DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL CANCER INSTITUTE
130th NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
June 2-3, 2004

Natcher Building, Conference Rooms E-1 and E-2
National Institutes of Health
Bethesda, Maryland

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
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The National Cancer Advisory Board (NCAB) convened for its 130th regular meeting on Wednesday, June 2, 2004, in Conference Rooms E-1 and E-2 of the Natcher Building, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Wednesday, June 2, 2004, from 8:30 a.m. to 4:30 p.m. The meeting was closed to the public from 4:30 p.m. until adjournment at 5:30 p.m. The meeting was reopened to the public on Thursday, June 3, 2004, from 8:30 a.m. until adjournment at 11:40 a.m. NCAB Chair Dr. John E. Niederhuber, Professor, Departments of Oncology and Surgery, University of Wisconsin-Madison, presided during both the open and closed sessions.

NCAB Members

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

President's Cancer Panel

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

Alternate Ex Officio NCAB Members

Dr. Michael A. Babich, CPSC
Dr. Raye-Anne Dorn, VHA
Dr. Peter Kirchner, DOE
Dr. Richard Pazdur, FDA
Dr. John F. Potter, DOD

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
Ms. Janice Mullaney, Acting Deputy Director for Management, Office of the Director
Dr. Dinah Singer, Director, Division of Cancer Biology
Ms. Sandy Koeneman, Executive Secretary, Office of the Director

Liaison Representatives

Ms. 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: WEDNESDAY, JUNE 2, 2004

I. INTRODUCTION, WELCOME, AND APPROVAL OF FEBRUARY 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 thanked Board members whose terms had ended with the February meeting for agreeing to attend one additional meeting until new members can be appointed. 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 welcomed Dr. James Doroshow, Director, Division of Cancer Treatment and Diagnosis (DCTD) and Chair, Clinical Trials Working Group (CTWG), to his first NCAB meeting since joining the NCI.

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 February 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

Dr. von Eschenbach, Director, NCI, reported that the President had not yet announced appointments to the NCAB to replace the five members whose terms of office expired with the February NCAB meeting. He thanked Drs. Stephen Duffy, Elmer Huerta, Susan Love, Larry Norton, and Amelie Ramirez for returning for an additional meeting, thereby ensuring that a quorum was present. He thanked the Board for their contributions to and support of the National Cancer Program.

Dr. von Eschenbach expressed regret that he would be absent from the meeting for periods of time to present a briefing on NCI strategic priorities at the White House, testify at a hearing on NIH authorization legislation before the House Commerce and Energy Subcommittee, and accompany Department of Health and Human Services (DHHS) Secretary Tommy Thompson to engage in a briefing and conversations at the Frederick Cancer Research and Development Center (FCRDC) regarding the FCRDC and the biomedical research complex at Fort Detrick, Maryland.

Dr. von Eschenbach announced the formal appointment of Dr. Karen Antman as Deputy Director for Translational and Clinical Sciences. Dr. Antman joins Dr. Anna Barker, Deputy Director for Advanced Technologies and Strategic Partnerships, and Dr. Mark Clanton, Deputy Director for Cancer Care and Delivery Systems, as members of the shared governance leadership team in the Office of the Director (OD). Other appointments are Dr. Joseph Tomaszewski to the position of Acting Associate Director for the Developmental Therapeutics Program, DCTD; Dr. Jeffrey Abrams to the position of Acting Chief, Clinical Investigations Branch, Cancer Therapy Evaluations Program (CTEP), DCTD; and Dr. Peggy Rhodes to the position of Special Assistant for Media Activities in the NCI Press Office.

Recruitment continues for the position of Deputy Director for Integrative Biology and Molecular Oncology, the fourth Deputy Director position in the OD.

Dr. von Eschenbach noted that the Executive Committee (EC) and members of the senior leadership team have been engaged in a process of leadership development, continuing to focus on creating a cohesive integrated team to manage the strategic opportunities and investments that are the charges to the NCI. In parallel with that effort, an ongoing process of strategic planning involves the broad cancer research community. An example of this is the recent Cancer Center Directors' Retreat, where 59 of the 61 Centers explored the challenges and barriers as well as opportunities with respect to the Cancer Centers. The retreat focused on identifying mechanisms to horizontally integrate the Centers into an effective network to enhance and expand the achievements already realized by individual Centers in discovery, development, and delivery. The NCI Cancer Bioinformatics Grid (caBIG) was discussed extensively at the retreat, and there was unanimous commitment among Cancer Center Directors to fully engage in the implementation of caBIG, especially as it relates to clinical trials activities. Dr. von Eschenbach noted that caBIG has started as a pilot project in 40 of the Cancer Centers and will undergo evaluation soon. He acknowledged the work of Dr. Kenneth Buetow, Director, NCI Center for Bioinformatics, and his staff in bringing caBIG to fruition.

Other interactions and collaborations included: (1) an EC and senior leadership retreat for planning to create mechanisms and opportunities for integration in areas such as bioinformatics and molecular and functional imaging, (2) the work of the CTWG, and (3) a meeting with the Children's Oncology Group and collaboration on adopting a pediatric central Institutional Review Board (IRB). Dr. von Eschenbach noted that the NCI is continuing the process of gathering input, refining its strategic planning and priorities, and introducing initiatives that will lead to the goal of eliminating suffering and death due to cancer. Emphasizing the importance of communication among the entire community of cancer stakeholders, he called attention to the recent introduction of the *NCI Cancer Bulletin*, and acknowledged the work of Ms. Nelvis Castro, Acting Director, Office of Communications (OC) and her staff for creating this Web-based weekly publication. He noted that circulation is rapidly increasing, with more than 15,000 hits to the site as well as many more individuals who receive the *Bulletin.* Evaluation of the pilot phase is in progress.

Next, Dr. von Eschenbach presented highlights of NCI's international initiatives. With NCI support and the leadership of Dr. Norman Coleman, Director of the Radiation Oncology Science Program (ROSP) and Associate Director of the Radiation Research Program, DCTD, NCI, a common bioinformatics infrastructure was created within the All Ireland Consortium, which is a collaboration between Northern Ireland and the Republic of Ireland to integrate their clinical trials and create a unified approach to cancer. The telesynergy initiative that was developed now is being disseminated beyond cancer as a model for addressing common problems associated with diabetes, hypertension, and a variety of health issues in that region. In the Middle East, the NCI has been instrumental with the Middle East Cancer Consortium in creating the King Hussein Cancer Center in Amman, Jordan, and progress has been made in helping to rebuild an infrastructure in Iraq by virtue of what has been occurring in the King Hussein Center. Health professionals from Iraq are coming to the King Hussein Cancer Center for training using programs developed by Dr. Samir Kalef of the NCI, and for meetings and educational programs.

In the national arena, Dr. von Eschenbach briefly noted that the NCI is working in a collaborative and cooperative way, not only on the NIH and FCRDC Campuses, but also with other federal agencies such as the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), and Centers for Medicare and Medicaid Services (CMS); with other cancer organizations around the country; and with professional organizations.

Turning next to the Fiscal Year (FY) 2005 budget, Dr. von Eschenbach noted that the President's budget request for the NCI is for a $134 M, or 2.8 percent, increase. That figure is lower than the $147 M, or 3.2 percent, increase received in FY 2004. Therefore, the NCI is taking a proactive stance in managing the budget, working in a redeployment mode in the absence of an infusion of new money. Dr. von Eschenbach noted that the portfolio of each Division will be reviewed for opportunities for redeployment, and efficiencies across the entire system are being sought to provide resources for strategic initiatives that have been identified. He pointed out that the FY 2003 redeployment effort was successful in that the R01 payline was maintained at the 20th percentile and 5,400 Research Project Grants were awarded, 300 more than in FY 2002. The NCI also was able to continue its commitment to the Cancer Centers Program, which increased by 6 percent to a level of about $13 M, as well as to the Specialized Programs of Research Excellence (SPOREs), which included funding for 12 SPOREs. Other challenges faced in FY 2004 include the Full Time Equivalent (FTE) reduction program to reach an FY 2005 target for NCI staffing levels, and Dr. von Eschenbach acknowledged the work of Ms. Janice Mullaney, Acting Deputy Director, Office of Management, and her staff in the FTE management process.

Questions and Answers

Dr. Niederhuber noted that the joint retreat of the NCAB, Board of Scientific Counselors (BSC), and Board of Scientific Advisors (BSA) held in the fall of 2003 to discuss and provide advice on budget, financial, and programmatic issues was helpful in communicating the planning process back to the community. He asked if another such retreat was planned for the fall of 2004. Dr. von Eschenbach replied that this was the case, noting that the Cancer Directors' Retreat also would be repeated and meetings with other organizations will continue under the leadership of Dr. Alan Rabson, Deputy Director, NCI, to inform and advise the planning process.

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

Dr. LaSalle Leffall, Jr., Charles R. Drew Professor of Surgery, Howard University College of Medicine, reported that the President's Cancer Panel has considered all of the testimony and written remarks received in the previous year's series of five meetings that examined issues and challenges associated with cancer survivorship. The Panel has prepared a report to the President, Congress, and the Nation that provides an overview of the challenges faced by cancer survivors in various age groups and as a whole. The report spells out the Panel's recommendations for short- and long-term steps that should be taken by the health care system, policymakers, and the research community in response to what was learned during these meetings.

Dr. Leffall reported that the Panel's next series of four meetings is titled "Translating Research To Reduce the Burden of Cancer," and will focus on the barriers to progress in translating research into reductions in cancer incidence and mortality. Issues the Panel will examine 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 will be 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, and industry. Participants will represent a wide range of disciplines. The dates for the Panel's 2004-2005 series are: (1) August 30, University of California, San Francisco Comprehensive Cancer Center, San Francisco, CA; (2) September 27, Arthur James Cancer Hospital and Richard Solov Research Institute, Columbus, OH; (3) November 1, The University of Texas M.D. Anderson Cancer Center, Houston, TX; and (4) January 24, Memorial Sloan-Kettering Cancer Center, New York, NY. Information regarding this series of meetings is posted on the Panel's Web Site at http://pcp.cancer.gov.

V. LEGISLATIVE UPDATE—MS. SUSAN ERICKSON

Ms. Susan Erickson, Acting Director, Office of Policy Analysis and Response, OD, NCI, briefly reviewed Congressional hearings since the February NCAB meeting in which NCI staff were called to testify, including: (1) Human Papilloma Virus and Cervical Cancer Hearing, March 11; (2) Senate and House Appropriations Subcommittee Hearings on the FY 2005 Budget, April 1 and 21-22, respectively; (3) Cancer Clinical Trials Hearing, May 13; and (4) House Energy and Commerce Oversight and Investigations Subcommittee Hearing on Conflict-of-Interest Issues, May 18. She noted that Dr. von Eschenbach will be participating in a hearing before the House Energy and Commerce Committee to discuss priority setting, in anticipation of the writing of the NIH reauthorization bill. She then called attention to provisions in legislation of interest to the NCI. The Family Smoking Prevention and Tobacco Control Act, introduced by both Houses, would allow the FDA to regulate the sale, advertising, and content of tobacco products; preserve the authority of states to regulate advertisements; require that warnings be more prominent; and prohibit the use of terms such as "light" and "low-tar" in relation to tobacco products unless approved by the FDA. It has been proposed that this regulation be combined with the tobacco buy-out that was introduced in separate legislation.

Questions and Answers

Questions from Board members pertained not only to the presentation materials, but also to the content of the Legislative Update document included in Board members' notebooks. In response to questions about the status of proposed health disparities bills from Dr. Moon Chen, Professor, Department of Epidemiology and Preventive Medicine, University of California, and Dr. Amelie Ramirez, Professor, Department of Medicine, Baylor College of Medicine, Dr. von Eschenbach noted that Dr. Harold Freeman, Director, Center to Reduce Cancer Health Disparities (CRCHD), NCI, has been working on behalf of the Patient Navigator, Outreach, and Chronic Disease Prevention Act and the complementary Closing the Health Care Gap Act of 2004 (S. 2091). Dr. Clanton pointed out that S. 2091, for the first time, calls for collection of data based on race and ethnicity, and has promise for moving standards of care forward in terms of quality of care, collection of data, and increasing access to care. In a related action by the NCI, the BSA recently approved a Patient Navigator concept to be released soon as a Request for Applications (RFA)/Cooperative Agreement.

VI. OVERVIEW OF CTEP CLINICAL TRIALS AND DATA—DRS. JAMES DOROSHOW AND MICHAELE CHRISTIAN

Dr. Michaele Christian, Associate Director, CTEP, described CTEP's organizational structure and the make-up and functions of its six operational branches (Clinical Grants and Contracts, Clinical Investigations, Regulatory Affairs, Investigational Drug, Pharmaceutical Management, and Clinical Trials Monitoring) and the Protocol and Information Office. The Biometrics Research Branch, formerly located within the CTEP, now resides organizationally in the OD, DCTD, because it provides service and statistical support to all DCTD programs. To highlight the scope of the Clinical Trials Program in Treatment, Dr. Christian noted that more than 5,000 sites are able to accrue patients to treatment trials, and 2,000 of those sites currently are enrolling to open trials. About 13,000 clinical trials investigators are registered, and approximately 30,000 patients are accrued to open trials annually. The CTEP holds 138 investigational new drug (IND) applications and has 88 clinical trials agreements with pharmaceutical and biotechnology companies in the form of either Cooperative Research and Development Agreements or Clinical Trials Agreements. CTEP efforts to reduce barriers to industry collaboration include the negotiation of Intellectual Property (IP) agreements for both single investigational agents and combinations. Terms of award to clinical sites include the IP option to collaborators who supplied the agents.

