DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL CANCER INSTITUTE
131st NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
September 14-15, 2004

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

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BETHESDA, MARYLAND
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The National Cancer Advisory Board (NCAB) convened for its 131st regular meeting on Tuesday, September 14, 2004, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday September 14, 2004, from 8:00 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 Wednesday, September 15, 2004, from 8:30 a.m. until adjournment at 12 noon. 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 (absent)
Dr. James O. Armitage
Dr. Moon S. Chen, Jr.
Dr. Kenneth H. Cowan
Dr. Jean B. deKernion (absent)
Dr. Ralph S. Freedman
Ms. Kathryn Giusti
Dr. James H. French (absent)
Mr. David Koch
Dr. Eric S. Lander
Dr. Diana M. Lopez
Dr. Arthur W. Nienhuis (absent)
Ms. Marlys Popma
Dr. Franklyn G. Prendergast (absent)
Dr. Carolyn D. Runowicz
Ms. Lydia G. Ryan
Dr. Daniel D. Von Hoff (absent)

President's Cancer Panel

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

Alternate Ex Officio NCAB Members

Dr. Michael A. Babich, CPSC
Dr. Allen Dearry, NIEHS
Dr. Peter Kirchner, DOE
Dr. Raynard Kington, NIH
Dr. T.G. Patel, VHA
Dr. Richard Pazdur, FDA
Dr. John F. Potter, DOD
Dr. R. Julian Preston, EPA

Members, Executive Committee, National Cancer Institute, NIH

Dr. Andrew von Eschenbach, Director, National Cancer Institute
Dr. Alan Rabson, Deputy Director, National Cancer Institute
Dr. Karen Antman, Deputy Director for Translational and Clinical Sciences
Dr. Anna Barker, Deputy Director for Advanced Technologies and Strategic Partnerships
Dr. J. Carl Barrett, Director, Center for Cancer Research
Ms. Nelvis Castro, Deputy Director, Office of Communications
Dr. Mark Clanton, Deputy Director for Cancer Care and Delivery Systems
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Dr. James Doroshow, 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. Paulette Gray, Acting Director, Division of Extramural Activities
Dr. Peter Greenwald, Director, Division of Cancer Prevention
Dr. David Elizalde, Deputy Director for Management and Executive Officer, Office of the Director
Dr. Dinah Singer, Director, Division of Cancer Biology
Ms. Sandy Koeneman, Executive Secretary, Office of the Director

Liaison Representatives

Ms. Roshundd 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
Dr. Monica Leibert, American Urologic Association
Ms. Judy Lundgren, Oncology Nursing Society
Ms. Mary Mitchell, American Society of Therapeutic Radiology and Oncology
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

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DAY ONE: TUESDAY, SEPTEMBER 14, 2004

I. INTRODUCTION, WELCOME, AND APPROVAL OF JUNE 2004 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. He 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. Members of the public were invited to submit to Dr. Gray, in writing and within 10 days, comments regarding items discussed during the meeting. Dr. Niederhuber extended a special welcome to and introduced newly appointed Board members: Ms. Kathryn Giusti, President, Multiple Myeloma Foundation; Mr. David Koch, Executive Vice President, Koch Industries; Dr. Diana Lopez, Professor, Department of Microbiology and Immunology, University of Miami School of Medicine; and Dr. Carolyn Runowicz, Director, University of Connecticut Comprehensive Cancer Center. Dr. Daniel Von Hoff, Director, Translational Genomics Institute, also has been appointed to the Board but was unable to attend this 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 June 2004 NCAB meeting. The motion was seconded, and the minutes were unanimously approved by the Board.

II. FUTURE MEETING DATES CONFIRMED THROUGH 2006— DR. JOHN E. NIEDERHUBER

Dr. Niederhuber called Board members' attention to future meeting dates listed in the Agenda, which have been confirmed through 2006.

III. NCI DIRECTOR'S REPORT—DR. ANDREW von ESCHENBACH

On behalf of the NCI, Dr. Andrew von Eschenbach extended a welcome, appreciation, and gratitude to current, new, and *ex officio NCAB* members. Continuing the interactions and collaboration with the agencies represented by the *ex officio* members in the ongoing efforts to contribute not only to the National Cancer Program but also to the entire health care agenda are critical. He pointed out that current and new members were selected for the NCAB because of their contributions to the cancer agenda and for their special qualities of compassion and commitment to patients and to alleviating the burden of disease. He noted that the NCI looks forward to a close relationship with the NCAB as it discharges the functions of serving as an advisory board to guide the Institute in many of its initiatives, providing stewardship and oversight to ensure responsiveness to the American people and the goal of eliminating suffering and death due to cancer, and serving as advocates and conduits of communication with the broad community for the exchange of information on NCI activities and the needs to be addressed as reflected in the community.

Dr. von Eschenbach announced the appointment of Dr. David Elizalde to the position of Deputy Director for Management and Executive Officer, Office of the Director (OD), NCI. Dr. Elizalde formerly was Deputy Director of Acquisition and Grants, Center for Medicare and Medicaid Services (CMS). Dr. von Eschenbach acknowledged the contributions of Mr. John Hartinger and Ms. Janice Mullaney, both of whom served as Acting Deputy Director for Management prior to the recruitment of Dr. Elizalde. Mr. Hartinger will continue to be part of the NCI senior leadership team working on long-range financial

planning. Ms. Mullaney has accepted a position with the NIH Foundation. Recruitment continues for other leadership roles within the NCI.

Board members received an update on conflict-of-interest issues within the NIH and how they are being addressed. Dr. Elias Zerhouni, Director, NIH, with the assistance of Institute and Center (IC) Directors, has developed an NIH ethics plan that serves to refresh, enhance, and, where appropriate, strengthen policies and procedures already in place. One objective is to increase transparency but, at the same time, maintain sufficient flexibility so that recruitment and retention of the best scientific expertise is not curtailed. Dr. von Eschenbach commended the work of Dr. Maureen Wilson, Assistant Director for Ethics, OD, NCI, and staff in the NCI Ethics Office for the degree of care and competency already that has been exercised in regard to the entire process of examination required in managing the relationships of NCI staff vis-a-vis their participation in outside activities. One step already being implemented is the inclusion of more specific requirements in performance evaluations with regard to education, monitoring, and enforcement of ethics issues and policies. The Board will be kept informed of the activities.

Next, Dr. von Eschenbach called attention to some NCI advanced technology initiatives that will enhance the tools that are available to the scientific community for addressing important scientific issues and questions. The concepts for a cancer nanotechnology initiative were approved by the NCI Board of Scientific Advisors (BSA) at its June meeting. A Request for Applications (RFA) has been issued, and the scientific community was briefed recently on the creation of the Nanotechnology Alliance in Cancer. This initiative is not only a step toward the integration of the emerging field of nanotechnology with applications in cancer research across the full discovery, development, delivery spectrum, but also a model for future collaborations with partners in these kinds of ventures. In this instance, an alliance has been established with the Food and Drug Administration (FDA), National Institute for Standards and Technology (NIST), and Department of Commerce through Memoranda of Understanding. This strategy will permit the simultaneous definition of standards and preparation of regulatory science to match the discovery science, thereby shortening time to development and delivery of interventions. Because nanomedicine and nanotechnology are important NIH priorities, the NCI also is participating in the NIH Roadmap's Nanotechnology Initiative and is the lead Institute in this regard. Under the Government Performance and Results Act (GPRA), the NIH Nanotechnology Initiative was selected by the Office of Management and Budget as one component of the budget to be analyzed for performance, and the NCI participated in this effort. Dr. von Eschenbach credited the leadership of Ms. Nichols, Dr. Clanton, and NCI staff for the satisfactory conclusion of the performance review.

The NCI is playing a role in the Medical Innovation Task Force, a major initiative within the Department of Health and Human Services (DHHS). The Task Force, which is chaired by Dr. Les Crawford, Acting Commissioner, FDA, is composed of representatives from the CMS, NIH, Centers for Disease Control and Prevention (CDC), FDA, and NCI. Dr. Anna Barker, Deputy Director for Advanced Technologies and Strategic Partnerships, OD, and Dr. Dan Sullivan, Associate Director, Cancer Imaging Program, Division of Cancer Treatment and Diagnosis (DCTD), are the NCI representatives on the Task Force. Another DHHS initiative in which the NCI is exercising a leadership role is the CMS-NCI Task Force, co-chaired by Dr. Clanton, to identify partnership opportunities. This Task Force is examining emerging issues such as the long-term, postmarketing surveillance of drugs and interventions as it relates to late-term, unexpected safety issues. The Task Force also is examining aspects of the health care delivery system to ensure that the system is adequately prepared and ideally structured to deploy the products of discovery and development, such as molecularly based diagnostics, therapeutics, and prevention interventions.

Dr. von Eschenbach reminded members of the examination of the NCI clinical trials infrastructure being conducted under the direction of Dr. James Doroshow, Director, DCTD, and Dr. Howard Fine. In an update of the 2-year-old NCI-FDA Task Force, he noted that new initiatives within

the FDA, such as the new cancer office and program, have evolved from that collaboration. In another collaborative effort, the NCI, CDC, and American Cancer Society (ACS) are working through organizations like C-Change to develop cancer programs within the states. As part of the implementation strategy, the NCI recently hosted the Advanced Comprehensive Cancer Control Leadership Institute, which was organized and executed by Dr. Jon Kerner, Assistant Deputy Director for Research Dissemination and Diffusion, Division of Cancer Control and Population Sciences (DCCPS), and DCCPS staff. The program was designed to help train state officials and health agency representatives for the implementation of cancer control plans at the state level, using tools such as Cancer Planet that have been developed within the NCI.

As another example of cancer-led but not cancer-centric initiatives, Dr. von Eschenbach noted that representatives from the Juvenile Diabetes Research Foundation (JDRF) visited the NCI to explore the possibility of applying angiogenesis research underway within the cancer program to address problems such as diabetic retinopathy and diabetic ulcers of the feet. Subsequent discussions between the NCI and JDRF ultimately included nationally recognized experts such as Drs. Judah Folkman and James Watson and representatives of the National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung, and Blood Institute (NHLBI). From this collaboration, the Trans-Institute Angiogenesis Research Program was created. Dr. von Eschenbach acknowledged the leadership of Dr. Steve Libutta and staff in bringing together the participating institutes in an initiative that will expand the angiogenesis portfolio in a way that will benefit many other diseases. Dr. von Eschenbach noted that cancer-led, but not cancer-centric is a principle that will guide future NCI activities and relationships to make use of NCI resources such as technology development and the clinical trials infrastructure.

Next, Dr. von Eschenbach commented that his visits in the community, especially to the Cancer Centers, have been of great benefit. In particular, he complimented the initiatives and activities within the Cancer Centers that have become gravitational forces, drawing to the Centers intellectual capital and opportunities for collaboration in their communities. He cited as an example the collaboration that has developed at Vanderbilt University between the Cancer Center and Mass Spectrometry Center, which has developed cancer proteomics capabilities. Their joint research project now is being linked to computational opportunities at Oak Ridge National Laboratory.

Finally, Dr. von Eschenbach highlighted NCI efforts to enhance communications for sharing reports and opportunities with the community. The year-old *Cancer Bulletin* has been an electronic vehicle for weekly communication. Members were introduced to a new publication, *The Nation's Progress in Cancer Research: An Annual Report for 2003.* Dr. von Eschenbach noted that this document is intended as a complement to the Bypass Budget, which is being revised more as a forward planning, financial document than a progress review. He commended the work of Ms. Nelvis Castro, Acting Director, Office of Communications (OC), and OC staff in developing the *Annual Report.*

Turning next to the budget update, Dr. von Eschenbach stated that the NCI budget for Fiscal Year (FY) 2004 of $4.7 B will be fully obligated by September 30. The FY 2004 budget resulted in a 3.9 percent, or $178 M, increase over FY 2003. However, not all of that new money was available for new programs. Because of reductions to the NIH appropriation, contributions to NIH and DHHS activities, and out-year commitments related to grant funding, the total of available dollars in FY 2004 was less than the previous year. Dr. von Eschenbach noted that the NCI has been working through a process of redeployment of dollars and has been successful in directing new dollars to new enterprise activities while meeting strategic commitments to NCI portfolio balance. The R01 payline has been maintained at the 20th percentile, and more investigators have been funded than ever before, including first-time applicants to a cancer research program. The overall success rate for Research Project Grants (RPGs) was 24 percent; 82 percent of available new dollars went into the RPG pool. Dr. von Eschenbach concluded by

noting that FY 2005 appropriations legislation has not yet been enacted. Currently, only the House version of the Labor-DHHS-Education bill has been passed, providing a 2.8 percent increase for the NCI.

