. Platforms for discovery, development, and delivery are: (1) investigator-initiated research; (2) centers, networks, and consortia; (3) integrated clinical trials system; and (4) the NCI intramural program.

Dr. Clanton noted that what was needed was to focus the NCI portfolio and planning in such a way that NCI's \$4.7 B budget is used to accelerate the process that develops knowledge, moves that knowledge into the intervention development and validation phase, and then into intervention delivery.



Ultimately, the knowledge and interventions must move into the public health domain and into programs that use the knowledge to have an impact on the population as it relates to cancer, or change medical practice in such a way that patients get better care. Using specific examples from the research portfolio, he showed how the progress of molecular epidemiology and integrative cancer biology discoveries can be accelerated across the entire continuum. Dr. Clanton summarized the planning concept as integrating the PRG information, Bypass Budget planning, and prioritization process to focus on the areas of discovery, development, and delivery such that knowledge is quickly moved to translation, diagnostics, and treatment, and then into the delivery system with provisions for funding and for ensuring that the knowledge is used appropriately to improve quality of care and reduce health care disparities.

### **Questions and Answers**

Dr. Freedman asked for and received clarification that implementation of the NCI programs in the public health domain will always be in collaboration with other Federal agencies and other organizations that are involved in health care delivery and advocacy. Dr. Chen asked for and received an explanation of how disparity reduction could be addressed in all parts of the continuum. Regarding the comments in relation to delivery, Dr. von Eschenbach made the point that the NCI is creating the knowledge upon which the health care delivery system has to be based. Delivery is included in the continuum because the NCI influences that aspect of the continuum and provides leadership even though it is not directly responsible for delivery. Dr. deKernion agreed that the NCI must assume a leadership role in delivery, but expressed concern about how the new and possibly expensive treatments can be delivered to the people who need them. Dr. Greenwald gave the examples of vaccines against nicotine and the DNA battery of a stool as colon cancer diagnostic interventions that promise to be easily administered and more accessible costwise.

### **Bypass Budget**

Ms. Cherie Nichols, Director, Office of Science Planning and Assessment, continued the presentation with an introduction to the Bypass Budget for FY 2005, copies of which had been distributed to members. In general, she noted that: (1) energy balance has been added as a new public health emphasis; and (2) progress and the plans have been laid out and tied to the framework of discovery, development, and delivery. She then described the overall approach to developing the budget beginning with the EC strategic planning sessions in early and mid-2003. This effort identified seven strategic priority areas and developed plans for those areas. In the second phase, input was received on strategic priorities through informal working groups that supported planning efforts and formal solicitation and responses from NCI staff. In the third phase of the Bypass process, external input was solicited (February 2004), and the 7 priority areas, disease-specific research, and 13 bypass areas were integrated to develop the Bypass Budget entitled “The Nation’s Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2005.”

Ms. Nichols noted that the NCI has begun planning for FY 2006, and the aim is that the final budget articulates the collective judgment of the entire cancer community on what is needed to achieve the 2015 challenge goal. Two areas of particular interest are: (1) what are the most compelling opportunities; and (2) what are the gaps. Ms. Nichols pointed out that this year’s solicitation of input from external stakeholders produced only a 10 percent response. She asked for advice and suggestions from the NCAB as to how the NCI could influence the community to respond. The NCI will begin by sending solicitation letters to about 400 organizations and individuals. She underscored the usefulness of reviewer input by listing examples of revisions the NCI made in the FY 2005 Bypass Budget as a result: (1) emphasized establishing new and strengthening ongoing efforts for reducing cancer health disparities; (2) developed an objective to ensure that partners employ evidence-based methods in generating health messages, screening recommendations, and patient publications; (3) expanded emphasis and increased

funding request for symptom management/palliative care efforts; (4) placed greater emphasis on partnerships with cancer centers; and (5) strengthened the intervention delivery component of plans for tobacco and tobacco-related cancers research.

Finally, Ms. Nichols reviewed the timeline for development of Bypass 2006, beginning with solicitation letters to stakeholders and identification of NCI integration teams this month. External input is requested back by mid-April; the budget will be drafted, reviewed internally, and submitted for final internal and NCAB review in September. Dr. von Eschenbach conveyed the Institute's gratitude for the work of Ms. Nichols and Office of Science Planning and Assessment (OSPA) staff in producing the Bypass Budget and their efforts in the planning process. He reiterated the call for help from NCAB members in accelerating and promoting stakeholder input early in the planning process.