Dr. Christian described the components of the Early (Phase I, II, translational) and Late (Phase III) Clinical Trials Program in Treatment. Most of the Phase I trials are conducted through 14 Cooperative Agreements at 16 Cancer Center and 6 SPORE sites. Disease-specific cancer consortia involving 18 sites conduct contract-supported Phase II trials. Cancer Centers, SPORES, and Cooperative Groups also conduct some of the Phase I and Phase II trials. Translational research is conducted through the Translational Research Initiative, SPOREs, and the Interdisciplinary Research Teams for Molecular Target Assessment, the latter a relatively recent resource. Phase III trials, both adult and pediatric, are conducted by the Clinical Trials Cooperative Groups and through the Community Clinical Oncology Program (CCOP). Dr. Christian noted that the NCI has about 900 active trials accruing patients at any one time and starts between 200 and 250 new trials in any year. Review of all concepts and protocols submitted to the CTEP is the responsibility of staff from all CTEP branches, together with specific expertise from other DCTD programs, for example, from the Radiation Research Program for radiation or the Cancer Diagnosis Program for correlative science. Decisions as to whether a proposed study is subject to full protocol review or not are based on whether the NCI holds the IND or provides funding for the sponsored research. Based on experience with Concept Evaluation Panels, which are broader and include extramural investigators, recurring themes in disapproved Phase III concepts include unrealistic advantage attributed to the experimental arm resulting in an underpowered study, weak preliminary data, and competing trials. For Phase II trials, the most common reasons are duplication and weak preliminary data.

Dr. Christian described how the CTEP approaches cancer therapeutics development, using the epidermal growth factor receptor inhibitors (EGFRis) as an example. Based on what was known from clinical investigations, nonclinical models, and preclinical investigations, collaborative development to identify EGFRis was considered a high priority. Initial goals were to: (1) emphasize translational research and the developmental work associated with bringing these agents to Phase III clinical trials; (2) conduct innovative studies to evaluate dose, schedule, and sequence issues for combinations; (3) conduct correlative studies; (4) evaluate activity in uncommon tumors and stages of disease for which there was strong rationale to bring agents to much broader development earlier; and (5) evaluate combinations of interest. Three EGFRis—gefitinib (Iressa), erlotinib, and lapatinib (Pan-HER)—currently are under development. Dr. Christian noted that 121 letters of intent (LOIs) were received and reviewed for gefitinib and 41 were approved; 159 LOIs were received for erlotinib, and 43 were approved; and 78 LOIs were received for lapatinib, and 21 were approved. Tumor specimens for correlative studies have been sought from all enrolled patients, and investigators have been successful 70-80 percent of the time. Proposals for potential biomarkers are evaluated based on supporting nonclinical and clinical data, investigator experience, and robustness of the assays. Potential correlative studies include pharmacokinetic evaluation of blood and tissue to determine target expression, biochemical modulation of target (for dose optimization) and pathway (for biological effect optimization); markers of biological response to identify possible surrogates for antitumor activity; and clinical response. Dr. Christian noted that these drugs are being studied in a variety of trials in many different tumor types, both single-agent and combination trials. Correlative studies have been incorporated into these investigations.

Dr. Christian reviewed a recent NCI/CTEP experience related to Phase III trials of small molecule EGFRis in nonsmall cell lung cancer (NSCLC). The CTEP received concepts for five Phase III trials in NSCLC. Because a number of Phase III trials in NSCLC had already been sponsored by the NCI/CTEP (some of them negative and some ongoing) and sponsored or planned by industry, extramural EGFR and lung cancer experts were consulted to discuss reasonable approaches to the continued evaluation of that therapeutic. On the basis of input from a group of experts in EGFRs and lung cancer, the concepts were not approved in the absence of new information on selection of appropriate patients or markers of activity. However, the NCI/CTEP continues to support smaller studies to explore mechanisms of pathway perturbation, markers of activity, and drug to target effects.

Dr. Christian discussed unanswered questions that remain in relation to EGFR as a target for cancer therapeutics development and what has been learned with regard to correlative studies. Despite the limitations, there are an increasing number of these agents in clinical development. The CTEP has initiated a strategy for moving forward based on critical molecular pathways to optimize targeted therapy with combination strategies. This plan of action is based on the belief that inhibiting a single target in a complex signaling pathway is unlikely to provide sufficient treatment for most of the complex human cancers, because of multiple activating signals and crosstalk as well as signal transmittal via multiple pathways. Three combination strategies are being pursued: (1) maximize the inhibition of a single critical target, (2) maximize inhibition of a critical pathway, and (3) target multiple cellular mechanisms or processes. Combinations for the studies would be agents with no adverse pharmacologic interactions, nonoverlapping mechanisms of resistance, and nonoverlapping toxicities. Dr. Christian stated that the CTEP sought the advice of about 25 experts in signal transduction to discuss issues such as which pathway to target and which agents and how many to use. She reviewed the challenges in targeted therapeutics development: (1) incomplete understanding of mechanisms of action; (2) inability to assess target effects because of the lack of assays, imaging tools, and assay standardization; (3) lack of preclinical models to evaluate efficacy, schedule effects, or biomarker utility; (4) clinical trials methodology that makes it necessary to screen large numbers of patients and obtain tumor biopsies; (5) the growing number of available agents and clinical need; and (6) IP issues related to novel combinations. She used the herceptin example presented by GenenTech at a recent meeting to illustrate the barriers to designing a clinical trial with the proper sample size and duration of treatment to produce the expected benefit.

Dr. Christian then described the Critical Molecular Pathways approach that CTEP is taking. The EGFR pathway and the P13 kinase AKT pathways are being targeted using a number of agents, many of which are in the NCI portfolio and can be combined now. To maximally inhibit the target, an antibody and a small-molecule inhibitor of EGFR will be combined. Critical decisions for the project relate to assay or imaging approaches that can be used now, centralized laboratory and standardized specimen handling, and tumor banking versus protocol-specified correlative studies. Dr. Christian noted that a number of investigational drug combinations are moving forward in multiple tumor types, including kidney cancer, melanoma, glioblastoma, as well as lung, ovary, pancreas, head and neck, colon, and breast cancers. As a result of an extraordinary amount of collaboration with more than a dozen pharmaceutical companies, some of the trials are underway and others will be started shortly.

Next, Dr. Christian presented updates on a number of CTEP initiatives:

- Cooperative Group funding increased by 62 percent during the period from FY 1998 to FY 2003 to address critical funding questions raised by the Armitage Report.

- The 166 percent increase during the same period for the Early Clinical Trials Program went to fund increases for Phase I and II sites and the clinical components, and provide new funding for the translational research initiative and interdisciplinary research teams.

- Significant increases were seen in accruals, including a 24 percent increase in Phase III Cooperative Group trials, and a 58 percent increase in the Phase I and II Early Clinical Trials Program, the latter devoted to preparing many new agents for definitive testing.

- Progress has been made in the standardization of data elements and electronic systems, including initiation of the CTEP Data Update and Adverse Event Expedited Reporting Systems and development of a model informed consent, common data elements, common case report forms, and common toxicity criteria.

Dr. Christian presented a brief update of the Cancer Trials Support Unit (CTSU), a pilot project that was initiated to facilitate operations of the national network of investigators by increasing and simplifying access to clinical trials, and to consolidate and off-load duplicative administrative and regulatory activities across the eight adult Cooperative Groups. Administrative functions now consolidated in the CTSU for the eight Groups are: (1) investigator credentialing and storage of IRB databases; (2) cross-Group protocol registration and transfer of study data to statistical centers; (3) training, education, and promotional materials development for CTEP-approved Phase III studies; (4) disbursement of funds and accounting; and (5) management of onsite auditing of Group and non-Group activities. Another important project is the CTSU Remote Data Entry (RDE) system, which will make it possible to collect data in a completely electronic form. The system is undergoing beta testing now in a large adjuvant colon cancer trial. The CTSU RDE is suitable for a large array of clinical sites with diverse informatics platforms and expertise, and it integrates with NCI clinical data standards, other NCI databases, and Group legacy databases. Potential benefits of the system are faster data collection, improved data quality, and cost savings in data entry and quality control personnel.

Turning next to a discussion of protocol history, Dr. Christian noted that the CTSU began with grandfathered protocols and has been adding new ones ever since. Currently, 64 Phase III trials and some Phase II trials in rare diseases are available for national accrual. The rate of accrual has increased substantially in the past few years. The 180 registered sites and 600 accruals in 2002 tripled in 2003 to 471 sites with nearly 2,200 accruals. This year, there are 711 participating sites, and 1,300 patients were accrued during the first 4 months, with projections of doubling the 2003 number of accruals. Dr. Christian pointed out that the increases have been realized even without complete resolution of issues—for example, the need for a Central IRB (CIRB)—that were deemed necessary for the system to work most effectively. In response to earlier questions, Dr. Christian described the design and setting of the CIRB as it is being established. Clinical trials receive initial IRB review at the national level by an expert CIRB prior to final NCI approval. Local IRB Chairs or a subcommittee may accept the CIRB's review, assure that any local context issues are adequately addressed, and then approve protocols rapidly without the need for full IRB review. This process is called facilitated review. If the local IRB accepts the CIRB review, the CIRB becomes the IRB of record for that protocol and takes responsibility for review of all subsequent protocol amendments, adverse events, and continuing review. Importantly, this process can result in IRB approval within as little as 1 to a few days, and only adverse events that occur at the local site are reviewed at the local site, thus ensuring a context in which to review them. Dr. Christian noted that the pilot CIRB was offered originally to about 22 sites and one Cooperative Group. To ensure a robust experience in the pilot project, the number was expanded in 2003 to approximately 160 sites, and facilitated review was used in that year about 409 times. Utilization of facilitated review is projected to rise to 510 sites in 2004. Enrollment in the CIRB pilot includes 7 Comprehensive Cancer Centers, 11 major academic centers, and 13 Community Clinical Oncology Programs.

As a final topic for review, Dr. Christian provided data regarding efforts to facilitate and accelerate approval of new clinical trials. An Expedited Review Process (ERP) has been initiated in which the CTEP works with the Cooperative Groups following concept approval to generate the protocol document, which then goes on to the CIRB for approval and activation by the Group. Currently, the time for generating an approved protocol has been decreased to 107 days, and with CIRB review, it is 198 days to activation. This compares favorably with 282 days to protocol generation and 405 days to activation for the nonexpedited review. Dr. Christian noted that the CTEP is working with the CIRB to reduce the review time even further. For reasons associated with Group logistics, only 16 of the total of 42 Phase III trials initiated since 2001 have utilized the ERP, the remainder using the standard process. Dr. Christian noted that the median time from concept approval to protocol activation for CTEP Cooperative Group Phase III trials has been reduced from 577 days (without CIRB) to 307 days in 2003 with CIRB, and efforts are ongoing to reduce that length of time even further.

Questions and Answers

Dr. Niederhuber expressed the view that CTEP progress in addressing the timeliness issue should be communicated more effectively, and that timeliness is an issue that should be shared by all in both the academic and private sectors. In response to a query from Dr. Eric Lander, Director, Whitehead Institute, Massachusetts Institute for Technology, about changes that would improve the program, Dr. Christian pointed out that this is the focus of the CTWG. She suggested some areas to continue to address, including providing industry with greater incentives to work with the NCI, providing clinical research sites with adequate resources such that funding is optimized and duplication/waste minimized, and continuing to work on timeliness. Dr. Jean deKernion, Professor and Chairman, Department of Urology, University of California School of Medicine, asked for clarification on CTEP's organizational configuration and functioning and CTEP's responsibility in relation to translational research and the testing of therapeutic agents through grant mechanisms, the Cancer Centers, Cooperative Groups, CCOPs, and SPOREs. Dr. Christian pointed out that the CTWG will be working to optimize interactions between all of those resources. In response to a question from Dr. James Armitage, Dean, University of Nebraska College of Medicine, Dr. Christian noted that the Cooperative Groups are grappling with the dilemma of making high-priority clinical trials available nationally and, at the same time, optimizing aspects of site participation so that an increase in accrual occurs in all sites approved for clinical trials participation. In response to a question from Dr. Antman about the interaction between the CIRB for pediatric studies and the adult CIRB, Dr. Christian explained that the members of Boards will be different but the support structures will build on the model that has been developed and piloted in the main central IRB project.

Dr. Ralph Freedman, Professor, Gynecologic Oncology, The University of Texas, asked about the lack of preclinical models on decisions as to which Phase I/II trials to support, the adequacy of NCI/CTEP funding allocated to early clinical trials with correlative studies, and the concern that only seven of the Comprehensive Cancer Centers are actually participating in the CIRB pilot. Dr. Christian reminded members that the CIRB pilot was not open to the entire community; she acknowledged, however, that all Cancer Centers probably would have been accepted as participants. She expressed the view that concerns about liability may have been an impediment and noted that the CTEP is open to suggestions and incentives to encourage participation by other Cancer Centers and academic institutions. After a brief review of NCI/CTEP efforts to create resources to address what are considered fundamental gaps, further discussion was tabled until presentation of the CTWG later in the meeting.

VII. OVERVIEW OF BIOTERRORISM/BIORADIATION STUDY AND NCI/NIAID COLLABORATIONS—DR. NORMAN COLEMAN

Dr. Norman Coleman explained that the ROSP is a semi-unique model in that it involves work in the Radiation Research Program (RRP), DCTD, and in both the Radiation Oncology Branch and Radiation Biology Branch (RBB) of the Center for Cancer Research (CCR), NCI. He acknowledged the contributions to and participation in the work of the ROSP by the Director, NCI, and colleagues in the OD, RRP, Division of Cancer Epidemiology and Genetics, RBB, and National Institute of Allergy and Infectious Diseases (NIAID). Dr. Coleman reviewed activities in the radiation oncology/biology community that indicate the long-standing interest of the NCI and various federal agencies in radiation biology and the consequences of radiation exposure. These have included studies of the Japanese atomic bomb survivors (60-year collection of data); biodosimetry and radiation protectives; low-dose effects; astronaut exposure in preparation for a future Mars expedition; radiation epidemiology; radiation sciences by funded NCI grantees; radiation protectors for oncology; and late effects (30+ years) in pediatric populations, Hodgkin's disease patients, and other populations. Dr. Coleman noted that treatment algorithms have been modified substantially over the past two decades to minimize late effects.