Questions and Answers

Dr. Ralph Freedman, Professor, The University of Texas M.D. Anderson Cancer Center, asked about plans for sustaining support for both the critical mass of R01 scientists for the future and important new initiatives, in the face of budget constraints. Dr. von Eschenbach explained the planning process put in place under Mr. Hartinger's leadership to aggressively manage the NCI portfolio. The methodology involves examining specific and individual investments in terms of both mechanism and important strategic priority to define an appropriate balance across mechanisms and opportunities. Dr. Niederhuber expressed the view that the cancer-led but not cancer-centric aspects of NCI collaborations should be communicated to the cancer community at large to create greater awareness of NCI leadership roles across the NIH and among other governmental agencies.

IV. PRESIDENT'S CANCER PANEL—DR. LASALLE LEFFALL, JR.

Dr. LaSalle Leffall, Jr., Charles R. Drew Professor of Surgery, Howard University College of Medicine, began by thanking Dr. Wilson and her staff for the excellent support they have given the Panel over the years. He reported that the Panel recently launched a new series of meetings under the title "Translating Research to Reduce the Burden of Cancer." The purpose in convening this series is to examine barriers to progress in translating cancer research into reductions in suffering and death due to cancer. Issues to be examined include the role of academic medical centers, NCI-designated Cancer Centers, and community cancer centers in translating research into practice, as well as how these organizations fit into the larger communities. Specific consideration is being given to the peer review process, current and future infrastructure, financing and design of clinical research and clinical trials, and the potential for effective partnerships among academia, government, industry, and others.

Dr. Leffall informed the Board that the Panel meeting structure has been modified to generate more targeted, concrete information. The agenda is being organized into three discussion panels, each to focus on one of the following areas: (1) barriers to translating research into reductions in the burden of cancer, (2) the role of academic medical centers in translating research into clinical practice, and (3) best mechanisms for moving research into communities. Invited panelists are asked to prepare and submit a short white paper prior to the meeting. Panelists then provide testimony at the meeting with time afterwards for questioning by the Panel. At the close of the meeting, designated Chairs of each discussion panel are asked to report to the PCP members a summary of key points and recommendations, in particular, avenues for change that were deemed innovative, affordable, and practical in application.

Dr. Leffall summarized key points and suggestions derived from the first of the series, which was held on August 30 at the Grand Hyatt Hotel in San Francisco, CA.

- The scientific discovery engine is accelerating at a rapid pace but the speed at which the information is disseminated to clinicians, patients, and communities lags behind. To eliminate death and suffering due to cancer, it is critically important for the National Cancer Program to focus on moving the results of research into practice in all communities of the United States.

- Although basic science discovery is traditionally a function of individual effort, multidisciplinary team science is necessary to elevate discoveries to proven cancer interventions. Current academic infrastructure does not reward this type of collaboration either through promotion and tenure tracks or peer review systems. Thus, the formation of a translational review research infrastructure is crucial to channel more discoveries into the development phase.

- In testimony about opportunities for expanded partnerships to create a more robust development system, it was acknowledged that the complexity, expense, and technological demands of biomedical research require a new paradigm of partnering. No one institution can single-handedly meet these demands. A large middle ground between academia and industry currently exists that needs to be strengthened.

- There also are opportunities for teams composed of nontraditional partners with a vested interest in the cancer problem. HMOs and other third-party payers have large patient populations and health-tracking databases that would be of value to translational research efforts, and they seem willing to partner with industry and government. In addition, the Panel heard about opportunities for more effective partnering with local communities to disseminate proven interventions.

- Issues of regulatory reform raised in testimony included: (1) FDA efforts to modernize and streamline the regulatory process in favor of development, and (2) the Health Insurance Portability and Accountability Act (HIPAA) as a regulatory barrier. It was noted that making progress against cancer means making use of medical information, some of which may be considered private under current HIPAA interpretations. It was suggested that the cancer research community, in cooperation with patient interest groups, address aspects of HIPAA that currently inhibit collaborative cancer research.

- The need for more shared resources and better research development tools was another key theme. To maximize existing resources, it was suggested that better tools (e.g., biomarkers, animal toxicology, modeling, and surrogate endpoints) be crafted for assessing the usefulness of compounds at the earliest possible stages of clinical research. Standardization and centralization of national cancer registries and tissue banks are needed to create more efficient and less costly development systems.

- The public and community play a large role in translating research to reduce death and suffering from cancer. Progress is impeded by misunderstandings and mistrust on the part of the public about the process of biomedical research, how the pieces fit together, and what is involved. Compliance with prevention and screening guidelines, as well as clinical trials participation, are impacted by public mistrust. It was suggested that the scientific community work more vigorously to inform the public and dispel myths about the scientific enterprise.

- Approximately 85 percent of patients are being treated in the community, yet barriers exist to getting the best research results to these patients. The Panel was told that the promise of discovery would not be fully realized without the infrastructure for disseminating proven practices and programs to all communities. Cancer Centers are known repositories of evidence and data, but many do not have clear strategies for translating what is known to be effective to their community-based constituents. A key question raised was how Cancer Centers can partner with community-based organizations to disseminate evidence-based findings. Perceiving cancer as a community problem, not just an individual problem, may lead to new models for translation.

In summary, Dr. Leffall stated that it is the Panel's challenge and goal through this series of meetings to develop recommendations for improving the way the research and health care communities discover, develop, and deliver science to everyone, all aspects of which are necessary to translate research to reduce the burden of cancer. Subsequent meetings in this series will be held on September 27 at the Arthur G. James Cancer Hospital and Richard Solove Research Institute, Columbus, OH; November 1 at The University of Texas M.D. Anderson Cancer Center, Houston, TX; and January 24 at Memorial

Sloan-Kettering Cancer Center, New York, NY. Information regarding the series is posted on the Panel's Web site at http://www.pcp.cancer.gov.

Questions and Answers

Dr. Niederhuber commented that well-defined recommendations appear to be likely from the Panel's investigations and asked how the NCAB could help now in beginning to address those issues. Dr. von Eschenbach suggested that the NCAB could take a position of directing and requesting the NCI to work with an NCAB subcommittee to begin a strategy-planning trajectory that is aligned with the agenda of the Panel so that programs are in place for implementation when the Panel's report is presented to the President.

V. LEGISLATIVE UPDATE—MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Policy Analysis and Response, OD, NCI, began her presentation of NCI- and NIH-related Congressional deliberations by reviewing the FY 2005 appropriations status. The President's Budget announced in February provided $4.87 B for the NCI. The Labor-HHS-Education bill containing the same amount for the NCI was reported out by the House Appropriations Committee in July and was passed by the full House on September 9. Senate action on its version of the bill is pending. Ms. Erickson highlighted items of interest to the NCI included in the House bill's report language:

- The NCI will be asked to provide an annual update on the progress in prostate cancer research as it relates to goals outlined in the plan submitted to Congress for the years 2004 to 2008.

- The Committee is encouraging the NCI to continue research on tobacco products intended to reduce harm, particularly as that relates to smoking cessation.

- A report on how the NCI will further develop its program involving human embryonic stem cell research is requested.

- In an NIH-related item directed to the National Library of Medicine, the Committee supported the proposal to make the complete text of articles generated by NIH-funded research available on a PubMed Central Database. In that regard, an NIH proposal was posted on the Web on September 3 for a 60-day comment period. This draft policy will make NIH-funded research freely available on PubMed 6 months after publication.

Ms. Erickson summarized the outlook for FY 2005 appropriations as follows: (1) target adjournment date is October 1, (2) a continuing resolution will be needed if the bill is not passed by that date, and (3) a lame-duck session after elections could be needed if neither the bill nor a continuing resolution is passed. Members were reminded that unpassed legislation will die on adjournment.

Ms. Erickson briefly reviewed Congressional hearings since the June meeting. Dr. von Eschenbach and the Directors of the National Institute of Allergies and Infectious Diseases (NIAID) and the National Institute on Drug Abuse (NIDA) were witnesses before the House Energy and Commerce Subcommittee on Health to discuss priority setting as a forerunner for the Committee's drafting of NIH reauthorization legislation. Discussion focused on options for improving the NIH structure and questions as to how the NIH decides which projects will produce the greatest gain and thereby sets priorities. Drs. Anna Barker, Carl Barrett, and Maureen Wilson were NCI's witnesses in an ethics hearing conducted by the House Energy and Commerce Subcommittee on Oversight and Investigations. The topic of the

hearing was consulting arrangements and outside awards. Three visits by Congressional staffers over the summer included presentations on Cancer Centers and the Radiation Oncology Sciences Program and a pre-dedication tour of the new Hatfield Clinical Research Center.

Questions and Answers

In response to a question from Dr. Kenneth Cowan, Director, Eppley Cancer Center, University of Nebraska Medical Center, about NIH reauthorization conversations, Dr. von Eschenbach noted that the witnesses were engaged in explaining the importance of the current authorizations, how they can continue to be used effectively, and what other opportunities could be available in the future by virtue of the authorizations.

VI. *AD HOC* SUBCOMMITTEE ON BIOMEDICAL TECHNOLOGY WORKGROUP UPDATE: ADVANCED TECHNOLOGY INITIATIVE FOR CANCER—DR. ERIC LANDER

Dr. Eric Lander, Director, Whitehead Institute/Massachusetts Institute of Technology Center for Genome Research, stated that the full report of the Subcommittee would be presented formally to the Board at a later meeting. He presented an interim report to review questions and opportunities that have arisen, as well as the type of recommendations that are crystallizing within the group, so that the Board would have an opportunity for input at this developmental stage. Board members were reminded that the charge to the Workgroup was to explore specific ways in which the NCI can take advantage of the potential power of technology to provide a technology infrastructure that has a transformative effect across the cancer research continuum. To avoid duplication of effort, the Workgroup received a briefing on the status of important technology initiatives underway at the NCI, such as the Cancer Genome Anatomy Project (CGAP), the emerging Nanotechnology Initiative, and the Division of Cancer Biology (DCB) think tanks.

Dr. Lander noted that the Workgroup met in December 2003 to discuss broad, overarching needs and themes and to develop strategies for approaching the task. Five smaller groups were created to address the following topics: (1) characterization of cancer in the cell (Dr. Lander, Chair); (2) characterization of cancer in the organism (Dr. Lee Hartwell, Chair); (3) public health (Dr. Margaret Spitz, Chair); (4) cancer therapeutics and clinical trials (Dr. Brian Drucker, Chair); and (5) technology, access, development, and dissemination (Drs. Benjamin Shapiro and Jeffrey Duette, Co-Chairs). With expertise recruited from throughout the community, the five focus groups were convened. Themes that emerged from the focus group related to the characterization of cancer in the cell were: (1) the ability to characterize the genomic basis of cancer is at a turning point; the availability of human genome sequencing and the technologies for amplifying and resequencing suggest that genomic characterization of cancer can now be accomplished definitively; (2) technologies becoming available have the potential for building a map of functional responses of the cells; and (3) systematic research is needed to understand what makes it possible to create cell lines from all cancers.

The group focusing on cancer in the organism identified detection as the key issue that would be transformative to both basic and translational scientists and have direct clinical application. Better tools are needed for detecting cancer in two different fashions: (1) through direct functional imaging in patients, which would involve the development of the right kinds of functional imaging probes combined with technology advances and informatics tools to process the information; and (2) through detection in bodily fluids from patients, which would involve the systematic and collaborative development of high-throughput proteomics technology.