### **Questions and Answers**

Dr. Niederhuber commended the organization and structure that is evident in the strategic planning as laid out in the Bypass Budget. He commended Ms. Nichols' leadership and the work of the OSPA team and division heads. Dr. Chen added his commendation and suggested that April 15 might be enshrined as the deadline day for Bypass Budget responses as well as taxes. Dr. von Eschenbach commented that the Bypass Budget was authorized by the National Cancer Act of 1971 and did go directly to the President in those early days. Now, the route is through the NIH, HHS, and ultimately to the Office of Management and Budget (OMB). Dr. von Eschenbach noted that the Bypass Budget has become a powerful tool to promote understanding of the hoped-for accomplishments and achievements behind the numbers that come through in the normal budget process.

### **XIII. ANNUAL DELEGATIONS OF AUTHORITY—DR. PAULETTE GRAY**

Dr. Paulette Gray, Acting Director, Division of Extramural Activities (DEA), reviewed the delegations of authority requested annually from the NCAB as stated in Section 413(b)(5) and Section 413(b)(7) of the National Service Act, noting that a motion and vote were needed from the Board. Delegation A grants to the Director, NCI, permission to obtain the "services of not more than 151 special experts or consultants who have scientific or professional qualifications to assist in accomplishing the mission of the Institute." Delegation B grants to the Director, NCI, permission to "appoint one or more advisory committees composed of such private citizens and officials of Federal, State, and local governments to advise the Director with respect to the Director's functions."

Dr. Gray then reviewed the provisions in the statement of understanding with NCI staff on operating principles in extramural awards set forth in the NIH Manual Issuance 4513. The first states that concurrence of the NCAB with recommendations of initial review groups will be required with the following exceptions: (1) NCI staff may award grants exceeding \$50 K annually, and they may be awarded without presentation to the NCAB for concurrence if they are within the payline. (2) Individual National Research Service Awards also may be awarded without presenting to the Board. (3) Applications over the 50<sup>th</sup> percentile will not have summary statements presented to the NCAB. For applications assigned raw scores that are not percentiled, the cutoff will be a priority score of 250 for all mechanisms except R41, 42, 43, and 44 awards. For the latter awards, all scored applications will be included.

The second provision is that a process of expedited concurrence may be used for R01 and R21 applications with percentiled or raw scores that fall within the NCI paylines for that mechanism. The Executive Secretary will alert the Board members with responsibility for expedited concurrence when review outcomes for eligible applications are available on the Electronic Expedited Concurrence portion of the Electronic Council Book.

The third relates to administrative adjustments. The NCAB delegates to the Director, NCI, permission to allow staff to negotiate appropriate adjustments in dollars or other terms and conditions of grant and cooperative agreement awards recommended by the Board. Administrative requests for increases in direct costs, which are the result of marked expansion or significant change in scientific content of a program after formal peer review, will be referred to the Board for advice and recommendations. In addition, NCI staff may restore requested time and support that were deleted by the initial review group. Those types of changes, however, will be included in the special actions package during the closed session to inform the Board of the changes and restorations that have been made. As circumstances evolve, the Director, NCI, may make exceptions to these guidelines if the Board so delegates.

**Motion.** A motion was made and seconded that the NCAB grant the authority to the Director, NCI, as set forth in Delegations A and B of Section 413(b) of the National Service Act and in the operating principles for extramural awards contained in the NIH Manual Issuance 4513 as listed above. The motion was approved.

#### **XIV. CLOSED SESSION**

*This portion of the meeting was closed to the public in accordance with the provisions set forth in Section 552b(c)(6), Title 5 U.S. Code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2).*

Members were instructed to exit the room if they deemed their participation in the deliberation of any matter before the Board to be a real conflict or that it would represent the appearance of a conflict. Members were asked to sign a conflict of interest/confidentiality certification to this effect.

The en bloc vote for concurrence with all other IRG recommendations was affirmed by all serving Board members present. During the closed session of the meeting, a total of X,XXX applications were reviewed requesting support of \$XXX,XXX,XXX. Funding for those X,XXX applications was recommended at a level of \$XXX,XXX,XXX.