In addition, a radioprotective agent (amifostine) developed initially by the Walter Reed Army Medical Center (WRAMC) has been approved for clinical use for salivary gland function.

Dr. Coleman described intensity-modulated radiation therapy, which enables the use of more sculpted tumor dose of radiation. The use of multiple fields increases tumor dose and decreases high-dose areas near tumor (sculpted dose) reducing toxicity, but more tissues are exposed to some low radiation dose. Dr. Coleman noted that in December 2001 after the terrorist attacks, a workshop was organized to bring together the radiation biology and oncology communities, including experts in normal tissue injury and drug development. The underlying rationale was that the radiation scatter in radiation therapy would be similar to what happens in a nuclear event where there would be a high-dose area surrounded by rings of lower and lower doses. Although the very low dose radiobiology has been studied by the Department of Energy (DOE) for population exposure and the very high dose for cancer, the workshop defined a moderate dose between 1 and 10 Gray (the single, fractionated radiation) as the doses that would be seen in a bioterrorism event and a time for successful intervention, and thereby worthy of additional research.

Dr. Coleman listed three general classes of radiation lethality, which depend on dose, exposure rate, and quality of irradiation. The single-dose exposure syndromes are: cerebrovascular syndrome (death within 24 to 48 hours); gastrointestinal syndrome (death within 3 to 10 days; survival possible in lower end of the range with intervention); and hematopoietic syndrome (death within 1-2 months; survival possible with intervention). The dose of radiation needed to kill 50 percent of the population in either 30 or 60 days is about 4.5 Gray, single dose, whole body. Dr. Coleman reviewed an analysis of what would happen during a major nuclear event: about 8 percent of the people would be lethally exposed in the higher dose range; 14 percent in the high-moderate dose range, requiring intensive care; 19 percent in the lower moderate range, requiring minimal to intensive care; 12 percent in the lower dose range, requiring minimal care; and 47 percent in the very low dose range. Dr. Coleman noted that the latter are described as the worried well who would have no obvious manifestations but would require some kind of reaffirmation or mild intervention. He listed elements of radiation exposure to be considered in addressing radiologic and nuclear device injury, including exposure fractionated over time; volume of exposure (partial or whole body, ingestion, combined injury); reaction by time and organ syndrome; and intervention (prophylaxis/radioprotectors, mitigators, treatment).

Turning next to a review of efforts in the radiation research community to address the nuclear and radiological terrorism issue, Dr. Coleman noted the longtime RRP interest in the field and listed topics of workshops organized by the RRP with various co-sponsors: normal tissue injury (2000); moderate dose (2001); normal tissue in which common toxicity criteria were established for clinical use (2002); radiation biology education and training (2003); normal tissue, animal models (2003); and late effects of normal tissues (2004). In addition, symposia are held at national and international meetings in an effort to bring the community together to reach consensus as to which research issues will move the field forward. In another initiative, the Armed Forces Radiobiologic Research Institute has conducted extensive research on a biodosimetry assessment tool that could identify markers in an individual patient that could indicate dosage received and potential biological consequences. This multi-assay strategy using high-throughput deployable systems was developed for military use, but could be used in the field in a nuclear event. In the field of radioprotective agents, the NCI has an animal models workshop to link the basic molecular biology of radiation injury to the development of agents for prophylaxis, mitigation, and treatment. A whole spectrum of models is being developed by which one could identify molecular biology targets and use high throughput screening to develop effective agents for prophylaxis, mitigation, and treatment of radiation injuries. As an example of the sophistication of the field, he cited several studies of the role of transforming growth factor beta in tissue fibrosis and its potential as a biomarker for radiation injury. One example of potential research approaches is a study published in *Science* using p53 inhibitors in an animal model to prevent injury from whole body radiation.

Additional activities involving NCI-RRP include: (1) NIH-wide action through the NIAID; (2) production of a working group report entitled "Cytokines for Marrow Suppression" in collaboration with the WRAMC; (3) the Countermeasures Working Group with the Office of Science Technology Policy, which resulted in the appropriation of new funding for normal tissue countermeasures; (5) the Subcommittee on Standards with the National Science and Technology Council (NSTC), which developed a draft of Protective Action Guidelines to standardize radiation exposure guidelines among all federal agencies; (6) the Critical Infrastructure Research Subcommittee with the NSTC; (7) the Radiation Biology Research and Training *ad hoc* group to coordinate and communicate among federal agencies; (8) an NCI/RRP Workshop in December 2003 on models for evaluating agents intended for the prophylaxis, mitigation, and treatment of radiation injuries; and (9) the NIAID-sponsored workshop in May 2004 on animal models for radiation injury, protection, and therapy.

Turning next to plans for future research, Dr. Coleman stated that the research and development (R&D) plan that has been more or less approved is designed to develop agents for human use for the strategic national stockpile (SNS). In characterizing the plan, he noted that although basic mechanisms research is vital, the emphasis will be on agent development, with support for education and training in radiation biology. It is a model for multi-agency, multidisciplinary, public-private partnerships and will clearly have a spinoff benefit for cancer treatment. Dr. Coleman briefly reviewed radioprotector drugs that are available for prophylactic pretreatment, as well as cytokines, other growth factors, and other agents that can be given as mitigators after radiation. In regard to the latter, he noted that patients with severe radiation fibrosis who are treated months or years later with pentoxyphylene exhibit some reversal in tissue fibrosis, suggesting that these chronic injuries are, in fact, chronic processes that may well be reversible. In addition to biomarkers and basic mechanisms, the R&D plan has considered other issues such as epidemiology, psychological effects, risk communication, information repository, and education and training.

Dr. Coleman noted that the NIAID is the lead Institute to develop and oversee the implementation plan for DHHS/NIH medical countermeasures against radiation attack. A recently proposed plan has been approved to protect the civilian population against radiation attack. Three major components of the plan are product development; resources and infrastructure development; and establishment of Centers for Medical Countermeasures Against Radiation, a centers-of-excellence initiative to focus on research, training, and education. Product development will involve formulating new indications for licensed drugs, facilitating movement of investigational drugs through licensure, and completing preclinical studies for new products. Examples of resources and infrastructure that will be developed are animal colonies, a preclinical testing core, centralized databases and informatics services, and small-scale product synthesis. Funding mechanisms for the Centers will be U19 grants (Cooperative Agreements). The NCI and NIAID will collaborate to develop the RFA over the summer for an expected public announcement in October 2004, to be followed by interested parties meeting at the NIH, also in October. Applications are due in February 2005, and grants will be awarded in September 2005. The allocated budget for FY 2005 is $47.4 M. The Centers could be either single institutions or collaborations and could focus, for example, on the following research areas: biomarker identification/dosimetry, radioprotectants and treatments, immune reconstitution and enhancement, training, drug screening assay development, animal model development, or epidemiology.

Finally, Dr. Coleman discussed plans for bringing the fruits of bioterrorism/bioradiation effort into the intramural program, particularly in the area of reducing normal tissue injury resulting from cancer and the treatment. The Molecular Oncology Therapy Technology Imaging Program has been proposed as a trans-NCI effort, with collaborators from the extramural community. It would provide an opportunity to bring together standard imaging of all types, innovative imaging (including nanotechnology), tissue analysis, and therapies of all types. The detailed study of a limited number of patients would provide robust datasets of both tumor and normal tissue biology. In conclusion, Dr. Coleman noted that the

importance of the radiation science to the national need has been recognized, and the radiation research community has come together rapidly and effectively. National need and scientific opportunity have been linked, and a state-of-the-science research agenda has been defined. The importance of collaboration and partnerships within the NIH and among federal agencies has been emphasized, which has helped set the stage for a national and international effort to benefit the general population and oncology research.

Questions and Answers

Dr. Freedman commented that work tied to the bioterrorism/bioradiation program could be beneficial in improving the long-term outcome of patients who are receiving radiation therapy. He asked about the interaction of the proposed program with the Radiation Therapy Oncology Group, Gynecologic Oncology Group, and others, particularly in regard to clinical trials for protective agents. Dr. Coleman pointed out that there has been a great effort to mobilize interest in this initiative among the entire community. He gave assurances that the Cooperative Groups would be involved through mechanisms other than the upcoming RFA. Dr. Armitage pointed out that drugs for the SNS should have been approved or at least have reached the IND stage, and large-scale clinical trials could not be done that would verify that the results obtained in animal models are translatable to humans. He asked whether solutions would be possible to the problem of getting agents approved for use that can be used, not only for traditional medical care, but also in response to a terrorist threat. Dr. Coleman noted that one of the next goals in the initiative is to bring the NIAID, FDA, and other groups together to try to determine endpoints for use in preclinical studies that would be acceptable to the FDA. He also noted that clinical experience in bone marrow transplant patients and patients undergoing lung radiation could help in developing methods for assessing gradations of tissue toxicity that are translatable to whole-body exposure incidences. Dr. Niederhuber commented that Cancer Centers and their radiation oncology units would be an ideal network to begin to disseminate information and regular updates as to how the community or country can respond.

VIII. SPECIAL RESOLUTION AND RECOGNITION FOR THE LATE DR. PAUL CALABRESI—DRS. LASALLE LEFFALL, JR., KAREN ANTMAN, AND JOHN NIEDERHUBER

Drs. Leffall and Antman, acting on behalf of Dr. von Eschenbach, joined Dr. Niederhuber at the podium to present the special resolution and recognition for the late Dr. Paul Calabresi to his wife and family. Following a brief personal memorial to Dr. Calabresi, Dr. Leffall read the following resolution on behalf of the NCAB and PCP:

"Whereas, Paul A. Calabresi, M.D., M.A.C.P., as part of his long and established association with the National Institutes of Health (NIH), National Cancer Institute (NCI), came to be appointed by the President in 1995 as a member of the President=s Cancer Panel at the National Cancer Institute; and,

"Whereas, he has served as chairman of the National Cancer Advisory Board; and through his participation in developing such seminal reports as *Cancer at a Crossroads: A Report to the Congress for the Nation;* and as a member of the Advisory Council to the Director of the NIH; and,

"Whereas, in that service to the NCI and the American people, Dr. Calabresi, through his gifted vision and profound scientific understanding of oncology and of the cancer community, served on nearly two dozen prominent committees and sections of the National Cancer Institute raising to new heights the capabilities of the Institute and the National Cancer Program to respond to the challenges and opportunities facing the Nation in its War on Cancer; and,

"Whereas, he shared his passion and deep commitment to the field of cancer research through his election to and active participation in the Institute of Medicine; and through his work as an Associate Editor for the journal *Cancer* and service as a member of the Editorial Board of the *New England Journal of Medicine;* his personal authorship of over 200 scientific and medical papers; and,

"Whereas, Dr. Calabresi exemplified through his own extraordinary dedication, capabilities, and achievements that the call to public service is a noble one; and,

"Whereas, he did all of these things, and more, with dedication, energy, intellect, grace, caring, compassion and humor;

"Therefore, be it resolved that the National Cancer Advisory Board and the President's Cancer Panel recognize and honor Dr. Paul A. Calabresi for his leadership, vision, and extraordinary contributions to the National Cancer Program."

Following presentation of the certificate and proclamation/resolution to Mrs. Calabresi, Dr. Niederhuber presented a personal memorial and expression of gratitude to Dr. Calabresi for his dedication as a medical oncologist, but also as mentor and advisor. Dr. Niederhuber then called attention to the newly instituted and released Paul Calabresi Award for Clinical Oncology. He described it as a K12 grant with the purpose of increasing the number of doctors, nurses, and basic scientists who are highly motivated and trained to perform the types of clinical oncology trials that Dr. Calabresi believed in and advocated throughout his career. Individuals receiving the grants will be trained to work together as teams, a concept advocated by Dr. Calabresi, to accelerate the translation of research and the delivery to patients. Dr. Niederhuber noted that the award will begin with applications submitted in July 2004, to be reviewed in the fall, and go to the January-February Council of 2005.

IX. HEALTH CARE DELIVERY UPDATE—DR. MARK CLANTON

Dr. Mark Clanton reminded Board members of Dr. von Eschenbach's belief that the basic science, translational science and health care delivery components must be addressed to make a fundamental impact on cancer in the United States. He noted that three components of the health care delivery system are financing care, pursuing quality and quality standards in the care of patients with cancer, and ensuring and improving access to cancer therapeutics and diagnostics and preventive services. He then gave an update on two programs focusing on the funding component, which are being developed to improve the U.S. health care infrastructure for cancer: (1) the proposed NCI and CMS collaborative Oncology Treatment Working Group, and (2) the Cancer Center Loan Program. The first initiative recognizes the fact that the CMS provides funding as it relates to health insurance and health care coverage to the highest risk population for cancer, those aged 65 years and older. The recently enacted Medicare Modernization Act created a demonstration prescription drug program that will become a full-blown program in 2006 to provide all drugs to Medicare recipients. The CMS/NCI collaborative will bring NCI's scientific resources to bear on CMS decisions about coverage for new drug therapies and oncology diagnostics, as well as on how CMS coverage decisions are made for the drug card program. A possible spinoff of the initiative would be its use in informing commercial health insurance coverage of oncology drugs. The second initiative relates to another provision of the Medicare Modernization Act, which allocates about $200 M to NCI-designated Cancer Centers and "State-designated Cancer Institutes" to improve health care infrastructure.

CMS/NCI Oncology Treatment Working Group

Dr. Clanton presented and discussed the five-fold purpose of the CMS/NCI Oncology Treatment Working Group: (1) focus on oncology drug treatment questions that could have major public health importance; (2) provide clinical and scientific expertise to CMS concerning oncology drug treatment questions; (3) explore the development of the off-label oncology drug coverage process, including looking for additional evidence-based ways to make decisions; (4) explore the possibility of an NCI/CMS/FDA collaboration to accelerate decisions to cover FDA-approved oncology drugs; and (5) facilitate a forward-looking discussion of the application of new technologies to oncology. Dr. Clanton cited nanotechnology as an example of a drug delivery system of the future that involves molecular diagnostic services, molecular therapeutics, and molecular imaging. He noted the relevance of this example to stimulate the thinking and planning by private, commercial, and public health plans about drug delivery systems that do not resemble the systems of today or combined therapy that is not necessarily covered in all drug card programs.