The public health group focused on ensuring that these technologies would get broad application in the community. Considerations in this regard were the need: (1) to understand inheritable risk factors for cancer (e.g., single nuclear polymorphisms that predispose to disease); (2) to have high-throughput proteomics and metabolomics technologies available in both large centers and smaller scale research settings and to have the technologies reconfigured for and available in the clinical setting; and (3) for data repositories and analytical tools, to include standardized methods for data collection and standardized systems for laboratory information management and analytical information management. This group also recognized that the support of team science requires careful attention.

An overarching theme that emerged from the cancer therapeutics and clinical trials focus group was that greater efficiency was needed in translating discoveries about the fundamental basis of cancer and prognostic and diagnostic markers into clinical trials. Four points in that regard were the need: (1) to standardize the collection of clinical samples from clinical trials for more systematic research; (2) for better animal model systems for developing cancer therapeutics; (3) to design better trials from a scientific point of view, to include a scientific base for characterizing patients and a scientific base in terms of the ability to evaluate drugs *in vivo*; and (4) for an organizational infrastructure that enables the development of more efficient clinical trials (i.e., smaller, faster, cheaper, smarter trials).

The fifth group focusing on technology access, development, and dissemination spoke more about general conditions for technology development, including the management of intellectual property, access to tools, models for cross licensing, consortia, and essential information resources. Included in these deliberations were a call for standardized collection of samples with appropriate consents and discussions about effective ways to organize centers.

Dr. Lander noted that the Workgroup convened to identify cross-cutting themes that emerged from the five focus group meetings. He summarized, for Board consideration and possible input, directions that are being considered in developing formal recommendations to be included in the Workgroup's final report. There was a sense that important technology opportunities exist that will continue in the future. The NCI, therefore, should consider establishing a cancer technology working group on a standing basis, whose job it would be to identify the most important opportunities for creating projects and initiatives that have a potential transforming impact across cancer. Moreover, the Workgroup believes this should be a sustained exercise and that the cancer technology working group should be proactive in turning general observations into an actionable program. In the meantime, the Workgroup plans to identify the most important from among the themes emerging from the focus groups and structure them into actionable programs as a recommendation to the NCI. Dr. Lander listed two themes to be recommended for immediate attention: (1) comprehensive characterization of the genomic basis of cancer, and (2) molecular detection of cancer in patients and in patient fluids. Specific plans to address these two areas will be included as recommendations in the Workgroup's report to the NCAB. Dr. Lander noted that other focus group recommendations bear mention but have not been fully developed. They include animal model systems for cancer therapeutics, functional characterization of cellular responses, and broad dissemination problems related to getting the technologies into smaller laboratories and clinics, the latter requiring technology development efforts.

Workgroup plans for moving forward are to incorporate NCAB member comments resulting from this update to develop a final report that will summarize the input from the focus groups, describe the proposed cancer technology working group, lay out draft plans for the two areas singled out for immediate attention, and identify other areas that merit attention on a going-forward basis. The report will be presented to the NCAB at the December or February meeting, pending completion.

Questions and Answers

Dr. Niederhuber commended the work of Drs. Lander and Hartwell in co-chairing the Workgroup effort, and he commented that the needs identified by the Workgroup also have been strongly expressed by those involved in bringing new agents to patient care in the academic scientific community and industry. Dr. T.G. Patel, Program Chief, Veterans Health Administration, asked what is intended in the proposal related to data repository and analytical data systems in terms of public health. Dr. Lander explained that the thinking of the group addressed standardization of laboratory and analysis information management systems and the need for rewards for building generally usable tools. In response to a question from Mr. Koch as to whether the Workgroup report would focus on structural changes at the NCI to facilitate rapid response to breakthrough discoveries in cancer research, Dr. Lander replied that the report will lay out the structures that the Workgroup thinks are needed to address the task assigned to it. Ms. Kathryn Giusti, President, Multiple Myeloma Research Foundation, Inc., described a national tissue bank that is being created by a myeloma consortium, in which tissue is standardized as it enters the system and Good Laboratory Practices quality standards are applied universally. Obstacles encountered in this initiative include gaining access to tissue at community centers where 85 percent of patients are seen, competing with large projects in academic centers such as Specialized Programs for Research Excellence (SPOREs), and working with industry to obtain samples from their clinical trials for validation. Dr. Lander asked Ms. Giusti to provide the Workgroup with a description of the consortium's experiences to add to its information base. Dr. Freedman asked whether the Workgroup had considered using technology to detect changes in the microenvironment of the cancer cell as an important research area and whether the Workgroup had identified specific barriers to conducting faster and more economical clinical trials. Dr. Lander pointed out that the cancer microenvironment is getting significant attention from DCB think tanks, and an organized technology focus is not indicated at this point. In regard to clinical trials, he briefly reviewed strategies suggested by the clinical trials focus group for designing and conducting smaller, faster, smarter, and less costly trials.

Dr. Barker requested that the Workgroup deal more specifically with the issue of reward systems, in recognition of the move toward much more of an engineering culture for initiatives such as systematic ways of looking at cancer genomics, proteomics, and biomarkers. Dr. Lander agreed to approach the Workgroup about taking on the additional task. Dr. Barker suggested that one approach may be to form another subcommittee of the Board. Dr. von Eschenbach thanked Drs. Lander and Hartwell and the Workgroup, and he commented that this is an extraordinary example of how the NCAB can provide guidance, advice, direction, and insight. He looked forward to contributions from members of the Board in the continuing effort to make the NCI more able to respond to scientific opportunities.

VII. MINI-SYMPOSIUM: THE SCIENCE OF NANOTECHNOLOGY—DRS. GREGORY DOWNING, ANNA BARKER, HAROLD CRAIGHEAD, JAMES HEATH, CHARLES LIEBER, JENNIFER WEST, AND MAURO FERRARI

Introduction—Dr. Anna Barker

Dr. Barker thanked the Board for reviewing the Nanotechnology Initiative and noted that the Initiative had been launched on the day before this meeting. The NCI considers nanotechnology a promising breakthrough technology for cancer and is working to inform the public and scientific community about it. The Initiative took 2 years to develop and launch. Dr. Barker thanked those who had been involved in this effort, including those from the NIH, NCI, NIST, and FDA.

Development of the Nanotechnology Initiative—Dr. Gregory Downing

Dr. Gregory Downing, Director, Office of Technology and Industrial Relations, NCI, stated that the Cancer Nanotechnology Plan is a comprehensive document, and the Nanotechnology Alliance represents the programs and initiatives that have evolved from the Plan. Board members received copies of both of these documents. Six Cancer Nanotechnology Symposia were held over the past year and informed the development of the Plan and Alliance. An October symposium will bring together Cancer Centers and engineering programs. These Symposia have resulted in the development of new ideas and the formation of new teams to address specific cancer issues on which nanotechnology can have an impact.

Programs in the Alliance focus on six key areas contained in the 5-year Cancer Nanotechnology Plan. Detailed performance measures were developed to address molecular imaging and early detection, *in vivo* imaging, reporters of efficacy, multifunctional therapeutics, prevention and control, and research enablers. Nanotechnology information, including details of the initiative, is available at http://www.nano.gov.

Dr. Downing explained that the goal of the Centers of Cancer Nanotechnology Excellence is to integrate nanotechnology in basic and applied cancer research with an approach to develop technologies that will impact clinics. The key features are described in more detail on the Web Site. Basically, the intent is to develop consortia of up to four programs or institutions within each Center with defined projects and identified investigators. Each Center will have approximately five to eight technology platforms on which to build interchangeable components to address specific problems in cancer. A vital aspect of this is to develop advanced biocomputing capabilities with connections through the Cancer Bioinformatics Grid (CaBIG). Also key is bringing technology to and from the Cancer Centers to be deployed through clinics in close affiliation with universities or research programs of engineering and physical science excellence. Thus, an affiliation will be developed between projects to be coordinated within engineering programs and the physical sciences and cancer biology. Also important is the development of partnerships with the corporate world geared toward technology development and commercialization.

The proposals themselves should focus on the six key programmatic areas. The funding mechanisms include the SPOREs, Cooperative Agreements, and the U54 mechanism. It is anticipated that up to five Centers will be funded for an approximate total of $91 M over 5 years. The receipt date for these proposals is March 2005.

A second major component of the Alliance is the development of multidisciplinary research teams. Supporting the training and multidisciplinary career development pathways is essential for advancing this field. The two funding mechanisms identified thus far are the F32 and F33 National Research Service Awards. Approximately $16 M is anticipated to be available over 3 years. After that, career talent will be reassessed to facilitate future technology development. The initial receipt date again is March 2005.

Nanotechnology platforms are the third major Alliance component and enable investigators to use the R01 mechanism to develop individual technology projects. The use of multiple Principal Investigators (PIs) is being explored as a possible option. Approximately $38 M is anticipated over 5 years for approximately 18 awards, and the initial receipt date again is March 2005.

The fourth major component of the Alliance is the Nanotechnology Characterization Laboratory. Input received from technology programs during the past 5 years has indicated the need for a public database of information regarding the characterization of nanoparticles and other nanomaterials in

biological systems. Collaborations have been established with the NIST and FDA to develop an assay cascade to provide researchers who are not biologists and who have not worked in this field with reference points regarding the assays and characterization materials needed to facilitate preclinical and clinical studies. Discussions with other governmental agencies are ongoing as well.

Dr. Downing noted that the RFAs for the above-described programs should be released in late October. A preapplication informational meeting will be held on December 14, 2004, and initial proposals are due in March 2005. Ongoing efforts include discussions with other federal agencies to leverage their investments in this fundamental technology and continued outreach programs and education through professional societies, Cancer Centers, and engineering programs. Additional symposia are expected in the near future to highlight research achievements and identify new opportunities.

In response to Mr. Koch's question regarding how the decision to invest so heavily in nanotechnology was made, Dr. Downing noted that the decision was based on internal and external evaluations of existing programs and on the view that this as an opportunity to bring these technologies to clinical development. The budget formulation was based on what is considered realistic in this environment, where the opportunities are, and what would be needed to ensure a successful initiative. The BSA and NCAB provided input throughout the process.

Nanotechnology Overview—Dr. Harold Craighead

Dr. Harold Craighead, Charles Lake Professor of Engineering, Professor of Applied and Engineering Physics, and Co-Director of the Nanobiotechnology Center at the School of Applied Engineering Physics at Cornell University, explained that the types of nanostructures that perhaps are mentioned most often are nanoparticles, the small, free-moving objects used to deliver drugs by coating the inside and outside of particles in different ways. Nanoparticles also are used to enhance the ability to identify molecular species by using quantum dots to replace organic dyes and using the ability to tailor the properties of these particles in ways that promote enhanced behaviors. This same philosophy is being applied in developing devices from other sciences and adapting them to biological and medical applications.

Dr. Craighead continued that this process involves exploring the physics and material science of addressing in a practical way the ultrasmall systems down to the molecular scale. This involves creating tools that can probe activity at the cellular level by observing the function of individual molecules, in their natural environments and otherwise, and then creating practical uses of these tools in detecting and observing the activity. In the long term, this may result in microscopes that function at the subcellular, molecular, and genetic levels to enable sensitive diagnostic approaches that can detect objects at much lower concentrations than before; tools that are sufficiently automated and inexpensive so as to be used more routinely to monitor, perhaps in real time, the activity of different therapies; and, perhaps, genetic analysis that can be used for individualized medicine. Advances continue to be made in manipulating solid and soft matter in ways that may be useful in attacking cancer.

The simplest construct is the chemical analog of an electrical wire—a small tube that carries individual molecules. If this tube is made small enough, it is possible to interrogate one molecule at a time by isolating individual entities. A goal is to examine the character of the molecules. Nanotechnology currently makes it possible to select a molecule of interest and link it to a "beacon" or identifier. Quantum dots are one class of such molecules. These kinds of objects can be linked to specific chemistries, and the particular biomolecule of concern can be interrogated or observed via the quantum dot as a reflection of what is occurring. From that reflection, the quantity and quality of various chemicals and solutions can be inferred. A simple spectrometer makes it possible to read information

encoded in various quantum dots. In principle, a single molecule could be detected in this manner. Distinguishing features of molecules also can be observed by applying various techniques.