### **DAY TWO: THURSDAY, FEBRUARY 19, 2004**

#### **XV. TUMOR MICROENVIRONMENT—DR. JOAN BRUGGE**

Dr. Joan Brugge, Acting Chair, Department of Cell Biology, Harvard Medical School, began by highlighting aspects of the tumor microenvironment, especially as it relates to potential for translation to cancer diagnosis, treatment, and prevention. Specifically, she discussed tumor microenvironment as a critical component of tumor progression and metastases, and as a target for therapeutic intervention. She first showed how the perception of the events associated with tumor progression have evolved. Previously, tumors were generally considered autonomous cell masses that can function independently and whose progression is driven by a series of genetic alterations. It is now generally recognized that tumor cells are not autonomous, and tumors are considered more as organs or complex tissues composed of many interdependent cell types that can contribute to tumor development and metastases. She stated that a growing body of evidence suggests that the interaction between tumor cells and the tumor microenvironment is key to the cancer program. Using the example of a developing mammary gland, she illustrated that cross talk between the luminal epithelial cells and the different surrounding cells are critical for both embryonic development and normal homeostasis. In like manner, neoplastic cells, which

generally are derived from the luminal epithelial cells, are dependent on interactions with the cells in the microenvironment.

Dr. Brugge stated that the tumor microenvironment can exert both positive and negative influences on tumors. As evidence that the microenvironment of tumor cells can strongly suppress tumorigenic capacity, she reviewed: (1) a study that demonstrated influences are needed both within the neoplastic cells and in the microenvironment for the tumor to succeed; (2) a study by Mintz and Illmensee showing that the malignant potential of microenvironment cells can be restrained during embryonic development; and (3) a Bissell study to identify tumor-suppressive influences of the environment, which showed that tumorigenicity can be reverted through the extracellular matrix receptors.

Next, Dr. Brugge listed tumor-promoting influences of the microenvironment: (1) growth and survival factors (e.g., growth factors produced in the stroma cells), fibroblasts, adipocytes that promote cell proliferation and survival; (2) chemokines and chemotactic factors that stimulate cell migration and invasion; and (3) proteases that are produced by the fibroblasts, adipocytes, or infiltrating leukocytes that break down basement membrane and alter the architecture of the tissue structures and promote migration and invasion. She gave examples of different components of the tumor microenvironment, the profound influence they have on tumor cell behavior, and the potential for developing interventions.

Tumor vasculature is one component. Extensive characterization of blood vessels has established that angiogenesis is orchestrated by a variety of different activating proteins as well as inhibitors. For angiogenesis to be successful, activators must be turned on and inhibitors turned off. These findings provide a potential for being able to specifically target the tumor-associated blood vessels, which are critical for the expansion of tumors. Lymphatic vessels serve as critical components of the tumor microenvironment. Lymphatic endothelial cells also are recruited by tumor cells, and lymph vessels provide a gateway for metastases. Critical molecules that mediate lymph angiogenesis have now been identified and found to be in the same family as those that recruit vascular blood vessels. There is potential that strategies targeting lymph vesicles when used in combination with other therapies may have utility in the treatment or prevention of metastatic lesions.

Inflammatory cells are another important component of the tumor microenvironment and have been found to influence tumor progression. They can produce cytokines and promote proliferation and survival, and they can facilitate genomic instability. In regard to the latter, Dr. Brugge noted that it has now been shown that the generation of reactive oxygen species by the leukocytes can actually induce DNA damage, so it could contribute as well to the genomic instability and promote angiogenesis.

Stromal cells also can influence tumor progression. Dr. Brugge cited studies by Kenneth Anderson of multiple myeloma (MM) biology as one example of the different components of the stroma that can contribute to tumor progression. The studies showed that MM cells are dependent on the environment within the bone marrow to survive and proliferate. They need to adhere to bone marrow stromal cells (BMSC), and these interactions lead to complex cross talk between the stromal cells and myeloma. These studies have led to investigations of the effects of a variety of potential therapeutic agents in influencing the cross talk. Two candidate therapeutics—a thalidomide analog called Revamid and a molecule called Velcade that was originally developed as an NFκB inhibitor—have been shown to induce MM cell death. Both compounds prevent the adhesion of the fibroblast and MM cells, and prevent the production of the supportive factors from the stromal cells. Both are in clinical trials. Results of the Phase I studies show promise for a reduction in the outcome.