Cancer Center Loan Program

Dr. Clanton noted that the purpose of the program as written into the Medicare Modernization Act is to provide cancer center capital improvements for construction and renovation. In addition, the mention of "health care infrastructure improvement" written into the Act might encompass improvements such as updated bioinformatics and imaging capabilities. Eligibility for funding from the $200 M appropriation is limited to NCI-designated Cancer Centers or "State-designated Cancer Institutes," and the program is scheduled to begin on 1 July 2004, and end on 30 September 2008. Dr. Clanton noted that the NCI is primarily responsible for developing review criteria and the application process, as well as for administering the review process. The plan is to establish a partnership through an interagency agreement with the Health Resource Services Administration (HRSA) for help in administering the technical aspects of the loans, which would be for capital improvements. Dr. Clanton noted that the number of institutions that qualify to apply for loans appears to be 61 NCI-designated Cancer Centers and 10-12 State-designated Cancer Institutes. Other language in the Act specifies that capital improvements proposed for funding must have the potential to make a substantial impact on regional or national health care delivery.

Questions and Answers

Discussion after Dr. Clanton's presentation focused primarily on the Cancer Center Loan Program provisions in the Medicare Improvement Act, including: (1) the types of capital improvements that might be covered, (2) the potential impact a $200 M fund for capital improvements could have on Cancer Centers' budgets, (3) criteria for loan forgiveness, and (4) the need for a strategic plan for deploying the funding. NCAB members were referred to the actual legislation for an understanding of Congressional intent in enacting the bill and for more detailed information about criteria for loan forgiveness. The announcement for the Cancer Center Loan Program, which will be published on July 1 in the *Federal Register*, is under development by the NCI, which will administer the scientific review of the applications and the HRSA, which will administer technical issues related to the loans. Suggestions from NCAB members were encouraged.

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

As background, Dr. Edward Maibach, Director, Center for Strategic Dissemination (CSD), NCI, reminded members that dissemination as related to the CSD is defined as an active process, the goal of which is to turn knowledge into applications that benefit people. The objective in creating the CSD was to enhance NCI's dissemination capability and success by embracing a strategy of promoting and enabling user-centered application development and distribution. He then presented updates on caBIG,

the Energy Balance Dissemination Initiative, and the activities of the Director's Consumer Liaison Group (DCLG) and its new focus—"NCI Listens and Learns."

Dr. Maibach described caBIG as the "poster child" for user-centered application development. It was established by the NCI Center for Bioinformatics in partnership with the Cancer Centers, one of NCI's major "customer" groups. Cooperative development meetings were held with 49 Cancer Centers to assess what the Centers considered to be their most pressing bioinformatics support needs. The results were used to determine three initial focal areas for caBIG development: integrative cancer research, clinical trials, and pathology and tissue banking. The CSD is conducting additional needs assessments through focus groups with cancer investigators and through a Web-based survey of investigators at all 61 Cancer Centers and of intramural NCI Principal Investigators (PIs). The objective is to expand beyond the inner circle involved in the development of caBIG to address the needs of all eventual users of caBIG in the cancer care community.

Dr. Maibach then presented an overview of the Energy Balance Dissemination Initiative (EBDI), which he described as emblematic of the CSD dissemination strategy. The objective of the Initiative is to stimulate adoption of evidence-based approaches for improving energy balance behaviors by organizations in the private, nonprofit, and public sectors of the community and to create an environment in which it is easy for people to maintain energy balance behaviors in the areas of both physical activity and calorie restriction. Dr. Maibach noted that there is a broad and deep evidence base with regard to approaches to promoting greater amounts of physical activity, and a smaller but growing evidence base with regard to how to change people's eating behaviors on a population basis. Two basic methods are being pursued in tandem. The first is to conduct marketing research to identify perceived benefits and barriers associated with those evidence-based approaches among citizens in the community and intermediary organizations. The latter are important because they have the wherewithal to adopt, implement programs, and offer evidence-based programming to their constituents. The second method is to develop partnerships with those intermediary organizations that can advance EBDI's objective by becoming members of the distribution channel for evidence-based energy balance programs. Dr. Maibach presented a schematic of the logic model of the Initiative, noting that the EBDI is the beginning of the effort to develop active distribution channels to move evidence-based approaches into practice in the community. The plan is to conduct academic research to study the success and effectiveness of the distribution channels that are developed to contribute back to the evidence base itself. Dr. Maibach pointed out that this is an important opportunity for reducing cancer health disparities. In research to build distribution channels for the EBDI, it has been found that the science base is growing in favor of addressing energy balance, obesity, and physical activity objectives through work-site health programs.

Dr. Maibach discussed EBDI progress to date. An NCI-wide working group has been established to include participants from the CSD, Division of Cancer Control and Population Sciences (DCCPS), CRCHD, and OC. The NIH Task Force on Obesity has been briefed on the EBDI, and a subcommittee has been formed to pursue the idea as an NIH-wide initiative. A letter has been sent to Special Populations Network (SPN) investigators asking them to submit pilot projects that would be conducted during the final year of their SPN awards to test the EBDI logic model in specific communities with known cancer health disparities. A Small Business Innovation Research Award has been developed and is pending BSA approval. The CSD has been engaged in conversations with extramural partners, including national organizations in the nonprofit sector, who are interested in helping to take the insights of this research process to organizations in communities to promote adoption of evidence-based approaches to energy balance.

A new focus for the DCLG is an initiative called "NCI Listens and Learns." The objective is facilitating dialogue between the cancer advocacy community and the NCI. As background, Dr. Maibach reminded members that DCLG's chartered function was to advise and make recommendations to the

Director, NCI, and to serve as a channel for consumer advocates to voice their views and concerns. As part of its deliberations over the past few years on how to achieve these objectives, the DCLG conducted a 2003 survey of 152 cancer advocacy organizations, which produced the key finding they did not believe that the NCI is effectively collaborating with the advocacy community, with the exception of the area of survivorship. Respondents to the survey also indicated that facilitating better collaboration is an appropriate priority for the DCLG. Dr. Maibach contended that creating effective collaboration between two such large decentralized communities as the NCI and cancer advocates is difficult, and that the role of dialogue is going to be pivotal in creating better collaboration—both in terms of increasing beneficial and decreasing problematic outcomes. Thus, the DCLG has begun to focus on creating effective dialogue.

A working group, chaired by Dr. Marisa Weiss, has been formed to develop the dialogue process, which is expected to be launched in September 2004. The DCLG will serve as the facilitator of dialogue between the advocacy community and the NCI, to monitor the process and modify it, as needed, to move toward a better outcome. Formal goals and objectives have been formulated as a basis for evaluating the year-long pilot study as to the degree to which the dialogue facilitation process is improving collaboration between the NCI and the advocacy community. Specifically, the evaluation will look for an increase in the input received regarding NCI strategic plans or other initiatives, an increase in the number and diversity of advocacy organizations that are providing the input, increasing perception among members of the advocacy community that the NCI is actively soliciting and listening to their input, and increasing satisfaction with collaboration among advocates and NCI staff. The dialogue will be launched and hosted on the newly redesigned Web site http://www.cancer.gov. The dialogue will be open to individual citizen advocates through a different process.

Dr. Maibach noted that the dialogue will focus on specific issues of strategic importance and will be completely transparent. He briefly described the dynamics of the process. The NCI will ask for input via the Web site, the community will respond, the NCI will publicize a summary of what was heard and learned, the community will have an opportunity to provide feedback on the summary, and NCI decisions to change plans or not will be communicated along with the rationale for the decisions. Dr. Maibach noted that the Web site is up and will undergo alpha testing with advocates at the SPORE workshop in early July and beta testing later in the summer with consumers on Dr. Weiss' Web site (http://www.breastcancer.org).

XI. NIH ROADMAP INITIATIVES—DRS. DUSHANKA KLEINMAN AND J. CARL BARRETT

Dr. Dushanka Kleinman, Associate Director for NIH Roadmap Initiatives, OD, NIH, briefly reviewed the history of the NIH Roadmap Initiative. Shortly after taking office, Dr. Elias Zerhouni, Director, NIH, convened a series of meetings of scientists, stakeholders from patient groups, and provider groups to address emerging scientific opportunities in the changing scientific, societal, and funding environment and roadblocks to moving the science to the benefit of the public. Institute and Center (IC) leadership applied several criteria to the series of initiatives brought forward from the meetings and identified 28 initiatives across three themes: (1) New Pathways to Discovery, which would provide new tools and technologies to accelerate the conduct of basic research; (2) Research Teams of the Future to focus on new ways of conducting and funding research and on creating a workforce for interdisciplinary research; and (3) Re-Engineering the Clinical Research Enterprise, which is geared toward policy issues, research workforce, translational research, and enhancement of the current infrastructure for clinical research networks. Operating principles for Roadmap management are to: (1) reflect the collaborative process used to develop the initiatives; (2) be informed by, but not bound to, current NIH practices; (3) maintain central administrative services; (4) provide routine updates and clear communication within the NIH and with the extramural community; and (5) include prospective evaluation. Regarding evaluation, Dr. Kleinman noted that a framework is being developed for an evaluation of the overall

Roadmap and success in achieving the goals of accelerating the conduct and transfer of research, as well as for evaluation of individual initiatives.

Dr. Kleinman stated that the Roadmap implementation and coordination reporting structure permits cross-matrix management with checks and balances. The Roadmap Implementation Coordination Committee (RICC) consists of Chairs of the nine Roadmap Implementation Working Groups (RIWGs); these are predominantly IC Directors and directors from many offices within the OD, NIH. The RICC provides governance for the overall Roadmap in the areas of policy setting and oversight and review of fiscal and human resources. The RICC also facilitates coordination and communication among the RIWGs and provides guidance for evaluation of the overall initiative. The RIWGs are composed of a series of project teams. Each team is focused on a given initiative; therefore, a large part of the NIH workforce is involved in working on the Roadmap across all ICs. Roadmap Liaisons are representatives from each Institute and Center and speak on behalf of the IC Directors. They inform IC staff and IC research and advocacy communities; serve as IC Roadmap points of contact for the extramural community; and serve as the point of contact for administrative aspects when they are the lead IC. Dr. Kleinman directed the Board's attention to current activities of the Roadmap initiatives that are organized according to Working Group and posted on the NIH Web Site.

Dr. J. Carl Barrett, Director, CCR, NCI, and NCI Liaison with the Roadmap Initiative, continued the update. He briefly reviewed the scientific and structural challenges, as well as the evolving public health challenges, faced by the NIH that are being addressed through the Roadmap Initiative. Moreover, he pointed out, the NIH budget for health care delivery has doubled since 1985, and the percentage of the gross national product represented by actual expenditures has been increasing rapidly, presenting the additional challenge of using the advances to reduce health care costs. Critical NIH priorities are to: (1) accelerate the pace of life science discovery, (2) translate research more rapidly from laboratories to patients and back, and (3) explore novel approaches that are orders of magnitude and more effective than those currently available. Dr. Barrett reemphasized the three questions the NIH Roadmap will address: (1) What are today's scientific challenges? (2) What are the roadblocks to progress? and (3) What can be done only at the NIH level that could not be done at the Institute level to overcome the roadblocks? Dr. Barrett noted that the Roadmap that evolved from the consultative process served as a framework for the priorities of the NIH as a whole so that the Institutes could work together to optimize the entire research portfolio. It provided a vision for a more efficient, innovative, and productive system for both biomedical and behavioral research. It also set forth a number of initiatives that are believed to be central to extending the quality of a healthy life for people in this country and around the world.

Dr. Barrett then discussed each of the three themes of the Roadmap believed to be essential to overcome the roadblocks and some of the initiatives envisioned in each. Initiatives within the New Pathways to Discovery theme address technologies and approaches necessary to meet contemporary research challenges. Two of the initiatives address the area of molecular libraries and imaging, recognizing the need to understand the complexity of biology as it relates to cancer and to all biological sciences. One initiative, technology development, will target bottlenecks in the development of compounds as basic research tools and drugs. A number of RFAs have been issued to develop the areas of chemical diversity; assays; robotics and instrumentation; and predictive absorption, distribution, metabolism, and excretion and toxicology. Another initiative along the New Pathways to Discovery theme is development of high specificity/high sensitivity probes to improve detection. A number of initiatives are being proposed to improve development of different molecular imaging probes, an area that also is of importance to the NCI. The last New Pathways initiative involves the Nanomedicine Implementation Group's plans to develop Nanomedicine Centers. A recently released RFA is associated with developing planning processes for the Centers.

Initiatives within the second major theme—Research Teams of the Future—provide mechanisms for interdisciplinary research, high-risk strategies, and public-private partnerships. One popular mechanism that came forward from this initiative was the NIH Director's Pioneer Award. This novel award mechanism supports an individual, rather than a research proposal. The selected individual is believed to have the potential to make extraordinary contributions to medical research. Dr. Barrett noted that 1,300 applications were received for the first offering, and only 5-10 will be awarded. A second set of initiatives under this theme are the Interdisciplinary Research (IR) Centers. A number of RFAs have been issued, and planning grants will be awarded to begin IR programs that address significant and complex biomedical problems, particularly those that have been resistant to more traditional approaches. Another subset of the Research Teams of the Future projects will develop IR training initiatives. A number of RFAs are planned for IR curriculum development for short training programs, as well as for long-range training programs to groom the research workforce for the future. A final initiative under the Research Teams of the Future theme was the use of the NIH Intramural Research Program as a model for interdisciplinary and multidisciplinary research.