Nanoshells in Cancer Imaging, Diagnostics, and Therapy—Dr. Jennifer West

Dr. Jennifer West, Isabel Cameron Professor of Bioengineering in the Department of Bioengineering at Rice University, discussed recent work with nanomaterial, a type of nanomaterial, and possible applications in cancer therapy, imaging, and diagnostics. Nanoshells have unique and tunable optical properties. They consist of a nonconducting dielectric core nanoparticle on which a thin metal shell is grown. Changing the thickness of the metal shell allows the nanomaterial to be designed to promote either absorption or scattering of light. What is important for biomedical applications is that nanoparticles can be made with optical properties in the near-infrared. This enables diagnostic and therapeutic applications that can probe inside the body using light sources that are external. Another advantage of the tunability of nanoshells is that they can be designed to be predominately absorbing or scattering, which is important for different types of applications. Therapeutic applications may require light to be absorbed, rather than scattered, and converted to heat. Diagnostic applications, on the other hand, may require predominately scattering so that light can be put in, scattered by the materials, and information sent back out of the system.

An application being studied is thermal ablation of tumors. Nanoshells are designed to strongly absorb in the infrared so they will generate heat. Targeting agents such as antibodies can be attached. Nanoshells can be injected intravenously and will tend to accumulate in tumor sites because of the enhanced permeability and retention effect caused by leaky vasculature. Nanoshells can be injected systemically, allowed to find the target site, and then near-infrared light is applied from outside the body. This light penetrates deeply and, wherever it hits the nanoshells, they heat up and kill the targeted cells. This therapy is attractive because the nanoshells are very biocompatible. No toxicity effects have been observed, no issues have arisen with injecting nanoshells, and the light by itself is not absorbed by anything in the tissue and is harmless. Studies to date have proved very promising.

Another area being explored is that of combining imaging and therapy. Nanoshells have proven attractive as contrast agents in procedures such as optical coherence tomography. Researchers hope to develop a system in which the same nanoshells can be used for both imaging and therapy. Toward this end, nanoshells can be designed so that they both partially absorb and partially scatter light. This allows the use of low laser intensity to accomplish imaging; if a problem is found, the light intensity can be increased and the tumor ablated during the same procedure. Nanoshells are seen as a platform technology that may have other uses as well. Additional areas in which nanoshells are being studied include whole blood immunoassays, photothermally modulated drug delivery, optically controlled valves and actuators, and microfluidics.

What Can Nanoscience Offer to the Field of Cancer?—Dr. Charles Lieber

Dr. Charles Lieber, Mark Hyman, Jr., Professor of Chemistry at Harvard University, discussed how nanoscience might enhance cancer diagnosis and treatment by facilitating real-time diagnosis and monitoring and semi-real-time capabilities for treatment and recurrence. Nanoscience can permit accessing or testing information in multiple ways, thereby helping to avoid false negatives and false positives and enabling more robust diagnosis. One technology being tested is a nanoscale wire with receptors. It functions as a field effect transistor and responds to charge, and most solution-soluble biological species are charged. Efforts also are underway to develop large arrays and sensor chips that may be usable at the clinical level. Such devices may be useful in detecting prostate-specific antigen, for example, and can help eliminate false negatives and false positives. It may be possible to use many such

wires, personalized with different receptors, to screen for known and emerging markers of cancer. Such devices may be applicable in the area of drug discovery as well.

Dr. Lieber stated that nanotechnology may be unmatched in its ability to highlight the biology of a single particle, which can be important in detecting viral-based infections such as HIV. It presents an opportunity to integrate clinical and diagnostic medicine and cancer biology research. Such systems have the opportunity to provide rapid parallel acquisition of information that is being defined from other fields that will make the definitive diagnosis, monitoring, and treatment of patients possible.

Nanotechnology Platforms and Cancer Issues—Dr. James Heath

Dr. James Heath, Elizabeth Gilloon Professor of Chemistry at the California Institute of Technology (CalTech), discussed efforts to use a systems biology approach as a way to drive the development of nanotechnology platforms in addressing cancer issues. He referred to informative diagnostics and stated that nanotechnology is making it possible to capture various levels of information in biological systems and understand how environmental perturbations that act at these levels cause the system to change. Changes in the system are related back to the fundamental code of the genome to help build a system model. Studies of model organisms have shown that genetic and environmental perturbations can yield a time-dependent fingerprint that is reflected in both proteins and gene-expression patterns. This model is considered applicable to human disease in that disease patterns and progression can be recorded through proteins, gene expression, and positive and adverse responses to therapy as detected in blood samples. Many measurements are involved but can be done and recorded in graphic form that will inform patients and practitioners. Analysis of gene expression and translation can be used to create a network hypothesis that can yield key nodal points in regulatory networks and drug targets. With regard to dissection and therapeutics, nanotechnology seems capable of providing a detailed view and of dissecting at the single- or few-cell level. Nanotechnology also can enhance efforts to locate a tumor via molecular imaging. Using a microfluidics environment has been found to dramatically decrease synthesis times and increase yields.

Dr. Heath concluded by noting that much work is needed in this area. Comprehensive, high-quality databases are paramount, regardless of the technology. Technology demonstrations are not sufficient; technology production and testing through Cancer Centers and the training of Cancer Center researchers are critical to the success of this program. He continued that early-stage NCI technologies, such as those discussed today, are possible, but developing needed nanotechnology capabilities is difficult and will take time. Collaborative efforts such as that between CalTech and the University of California at Los Angeles, Johnson Cancer Center, Sloan-Kettering Cancer Center, and Winship Cancer Center are underway. In addition, attention must be paid to complicated issues such as intellectual property, clinical trials, and commercialization.

In response to a question about the boundaries for nanotechnology initiatives, Dr. Barker stated that the area has been defined basically as within the 1-100 nm range. The focus is on creating new devices and on ways to integrate the new devices with biology at the nanoscale. Multidisciplinary efforts to enable this technology, which includes microfluidics, are key.

Concluding Remarks—Dr. Mauro Ferrari

Dr. Mauro Ferrari, Edgar Hendrickson Professor of Biomedical Engineering and Professor of Internal Medicine at The Ohio State University, cited “smart” or multifunctional therapeutics as an area of interface with patients that can be enabled by nanotechnology using a variety of different capabilities. Examples include the ability to monitor the effects of therapeutic agent release, and perhaps self-regulation or remote activation of therapy by a physician or the patient. The notion of getting therapeutic

agents to sites where they are needed requires avoiding biological or physical barriers and could include sequestration of nanoparticles by the endothelial system. Cancers, as they grow, may push the drugs out; thus, the notion of avoiding barriers is vital. Another aspect is that of personalizing treatment and delivery of care, even with nominally identical therapeutic regimens. He stressed the importance of a multidisciplinary approach in these efforts.

Dr. Ferrari described an implanted nanodelivery system that provides controlled drug release as an example of such techniques. He noted the importance of mathematical modeling in developing and perfecting the device at the nanoscale. He also discussed the notion of developing novel markers of disease that are architectural, multiscale, and based on appropriate mathematical models. Detecting differences from otherwise standard technologies in tissue responses and linking those responses to pathologic states requires appropriate modeling of biological matter. With regard to implantable or biological sensors, Dr. Ferrari noted that nanoparticulates may be useful for acquiring information not only on molecular presence or absence but also on molecular distribution, architecture, scaling factors, decoupling, and deconvoluting signals from confounding effects.

Dr. Ferrari noted that a clear focus on solving significant problems in cancer is the spirit in which the Cancer Nanotechnology Plan was written. The effort is not technology focused; it focuses on cancer-solving and involves technologies toward that end. The problems will dictate the proper technologies to involve. The objective is to solve real problems as quickly as possible via a pragmatic, operational approach that leads to effective clinical translation. There are important opportunities to coordinate with the private sector to efficiently translate discoveries into the clinic. Such opportunities should be pursued whenever appropriate. With regard to a regulatory perspective, the effort is being coordinated with the FDA. Although the FDA currently does not have specific requirements for approval of nanotechnological devices, its past experience—with liposomes, for example—is relevant. Technology standardization is another important aspect of this effort, as are education and training

VIII. GRANTS SUCCESS RATE REPORT—MR. STEPHEN HAZEN

Mr. Stephen Hazen, Chief, Extramural Financial Data Branch (EFDB), OD, NCI, presented background information on success rates and percentiles because the topic is a source of confusion to many in the extramural community. The R01 payline has been provided as a standard for applicants to use in determining how good or poor the chances are for success. He pointed out that the R01 payline is not a sufficient way of explaining the grant portfolio. At the request of the BSA, the EFDB has devised alternative formats for presenting information on the NCI grant portfolio and grant policies in a way that more fully explains what is happening.

Mr. Hazen presented an illustrative example of success rate rules using R01 data from FY 2001 to demonstrate how the official success rate is calculated for each grant cycle and for total R01s funded in FY 2002, then compared it with totals and the calculated success rate for all research project grants (RPGs). The success rate is the percent of the grants that are funded calculated by using the number of grants awarded as the numerator and the number of applications received (excluding amended applications [success rate base]) as the denominator. As a preliminary step to comparing percentile and success rate, Mr. Hazen reminded members that percentiling is a method to identify the relative rank of a particular application related to all the other applications reviewed by a specific study section over the most recent three rounds. Percentiling helps the reviewers to be consistent over a longer time frame and it helps areas of research that are emerging to be better funded, the latter because funding is assured for a certain number of applications in each study section. Percentiling also allows an Institute like the NCI, which receives applications from a wide variety of study sections, to make choices with some degree of standardization. The percentile counts apply only to the R01s that are funded within the payline,

whereas the R01 success rate includes the approximately 10 percent of R01s that are funded as exceptions.

Mr. Hazen then presented the Grant Success Rate Report developed by EFDB staff in response to the BSA request for a more detailed examination of the grant numbers. The report is included on most BSA meeting agendas. The graphics tables that make up report display the number of competing awards, overall awards, and competing applications for several key grant mechanisms for the period from FY 1998 (baseline year for the near doubling of the NCI budget) to date. In the graph comparing total RPGs and R01s, Mr. Hazen pointed out that the total number of awards increased consistently over that period, and that even with less than a 3 percent budget increase in FY 2004, the NCI received the largest number of competing applications ever and funded the largest number of grants in NCI history. In the comparison of program projects (P01s) and SPOREs (P50s), Mr. Hazen pointed out that the success rate for SPOREs has been lower (sometimes considerably) than that for P01s. In another comparison, Mr. Hazen noted that the RFA success rate is in line with the R01 success rate and lower than the P01 rate. With regard to developmental grants (R21s), Mr. Hazen pointed out that the mechanism has experienced considerable growth since initiation of the program in 1998. Competing awards showed consistently good growth; however, between FY 2003 and FY 2004, even though the number of awards increased by over 10 percent, the number of applications increased by about 50 percent, causing the success rate to fall from 23 percent in FY 2003 to 15 percent in FY 2004.

Questions and Answers

Dr. Lander reminded the Board that the NIH Center for Scientific Review (CSR) implemented new criteria for grant review several years previously. He suggested that the Board consider proposing an evaluation of the effectiveness of the new review process in ensuring the quality and innovation of the science that is funded. Dr. Runowicz commented that although the total dollars awarded has increased, the drop in the success rate is a discouraging message for young investigators. Dr. von Eschenbach pointed out that the payline (percentile) is not the only indicator of opportunity. The NCI continues to develop and promote mechanisms that will enhance the development of new investigators; the number of grants to compete for has increased substantially within the past few years and the pool has increased. Moreover, other mechanisms have opened tremendous opportunities for investigators to be funded in ways that do not reflect the R01 pool, and new mechanisms are being examined to address the funding of the team scientists of the future. Dr. Lander suggested that accelerating the grant review process would significantly improve the situation for investigators.