Turning next to the topic of metastasis, Dr. Brugge cited a study by Stephen Padgett that first recognized that the tumor environment has a profound effect on the survival, proliferation, and outgrowth of metastatic lesions; metastasis requires compatible “soil and seed.” One study to determine what it is

that decides which organ shall suffer in the case of disseminated cancer led to the conclusion that metastatic inefficiency is due largely to postextravasation events. Dr. Brugge noted that finding what it is within the microenvironment of metastatic sites that allows the tumor cells to survive and to answer the question “what is the molecular basis of site-specific metastasis” is important to the task of developing interventions. She discussed work being conducted by Jean Massague to define the specific mediators that are critical for survival and expansion within the bone. She noted that findings from these initial studies in the field highlight the opportunity and provide the basis for developing therapeutic interventions. Understanding the tumor microenvironment could lead to: (1) the development of therapeutics that would kill the altered cells in the tumor environment, thus preventing the feeding of the tumor by these cells; (2) reduce the likelihood of drug resistance by targeting the tumor microenvironment; and (3) lead to diagnostic tests that assess the state of the microenvironment for evidence of predisposition for the tumor or the outcome in the tumor.

Given this potential, according to Dr. Brugge, workshops were convened by Drs. Suresh Mohla, Dinah Singer, and Ellen Wilson, DCB, bringing NCI-funded investigators together to identify the most important questions to address and how the NCI can facilitate the best research in this area. The workshops focused on epithelial-stromal interactions in tumor progression, mechanisms of tumor metastases to the bone, and marrow microenvironment and hematology. The resulting summary of the workshops was published to disseminate the information to the scientific community. Subsequently, a tumor microenvironment think tank was organized by Drs. David Rudman and Brugge to make recommendations concerning strategies to define the role of the tumor microenvironment in tumor initiation and progression to metastases. The think tank also addressed strategies for using the information from the initial, defining studies to develop applications that will impact diagnosis, prevention, and treatment of cancer, as well as how the NCI could best facilitate acquisition of this information and its application. Participants in the think tank included basic and clinical scientists, people focused more on mechanistic studies and people with technological expertise.

The committee concluded that the initial goal of the preclinical studies would be to further the understanding of how the tumor microenvironment contributes to tumor cell progression. In stage 1, a concerted effort would be devoted to identifying the key components and defining how they are altered during tumor development. In stage 2, the work would focus on how to define the changes and decide which mechanisms are critically involved in the development, progression, and metastases of tumors. Dr. Brugge noted that defining the critical alterations associated with the microenvironment will require the further development of new *in vitro* and animal models in which conditions mimic the environment *in vivo*. Models to address microenvironment questions in mice are currently being developed by the Mouse Models for Human Cancer Consortium and present an opportunity for effective collaboration.

Dr. Brugge noted that the next step will be to translate the information from stages 1 and 2 into clinically relevant applications. Possibilities include the development of drugs that: (1) induce death or inhibit the function of the altered cells in the microenvironment; (2) target factors produced by the microenvironment that are responsible for tumor progression; or (3) block the induction of the factors responsible for tumor progression. Another possibility would be the further elucidation of diagnostic information from stage 1 and 2 studies, for example, to establish whether any of the alterations in the microenvironment correlate with outcome or specific treatment responsiveness. Ultimately, the goal would be to pursue strategies and therapeutics to prevent the development of tumors, based on an understanding of the microenvironment changes that are required for tumor development.

Finally, Dr. Brugge listed think tank recommendations for funding initiatives: (1) assemble small to mid-size groups at each of the participating institutions to define the components and ensure that there is effective communication and collaboration; (2) initiate a funding format that would facilitate cross talk and dissemination of information and reagents, and involve NCI staff support to coordinate the different

efforts; (3) generate a format for reagent generation and dissemination of research tools and biologics; (4) create core laboratories to conduct the highly technologic and sophisticated genomic and proteomic analyses; (5) develop new paradigms to establish the mechanisms whereby the tumor microenvironment influences tumor development; (6) develop new organotypic models in which the organ-like environment within the tumor can be reconstructed *in vitro*; and (7) bring more scientists into this area of research through the initiation of transdisciplinary training grants and training workshops.

### Questions and Answers

Dr. Niederhuber asked if the up and down regulation processes that occur in the microenvironment cells induce genetic instability similar to that seen in the tumor, where the cells become permanently abnormal and established as part of the tumor. Dr. Brugge stated that there is evidence to that effect, and she discussed the various findings. Dr. Love described studies of ductal lavage from women without cancer that are providing a hint of the intraluminal environment of the breast. Preliminary results from these studies to determine what is normally present in ducts have shown that some have large amounts of macrophage and others none, ducts have higher levels of estrogen than blood, and macrophages have aromatase as do the stromal cells and some of the adipocytes. She discussed with Dr. Brugge the possibility that these findings suggest that macrophages or stromal cells may be contributing to estrogen that may be in the tumor, even when the systemic estrogen levels are not high. These studies are in the early stages.