Reengineering the Clinical Research Enterprise is the third theme of the NIH Roadmap. Initiatives address the need for creating better integrated networks of academic centers that work together in developing new strategies to reenergize the clinical research workforce. Dr. Barrett noted that a Senior Advisor for Clinical Research is needed; this individual will be the key point person for the NIH for clinical research across the different Institutes. Recruitment is awaiting the definition of the role, function, and responsibilities of the position. A Clinical Research Implementation Group has been established at the NIH level with responsibility for enhancing the leadership and coordination of efforts to harmonize, standardize, and streamline federal policies and requirements pertaining to clinical research. The NCI is involved in these discussions. Also envisioned under the Reengineering theme is a National Electronic Clinical Trials and Research (NECTAR) Network with the objective of developing a bioinformatics system for the NIH community. This standardized data system will allow community-based clinicians to participate in national studies, facilitate the sharing of data and resources, and augment clinical research performance and analysis. Other Reengineering initiatives are the development of translational research core services and a network of Regional Translational Research Centers (RTRCs). Dr. Barrett noted, in summary, that nine implementation groups have been created around the three themes to address each of the key elements of the NIH Roadmap.

Dr. Barrett listed Roadmap initiatives with the NCI as lead and NCI staff who head them: (1) Comprehensive Trans-NIH Imaging Probe Database (Dr. Daniel Sullivan); (2) Clinical Research Informatics: NECTAR (Dr. Kenneth Buetow); and (3) Translational Research Core Services, a Rapid Access to Intervention Development-like program (Dr. James Doroshow). Dr. Barrett briefly reviewed key elements of Roadmap funding and management. All Institutes participate with their scientific communities in defining all components of the Roadmap; contribute equally and proportionately; and participate directly in decision making and have a direct liaison to the Roadmap. All Roadmap initiatives are offered for competition to researchers from all fields and communities. The peer-review process will ensure appropriate expertise. In FY 2004, Roadmap funding totals $128.3 M, 0.34 percent of the NIH budget, with the largest amount allocated to New Pathways to Discovery at this point. Five-year projections suggest that Roadmap funding will increase as a proportion of the NIH budget to about 0.9 percent. These dollars are to be competed for in a common pool of initiatives by all researchers from every discipline.

Finally, Dr. Barrett discussed the benefits to cancer research realized from the NIH Roadmap Initiative: accelerated removal of major and fundamental roadblocks common to all diseases, promotion of collaboration among the Institutes to solve problems, and availability through the trans-NIH pool of transforming investments open to all disease areas for competition. He reminded members of the seven

strategic priority areas that make up NCI's 2015 Challenge Goal and reviewed NCI's strategic initiatives consistent with and complementary to the three themes of the NIH Roadmap Initiative.

Questions and Answers

Dr. Ramirez pointed out that the area of cancer and other health disparities was not specifically addressed in the Roadmap Initiative and suggested that health disparities elements be laid out more explicitly in the three theme areas. Dr Kleinman noted that in addition to elements throughout the Roadmap that have the potential to address health disparities, the Council for Public Representatives for the Director recently launched an initiative that will examine the intersect of public trust and health disparities. Dr. Lander asked what type of NCAB response was expected as a result of the comprehensive informational presentation on the Roadmap, noting that there appeared to be no open questions inherent in it. Dr. Barrett explained that the presentation was intended to provide fundamental knowledge of the Roadmap and its relation to NCI programs inasmuch as the Board might be presented with different Roadmap-related proposals for approval or disapproval in the future. In the meantime, input from the Board was welcomed for adjustments in terms of different areas for investment that could be integrated into future plans.

Dr. Lander pointed out that many of the RFAs were issued as one-time RFAs and asked whether they are likely to be reissued in some related form or whether other one-time RFAs would be issued. Dr. Barrett replied that the issue of whether and how some of the initiatives need to be reissued is under consideration, and more will be known in September when the initial awards are made. However, the philosophy of working across all ICs with a limited percent of the funding to experiment from individual portfolios on research that benefits the whole agency is a concept that seems to have gained interest and popularity. Dr. Lander asked for an elaboration of the envisioned process by which experts will be convened to help evaluate the results of the Roadmap RFAs and make midcourse corrections. Dr. Kleinman explained that the framework for an overall evaluation has been put together and is pending development by the RICC. Within that framework, there is an advisory group that is at this point primarily internal. The concept in terms of the evaluation is to solicit competitive bids to add a third party that is experienced and able to help solidify a design and have an advisory oversight capacity within the context of that design. Dr. Lander suggested the need to have an internal process that takes advantage of peer review by taking it to a higher level, drawing on both the councils of the Institutes and a wide range of excellent scientists throughout the community. He also suggested the need to commission independent groups and engage them in the opportunity to improve the Roadmap in an ongoing process to cement the connection with the community. Dr. Barrett pointed out that the Board should be aware of and watch several management experiments that are ongoing. Two of them are in the area of molecular targets and bioinformatics and finding answers to questions about the most efficient ways of conducting those activities in terms of scale. Another is the special authorities associated with the nanomedicine centers. Dr. Elmer Huerta, Director, Cancer Prevention, Washington Cancer Institute, emphasized the need to communicate the Roadmap programs to the general public to ensure that science is transferred into use by the public and that change can take place.

Dr. Niederhuber expressed concern about how the envisioned centers, for example, the Translational Research Centers, will interact in institutions that already have longstanding clinical research center programs. Dr. Antman noted that a workshop scheduled for July 19 would address that issue, and she invited participation by interested NCAB members. Dr. deKernion suggested that future presentations on the Roadmap be broken down into specific areas, with updates on problems encountered, metrics for success, and future plans to facilitate discussion and input from the Board.

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 2,677 applications were reviewed requesting support of $ 725,210,289 . The subcommittee meeting adjourned at 5:30 p.m.

DAY TWO: THURSDAY, JUNE 3, 2004

XIII. CANCER NANOTECHNOLOGY STRATEGIC PLAN—DRS. ANNA BARKER, MAURO FERRARI, AND GREGORY DOWNING

Dr. Barker introduced Dr. Mauro Ferrari, Edgar Hendrickson Professor of Biomedical Engineering and Professor of Internal Medicine at The Ohio State University, as well as Dr. Gregory Downing, Program Director, Office of Advanced Technologies and Strategic Partnerships, NCI. She called Board members' attention to the handout of the draft *Cancer Nanotechnology Strategic Plan* that has been developed during the past year by Drs. Ferrari and Downing as well as a large contingent of NCI's intramural and extramural communities. The NCI has held symposia at a number of institutions, including the Salk Institute, University of Washington, Fred Hutchinson Cancer Research Center, and others that brought together oncology and nanotechnology experts to generate interest in nanotechnology applications related to cancer. Dr. Barker added that the cancer community has demonstrated a great deal of interest in nanotechnology.

Dr. Ferrari reported that the *Cancer Nanotechnology Strategic Plan* has progressed remarkably during the past year because of the input and wisdom acquired from broad sections of the cancer community both within and outside of the NCI. Throughout communications with the cancer community, including clinicians, basic researchers, and community leaders of many different types, Dr. Ferrari and his team have become convinced that nanotechnology can be a very fundamental enabling toolbox for cancer researchers and clinicians, with a broad spectrum of possible applications. He briefly described the activities that led to the formulation of the draft strategic plan, noting that some of these activities are ongoing and future activities are scheduled so that the plan will continue to be refined.

Nanotechnology can be a very powerful tool to help in every aspect of the fight against cancer, from fundamental science to early diagnostics and targeted therapeutics. Dr. Ferrari explained that it also holds promise for developing and implementing effective ways to increase therapeutic efficacy, diagnosing cancer earlier, understanding the foundations of the disease, and reducing the adverse impacts of cancer therapy. Furthermore, it is believed that nanotechnology may reformulate the taxonomy of the disease and help eliminate artificial barriers in the current treatment of cancer. Devices or components constructed at the nanometer scale approach atomic dimensions. Tens or hundreds of millions of nanoparticulates—carrying different functionalities or signatures—could fit into a single cancer cell. This makes the notion of instrumenting the search for markers of disease and implementing targeted therapeutics very realistic.

Dr. Ferrari argued that the timing is right to develop nanotechnology applications for cancer because of tremendous advances in the biological sciences (e.g., the genomic revolution), understanding of the fundamental nature of cancer, and information technology sciences and computational sciences. A technology linkage between fundamental biology and the capability to interpret enormous amounts of data is missing, and nanotechnology is expected to fill this niche. He provided some examples of nanotechnologies that could help address this need:

- **Carbon Nanotubes/Nanowires.** These constructs, made from carbon, silicon, and other materials, have the capability of interrogating biological systems to pick up hundreds, thousands, even tens of thousands of molecular signatures at the same time; monitor the complexity of biological phenomena; and relay the information.

- **Cantilevers.** Nanoscale cantilevers take advantage of extraordinary physical properties that can only be found in devices that have these dimensions. A University of California, Berkeley, researcher has developed cantilevered nanoscopic fingers that can be designed to detect specific molecular expression from a cancer cell. As a cancer cell expresses its molecular products, the physical properties of these fingers changes. Researchers can read the change in real time from hundreds or thousands of these fingers and obtain information about the presence, absence, and concentration of different molecular expressions.

- **Nanoparticles.** Nanoparticles can be injected safely in large numbers in the body to provide a signal amplifier to reach tumor sites and/or sites that are associated with progression or onset of disease and provide information through imaging or other tools, and possibly deliver therapeutics as well. Dr. Ferrari noted that the first use of a nanoparticulate agent for targeted delivery is the use of liposomes, currently the standard of care for a number of diseases, including refractory ovarian cancer. A recent article published in *Neurosurgery and Applied Neurobiology* described the work of researchers who used injected nanosized iron oxide particles coated with sugars as an imaging modality in conjunction with MRI to identify brain cancer lesions before and after surgical intervention.

- **DNA Chips.** DNA chips are made from photolithographic processes that have developed over the years from the micro scale to the nano scale. They represent future developments that will allow researchers to examine the proteome in a sophisticated multiplexing fashion.

Dr. Ferrari also noted that nanoparticulates can traverse the blood-brain barrier very effectively and obtain a large amount of information from inside the blood-brain barrier; a daunting obstacle for drug delivery and contrast agent delivery. This point underscores one of the tremendous potentials of nanotechnology—the ability to overcome the many biological, biophysical, and biochemical barriers that the body puts up against a standard intervention such as the administration of drugs or contrast agents. He described work recently published in the *Proceedings of the National Academy*. Researchers from Rice University developed nanoshells that have been safely injected in animals and that preferentially concentrate in cancer lesion sites because of their size via a phenomenon known as enhanced permeation and retention. These nanoshells can be modified to carry molecular conjugates to antigens that are expressed on the cells themselves or in the tumor microenvironment.

The NCI has taken the lead for a number of years in supporting nanotechnology and other innovations for cancer therapeutics and diagnostics. One of the Institute's overall goals in its nanotechnology strategic plan is to incorporate multiple functionalities on a single nanotechnological platform. Another is developing the ability to generate a signal amplification property to allow

researchers to see cells and molecules that otherwise cannot be seen using conventional imaging technologies.

Other goals related to nanotechnology applications in the cancer field include the ability to monitor therapeutic interventions and determine when a cell is mortally wounded or activated. Dr. Ferrari also restated other applications, including therapeutic delivery, cell targeting, overcoming biological barriers (e.g., the blood-brain barrier), and providing an early indicator as to whether treatment is effective. In terms of clinical management, knowing whether or not a therapy that works for one patient also works for another patient before having to administer weeks of therapy can increase effectiveness and reduce suffering. In addition, the ability to monitor the effectiveness of a therapy could result in a significant acceleration in the regulatory approval of many promising therapeutic agents under development.

Dr. Ferrari concluded his remarks by listing the multiple functionalities to be incorporated in a nanotechnology development plan, including the ability to: (1) explore and interrogate fundamental science at the cellular level, tumor microenvironment level, systems level, and at the level of linkages between molecular pathways; (2) detect the signs of disease early from serum or by biological fluids analysis, through proteomics, or from imaging technology; (3) follow what happens to the tumor lesion as it evolves and as it gets modified and, hopefully, contained or eliminated by therapeutic intervention; and (4) identify the molecular differences *in vivo* between an identical pathology in two different patients, thereby personalizing the understanding of the disease and the therapy that follows.

Dr. Downing explained that development of NCI's Cancer Nanotechnology Strategic Plan has been a team effort involving many intramural and extramural program scientists as well as input from a large number of extramural biologists and technology developers. He noted that the draft plan includes clear goals for the next 5 years, and that the plan intends to bring together institutions and scientists in developing strategies for technology development and its integration into NCI's cancer clinical trials programs and ultimately, into the clinic.

The plan calls for the formation of an alliance—a comprehensive, systemized initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnology to cancer. Goals in the strategic plan that have been applied to the alliance include developing: (1) research tools to identify new biological targets; (2) agents to monitor predictive molecular changes and prevent precancerous cells from becoming malignant; (3) imaging agents and diagnostics to detect cancer in earliest, most easily treatable, presymptomatic stages; (4) multifunctional targeted devices to deliver multiple therapeutic agents directly to cancer cells; (5) systems to provide real-time assessments of therapeutic and surgical efficacy; and (6) novel methods to manage symptoms that reduce quality of life.

The plan, starting with an active technology development program, involves integrating teams and concepts that already have been successfully brought together. The goal is to streamline and interface with NCI's existing cancer research infrastructure as its Comprehensive Cancer Centers and SPOREs. The approach includes creation of dedicated Centers of Nanotechnology Excellence, which will foster multidisciplinary physical, engineering, and chemical science research teams interfacing with cancer biology in clinical applications. Interagency collaborations will be important in developing training initiatives tied to the plan. Existing contracts and grants programs that have been very successful in developing technologies and commercialization pathways will be utilized.