IX. NCI INTERNATIONAL ACTIVITIES—DR. JOE HARFORD

Dr. Joe Harford, Director, Office of International Affairs (OIA), OD, NCI, reminded members that the National Cancer Act of 1971 explicitly directs the NCI to support: research in cancer fields outside the United States by foreign nationals which can be expected to benefit the American people; collaborative research involving American and foreign participants; and the training of American scientists abroad and foreign scientists in the United States. To characterize the global burden of cancer, he pointed out that: (1) there are 10 million new cancer cases per year (87 percent outside the United States) and 6.4 million cancer deaths per year (91 percent abroad); (2) a great diversity exists in genes and environment; (3) cancer kills more people worldwide than malaria, HIV, and tuberculosis combined and cancer incidence is rising; and (4) cancer mortality disparities are greatest in developing countries. The initial impact of discovery is to increase disparities because new interventions are developed and delivered first to the “haves.” Ultimately, discovery has the potential to eliminate disparities, but only if the interventions are delivered to the “have nots.” The most effective way to eliminate disparities is to prevent or eradicate the disease. Factors contributing to the increase in cancer are the increasing age of

the population, decrease in cardiovascular diseases, and increased incidence of certain forms of cancer, particularly those related to tobacco use.

Located within the Office of the Director, the OIA monitors international activities across the NCI, including grants or contracts involving foreign investigators and foreign researchers in intramural laboratories. The OIA also manages NCI's international projects, including multi- and bilateral interactions, individual and group training activities, and sponsorship of workshops. About 92 percent of the NCI international budget of approximately $65 M is allocated to grants, contracts, and training. The remainder is used for exchanges, conferences, and program support. Dr. Harford highlighted two programs with large participation by international visitors to the NCI. About 200 scientists from 48 countries have attended the summer course on cancer prevention conducted by the NCI Division of Cancer Prevention (DCP). More than 1,000 scientists from 75 countries were working in NCI laboratories in the Center for Cancer Research (CCR) in 2003. For OIA, a major objective is enhancing the capacity for research in countries worldwide and especially in developing nations. NCI international activities also serve to enhance U.S. relations with other countries.

Dr. Harford quoted excerpts from State Department documents to underscore the role of international science in diplomacy, and from the Institute of Medicine (IOM) publication to emphasize that America has a vital interest in global health. He then gave examples of NCI activities intended to support infrastructure building and good science for research and at the same time have a diplomatic component. The Middle East Cancer Consortium (MECC) was founded in 1996 with NCI leadership. Membership includes Israel, Egypt, Cyprus, Jordan, the Palestinian Authority, and Turkey. MECC objectives are to encourage cancer research in the Middle East to drive public health activities in the region; build a regional population-based cancer surveillance program; facilitate exchanges of and interactions between clinicians and scientists in the region; and enhance cancer information dissemination. As one measure of MECC success, the first ever comparison of population-based cancer data from Israel and Jordan was published last year, and other registries are beginning to produce quality data worthy of comparison and publication.

The Ireland-Northern Ireland-NCI Cancer Consortium was formed in 1999 as a direct result of the Good Friday peace accords. Consortium activities include identifying infrastructure improvements needed; formalizing and facilitating interactions among the research communities; developing joint programs that will enhance the environment for clinical cancer research and improve patient care; and developing educational exchange programs. Governance is provided by the Board of Directors, on which Dr. von Eschenbach serves with the Medical Officers of Ireland and Northern Ireland; the Implementation Group appointed by the Board and chaired by Dr. Harford to establish and manage programs; and Working Groups in the areas of scholar exchange, clinical trials, epidemiology, telecommunications, and prevention.

The King Hussein Cancer Center (KHCC) was founded in Amman, Jordan, in a bilateral agreement between the NCI and the King Hussein Cancer Foundation that was signed by Dr. von Eschenbach. The KHCC is intended to be a comprehensive cancer center for Jordan and the surrounding region, and is run by the nonprofit Jordanian Foundation. The NCI is providing expertise and logistical support in building programs and clinical infrastructure; training and education; informatics; teleconferencing; and research development, both basic and clinical. For example, Telesynergy® was developed by NIH's Center for Information Technology and deployed by the NCI in the KHCC, and sites in Belfast, Dublin, and Brussels, in addition to U.S. sites. The KHCC also serves as the primary coordinating center and site of treatment for a project involving Iraqi children with cancer and as a training center for Iraqi health care workers to begin to build capacity in Iraq. Activities to date include a conference in Amman of potential public-private partners in the region; a training course in pediatric oncology for Iraqi doctors; training courses and practical training for Iraqi nurses; formal assessment of

needs in pediatric oncology in Iraq; treatment of Iraqi patients in consultation with Iraqi doctors; short-term training for doctors and nurses; longer term fellowships and residencies for Iraqi doctors at KHCC; and exploration of Telesynergy® for Baghdad. Dr. von Eschenbach and DHHS Secretary Tommy Thompson visited Baghdad in regard to the proposed Telesynergy® site and then visited the KHCC.

The International Network for Cancer Treatment and Research (INCTR) is a not-for-profit organization headquartered in Brussels that is focused on countries with limited resources for cancer research. Dr. Ian Magrath of the NCI serves as the current President. Support is derived from the NCI and other sources. The INCTR mission is to build capacity for treatment and research in the developing world, thereby reducing suffering and death and promoting the highest quality of life for people with cancer, and to increase the quantity and quality of cancer research throughout the world. An example of INCTR activity is the cervical cancer screening project in Nepal in conjunction with the Gates Foundation and the International Agency for Research on Cancer. Dr. Harford noted that 45 countries participated in the INCTR Annual Meeting in 2003, and many more are expected for the upcoming 2004 meeting. Issues to be addressed in these countries are the lack of access to cancer care and health care generally and the lack of prevention and early detection programs leading to presentation at later stages and the serious health care implications of late-stage disease.

Dr. Harford noted that the OIA, with strong backing from Dr. von Eschenbach and Secretary Thompson, recognizes its responsibility for continuing to share U.S. technology and experience worldwide. Ongoing OIA activities and near-term plans include: revamping the OIA Web Site to make it a more complete and user-friendly portal for NCI international activities; creating a comprehensive OIA database of NCI international activities; forming regional interest groups to build networks across NCI Divisions and Offices; providing support for divisional research activities through sponsorship of workshops and exchanges related to these activities; strengthening contacts with individuals and institutions in the extramural research community that might be "twinned" with counterparts in developing countries; extending the paradigms of MECC and All-Ireland to other countries and regions; enhancing proactive outreach to the developing world with particular emphasis on research capacity building, cancer prevention, and palliative care; and strengthening links with other ICs to collaborate on overlapping international issues such as AIDS-related malignancies.

Questions and Answers

Dr. Lander asked whether the NCI had programs to help other governments think about proactively addressing the global tobacco problem. Dr. Harford pointed out that the NCI works internationally in collaboration with the ACS and International Union against Cancer and that in the NCI, the biggest focus of global tobacco activities has been within the DCCPS. Dr. Robert Croyle, Director, DCCPS, added that as a result of an RFA issued jointly by the NCI and the Fogarty International Center to develop international tobacco control research infrastructure, it was found that many international organizations lack a good surveillance system and baseline data on use, creating difficulties in planning and priority setting. The NCI, therefore, has collaborated with the CDC to support an international youth tobacco survey in developing countries to provide baseline and targets for these nations. The NCI and DHHS also are involved in the World Health Organization's Framework Convention on Tobacco, a treaty that has goals and objectives not only in terms of research but also policy, taxation, and importation. Dr. Freedman cautioned against raising unrealistic expectations and questioned whether NCI goals are realistic in light of the size of the OIA budget. Dr. von Eschenbach pointed out that NCI contributions go far beyond the OIA budget and that in many ways, the NCI shares intellectual capital, as was the case in the King Hussein Cancer Center. He noted also that Dr. Harford has moved the NCI international program beyond training and scientist exchange to work at the programmatic levels of government and institutions within those countries to begin to create infrastructure. International initiatives such as KHCC, MECC, and All-Ireland already have influenced policy and practice within those communities.

Dr. von Eschenbach emphasized that the NCI international effort is a long-term commitment because cancer is a global problem, and that the Secretary, DHHS, regards this as an opportunity for this Nation to share its health care excellence with the rest of the world as part of health diplomacy.

X. NEW NIH CLINICAL CENTER—DR. JOHN GALLIN

Dr. John Gallin, Director, NIH Clinical Center, Associate Director for Clinical Research, NIH, reminded members that the Warren Grant Magnuson Clinical Center (CC) opened in 1953, and the Ambulatory Care Research Facility (ACRF) for outpatient clinics, surgery, and diagnostic services was added in 1981; together they accounted for about 40 percent of all the laboratory space on the Campus. Planning for the Mark Hatfield Clinical Research Center (CRC) began in the early 1990s; the building was designed by stakeholders (users in the 17 Institutes and patients). Ribbon cutting for the completed new facility is scheduled for September 22, and patient transfer will begin on December 4. Together, the CC and CRC make up the NIH Clinical Center, the largest and most technologically advanced clinical research complex ever built. Dr. Gallin reviewed the long list of medical breakthroughs accomplished by CC basic and clinical scientists, and noted that the new facility is expected to provide an environment conducive to continuing the tradition.

In addition to Dr. Gallin, governance for the complex includes the Secretary, DHHS; Director, NIH; and NIH Deputy Director for Intramural Research. Advisory boards are the NIH Steering Committee made up of Institute Directors, the extramural Advisory Board for Clinical Research, the DCTD Board of Scientific Counselors, and the Medical Executive Committee, which functions as a medical board.

Dr. Gallin reviewed the year-long process for developing the Clinical Center budget, which must respond to the program needs of the different Institutes. Budget development lasts from September through December and budget review by the various advisory boards, working groups, and IC Directors is completed by June. Clinical Center funding comes from direct taps from Institute budgets at the beginning of the fiscal year. Dr. Gallin noted that the Clinical Center budget has experienced modest growth since 1999, and an increase of 0.3 percent has been forecast for FY 2005. Taps from the Institutes are proportionate to the size of each Institute's intramural program, providing incentives for all Institutes to use the facility. The NCI assessment is 28.2 percent of the cost of the Clinical Center, but because of its robust clinical research program, the NCI consumes more of the resources than it pays for.

To give an idea of the extent of Clinical Center activity, Dr. Gallin quoted current figures on patients, program, and staff: 267-bed capacity at present; 82,888 active patients in 2003; 1,100 active clinical research protocols; 1,398 credentialed physicians (410 NCI); 6,782 admissions; 98,769 outpatient visits; and 1,900 employees. He then listed characteristics that make the NIH Clinical Center unique: (1) every patient is admitted to a protocol, (2) no billing, (3) largest group of patients with rare diseases in the world, (4) patients and investigators form unique relationships as partners in discovery, (5) extraordinary and flexible infrastructure, (6) capacity to synthesize candidate drugs and conduct special laboratory tests, (7) special equipment such as cyclotrons and imaging equipment, (8) capacity for cell processing in transfusion medicine and stem cell harvesting for direct patient care or for supporting laboratories, and (8) human leukocyte antigen immunogenetics capability. Dr. Gallin reminded members that the Clinical Center can conduct long-term and difficult studies, but also can respond rapidly to public health emergencies and scientific opportunities. The NCI makes contributions to essential services in the areas of anatomical pathology, general surgery, and radiation oncology.

In addition to its role in clinical research and support for other types of Institute programs, the Clinical Center has built an extensive training program with a curriculum in clinical research that includes an introduction to the principles and practice, clinical pharmacology, and ethical and regulatory aspects of

human subjects research. A Masters degree program was initiated in 1997, with on-Campus and extramural classes by means of teleconferencing to 13 sites located in academic centers across the Nation and in Puerto Rico, Peru, Chile, and Argentina. A clinical research training program for medical students was set up in response to a blue ribbon panel review. This public-private partnership is co-funded by the NIH and a grant from Pfizer to the NIH Foundation.

Next, Dr. Gallin reviewed the numbers and types of protocols undertaken in the NIH Clinical Center: 535 (43 percent) interventional/clinical trials; 622 (50 percent) natural history; 49 screening; and 33 training. Of those, 292 are NCI studies, and 204 are Phase I through Phase III clinical trials. Dr. Gallin reviewed the weekly inpatient census, number of inpatient days, and number of outpatient visits. He pointed out that they demonstrate the consistent growth in patient activity in the Clinical Center and show that the NCI is a major driver of the growth, due primarily to an increasing number of investigators coming into the system.