In response to questions from Dr. Freedman about (1) the possibility that investigators expect to find, in studies other than those in cloned cell lines, that there will be common changes within the microenvironment for tumors of a specific subtype; and (2) whether those changes can be targeted to cause specific elimination of the tumor cell compared with the normal environment, Dr. Brugge discussed the status of current research and expectations. In response to his third question about the interest of industry, Dr. Brugge noted indications that the pharmaceutical industry is pursuing microenvironment targets. There was further discussion on the status of research in relation to questions posed by Drs. Huerta and deKernion about (1) the association between antibiotic use and breast cancer in women and possible changes in the microenvironment; and (2) about the theories that there is an inflammatory basis for prostate cancer. In closing, Dr. von Eschenbach thanked Dr. Brugge for her leadership, together with Drs. Singer and Mohla, and for the contributions made in this important research area.

### **XVI. NCI ENERGY BALANCE PRIORITIES: NEW INITIATIVES AND RESEARCH HIGHLIGHTS—DRS. ROBERT CROYLE AND RACHEL BALLARD-BARBASH**

Dr. Robert Croyle, Director, DCCPS, reminded members that this presentation was a requested followup to a previous mini-symposium on energy balance and cancer. The mini-symposium reviewed the state of the evidence concerning the relationship between obesity, body mass index, physical activity, and nutrition and cancer incidence and mortality, as well as some of the possible mechanisms showing those relationships. The mini-symposium provided the scientific background and foundation for NCI's entrance into that area of research. He noted that, on behalf of the NCI Energy Balance Working Group, Dr. Rachel Ballard-Barbash, Associate Director, Applied Research Program, DCCPS, would update the Board about activities, progress, and NCI initiatives in regard to optimizing energy balance—the intersect of weight, diet, and physical activity.

Dr. Ballard-Barbash reminded members that the NCI Energy Balance Priority Working Group was formed over the year following Dr. von Eschenbach's call in July 2002 for an energy balance initiative. In the fall of 2003, optimizing energy balance to reduce the cancer burden was included in the FY 2005 Bypass Budget. The goals of the initiative are to understand the causes of adverse patterns of body weight, physical activity, and diet; define their contribution to cancer; and apply this knowledge to

cancer prevention and control. The first objective within the initiative focuses on mechanisms by which these factors, along with genetic and environmental factors, interact over a lifetime to influence the cancer process. The second objective is to understand at the population level what are the determinants of these factors and how they might be operating at the population level. The third objective is to develop improved measurement methods of body mass and composition, physical activity and fitness, diet, and bioactive components of food through self-report measures and advances in the technology for objective reference measures. The ultimate objective is to improve and develop interventions that may improve cancer-related outcomes.

Next, Dr. Ballard-Barbash listed and briefly described a series of efforts that are moving forward to address the first objective: defining mechanisms. The first is a Transdisciplinary Research on Energetics and Cancer (TREC) request for applications (RFA), which will be issued later this month. The conceptual model developed for TREC focuses on how the macro-level (contextual) and micro-level (individual) factors influence energy balance, energetics, diet, activity, and obesity, and how this, ultimately, will influence cancer outcomes. Barriers to progress have been the need to broaden research beyond the intersection of diet, weight, and physical activity to: (1) make it transdisciplinary; (2) engage other disciplines such as urban planning, transportation, and communications if environmentally and culturally based research are part of the picture; and (3) bridge multiple disciplines to identify individual and population-level solutions to this complex health problem. Dr. Ballard-Barbash noted that the TREC RFA is calling for research to enhance understanding of mechanisms that may underlie the association between energy balance and carcinogenesis across the cancer continuum and throughout the life cycle. In addition, it is calling for the development of effective approaches with broad population impact at the social-environmental and policy level for the prevention and control of obesity, for example, focusing on children and adults during critical periods for excessive weight gain.