Dr. Downing explained that the Centers for Cancer Nanotechnology Excellence are intended to integrate nanotechnology development into basic and applied cancer research to rapidly facilitate clinical applications. Some of the key components are integrating with current NCI infrastructure, including, for

example, NCI's Comprehensive Cancer Centers through caBIG, as well as NCI intramural programs that are specialized in imaging and clinical trials. Affiliation with a university or with research centers of engineering and physical sciences will be critical to identifying particular technologies that have not yet made their way into medical applications. The Centers for Cancer Nanotechnology Excellence also are anticipated to have advanced biocomputing capabilities because of the massive amount of data that nanotechnology can capture from living systems. Also, it is hoped that the Centers will develop strong relationships with nonprofit and private technology development organizations.

Dr. Downing noted that the NCI has taken the lead from NIH's Bioengineering Consortium in framing a multidisciplinary research teamwork approach in the plan that addresses the different communication barriers and the training backgrounds of engineers and physical scientists, chemists, mathematicians, cancer biologists, and clinical trialists. He and his colleagues have worked with Cancer Centers and engineering programs to bring these disciplines together—when discussions are focused on a particular cancer biology problem, the barriers quickly evolve into new ideas and opportunities for teams and partnerships. One key is working within interagency collaborations. In this regard, the NCI has had a very strong and productive relationship with the National Institutes of Standards and Technology (NIST), focusing on establishing some of the physical and chemical aspects of understanding nanotechnology. Dr. Downing commented that new mechanisms for developing inspirations and aspirations for multidisciplinary teams that incentivize new investigators to come into this field may need to be explored as well.

Dr. Downing briefly highlighted the focused areas for technology development described previously by Dr. Ferrari. He pointed out that there is not a central database or location where one can go to develop basic reference data on how nanotechnology interfaces with cells and in living systems. Therefore, it is planned to develop a facility at NCI's Frederick campus to develop a cascade of biological assays that can be used to characterize nanoparticles and other nanomaterials in these biological systems. The output would involve building a knowledge base that will help inform the investigator community as well as the regulatory science field. The NCI/FDA Interagency Oncology Task Force has started to address nanotechnology and is developing a critical pathway for technology development and assessment. It is felt that the Frederick facility, in combination with NIST and FDA efforts, will be an important accelerator to developing the technology pathways for NCI's academic and private-sector partners. The Frederick laboratory also is intended to facilitate collaborations among the NCI, academia, and private sector primarily through the use and development of public databases and knowledge as well as assay development mechanisms—serving perhaps as a nexus for developing a multidisciplinary research team and focusing on potential new clinical applications.

Dr. Downing explained that technology development takes place in many different capacities in university and cancer centers across the country. The Technology Centers of Excellence that this nanotechnology alliance will provide will be an integrator for helping focus and streamline entry of technologies into the clinical paradigm. Additionally, other national laboratories (e.g., NIST, DOE, Department of Defense) have facilities in technologies that could be tapped into to help build multidisciplinary teams. These technologies then can be focused back to a characterization laboratory to help develop the data, protocols, and knowledge base that will help inform the clinical paradigm and ultimately lead to the applications of these technologies in the clinic.

Dr. Downing concluded his remarks by noting that the alliance offers the scientific opportunity for accomplishment in leadership and transforming the field of cancer biology to examine ways that technologies can be developed in the laboratory and translated into the clinic in a streamlined approach, and to understand how the physical world interacts with the biological world. Ultimately, it offers a new strategy for providing cost savings for health care programs and offering new approaches to personalized

medicine, as well as the opportunities for expanding biomedical careers and new avenues for career development.

Questions and Answers

Dr. deKernion asked about the development of the five Centers of Nanotechnology Excellence. Dr. Downing noted that these proposed Centers would address needs for reaching the principal goals identified in the presentation made by himself and Dr. Ferrari. Each of the five targeted areas that they highlighted likely would need at least one Center focused on that issue. Dr. deKernion asked about funding for these Centers, and Dr. Downing explained that he and his colleagues have been working on the strategies for the RFAs and the concepts for them. These proposed Centers are viewed along the same lines as other types of centers funded by the NCI, but with more of an integrative capacity. Dr. deKernion then asked about the level of nanotechnology research in biological systems being conducted across the country. Dr. Ferrari responded that research on the applications of nanotechnology to biological systems is conducted to some degree at almost every major university in the country.

Dr. Niederhuber asked about nanotechnology efforts underway at the NCI. Dr. Ferrari explained that they have conducted a preliminary census of intramural and extramural working groups on nanotechnology and found that there are approximately 70 laboratories and programs that work on cancer nanotechnology applications. Dr. Downing added that there also are virtual connections within and between laboratories. In addition, several of NCI's contracts and grants programs in technology development have collaborations with intramural laboratories. Dr. Kenneth Cowan, Director of the University of Nebraska Medical Center, Eppley Institute for Cancer Research, asked for a sense of the research portfolio at the NIH overall as well as at the NCI level. Dr. Downing responded that the grants and contracts programs have been a primary driver at the NIH in this regard. In 2003, the NIH reported funding $78 M for the National Nanotechnology Initiative, placing it as the third or fourth highest ranking federal agency that has nanotechnology development in its portfolio. NCI's Innovative Molecular Analysis Technologies (IMAT) Program and Unconventional Innovations Program (UIP) have fostered a great deal of growth in this area. For example, eight UIP contracts are focused on nanosensors and nanoparticle development, and nanotechnology scale development is represented by 10-15 percent of the IMAT portfolio. Dr. Downing also noted that he envisions programmatic contributions increasing significantly for training, and the grants and contracts program developing approximately five-fold over the next 5 years.

In response to a question about developments in the private sector, Dr. Downing explained that grants and contracts programs in technology development have heavily advertised annual PI meetings. The broad agency announcements for contracts programs are disseminated to many small businesses, and there have been collaborations with NIH's small business programs. There also are collaborative efforts underway with larger companies (e.g., Dupont, Dow). Dr. Downing estimated that approximately 70 percent of the telephone calls he receives each day that ask about nanotechnology initiatives come from the private sector. He and his colleagues are trying to develop a streamlined approach to help integrate those technologies with academic centers and helping virtually put teams together that will help bring those technologies to the cancer biology forefront. Many of these academic centers do not have adequate resources, laboratories, or knowledge base, and Dr. Downing's office spends a great deal of time trying to identify opportunities for collaboration between academic centers and the private sector.

Dr. Freedman asked about how many graduate school programs focus on nanotechnology. Dr. Downing commented that graduate schools have asked the NCI for input on curriculum development, and there are plans to develop curriculum programs for undergraduate as well as medical school programs. Dr. Ferrari added that universities typically have difficulty in accommodating interdisciplinary programs. However, because of the enthusiasm centered around nanotechnology, universities will have to adapt. There are

Ph.D. programs in nanotechnology at this time, although there is no undergraduate major in nanotechnology as of yet.

When asked to compare nanotechnology efforts in the U.S. with the rest of the world, Dr. Ferrari explained that there are three major contributors to nanotechnology research: the United States, Europe, and Japan. Currently, the United States spends more on nanotechnology research than Europe and Japan, although not by much. The United States also is firmly in the lead in terms of conducting research on the medical applications of nanotechnology (the NCI conducts the majority of this research), particularly in terms of having a much broader portfolio of researchers. In response to a question about the availability of information on the applications of nanotechnology for cancer on the Internet, Dr. Downing mentioned that the most relevant Web site at the moment is http://www.nano.gov, which is the Office of Science and Technology Policy's National Nanotechnology Initiative. A robust nanotechnology Web site for the NCI is under development. Dr. Clanton noted that a list of relevant Web sites appeared within a cancer nanotechnology brochure that was distributed at this meeting.

Dr. von Eschenbach asked Dr. Clanton to comment on the Government Performance Reporting Process (GPRP). Dr. Clanton explained that almost all federal agencies are undergoing the GPRP to determine whether research programs are achieving their intended results. The NIH is undergoing one of its first evaluations, and five programs were selected for evaluation. Nanotechnology was selected for evaluation by the Office of Management and Budget (OMB), and the NCI was chosen as the lead Institute for that performance evaluation process. The evaluation was conducted approximately 2 weeks before this Board meeting, and initial feedback indicates that the NCI represented the NIH extremely well. Results of the evaluation are not yet known, and although the NCI will not receive individual scores (collective scores will determine whether the NIH passed this performance evaluation), the OMB examiner mentioned that the NCI performed extremely well. Dr. von Eschenbach expressed appreciation and gratitude for the work that is being led by Drs. Downing and Ferrari.

Dr. Barker closed the session by thanking all involved and noting that their work has created an exciting vision for the ways that the NCI can apply these new tools. She explained that next steps involve aligning these programs and obtaining feedback from the BSA.

XIV. STATUS REPORT: CLINICAL TRIALS WORKING GROUP— DR. JAMES DOROSHOW

Dr. James Doroshow provided an overview of CTWG activities. It is hoped that with the help of the NCAB, the development of the CTWG will advance the clinical trials process across the NCI and beyond. The charge of the CTWG is to advise the NCAB and its Subcommittee on Clinical Investigations on the development, conduct, infrastructure, support, and coordination of clinical trials. In addition, the CTWG is to help examine the range of clinical trials supported by the NCI and how the clinical trials process might be broadened to develop not only constituencies in the consumer and advocacy communities but also across a variety of governmental agencies.

Dr. Doroshow noted that the landmark work performed by Dr. Armitage and his committee of external advisors and internal NCI investigators during 1996-1998 formed the basis of the rationale for the CTWG and its charge. The report of the Armitage Committee on Clinical Trials outlined essential issues related to clinical trials progress, including the training and retention of clinical investigators, development of novel methodologies for cancer clinical trials, evaluation of the framework in which clinical trials were/are conducted within the NCI, and identification of science-based processes to be developed to enhance the clinical trials process. Dr. Doroshow urged those who had not read the Armitage report to do so. He noted also that the report was the basis for the efforts of the Implementation Committee led by Drs. Michaele Christian and John Glick. A followup report of specific issues to be

addressed that were raised in the Armitage report was developed, and these implementation issues led to the formation of the first centralized IRB, which has made substantial progress over the past 3-4 years, and led to the development of the critical state-of-the-science meetings that have helped advance the areas of investigation that the NCI and the oncology community need to address.

The Implementation Committee's report also led to the formation of the Clinical Trials Support Unit, a paradigm for national efforts to organize the infrastructure for clinical trials. Dr. Doroshow noted that this process has reached the point that a major national clinical trial, which is being conducted at more than 100 sites, is using electronic data entry. He characterized this pilot as critical because, if the bioinformatic infrastructure can be developed to allow national data entry on a national trial, this may facilitate development of a national structure in which patients can be entered and their data collected at numerous venues across the range of sites at which clinical trials are conducted. The CTWG has evaluated the Armitage Committee's report and the Implementation Committee report as well as the P30 and P50 reports that outline the importance of including Centers and SPOREs in the national clinical trials effort and the need to coordinate efforts that are ongoing in various sites under various mechanisms. Thus, CTWG's starting point was a review of these three reports and an evaluation of the issues to be addressed.

Dr. Doroshow characterized CTWG membership as "broadly representative," including members from the NCAB, Cancer Centers, and SPOREs, as well as PIs from program project grants and other investigators. He characterized FDA's representation in the CTWG as "outstanding" and stated that Dr. Richard Pazdur, Director, Division of Oncology Drugs, FDA, has been a vital part of the process thus far and will continue to play a key role in reaching CTWG's short- and long-term goals. The group also includes representatives from the CMS, the Office for Human Research Protections (OHRP), and the advocacy community. Membership also includes representatives from the pharmaceutical industry as well as representatives from essentially every oncologic medical discipline involved in the clinical trials process. All CTWG members are active clinical trialists and have extensive experience and involvement in the day-to-day conduct of clinical investigations.

The CTWG advises the NCAB, implements solutions for critical issues currently impairing the efficiency of the NCI-supported clinical trials system, develops a blueprint for the conduct of cancer clinical trials in the future, and guides the construction of the informatics infrastructure for managing and organizing clinical trials information at the local and national levels. These opportunities are especially exciting in light of Dr. Buetow's presentations about caBIG and the not-too-distant possibility that credentialed investigators will be able to enter a patient eligible for a trial at almost any credentialed site. In effect, this will revolutionize how clinical trials are conducted.

Dr. Doroshow summarized the four immediate impediments identified by the group at its initial meeting. The first issue is prioritization. Given budget restraints, it is critical to enhance the ability to prioritize the studies to be conducted, by whom they will be conducted, and how they will be conducted. The second issue is coordinating clinical trials. Because many individuals involved in conducting clinical investigations assume multiple roles in the process, the process must be transparent and flexible so as to accommodate these multiple positions and so the highest priority studies can be conducted. Data concerning clinical trial accruals, detailed outcomes, and adverse events must be reported in detail to the NCI so that they may be evaluated to facilitate prioritization and coordination. The third issue is that of timeliness of completion. Improvements have been made in this area, but more needs to be done to address important questions more quickly. The fourth immediate issue is that of regulatory affairs—the ever-increasing amount of paperwork and regulatory hurdles that slow the process and progress of research. This issue highlights the importance of involving the OHRP in deliberations and of supporting a centralized IRB mechanism to allow studies to be made available much more quickly after final approval is received.

To address CTWG goals and priority areas, specific objectives include: (1) implementing an oversight mechanism for the clinical trials process as a whole; (2) defining new methods for the prioritization, coordination, and integration of NCI-supported clinical trials; (3) establishing a complete database of clinical trial outcomes for NCI-supported studies; (4) addressing regulatory issues that slow the completion of clinical trials; and (5) defining the elements of the clinical trials system of the future. In addition, the CTWG has established a Web site at http://integratedtrials.nci.nih.gov.