Dr. Gallin concluded with a review of the key differences between the Magnuson Center and the Hatfield Center, highlights of the CRC design process, CRC design principles (flexibility, soothing environment, community, generic laboratories), and layout of the patient care unit. Approximately 3,100 people will work in the new building. All inpatient units and the ancillary services (e.g., pharmacy, rehabilitation medicine, respiratory therapy, spiritual ministry, nutrition, social work) are located in the Hatfield Center. Units remaining in the Magnuson Center include the general outpatient clinics, transfusion and laboratory medicine, the surgical facility (ACRF) and various other services. Dr. Gallin pointed out that although the new center will have fewer beds, a greater number of day hospital stations has been added where patients can be seen for 12-14 hours. The number of patient care units has been reduced in the new Center, reflecting the change from Institute-owned units to program-based units that will be shared. Board members were then given a pictorial tour of the new CRC, the new Edmond J. Safra Family Lodge (jointly financed by Mrs. Safra and industry partners), and the expanded Children's Inn.

In closing, Dr. Gallin called attention to a few special features of the new facility: the day hospital stations will permit intense studies and care for patients on an outpatient basis; NCI and NHLBI scientists will work together in the new bone marrow transplant unit; the new biomechanics laboratory in the medicine department will support every Institute, with a special emphasis on building artificial limbs; the Center has an expanded behavioral health capacity, including a new obesity unit; the positron emission facility has three cyclotrons and an expanded radiation oncology unit; the Center has a facility for making ligands for study in patients; and the prototype for a completely new clinical research information system was recently activated to provide new tools for clinical investigators and harmonize with informatics in other agencies.

Questions and Answers

Ms. Giusti noted the predominance of Metropolitan Washington, DC, patients and asked whether an attempt would be made to ensure diversity in the patient population. Dr. Gallin replied that the patient population is constantly tracked to assure that the NIH Clinical Center is a national hospital for studying patients; moreover, a goal is that people not ever be denied access because of their financial situation. In response to a question about training programs in the new facility, Dr. Gallin stated that a major emphasis has been placed on training at multiple levels, ranging from high school through postgraduate. The facility is expected to draw on trainees in terms of both faculty and students from across the country and worldwide. Dr. Armitage asked for clarification of the policy regarding patients who were no longer actively enrolled on a study. Dr. Gallin explained that an attempt is made when a patient is enrolled to a protocol to identify the patient's primary care doctor so that participation in research is carried out in a partnership relationship with that individual and he or she does not lose the context of the patient's

experience. The Clinical Center does not become the primary care provider for a patient when a protocol ends.

XI. SUBCOMMITTEE ON CANCER CENTERS—DR. KENNETH COWAN

Dr. Cowan raised for Subcommittee discussion the most recent draft of the revised Cancer Center Guidelines. Members were reminded that the Subcommittee had an opportunity for input at the beginning of the revision process, reviewed the draft with changes from the first 20 Cancer Center Directors who vetted that draft, and then reviewed another iteration of the draft after it had been vetted by all 62 Cancer Center Directors and the CSR Parent Committee. Dr. Antman entertained final questions or change suggestions from the Subcommittee, noting that the Subcommittee would file its report to the NCAB as a whole. Following NCAB approval, the proposed Guidelines will be submitted for a review by the NIH Office of Intramural Research for adherence to regulatory and other NIH policies and for a final stamp of approval. The revised Guidelines will become the document by which Cancer Center grants are reviewed.

In response to a request from Dr. Cowan, changes since the last Subcommittee review were highlighted. The latest draft: (1) clarifies definitions of translational, transdisciplinary, and interdisciplinary; (2) provides definitions of clinical trials (e.g., prevention, behavioral); (3) clarifies new tables inserted in summary three for tracking shared resources were clarified; (4) ensures that definitions and categories in summary four correlated with the table in the text that summarized those data; and (5) adds a new procedure that will apply in lieu of the usual site visit if a Center chooses the no-site-visit option. In further discussion, the rationale behind the recommended ratio for requesting budget increases in future Cancer Center grant applications was clarified.

Motion. A motion was made that the Subcommittee on Cancer Centers recommend approval by the NCAB of the Cancer Center Guidelines draft as presented. The motion was seconded, and approval was unanimous. The Guidelines as revised will be presented to the full NCAB for approval.

XII. CLOSED SESSION

This portion of the meeting was closed to the public in accordance with the provisions set forth in Section 552(b(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 2,292 applications were reviewed requesting support of $648,431,279. The subcommittee meeting adjourned at 3:55 p.m.

DAY TWO: THURSDAY, JUNE 3, 2004

XIII. PRG REPORT: CANCER HEALTH DISPARITIES—DRS. MARK CLANTON AND GARTH GRAHAM

Dr. Mark Clanton, Deputy Director of Cancer Care Delivery Systems, stated that the purpose of the session was to introduce the progress review report on reducing cancer health disparities in the DHHS. NCI Progress Review Groups (PRGs) are developed via a structured process focused on cancer sites and implemented and supported by NCI's Office of Science Planning and Assessment. This process allows those involved to survey an entire field of knowledge, both state-of-the-art and state-of-the-science, by cancer site using principally external advisory resources and internal staff resources to provide data and support.

Historically, PRGs have been an internal tool. In this case, however, the focus was on reducing cancer health disparities throughout the DHHS. This type of effort, in which one federal agency pulled together resources and helped another group of federal agencies examine priorities and develop recommendations, had not been done before. If this effort is deemed successful, the PRG model could be used to focus on other diseases and health-related issues that might need to be coordinated to reduce health disparities. Previous PRGs have addressed various cancers and taken approximately 15 months to conduct their investigations and produce a final report. This group, which consisted of about 30 members and more than 100 outside experts, operated in a much shorter time frame.

Some of the agencies involved in this PRG included the Office of Minority Health, Office of Women's Health, Administration on Aging, Agency for Health Care Research and Quality, CMS, FDA, and Health Resource Service Administration (HRSA). Various components of the NIH participated, as did the Substance Abuse and Mental Health Services Administration (SAMHSA) and others. NCAB members Drs. Diana Lopez and Moon Chen chaired the group.

Phase I of the PRG process involved leadership meetings. DCCPS specialists produced a concept map that was an important resource for the group. A roundtable meeting took place in Chicago and included approximately 115 people. An overall report was developed and presented to the Secretary's Health Disparities Council. This report included 14 recommendations, which were distilled from approximately 400 ideas and staged according to when they might be accomplished. This PRG process now is in Phase II, and the Council on Health Disparities is reviewing the report to determine which recommendations should be implemented.

Year 1 recommendations included a budget review of all relevant DHHS programs, establishing a federal leadership council, evaluating specific grant and contract processes to advance and support disparity-reduction research, and implementing evidence-based tobacco control strategies. Year 2 recommendations included establishing new data collection and sharing approaches; standardizing data; increasing the proportion of DHHS agency support specifically targeted toward disease prevention, health promotion, evaluation, and translational research; designating certain geographic areas as high disparity and developing programs for those areas; and creating a diverse and culturally competent work force to implement programs throughout the DHHS to support such programs. Year 3 recommendations included implementing recommendations from IOM's report titled *Confronting Racial and Ethnic Disparities in Health Care*; establishing partnerships for and in support of sustainable community-based networks for participatory research; ensuring that every patient has state-of-the-art, science-based care; and collaborating with the private and voluntary health sectors on information, services, and quality of care.

Dr. Garth Graham, Acting Director, Office of Minority Health, DHHS, discussed the Council on Health Disparities and its reaction to the PRG report. Dr. Graham noted that Secretary Thompson

established the Council on Health Disparities in February 2004. The Council consists of senior leadership from across the DHHS. Prior to the establishment of the Council, the DHHS established health disparities as one of its top three priorities. Agencies were conducting a variety of disparity-related activities, but there was little overall coordination. The Council was established as a single umbrella organization to speak with authority and leadership regarding DHHS activities in this area. Dr. Christy Biatis was selected as Chair of the Council, and Dr. Graham was named its Executive Director.

As its first task, the Council undertook a review of all DHHS health disparity-related programs. This endeavor began before the PRG process was implemented. The work of the PRG in this area served to reinforce the importance of the Council's efforts, and the PRG's recommendations often paralleled those of the Council. The PRG made additional recommendations that the Council will explore to determine how they may be implemented and additional recommendations to be made to Secretary Thompson. The Council also has been developing disparity-related strategic plans for the DHHS. The Council's recommendations include establishing more formal community partnerships and engaging private and public entities in the process of addressing disparities. The Council will continue to incorporate the PRG's recommendations into its efforts and recommends that operating divisions within DHHS do the same.

Dr. Niederhuber called on PRG Chairs Drs. Lopez and Chen for remarks. Dr. Lopez thanked those who had been involved in the process. Dr. Chen noted that the title of the PRG report, *Making Cancer Health Disparities History*, was been chosen deliberately for its two meanings. The first meaning is that the PRG approach to health disparities issues was unique and unprecedented; the second meaning is that the aim is to make health disparities a "thing of the past." Dr. Niederhuber asked that Dr. Clanton provide the group with copies of the report and of his slide presentation.

Questions and Answers

Ms. Kathryn Giusti, President, Multiple Myeloma Research Foundation, Inc., stated that the one area of communications regarding PRGs in which the NCI might improve is to indicate what is being implemented with regard to each PRG. Mr. Koch asked what methodology was used to measure health disparities in the United States, how severe the problem is, and what the difference in health care is between the "haves" and the "have nots." Dr. Kerner responded that the NCI conducted a comprehensive review of the published literature on the magnitude of cancer health disparities and what evidence there is of interventions that have been shown to be effective in reducing them. The magnitude was found to vary from cancer to cancer. With regard to esophageal cancer, for example, rates among African Americans are two- and threefold higher than they are among whites and, in fact, are some of the highest rates in the world. Cervical cancer is a cancer that could and should have been eliminated because it is known how to find it early and how to treat it, but approximately 5,000 people still die annually from it, and they are concentrated in low-income, rural areas.

With regard to the "haves" and "have nots," the DHHS has set as a goal of eliminating racial and ethnic differences in cancer health disparities by 2010. Low-income populations across racial and ethnic groups tend to have less access to quality care and state-of-the-art prevention and early detection services. These issues persist and are endemic in this country, and this PRG process was developed to address them. The magnitude is quite large. In response to Mr. Koch's comment that the report does not include statistics on the differences, Dr. Kerner offered to provide him with a copy of the background paper and referred him to the biannual *Cancer Progress Report* and to a handout on racial and ethnic differences from the *Annual Report to the Nation*.

Dr. Graham commented that efforts are underway to see how the PRG process can be applied to other diseases across the DHHS. Dr. Chen asked what milestones might be expected in the next year or

two regarding either the Health Disparities Council or the PRG. Dr. Graham responded that the Council is proceeding with its overall strategic plan for addressing cancer health disparities within the Department and will include salient recommendations from the PRG process in that plan. The Council is looking specifically at various diseases and also is exploring issues and components that affect health disparities at large. Dr. Clanton noted that the report includes recommendations tailored to specific federal agencies and their roles in delivering cancer control programs and promoting and executing cancer control research.

In response to a question about how results would be measured, Dr. Clanton noted that an evaluation cycle and a data collection cycle had been built into the structure of the process. Dr. Chen stated that one way to measure outcome would be to compare what was recommended with what is accomplished in a phased manner. Dr. von Eschenbach thanked those who had been involved in and supportive of these efforts. The PRG model was applied to contribute to and serve the larger vision in a way that subsequently can be applied to other diseases associated with minority and socioeconomically underserved communities. This effort will not only contribute significantly to the mission of eliminating suffering and death due to cancer, but also will promote improvements in diabetes, obesity, hypertension, and other diseases that affect minority and underserved communities in a disparate kind of way. Dr. von Eschenbach cautioned that unrealistic expectations can be created during these kinds of efforts. There is an urgent need to select a few specific goals and to focus on accomplishing them.