Dr. Ballard-Barbash noted that the NIH Center for Cancer Research (CCR) also is involved in the effort to discover mechanisms. Research is focusing on the Insulin-like Growth Factors pathway and on the role of calorie restriction in cancer prevention and control. In addition, the interactive effects of physical activity and diet on body composition, gene expression, and carcinogenesis are being examined in mouse models of breast and colon cancer. These studies should help understand the biological basis of epidemiological associations between physical activity and cancer. Also in the CCR, physical activity interventions have been initiated in Phase II studies in primary and secondary breast cancer prevention, together with molecular studies to examine various measures that may be influencing risk for women. Extramurally, NCI-funded epidemiologic studies are exploring energy balance and cancer risk in the areas of breast and rectal cancer, and energy balance-related biomarkers are being analyzed in population studies.

In the implementation of objective 2—to monitor trends and determinants of diet, weight and physical activity and their cancer-related consequences within both national and regional populations, there have been efforts to expand NCI support of surveillance of these factors within the National Health Interview Study (NHIS) and the California Health Interview Study (CHIS). In addition, the NCI and other Institutes are providing input for the development of the trans-NIH Obesity Research Task Force RFA and conference entitled “Obesity and the Built Environment: Improving Public Health Through Community Design.” The National Institute for Environmental Health Sciences is the lead institute for this initiative. The NCI also is adding an objective measurement of physical activity to the National Health and Nutrition Examination Survey (NHANES). The measurement device is a mail-back monitor, which records both the duration and intensity of the physical activity. A program announcement (PA) entitled “Improving Diet and Physical Activity Assessment” co-sponsored by the NCI, National Institute on Aging, National Institute for Diabetes and Digestive and Kidney Diseases, and National Institute for Nursing Research is in the review and award stage.

In the implementation of objective 3—to improve assessment methods, a trans-NCI study called Observing Protein and Energy Nutrition (OPEN) used objective measures such as labeled water to quantify the extent of measurement error for factors such as energy intake and diet. OPEN II is in the planning stages by a trans-divisional working group to replicate the OPEN findings in diverse populations and to incorporate additional assessment instruments. A trans-NIH PA, led by the NCI, entitled “Improving Diet and Physical Activity Assessment” elicited a good response, and workshops are being held to identify new technologies that can capture this information in real time. This initiative has relevance for both monitoring and intervention purposes. Another trans-NIH effort, led this time by the National Heart, Lung, and Blood Institute, is exploring bioengineering approaches for prevention and treatment of overweight and obesity. A working group of nationally recognized experts in the area met in January 2004 to discuss opportunities and challenges of using real-time methodologies to assess and modify physical activity, diet, and obesity/energy balance. Based on these conversations, areas of promise for the support of future research activities will be identified.

Finally, Dr. Ballard-Barbash discussed efforts to improve cancer-related health outcomes through the development of effective interventions (objective 4). She noted first of all that the TREC initiative will address this issue. In addition, the DCCPS is tracking physical activity and nutrition-related legislative policies and their impact. The pilot effort was funded this past year and has been coordinated with CDC efforts and with other groups. In addition, the NCI has added questions to the 2003 Health Information National Trends Survey (HINTS) related to understanding public health recommendations in physical activity and nutrition. The NCI Office of Cancer Survivorship has a number of research activities in this area: (1) examine the feasibility and benefits of a home-based moderate exercise program among breast cancer survivors; (2) measure the effects of exercise or an exercise plus diet intervention to prevent weight gain and adverse changes in body composition, reduce depression, improve quality of life (QOL) and influence biomarkers associated with breast cancer and other comorbid conditions; and (3) establish feasibility and generate initial outcome data concerning the physical and psychological health benefits of a group exercise training program for women with recently diagnosed metastatic breast cancer. Dr. Ballard-Barbash noted that the NCI also has a number of synthesis and dissemination efforts underway, including: (1) support of evidence-based reviews through the Agency for Healthcare Research and Quality (AHRQ); (2) update of NCI Fact Sheets on obesity and fruits and vegetables; (3) highlights in the *NCI Cancer Bulletin*; and (4) efforts within the OD, NCI, to address the issue on the national level.

Dr. Ballard-Barbash closed with a brief description of the trans-NIH Obesity Research Task Force and its activities. The Obesity Research Strategic Plan, which was released on the NIH Web Site on February 12 for a 2-week comment period, spans the research continuum from basic to population sciences. Research outcome goals of this effort are to: (1) ensure translation of effective strategies at the population level across multiple environments; (2) use knowledge of regulation of energy storage and food intake to develop new therapeutic modalities; and (3) understand mechanisms that increase the risk for comorbidity so that therapeutic approaches can be developed that may not require weight loss in these populations in as much as near-term gains in controlling obesity and increasing physical activity in the United States.