Questions and Answers

Dr. Niederhuber noted that the NCAB is excited about the process and likely will ask for regular updates on the CTWG. Dr. Doroshow agreed to provide CTWG updates to NCAB's Clinical Trials Subcommittee at each NCAB meeting. Dr. Ramirez asked whether the CTWG would address the accrual of underserved populations into clinical trials and the barriers faced by such groups. Dr. Doroshow responded that the enhancement of accrual of minority populations to trials is one of the issues identified by the group. He noted that his personal bias (which has not been tested yet) is that accrual will be enhanced as trial enrollment becomes easier and trials become more accessible to the population of patients beyond Cancer Centers. A system that simplifies entry into studies may have significant impact on the ability to accrue minority patients. Dr. Ramirez also asked about outreach and education of minority physicians. Research indicates that there are differences in referral patterns between Hispanic and non-Hispanic white physicians. Dr. Doroshow responded that patient advocate members of the CTWG have spoken passionately about the need to market the availability of trials to all communities, both patient and physician. He noted that such marketing efforts are likely to be more effective once the trials process itself is simplified. Patient advocates are expected to keep the group on track with regard to such efforts.

Dr. Chen asked whether the new effort could be enhanced by the Office of Strategic Dissemination and the Cancer Information Service (CIS) to promote the effort publicly. Dr. Clanton responded that a meeting is planned between Drs. Doroshow and Maibach to discuss needs and dissemination capabilities. Dr. Freedman asked whether the CTWG will address the issue of standardizing monitoring and auditing policies and practices in the community. Dr. Doroshow noted that the lack of standardization is one of the reasons that the pharmaceutical industry has in part disengaged from its participation with the NCI. Dr. Christian previously discussed the development of standardized case reporting forms as part of a broad bioinformatics initiative. Pharmaceutical industry personnel have indicated that the implementation of such a system that is acceptable to both the FDA and the industry would lead to increased participation by the pharmaceutical industry. She identified this issue as being critically important.

Dr. Freedman noted also the need to standardize auditing procedures and interactions with the IRBs at an individual level; this is important for ensuring research integrity. Dr. Doroshow noted that the blueprint likely will include a national quality assurance program with standard procedures. Knowing in advance the criteria for evaluations, audits, etc. will enhance efficiency and effectiveness. Dr. Franklyn Prendergast, Director of the Mayo Comprehensive Cancer Center, commented that the idiosyncratic nature of IRBs is a clear problem, and it remains to be seen whether all or most IRBs would agree to a set of standards. He asked how CTWGs actions would interface with the CIRB. Dr. Doroshow responded that Dr. Abrams is part of the CTWG, and there is no question that the group will need to do whatever it takes to enhance the acceptance of the CIRB.

Dr. Prendergast asked whether Dr. Doroshow is satisfied that the way in which clinical trials currently are designed appropriately takes into account advances in biology. Dr. Doroshow answered that scientific developments now make it possible to examine areas at a level that has not been possible until now. A major impediment to doing something more than a large, randomized Phase III trial, for example,

is the implementation of a strategy that allows the use of resources for centralized national laboratory facilities to support national trials focusing on a particular set of assays essential for employing the best science for a particular study. He noted that in the future, there will be a need to consider whether it would be better to conduct fewer trials so that resources would be available to conduct the trials at a scientific level that might lead toward gaining more information than may be gained via the current process. Dr. Niederhuber summarized a number of comments to the effect that in the future, trials may be smaller and patients may be studied more intensely. He suggested that this model may take the place of Phase I, Phase II, and Phase III trials.

Dr. Prendergast cited one study under consideration for 5 years that has not been implemented because the tools are not available, adding that the notion of using a single analyte as the actual marker or surrogate marker does not hold. The idea of how to implement a panel based on diagnostics must be considered. Questions include: (1) What are the statistics of multiple analytes? (2) How should they be applied? (3) What are the implications for disease stratification and study design? (4) How many patients are needed? (5) What are the selection criteria? (6) How should they be randomized or double-blinded? and (6) Is it ethical? With regard to the last question, he explained that patient selection can raise ethical issues. For example, if a patient is known to have a particular single nucleotide polymorphism that will change the pattern of their responsiveness to a particular agent, is it ethical to consider conducting a randomized trial under those circumstances? Dr. Prendergast suggested that this topic requires a greater intensity of focus.

XV. UPDATE: OFFICE OF COMMUNICATIONS—MS. NELVIS CASTRO, DR. GISELLE SAROSY, AND MS. MARY ANNE BRIGHT

Ms. Nelvis Castro, Acting Director, OC, NCI, explained that proactive minority media outreach is one of OC's top priorities. In part, this effort involves communicating news and information to minority communities impacted by cancer health disparities. This includes seizing opportunities to expand communication efforts during community events, actively working with the Divisions and senior staff to communicate important research results to these communities, and tailoring information to specific minority media outlets. As an example, she noted that Dr. Brenda Edwards, Associate Director, Surveillance Research Program, DCCPS, was interviewed about the release of the *2004 Annual Report to the Nation* by the National Newspaper Publishers Association, which has a distribution of approximately 210 mostly African American members. The National Association of Hispanic Publications also prepared a story on the report, and an audio news release for African Americans and Spanish-language media outlets was prepared and is set to be released through the NIH radio news service. In addition, Dr. Huerta plans to comment on the report during his daily radio and weekly television shows. Additional activities highlighting the release of the report also are planned.

Ms. Castro discussed activities that took place during National Minority Cancer Awareness Week in April. The OC released information on incidence and mortality in minority populations and tailored the dissemination of this information to specific populations and media outlets. Radio network interviews were conducted with NCI experts, and columns by NCI experts also were distributed. Participants in these activities included Dr. Mark Clanton (for the Native American press and picked up by the Knight-Ridder business wire). NCI officials also appeared on more than 700 broadcasts and print outlets serving minority audiences. Dr. Harold Freeman, for example, was heard on more than 400 stations of the American Urban Radio Network and was featured on the National Native News Radio Network, which has 190 American Indian and Alaska Native stations nationwide. Dr. Clanton also moderated a forum on health disparities among minorities on CSPAN and was interviewed on Washington, DC's WHUR FM during morning drive time. In addition, he wrote an article that was circulated to *Indian Country Today*. Dr. Jorge Gomez, Chief of the Organ Systems Branch, was featured on the news broadcasts of 50 Spanish-language television stations affiliated with the Univision Network. Dr. Gomez also wrote an

article that was distributed to the National Association of Hispanic Publications. In addition, a special press release was distributed through the National Newspaper Publishers Association and to *AsianWeek*.

The OC believes that these efforts are having a significant impact because the minority broadcast networks and print publications involved have a large traditional following and high levels of trust and credibility within their communities. Some of the larger minority networks that the NCI works with include the American Urban Radio Network, Radio Bilingual, Univision and Telemundo (the two largest Spanish-language networks in the country), the Hispanic Radio Network, and the National Native News. She noted that the OC also is beginning to work with minority magazines to encourage and develop story ideas about various aspects of cancer as they relate to their audiences. The OC also provides these outlets with ideas that may be used in opinion columns, letters to the editors, and question-and-answer/interview articles. OC staff will attend major media conferences and meetings this year to expand the Office's networking capabilities. The National Association of Hispanic Publications will hold its annual Media Summit in Washington, DC, this summer, and OC staff will attend the event. OC staff also will exhibit and network at the Unity Conference, a national meeting of all minority journalists being held in Washington, DC, this August. These activities will be tracked and evaluated, and Ms. Castro will share this information in the near future.

Ms. Castro then provided an update on the Hollywood Health and Society Project. This project is designed to encourage the inclusion of positive health messages and images in popular television shows. NCI staff met recently with Hollywood Health and Society staff and entertainment industry officials in Los Angeles and New York to discuss program possibilities for the fall season. Staff also facilitated scientific briefings on health messages and information for industry representatives. The current focus is on fruits and vegetables, clinical trials, and promoting 1-800-4-CANCER. DCCPS staff and others across the Institute are involved in these efforts.

Ms. Castro then invited Dr. Giselle Sarosy, Acting Associate Director of the Office of Cancer Information Products and Systems, to discuss the redesign of www.cancer.gov. Due to technical difficulties, Dr. Sarosy was unable to connect directly to the cancer.gov Web Site to show it to Board members during her presentation. She suggested that participants visit the Web site at some later time to see the changes that had been made. She also expressed her appreciation for the opportunity to discuss the redesign of the Web site that had been implemented the previous week. The redesign was based on extensive user research, including interviewing users, analyzing usage logs, and observing users interacting with the site. In addition, a panel of usability experts was convened in collaboration with the Center for Strategic Dissemination and the DCCPS to provide input during the redesign process. Survey data, including data from a popup survey on the cancer.gov home page, were analyzed and user input was sought at all points of the redesign process. Input first was invited from the NCI community and then from the larger cancer community via a March *NCI Cancer Bulletin* article. In addition, trans-NCI working groups were convened for each of the subject areas, including cancer topics, clinical trials, statistics, research programs, and funding to help inform the redesign process, identify content, and advise on content presentation.

Dr. Sarosy explained that the redesigned Web site better addresses the needs of current users who, according to research, most likely are looking for information by cancer type. The major section of the home page is devoted to information by type of cancer. Other changes made to the home page include the use of red and grey (NCI's official colors) and emphasizing the NCI over cancer.gov so that users clearly are aware that they are visiting the NCI Web Site. The navigation bar at the bottom of the page allows users to move easily from one location to another—improved navigation and visual appeal were key goals of the redesign. Types of cancer are located in the middle of the home page to make them readily accessible to users. Dr. Sarosy drew Board members' attention to the "quick links" located in the upper left corner of the page. These allow users to easily locate resources such as the dictionary of

cancer-related terms. A box entitled "NCI Highlights" appears on many high-level pages and highlights newly posted content such as NCI press releases. An area for highlighting featured content is located on the right side of the page.

In summarizing the major navigation improvements, Dr. Sarosy noted that information about cancer type now is within one click of the home page. A user seeking information on breast cancer, for example, now can scan the home page for the breast cancer listing and click on it to be taken to the breast cancer home page. The redesigned breast cancer home page contains research and related information to enable users to quickly scan and find useful information from throughout the NCI environment. Quick links and NCI highlights again appear on many of the high-level cancer-type pages, and related pages appear on the right to highlight additional information such as publications of interest. Information about help available from the NCI also has been centralized in an icon on the left to enable users to easily determine how to get information from NCI's CIS, how to contact live help, and how to get help via e-mail.

Another important navigation enhancement has made clinical trials information available within one click of the home page and many other areas of the site. Within one click of the clinical trials tab is the clinical trials portal page, which now includes the basic clinical trials search form. This enables visitors to quickly search NCI's repository of more than 2,000 clinical trials, including both NCI-sponsored trials and trials sponsored by pharmaceutical companies. Also included are trials listed at http://www.clinicaltrials.gov. For more sophisticated users, a more advanced search form is located one click away from the basic search form.

In closing, Dr. Sarosy stated that the recent enhancements are a step in an evolving process. Those involved in making the changes see the site as having been improved greatly for current users, but efforts continue to create a Web site that will meet the needs of the entire NCI community. Staff will continue to work closely with the Center for Strategic Dissemination and DCCPS to implement further enhancements based on ongoing and future research.

Ms. Bright explained that she and Dr. Corrine Husten, Chief of the Epidemiology Branch, Office of Smoking and Health (OSH), CDC, have been working together on the National Network of Tobacco Cessation Quitlines since the initiative was announced in February 2004. The purpose of the initiative, announced by DHHS Secretary Thompson, is the establishment of a national network of quitlines to ensure national access to quitline services. The Cessation Subcommittee of the Interagency Committee on Smoking and Health released recommendations in February that called for the establishment of a federally funded national quitline network in 2004 to provide universal access to evidence-based counseling and medications for all tobacco users. The network would provide a national portal to state and regionally managed quitlines. Dr. Robert Croyle, Director, DCCPS, was a coauthor of the report.

NCI's CIS and CDC's OSH have been working toward implementing this initiative. The CDC will provide funding to enable states that currently do not have quitlines to implement them. The CDC also will provide supplemental funding to states with quitlines to enable them to enhance their services. Current funding amounts may not be adequate to allow states to implement full-service quitlines, but some monies are available. The CIS will establish and implement a national toll-free telephone number and will continue to provide smoking cessation services through NCI smoking quitlines. CIS' advanced telecommunications system will be used to operate the national quitline network number, which will route calls into state quitlines during national promotions. The CIS will answer calls during national promotions for states that elect not to establish a quitline.

Ms. Bright commented that there is an opportunity for states to become familiar with the CIS Partnership Program. The CIS has developed partnerships to reach minority medically underserved

populations and provide technical assistance and cancer information. Developing the new national quitline network should provide additional opportunities to collaborate with state tobacco control managers. The effort also will provide additional opportunities for the CIS to distribute tobacco cessation materials and to provide important cessation services to more Americans.

Dr. Husten explained that the CDC in essence provides funds to all 50 states and the District of Columbia for tobacco prevention and control. The CDC also funds seven territories and several tribal support centers. She identified the four basic goals of CDC's tobacco control program: (1) reduce/prevent initiation among youth, (2) increase cessation among adults, (3) eliminate exposure to secondhand smoke, and (4) identify and eliminate disparities among populations. She noted that the disparities goal is an overarching one that covers all of the other areas. It is listed separately, however, so that states would provide explicit funding for such efforts and report explicitly on them. In addressing these goals, states are asked to develop community interventions, address policy/legislative issues, work with the media on countermarketing to implement tobacco prevention and control programs, and conduct surveillance and evaluation activities.

Dr. Husten noted that states may have other monies as well; several have instituted excise taxes on tobacco and use some of those proceeds for tobacco control programs. Some states have used monies from the master settlement agreement for tobacco control efforts. Thus, in some states, CDC money is only a small part of the tobacco prevention and control budget; in other states, CDC money may be all the state has to put toward these efforts. State capacity to conduct comprehensive tobacco prevention and control programs varies widely. Dr. Husten noted that quitlines generally are not funded with CDC monies—they typically are funded using excise taxes or proceeds from the master settlement agreement. Most states operate their quitlines through their health departments; others, especially states that use master settlement agreement money, have established a foundation that runs the quitline. Dr. Husten noted that these different types of arrangements can present logistical challenges for initiatives such as the National Network of Tobacco Cessation Quitlines.