XIV. NCI BYPASS BUDGET PROCESS—DR. MARK CLANTON AND MS. CHERIE NICHOLS

Ms. Cherie Nichols, Director, Office of Science Planning and Assessment, noted that the Bypass budget is due to be released within the next 30 days. NCAB members will receive copies when it becomes available. Ms. Nichols explained that NCI planning involves three major components: the annual Bypass plan and budget, disease-specific research (PRGs), and the development of strategic priorities in pursuit of NCI's Challenge Goal. Previous Bypass plans have been framed around 14 strategic priorities in broad science (e.g., genes and the environment), public health (e.g., survivorship, quality of care), capacity building (e.g., investigator-initiated research), and research enablers (e.g., bioinformatics). Simultaneous PRG efforts help to identify disease-specific recommendations. Eleven PRGs have focused on 17 disease sites. All of these PRGs have completed Phase I, the recommendation phase, and most are in the implementation phase. Prostate Cancer and Breast Cancer, the first PRGs, are in the progress review stage. With regard to strategic priorities, the NCI has been involved in a year-long planning effort to realign its activities around seven strategic areas.

In developing the 2006 Bypass, the Bypass, strategic priority, and disease-specific areas were integrated into a single plan that was informed by most planning and priority-setting activities, including think tanks, task forces, and special advisory panel reports. This includes the P01 and the P30/P50 reports from the NCAB. The result is a set of "new" investments for 2006. The process also serves as an early step in developing a long-term strategic plan. The process began with the solicitation of input from the community in February 2004. Analyses were conducted, and crossovers among the three sets of priorities were mapped. In March, teams were assembled for each of the seven priority areas. These teams identified a comprehensive set of milestones (in May), selected the milestones to be used for the 2006 Bypass (in June/July), and helped identify resources (in August).

Ms. Nichols explained that this Bypass has a "new look and feel." Progress reporting will appear in the Director's *Annual Report* (January 2005), and will reflect 2004 achievements. The Bypass describes up front the final destination, which is eliminating suffering and death due to cancer, and the broad investment areas (capabilities). The remainder of the document focuses on the strategic priorities and on specific new investments needed in FY 2006. In describing what it will take to reach the

destination, the Bypass cites a more complete understanding of the causes, initiation, and progression of cancer; prevention as the first line of defense against cancer; early detection to make successful treatment possible; elimination of many cancers through improved care, molecularly targeted diagnosis and treatment, effective imaging technology, and nanotechnology; managing other cancers as a chronic disease through new molecular approaches and through monitoring and validating health care patterns and outcomes; and improving the quality of life for cancer survivors through medical advances that increase the length of survival, evidence-based supportive care, symptom management, and rehabilitation.

The NCI will concentrate on four areas to eliminate the suffering and death due to cancer by 2015. The first area is to invest in scientific research via a network of PIs, academic hospitals, and other sites; the intramural program; and extramural program experts. Second, the NCI will provide technology leadership and support capacity building through recent advances in bioinformatics, nanomedicine, and NCI-supported centers, networks, and consortia. Third, the NCI will partner for application in public health and patient care via the FDA and the CMS task forces, patient navigator programs being piloted around the country, and DHHS-wide efforts to eliminate health disparities. Fourth, the NCI will optimize communication and the transfer of results through Web-based information on cancer and clinical trials and the Cancer Information Service (CIS) Partnership Program.

Ms. Nichols identified the seven strategic investment areas and the key NCI personnel for each area. They are: Prevention, Early Detection, and Prediction (Drs. Peter Greenwald and Robert Croyle); Overcoming Cancer Health Disparities (Dr. Harold Freeman); Strategic Development of Interventions (Dr. Ann Barker); the Integrated Clinical Trials System (Dr. James Doroshow); Advanced Technologies (Drs. Ken Buetow, Daniel Sullivan, and Gregory Downing); Integrative Cancer Biology (Dr. Dinah Singer); and Molecular Epidemiology (Dr. Joseph Fraumeni).

Ms. Nichols made the following comments with regard to specific strategic areas in the 2006 Bypass budget:

- Prevention: NCI's tobacco control efforts will focus on multidisciplinary research on the interplay between behavior, chemistry, toxicology, and biology to determine cancer risk potential and reduce exposure to tobacco products. Energy balance research will focus on mechanisms that underlie the association between energy balance and cancer and new technologies for assessing energy intake and energy balance. The development of prevention vaccines and drugs will focus on a second generation of vaccines and trials of new chemopreventive agents. The translation of prevention research will emphasize increasing the adoption of evidence-based medicine and developing effective strategies for communicating risk prediction and perception to health professionals and patients.

- Early Detection: The NCI plans to expand the capacity of the biorepository to include tissues from diagnosed cancer patients; develop and optimize the use of computer-aided diagnostic programs; develop screening approaches that use a combination of body fluids, biomarkers, and imaging technologies; and create national standards for performance measures and public-private partnerships to collect and analyze data.

- Prediction: The NCI intends to develop risk-prediction markers and models for individual cancer risk and success of treatment, and to explore ways to significantly reduce the cancer burden.

- Overcoming Cancer Health Disparities: The NCI is developing multidisciplinary intervention studies on disparities and the economics of cancer; research on cancer survivorship in medically underserved, low-income, ethnic, and minority populations; tobacco and health disparities research networks; and programs designed to create a diverse and culturally competent research and cancer care workforce.

- Integrated Clinical Trials: The NCI is developing flexible collaborations to oversee the conduct of clinical trials; new approaches for clinical trials networks; broadly based working groups to identify, analyze, and validate clinically relevant surrogate molecular endpoints; and health-related quality of life economic endpoints in NCI-supported Phase III trials.

- Advanced Technologies: The NCI wants to evaluate and extend CaBIG, develop publicly available imaging archives to link outcomes to clinical data, assess and integrate the best technologies for biomarker discovery and development, and, for human tumor sequencing, develop a comprehensive database of genomic sequence data as discussed by Dr. Lander.

- Integrative Cancer Biology: The NCI wants to develop better computational models; expand intramural discovery of compounds that can serve as bioprobes for functional genomics, proteomics, and molecular target validation; and investigate the relationship between autoimmune diseases and the risk of cancer.

- Molecular Epidemiology: The NCI wants to conduct large-scale studies of highly lethal cancers; develop programs to implement public health measures and educational activities based on emerging genomic, epigenomic, and proteomic technologies; and establish joint training programs and new curricula in genetic and molecular epidemiology.

- Long-Term Strategic Plan: NCI's plan will be integrated, comprehensive, focused on the Challenge Goal, used as a reference for NCI's annual plan and budget proposal, and integrated into operational planning.

There are three main entities within the Institute that will work together to accomplish these goals. The Director and Deputy Directors will provide oversight for priority-setting and resource allocation. The Executive Committee, the Institute's senior leadership, will have overall responsibility for prioritizing. Finally, there will be one Integration/Implementation (I2) Team for each of the seven priority areas. These Teams will integrate, refine, and clarify existing plans and priorities; specify desired outcomes; develop milestones for the annual Bypass budget; propose initiatives that fill critical gaps; facilitate implementation; and communicate and disseminate. Currently, there are two I2 teams, one in molecular imaging, chaired by Dr. Sullivan, and one in bioinformatics, chaired by Dr. Buetow. A third, in lung cancer, will be co-chaired by Dr. Margaret Spitz.

Community input and advice are important, and NCI will continue to solicit these via the annual solicitation of comments on the Bypass budget and through a new Web Site, NCI Listens and Learns, which is being piloted to gather responses to the Bypass budget; as well as through advisory committees such as the NCAB and the BSA.

Questions and Answers

In answer to a question regarding how molecular imaging, bioinformatics, and lung cancer were selected as the topics for the first three I2 groups, Dr. Clanton noted that the integration/implementation process is new and designed to bring together personnel from different departments and Divisions to identify major priorities in specific areas. Interdisciplinary molecular imaging and bioinformatics groups were ready to begin identifying priorities in those areas. The lung cancer group evolved from the recent PRG in that area.

Dr. von Eschenbach added that lung cancer is the disease that is responsible for the greatest number of cancer deaths and, therefore, is an appropriate place to begin prioritizing with regard to the goal of eliminating suffering and death due to cancer by the year 2015. He added that recent work in lung

cancer makes it appropriate as an operational model for other cancers with regard to the prevention, detection, modulation, and elimination continuum. Dr. Niederhuber asked whether the work of the Lander-Hartwell committee could impact the 2006 Bypass budget. Dr. Barker responded that the Bypass budget will be a simpler document in the future, and the *Annual Report* is complementary to it. The advanced technology topics to be covered by the Lander-Hartwell committee, such as bioinformatics, proteomics, and genomics, already are addressed in the 2006 Bypass budget.

Ms. Giusti noted the importance of emphasizing that lung cancer has been chosen as an operational model, versus having been chosen as a cancer to be looked at separately. She also praised the *Annual Report* for providing a review of NCI's accomplishments and activities and a better perspective for those who are reviewing the Bypass budget. Ms. Giusti raised the issue of noncompeting grants and making sure that the seven priority areas are addressed in view of the "flat" budget. She asked if there is a framework to help ensure this. She also noted the importance of identifying areas in which public-private partnerships can be implemented to address the priorities. Dr. von Eschenbach responded that the NCI is exploring various strategies for managing the budget during times of flat or diminishing funds. These strategies include matching grants, funder's conferences, redeployment, and examining the use of full time equivalent positions. Dr. Clanton noted that the 2015 goal to change the public health impact of cancer has created pressure to move from broad categories of activities to a first set of strategic initiatives. The seven areas that have been outlined to date are high-impact areas, but they will not be the only areas of focus.

Mr. Koch asked for an explanation of the word "bypass" in the term "Bypass budget." Dr. von Eschenbach responded that an authority provided to the NCI Director by the National Cancer Act in 1971 allowed the budget for the National Cancer Program to be presented directly to the President. While that is no longer done, the Bypass budget is separate from the Operational budget and is presented to the President without change by the NIH Director or DHHS Secretary.

XV. UPDATE: CLINICAL TRIALS WORKING GROUP—DR. JAMES DOROSHOW

Dr. James Doroshow presented an update of the Clinical Trials Working Group (CTWG) after first presenting a brief history of CTWG. The group started after a review of the Armitage Report and the implementation of the P30 and P50 Reports. A first challenge was to prioritize the major issues impairing optimal clinical trials conduct. Dr. Doroshow said that the group has, in fact, developed a process for addressing these issues. The following are six primary concerns: (1) a lack of uniformity and standardization for procedures and infrastructure; (2) research is not coordinated across venues or by mechanisms of support; (3) mounting regulatory burdens and limited interface between the clinical research community and the various agencies; (4) increasingly sophisticated scientific requirements for successful novel therapy trials; (5) more protracted time frames for trial implementation and completion; and (6) a frequently fragmented, duplicative, competing national effort to study adult cancers

The CTWG created six working subcommittees, led by six members of the external clinical trials community, to address each of these major issues. The first group, chaired by David Parkinson, will work on standardization of clinical trials procedures. The second group, chaired by David Johnson, will help coordinate clinical trials across centers, SPOREs, P01s, and cooperative groups. Dr. Richard Pazdur will chair the third subcommittee, which will identify areas to help enhance the interactions among members of the clinical research community, the NCI, regulatory agencies, and patient advocates. Group four will develop core facilities to improve scientific support for trials and will be chaired by Dr. Fred Applebaum, while a fifth subcommittee, chaired by Dr. Rick Schilsky, will work to improve clinical trial accrual management. The sixth and final subcommittee will help refine the protocol prioritization process and will be chaired by Dr. Jim Abbruzzese.

Dr. Doroshow stated the specific goals for each of the subcommittee as follows:

- Subcommittee one: create specifications for infrastructure.
- Subcommittee two: create vehicles for communication and to foster cooperation.
- Subcommittee three: create a culture of early regulatory consultation.
- Subcommittee four: enhance scientific infrastructure for trials.
- Subcommittee five: create systems and an environment to speed accrual.
- Subcommittee six: improve effectiveness and efficiency.

The next steps include biweekly conference calls to develop a work product. Dr. Doroshow expects to present updates at each NCAB meeting on the progress being made by the CTWG.

Questions and Answers

Dr. Doroshow was asked about the difficulty of implementing the recommendations of the subcommittees. He expressed hope that an extramural committee could be created to oversee clinical trials. This would ensure a permanent basis for a reporting structure and an actionable committee to follow up on the recommendations of the CTWG subcommittees. The issue of how to address the complexity of correlative science, particularly with the genomic efforts was raised. Dr. Doroshow stated the importance of understanding that the ability to carry out correlative science varies among institutions, yet there frequently are outstanding opportunities to conduct studies in a variety of different venues. Dr. Barker suggested that the FDA-NCI task force currently working on selected topics (i.e., surrogate endpoints, imaging endpoints, etc.) would help the CTWG goals. Dr. Runowicz commented that at this point, the CTWG was focused on the regulatory administrative side of clinical trials. She said the next phase might be actually changing how large trials are conducted with the possibility that many trials may not require such large numbers.