## **XVII. UPDATE: CENTER FOR STRATEGIC DISSEMINATION—DR. EDWARD MAIBACH**

Dr. Edward Maibach, Director, Center for Strategic Dissemination (CSD), NCI, presented an update of the CSD. He began by emphasizing that dissemination is a proactive process, the goal of which is to turn knowledge into applications that benefit people. The CSD was described as an inward-focused strategy for overcoming the dissemination problem, created to promote and enable “user-centered” application development and promotion. He briefly reviewed the steps in the dissemination process and the capabilities that are required within the NCI to carry out the process effectively. The first step is to



conduct research on applications being developed with end-users and critical intermediaries, which requires operations research (OR) capabilities. The second step is to harness these insights in the design and promotion process, which requires teamwork between OR and program development staff. The third step is cultivating partnerships to expand NCI's distribution channel and leverage resources, which requires partnership development and management expertise. The fourth step is to promote the applications through appropriate media and interpersonal channels, which requires communications expertise. Dr. Maibach noted that education, training, and technical assistance should be provided, and educational materials and technical assistance training tools should be developed, if necessary.

Dr. Maibach then introduced the Board to the cancer bioinformatics grid through a multimedia tour accessed at <http://www.cancer.gov/directorscorner/caBIG>, which he characterized as a "stellar example of the user-centered application development process." He described briefly how the NCI Center for Bioinformatics (NCICB) implemented the process through cooperative development meetings (i.e., research with end users and critical intermediaries) with the 49 NCI-designated Cancer Centers that elected to participate in the 3-year pilot to test the concept. The meetings were a vehicle for explaining the goals of the pilot and the types of information needed from the spectrum of Cancer Centers with varying needs and capabilities to create a common grid of communications, shared data, applications, and technologies. Other goals of the pilot were to demonstrate that Cancer Centers, in collaboration with the NCI, will develop new enabling tools and systems that could support multiple Cancer Centers, and demonstrate that the Centers will actively use the grid and realize greater value in their cancer research. Through this process, the 49 Cancer Centers identified the areas of greatest opportunity and greatest need. The NCICB integrated this information to create the three caBIG domain workspaces: (1) Clinical Trials Management Systems, (2) Integrative Cancer Research, and (3) Tissue Banks and Pathology Tools. In addition, Crosscutting Workspaces 1 and 2 were established to deal with overarching issues and make it possible to develop successful applications in the three domains: (1) Cancer Bioinformatics Infrastructure Objects, (2) Cancer Data Standards Repository, and (3) Enterprise Vocabulary Services. Dr. Maibach noted that as the NCICB and caBIG partners move forward with application design, the CSD and NCICB are conducting additional research with users and intermediaries to extend the current plans.

Finally, Dr. Maibach introduced Dr. Jill Bartholomew as the Deputy Director, CSD, and identified the two CSD components. The Operations Research Office is responsible for marketing research and usability testing, and the Office of Education and Special Initiatives houses the capability for educational program development and training. He noted that the Energy Balance Dissemination Initiative is housed in the CSD. In closing, he emphasized that the CSD works closely with internal partners in the NCI OD, Divisions, and Centers to proactively identify how best to develop user-centered applications and then promote them in such a manner that the user communities understand the value of the applications to meet their needs.

## **Questions and Answers**

Dr. Moon Chen, Associate Director for Cancer Prevention and Control, University of California, Davis Cancer Center, asked how the Office of Education and Special Initiatives integrates within the NCI. Dr. Maibach explained that the CSD is a service unit to the NCI at large in support of overarching priorities. Dr. Freedman observed that it would be interesting to monitor over time whether the caBIG is effective in enhancing interinstitutional collaboration in clinical trials as well. Dr. Maibach noted that it is one of the evaluation endpoints for the 3-year pilot. Dr. Niederhuber asked that Dr. Maibach report to the Board on a regular basis because of the importance of the CSD effort to the overall NCI mission and agenda.

## **XVIII. SUBCOMMITTEE REPORTS**

### **Subcommittee on Activities and Agenda**

Dr. Niederhuber reported that the Subcommittee has been working with Drs. Gray and von Eschenbach on the agenda items that came from the NCAB planning sessions and has essentially completed their implementation in future meetings over the year to keep the Board informed and maximize its ability to be effective advisors.

### **Subcommittee on Cancer Centers**

Dr. Nienhuis reported that the Subcommittee discussed proposed changes in the P30/P50 guidelines as recommended by the P30/P50 Working Group. Goals of the revisions are to simplify the guidelines to facilitate translational research objectives, improve data collection, promote accomplishments, and make the guidelines more user-friendly. It was noted that the revisions will focus on those pertaining to the Cancer Centers at this time, and will address issues related to the Specialized Programs of Research Excellence (SPOREs) at a later time. Subcommittee responses to the recommendations will supplement those received from other sources. The next step will be a review of the Working Group recommendations at the Cancer Centers Directors Retreat in March. All comments will be addressed and a final version of the guidelines will be prepared, with the goal of submitting them for review by the Subcommittee and the NCAB at the June meeting.

### **Subcommittee on Clinical Investigations**

Reporting for Dr. deKernion, Dr. Niederhuber reminded members of previous discussions regarding the need for a Clinical Investigations Working Group similar to the P30/P50 Working Group to address broad issues relating to clinical trials, both within the intra- and extramural programs. He asked Dr. Ellen Feigal, Acting Director, DCTD, to give an update on the progress in organizing such a group. Dr. Feigal reported that the external components of the Clinical Investigations Working Group have been put together. That group has met by teleconference to review the charge and discuss logistics for bringing the participants together. The NCI component is being organized and will meet by teleconference with the external component. Information about the final membership will be disseminated to NCAB members by e-mail.

### **Subcommittee on Planning and Budget**

Reporting for Dr. Norton, Ms. Cherie Nichols noted that the Subcommittee discussed the followup to the presentation on the FY 2006 Bypass Budget and strategies for improving the response rate for external comments on the Bypass Budget at its meeting. A final copy of the meeting minutes will be distributed to members.

### ***Ad Hoc* Subcommittee on Communications**

Dr. Love reminded members that at the request of the Subcommittee after the September meeting, NCI staff had developed a marketing and action plan outlining the strategy for the CIS, with particular attention on the Hispanic community. The completed plan, which was presented at this current Subcommittee meeting, builds a promotional effort on the foundation provided by the CIS Partnership Program. The implementation cost for the plan is \$10 M per year for 5 years—\$8 M for the mass media campaign and \$2 M for media relations activities. Dr. Love noted that discussion in the Subcommittee meeting focused on identifying strategies for obtaining this funding in as much as it may not be included in the NCI budget in the current fiscal climate. Drs. Love and Huerta conveyed the concern of the

Subcommittee that relatively few people (an estimated 25 percent nationwide), particularly in underserved populations, are aware that an entire portfolio of potentially life-saving information on cancer prevention and treatment is available through the 1-800-4-CANCER telephone number, the cancer.gov Web site, and now the Chat Instant Line, and that funding may not be available to market that information. Dr. Niederhuber asked for Board discussion on this issue. Dr. von Eschenbach agreed that this is a core issue, and he stated that he and the NCI are committed to working with the NCAB to address it.

***Ad Hoc Subcommittee on Confidentiality of Patient Data***

Before hearing the report from the Subcommittee, Dr. Niederhuber stated that he had received a letter dated February 4 from the Secretary, HHS, in response to the NCAB letter concerning issues of confidentiality of patient data and the privacy rules. A compact disc of educational materials developed by the DHHS accompanied the letter. Dr. Ramirez reminded members that two major concerns expressed in the letter were whether researchers were given enough information in terms of applying the Health Insurance Portability and Accountability Act (HIPAA) rules to their research and how the rules applied to the tissue repositories and large databases. She stated that the Office of Civil Rights has developed some fact sheets to address some of the questions they have been receiving with regard to HIPAA. Noting that there was not time for review before the meeting, Dr. Ramirez recommended that the Subcommittee ensure that the issues raised are addressed in the new materials.

**XIX. FUTURE AGENDA ITEMS**

Suggested agenda items were: (1) advances in the minority training program, and (2) research update on NCI's proteomic initiative.

**XX. ADJOURNMENT—DR. JOHN NIEDERHUBER**

The 129<sup>th</sup> meeting of the National Cancer Advisory Board was adjourned at 11:30 a.m. on Thursday, February 19, 2004.

\_\_\_\_\_  
Date

\_\_\_\_\_  
John E. Niederhuber, M.D., Chair

\_\_\_\_\_  
Date

\_\_\_\_\_  
Paulette S. Gray, Ph.D., Executive Secretary