XVI. UPDATE: CENTER FOR STRATEGIC DISSEMINATION—DR. EDWARD MAIBACH

Dr. Edward Maibach, Director, Center for Strategic Dissemination (CSD), NCI, reiterated three important ideas underlying why the CSD was established at the NCI. First, the Center defines dissemination as an active process, the goal being to turn knowledge into applications that benefit people. Second, CSD's objective is to enhance NCI's dissemination capability and success. Third, the primary strategy of the CSD is to promote and enable "user-centered" application development and distribution across NCI, as appropriate. Dr. Maibach then presented updates on the Body&Soul Program and the Dialogue on Dissemination, which he described as conceptual at this point.

The Body&Soul Program as well as its parent program, Five-a-Day, recently moved from the DCCPS to the CSD. The move was initiated by the DCCPS, because it was felt that both programs were ready for full dissemination, and the CSD could better accomplish that goal. According to Dr. Maibach, the Body&Soul Program is a proven program aimed at increasing consumption of fruit and vegetables. Its specific delivery venue is African American faith communities. The Program uses a social ecological model to try to change not only individual behavior, but also the physical environments in which that behavior occurs thus sustaining behavior change over time. Body&Soul has the following four components: (1) pastoral leadership, (2) educational activities, (3) peer counseling, and (4) changing the

church environment to support individual behavior change. The Program was developed using principles of user-centered design, which included two R01 grants to develop and test the approach. The NCI and the ACS conducted a Phase IV effectiveness test. Following the Phase IV testing, the NCI developed a "turnkey kit," making it possible for any church congregation with this kit to develop and implement the Program on their own.

Dr. Maibach next discussed a second example of user-centered design for successful dissemination, "Dialogue on Dissemination," which still is in the conceptual stage with members of his team along with Dr. Mark Clanton, Dr. Jon Kerner and others engaged recently in what he called "blue sky brainstorming." The objective of these sessions is to identify steps that can be taken—near-term and long-term—to improve the uptake of evidence-based clinical and public health practices that reduce the burden of cancer. The rationale behind these sessions is to develop a systematic effort to identify and integrate knowledge and information into a practical framework for improving dissemination. Besides the brainstorming meetings, the panel used the focal question, "How can we—the community of organizations involved in cancer research, cancer care, and policy—do a better job of translating research results into practice?"

The following seven themes emerged in the brainstorming sessions:

- To enhance success (i.e., uptake), dissemination should begin early in the "intervention" development process.
- The perceived needs of potential adopters (or learners) are critical to their motivation and subsequent actions.
- The notion of "evidence-based" must be broadened to ensure that evidence and interventions are produced that are valued by practitioners.
- Organizational culture and local barriers influence the adoption of innovations.
- Efforts to drive dissemination and translation have placed too much emphasis on the researcher and not enough emphasis on the manager.
- There is a pressing need for dissemination research to enable greater evidence-informed practices of dissemination.
- There also is a pressing need to realign the efforts of the organizations that fund intervention development and dissemination efforts.

Dr. Maibach noted that the members of this dialogue adopted the objective of producing a set of products with January as a target date for the first tangible product—a draft dissemination research agenda. In partnership with the dissemination research agenda, the group would like to help develop an implementation agenda that will identify tools that provide greater continuity between the development and the dissemination process. In addition to these two agendas, members of the brainstorming sessions believe the agencies that fund these programs would benefit from participating in a process to identify an interorganizational collaboration plan. Finally, members want to develop case studies of successful dissemination that can serve as inspiration and models for future programs.

Questions and Answers

Regarding the Body&Soul Program, Dr. Runowicz asked how the real outcome is measured and what is being done to enhance sustainability. According to Dr. Maibach, the challenge of dissemination is building distribution channels for programs and ideas and for scientifically proven information that has value to the communities that can benefit from it. He stated that the unique brilliance of the Body&Soul Program is that it provides and promotes interaction with communities, which is based not only on scientific evidence and value, but is a direct reflection of what community members are trying to achieve in their lives, thereby increasing sustainability.

In answer to a question about the distinction between delivery and dissemination, Dr. Maibach explained that he views dissemination as shaping the work of the CSD to ensure that people carrying out the delivery are able to take advantage of the resources that have been developed to benefit them. He emphasized that the job of CSD is not complete until dissemination, specifically uptake, has been accomplished.

Ms. Giusti raised the issue of awareness of the NCI on the part of the lay population. Dr. Maibach stated that public awareness of the NCI is relatively low, which the NCI is working to change. There is inherent value in the public understanding what the NCI is and how it can and does serve the community. Dr. von Eschenbach added that he believes the problem from the point of view of the endpoint, the user, has not been properly understood by the NCI. The CSD is charged with helping the Institute to understand how to create and build programs and initiatives that connect with and impact the community.

XVII. UPDATE: OFFICE OF COMMUNICATIONS—MS. NELVIS CASTRO AND MS. MARY ANNE BRIGHT

Ms. Castro provided an overview of the OC and highlighted priorities and key activities for 2005. Ms. Bright shared the NCI Cancer Information Service National Partner and User Survey results, noting that in 2005, the OC will continue to: (1) leverage new and existing communication mechanisms to increase access to NCI cancer information; (2) increase media outreach, particularly with minority media outlets; (3) expand communication planning and support across the Institute; and (4) lead the effort to increase access to smoking cessation programs nationwide.

Ms. Castro highlighted the success of the *NCI Cancer Bulletin*, which is now a permanent weekly electronic publication of the Institute with more than 16,000 subscribers. According to a recent NCI study, readers include NCI staff, cancer researchers, clinicians, advocacy and voluntary organizations, cancer patients, and the general public, among others. The survey found that 94 percent of respondents found the content valuable, and 98 percent were satisfied with the *Bulletin*. Plans are underway to address respondents' suggestions and promotional efforts to increase readership are being implemented.

The OC coordinated the development and production of *The Nation's Progress in Cancer Research: An Annual Report for Fiscal Year 2003,* which was distributed to NCAB members. Plans are currently underway to develop and produce the 2004 *Annual Report*. In May of this year, the redesign of cancer.gov was launched, and Ms. Castro stated that OC will continue to work with NCI Divisions and Centers to create a common look and feel for all NCI Web sites. The NCI continues to spearhead the DHHS National Network of Tobacco Cessation Quit Lines. According to Ms. Castro, the Institute hopes to: (1) create an infrastructure for a single national number, (2) route calls to individual states, and (3) enhance the CIS services. The NCI continues to work with the CDC, state tobacco control program managers, quit line vendors, and the North American Quit Line Consortium to accomplish these goals.

Ms. Castro then introduced Ms. Bright to discuss the results of the CIS National Partners Survey. Ms. Bright stated that a partner survey as well as a user survey had been completed over the past year. The goal of the evaluation was to demonstrate the effectiveness and value of the CIS program to NCI's key stakeholders, including the public. Types of evaluation included process (ongoing) and outcome. Funding included $100,000 from funds used by the NIH to evaluate NIH-related programs. Ms. Bright then discussed the National Partners Survey. The survey was conducted by an independent research firm. It included 288 partners surveyed, a 25-minute interview, and had an 89.4 percent response rate. Baseline measurements included: (1) partnership function and effects; (2) perceived capacity to disseminate information; (3) satisfaction with the partnership; and (4) use of and satisfaction with NCI programs, products, and services.

According to Ms. Bright, the NCI emphasizes high performing partnerships to reach underserved populations. Survey results show that 81 percent understood their roles and responsibilities as a CIS partner, with 96 percent stating that they felt their relationship with the CIS was collaborative. Approximately 95 percent of respondents either strongly agreed or agreed that partnership activities were important to their organization's cancer-related programs, and 96 percent felt that the partnership had an effect on the population they serve. In terms of increased awareness, access, and use of NCI programs, products, and services, 94 percent use NCI information and materials, and 95 percent of partners found the CIS to be effective in disseminating cancer information and materials. A smaller percentage (75 percent) reported that the CIS is helpful in enabling access to NCI materials. The fourth domain of the National Partners Survey was whether the partners were satisfied with their relationship with the CIS and whether they expected to continue the partnership. About 98 percent of respondents indicated that they were either very satisfied, or satisfied with 93 percent very likely or somewhat likely to continue the partnership.

Ms. Bright then discussed the National User Survey, which also was conducted by an independent research firm and involved 2,485 first-time users (patients and nonpatients) of the CIS and had a 39 percent response rate. Concerning the low response rate, Ms. Bright pointed out that the population comprises many sick people with new cancer diagnoses or those in treatment and who may, in fact, not be readily available when contacted. Access points included the toll-free cancer line, the smoking quit line, and LIVEHELP, a real-time instant messaging service through the NCI Web site. Baseline measurements were: (1) satisfaction and trust of the CIS Program, (2) increased knowledge and awareness after contacting the CIS, (3) enhanced self-efficacy, and (4) intention to make behavioral changes.

Satisfaction rates were high, at 95 percent. Ninety percent of respondents indicated that their expectations were met or exceeded. Approximately 98 percent of users perceived the CIS information specialist as knowledgeable, and 83 percent reported a high degree of trust in the information they received. Ms. Bright noted that three-quarters of users reported an increase in knowledge, with 67 percent more confident in their ability to seek more information. Regarding intention and behavior, 71 percent reported using (or planning to use) CIS information to speak with a health professional. Regarding tobacco users, 94 percent said CIS suggestions helped them to make a tobacco-related change in their lives, with 49 percent quitting or cutting back and 45 percent planning to quit in the future. Ms. Castro invited the NCAB Subcommittee on Communications to work with and advise the OC in the development of an NCI strategic communications plan. She also suggested that the Subcommittee serve as a conduit for the exchange of information between the OC and the NCAB.

Questions and Answers

Mr. Koch asked how decisions were made on when and how to publicize NCI programs. Dr. von Eschenbach explained that communications fall into the two broad categories of education and information. Historically, the NCI has not been effective at informing the community about what is occurring at the Institute. However, Dr. von Eschenbach emphasized that he would like that to change. He believes different tools and vehicles such as the *Cancer Bulletin* will help the organization become more open and visible. Ms. Giusti asked if the results of the surveys were going to be publicized through a press release. She suggested that in addition to the survey results, including information such as how many telephone calls are taken would be an excellent way for the NCI to demonstrate how they are helping and reaching out to the community.

XVIII. SUBCOMMITTEE REPORTS—DR. JOHN E. NIEDERHUBER

The NCAB Subcommittee on Cancer Centers met on the first day of this meeting, and the Subcommittee's report was included in Board members' meeting binders. Dr. Niederhuber asked NCAB members—particularly new members—to review the list of NCAB standing and *Ad Hoc* Subcommittees found in their meeting materials as well as the Subcommittee Mission Statements and consider volunteering to serve on at least one Subcommittee. He also asked Board members to consider whether the Ad Hoc Subcommittee on Communications should become a permanent Subcommittee of the NCAB. Subcommittee Chairs were asked to contact Dr. Niederhuber or Gray if their respective Subcommittees need time to meet or make presentations at future NCAB meetings.

XIX. FUTURE AGENDA ITEMS—DR. JOHN E. NIEDERHUBER

Before adjourning the meeting, Dr. Niederhuber asked Board members to suggest future agenda items. Dr. Chen noted that because CaBIG has been launched, it may be time to consider retiring the *Ad Hoc* Subcommittee on Bioinformatics and Vocabulary. A presentation on CaBIG at the next Board meeting might be a fitting way to retire this *Ad Hoc* Subcommittee.

XX. ADJOURNMENT—DR. JOHN E. NIEDERHUBER

There being no further business, Dr. Niederhuber thanked Board members for attending and participating in the meeting. The 131st meeting of the National Cancer Advisory Board was adjourned at 11:56 a.m. on Wednesday, September 15, 2004.