In describing how the Network is envisioned, Dr. Husten noted that the plan is to have a single number—a single national portal to the various quitlines. When a call is received by the national number, it will be routed seamlessly and electronically by area code to the state quitline, if there is one, and to the CIS if there is no state quitline. This national number provides an opportunity for national promotion of the quitline. Also, as people move from state to state, they will be able to use the same number for quitline services. States will maintain their quitline numbers and branding and will continue to serve their regional populations, provide services tailored to the needs of those populations, and implement state-based quitline promotions. In addition, states will continue to integrate their quitlines into their comprehensive state cessation strategy within their comprehensive tobacco and prevention and control program. A problem that may arise is that state capacity varies, and a national promotion could overwhelm a state's capacity, especially in states that do not have much and perhaps have only CDC monies to fund their operations. Dr. Husten also noted that the planned implementation of the initiative does not fully implement the Cessation Subcommittee's vision. For example, there are no plans to provide free medication to all quitline callers, either through the states or the CIS.

Ms. Bright listed the key partners in the initiative, including CIS national and regional staff, OSH staff, state tobacco program managers, service providers, the DCCPS, and the North American Quitline Consortium (a large group of stakeholders interested in tobacco-related issues that will be launched formally in July). The Consortium's charge is to maximize access to, use of, and effectiveness of quitlines; provide leadership and a national voice to promote quitlines to policymakers and the public; and offer a forum to link all those involved in quitline services. Dr. Husten discussed current state quitline activities, noting that the master settlement agreement facilitated an expansion of quitline services such that most states (38) now have some degree of service. Capacity, however, varies from state to state and

depends on funding. Thus, a few quitlines provide comprehensive, multisession counseling and free medication, but states with more limited funding may provide counseling with no medication only to those who are uninsured and/or on Medicaid. Because state quitlines are funded through state legislatures, they sometimes lose their funding.

Another issue surrounding funding of state quitlines is that funding amounts generally are not based on any true study of what it would take to fund a comprehensive state quitline. State legislatures may provide a certain amount of money to health departments for the program or, in the case of master settlement agreement monies, foundations may specify an amount; and then states must determine whom they can serve, what services they can provide, and how much they can promote the quitline so as to use the resources provided without overwhelming the quitline's capacity. Dr. Husten also noted that states providing free medication have found that the offer of such medication often drives many calls to the quitline. In such cases, a newspaper article may have an effect similar to that of a broader media campaign.

With regard to funding sources, Dr. Husten explained that last year, for the first time, the CDC began providing small amounts of funding to states that did not have quitlines to enable them to conduct pilot studies. The Legacy Foundation matched these funds to some extent, but the funds were not sufficient to enable states to establish a quitline. She also commented that there may not be a separate call center in each state with a quitline. Currently, there are five major service providers that provide quitline services to most states. Some state legislatures, however, require the use of in-state resources. In such cases, the quitline usually is operated by a university or some other service within the state. These arrangements can have implications with regard to national promotions, because larger call centers have a greater capacity than smaller call centers to absorb the increased calls that may result from such promotional efforts.

Dr. Husten displayed a map showing the current distribution of quitlines among states, emphasizing that the map changes frequently as a result of funding changes that occur within states. It is hoped that the new initiative will enable further expansion of quitline services. The National Network of Tobacco Cessation Quitlines will conduct a series of five regional meetings during June and July of this year that will involve national CIS and OSH staff, state program managers, CIS Regional Coordinators, and service providers. The meetings will last for 1.5 days and will enable stakeholders to share information and discuss opportunities provided by this initiative, challenges involved in implementing it, and solutions to those challenges. The input provided by these meetings will be used to fine tune implementation plans for the initiative.

Ms. Bright discussed challenges involved in implementing this initiative. Coordination will be key in terms of promotion and understanding. For example, CIS staff must get to know and understand how the states operate and what services they provide, and state personnel must learn what the CIS is and does as well as the kinds of support it offers. Capacity and how it relates to promotional efforts will be another key challenge and will require very careful planning. The uncertainty of funding in a time of competing priorities for state legislatures is another issue. With regard to promotion, additional partners are being looked to for additional resources. The Departments of Defense and Veteran's Affairs (VA) have expressed an interest, and the VA has allotted funds toward the initiative. It is hoped that additional partners can be drawn from the private sector, pharmaceutical companies, and large corporations. The quality and standardization of quitline services represents another challenge. The North American Quitline Consortium is taking a leadership role in this area, along with other stakeholders. Evaluation will be another key challenge in the implementation of this initiative.

Questions and Answers

Dr. Niederhuber asked how the investments in this initiative will be monitored over time to ascertain whether goals are being accomplished and whether the CDC and state departments of public health are getting a good return on their investments. Dr. Husten replied that this will be a challenge because CDC and state monies are not the only funds being used to implement quitlines. Efforts are underway in conjunction with the North American Quitline Consortium to develop a minimum dataset to be incorporated into the RFA. She also noted that perhaps the ultimate information to be learned is whether the initiative allows more people to receive quitline counseling than was possible before the initiative; or whether state legislators may decide that they do not need to fund such services because it is being done at the national level, resulting in an actual loss of services. This would be one of the areas states are asked to monitor, in addition to call volume and quit rates.

Dr. Niederhuber commented that there always is some concern when monies are given to state departments of health because of the demands on such departments. Dr. Chen asked about the capacity to handle Spanish- and Asian-language inquiries. Dr. Husten noted that most states offer services in English and Spanish; some offer other language capabilities, depending on the size of the population needing them. California, for example, offers services in multiple Asian languages. Minnesota is exploring offering services in Hmong because the state has a large population that could use such services. Ms. Bright stated that one of the exciting aspects of the regional meetings is that they will provide a national view of what exists in terms of types of services provided, service capacity, and the like. Data from each of these meetings will be summarized.

Dr. Chen asked whether it would be technologically possible to transfer inquiries from Spanish- and Asian-language callers to specific lines (such as California) that may have the capacity to respond in that language. He also noted that a lesson learned from the 1-800-4-CANCER line is that it may be desirable to have a separate telephone number for Spanish-language callers to encourage more calls from Spanish speakers. He suggested that different telephone numbers for different languages, if possible, might be desirable. Dr. Husten responded that these are the types of comments and suggestions that coordinators hope will come from the regional meetings. In California, it was found with Asian-language callers that family members tended to call the main number, and smokers themselves tended to call the Asian-language number.

Dr. Samir Abu-Ghazaleh, Gynecologic Oncologist at the Avera Cancer Institute, asked what is being done to promote prevention in elementary, middle, and high schools, where the percentage of smokers has been increasing yearly, and why more is not being done to prevent children from starting to smoke as opposed to reaching adults who may have been smoking for 50 years. Dr. Husten responded that both groups must be addressed in a combined strategy. Children need to be targeted with prevention efforts to avoid continuing the cycle of having to help new generations quit smoking. Prevention is a main component of current funding, and traditionally, more funding has gone toward prevention and secondhand smoke than for cessation. On the other hand, to reduce the burden of disease within the next 30 to 50 years, current smokers must be encouraged to quit. Smoking rates among adolescents increased dramatically during the early 1990s until 1996 or 1997, but have fallen dramatically since then. A variety of interventions have been successful in preventing young people from starting to smoke. Price increases, for example, are a major factor in keeping youth from starting to smoke. Aggressive, targeted media campaigns also have been successful in preventing young people from starting to smoke. Community interventions combined with school prevention programs also are recommended. Combinations of all of these strategies are being recommended to states, because no single strategy is likely to be successful.

Dr. Jon Kerner, Deputy Director for Dissemination and Diffusion, DCCPS, noted that 17 tobacco control and prevention programs that have been tested in research funded by the NCI, CDC, or ACS are

listed on the Cancer Control PLANET Web Site. Interested states can download and use available non-copyrighted programs. The site also contains links to programs that are available for sale. This effort to move research-tested intervention programs into practice more quickly complements work that the CDC is doing at the policy and legislative levels.

Ms. Lydia Ryan, Service Line Clinical Director at Children's Healthcare of Atlanta/AFLAC Cancer Center, commented that her recent experiences in speaking to patients, families, and advocacy groups in Georgia about access to care and clinical trials suggest that cartoons might be a useful form of communication on the complicated topics involved in these issues (e.g., randomization, standard versus experimental arms and how they lead to improved outcomes, biology sampling at initial diagnosis, and tumor banking). These topics can be difficult to explain, especially when presenting to families from which multiple informed consents must be gathered at one time. She added that the cancer.gov and PLANET Web Sites are used frequently in Georgia.

XVI. *2004 ANNUAL REPORT TO THE NATION*—DR. BRENDA K. EDWARDS

Dr. Edwards informed Board members that the online version of the *2004 Annual Report to the Nation* was released that day (June 3). The print version will be released on July 1, 2004. This report is a collaborative effort between NCI, CDC, and many other partners. The American Cancer Society (ACS) is listed as the first author, and at least three NCI staffers contributed to the report. A key feature of the new report is that the number of cancer sites reported on has increased. For the top 15 sites, information is presented by race/ethnic group. Information on survival by cancer stage is included for one of the first times, including information on stage distribution for four major sites and by state. This information was provided by the CDC. In describing the sources of data for the report, Dr. Edwards noted that long-term trend data come from the nine registries that have been part of the Surveillance, Epidemiology, and End Results (SEER) Program since 1973. Information over the last 10 years comes from the expanded San Francisco and Los Angeles registries. In the future, that information also will come from expanded registries in Kentucky, Louisiana, and New Jersey. The report includes data from state registries that are funded by the CDC as well.

Dr. Edwards displayed ACS estimates for the 2004 U.S. cancer burden. These projections are based on data from incidence reports that were used to generate an expected number of cancers for the year 2000. Four cancers (prostate, breast, lung, and colon/rectum) represent more than 50 percent of all cancers. The report attempts to identify other sites and provides estimates on incidence, mortality, and survival rates. With regard to death, Dr. Edwards explained that there now are more deaths attributed to pancreatic cancer than to prostate cancer. Although prostate cancer death rates apply to men, pancreatic cancer deaths affect women as well, which adds to the total count for pancreatic cancer deaths. She characterized a slide showing cancers of all sites between 1975-2001 as perhaps the "hardest to interpret in terms of incidence." It appears to show an increase followed by a decrease during 1991-2001—she attributed the difference to reporting delays and concluded that, after adjusting for such delays, the overall incidence rates appear to be stable. Another slide portrayed incidence trends for men and women during the period 1975-2001. Recent incidence for men has been stable, but there has been an increase in incidence for women. Dr. Edwards commented that incidence is difficult to summarize because it varies and is susceptible to increases from early detection screening.

In discussing 10-year cancer incidence trends from 1992 to 2001, Dr. Edwards indicated that, based on SEER data, incidence of the following cancers appears to be increasing: all sites for females, breast, kidney and renal, liver and inflammatory bowel disease (IBD) for females, non-Hodgkin's lymphoma (NHL), melanoma, prostate (1995-2001), esophagus, thyroid, and testis. Incidence of the following cancers appears to be decreasing: lung for males, lung for females (not statistically significant yet but expected to be in the near future), colorectal, prostate (1992-1995), stomach, ovary and cervix,

oral cavity and pharynx, larynx for males, bladder, other skin and Kaposi's Syndrome in males. She noted that SEER areas are not totally representative of the United States because they do not include the southeast, where smoking rates are very high. In the past, however, SEER data have tended to be predictive of the future for the country as a whole. She also noted some ambivalence with regard to prostate cancer incidence. Prostate cancer rates increased rapidly between 1992 and 1995, but then declined. More recently, however, there has been an upswing in the rates from 1995-2001. In summarizing incidence over the last 10 years, Dr. Edwards noted that there is a discrepancy between the most recent trends and the trends during the past 10 years. Overall, incidence is declining, but the effects are mixed.

With regard to U.S. death trends for cancer of all sites, 1975-2001, Dr. Edwards noted that death rates for both men and women have declined for all cancers combined at a rate of approximately 1.5 percent per year since 1993. The decline for women alone is somewhat lower and began in 1994. Lung cancer death rates among women now are considered to be stable. The expectation is that lung cancer deaths in women will decline as the effects of tobacco control activities become apparent. With regard to overall 10-year U.S. cancer mortality trends for 1992-2001, death rates are increasing for: esophagus, liver, lung (for females; stable since 1995), and thyroid (for males) cancers. Death rates are declining for: all sites; lung (for males); colorectal; prostate; breast (for females); stomach; ovary, cervix, and corpus; urinary bladder; oral cavity and pharynx, gallbladder, larynx; and brain cancers.

In discussing lung cancer incidence and mortality 1975-2001 and long-term trends, Dr. Edwards noted that the decline in incidence rates for men was evidenced earlier in SEER data and then later in data from the country as a whole. There is some evidence of incidence decline for women as well, and the rate of decline is expected to increase. In more closely examining the trend among women, Dr. Edwards presented incidence rates by age group. These data show declines in incidence among younger women. Current data show declines across all age groups, including the oldest women, although mortality rates still are increasing among the older age groups. Dr. Edwards noted that, as incidence rates in the older age groups continue to decline, the mortality rates also eventually will decline.

Dr. Edwards highlighted recent increases in incidence of prostate cancer among white men during the late 1980s and early 1990s. Rates then fell in the 1990s and now are increasing again (prostate cancer incidence rates are considered to be very volatile). Mortality rates for both African Americans and whites, however, have been declining for some time. SEER data on cancer incidence rates by distant disease also show declines for both African-American and white men. This trend is seen as another contributing factor in decreasing prostate cancer mortality rates. In examining 5-year relative survival and incidence trends, Dr. Edwards noted that the 5-year relative survival rate for prostate cancer has been increasing over time. Data show that survival rates are increasing at least in part because cases increasingly are being diagnosed at earlier stages, when the disease is more localized.

With regard to female breast cancer, Dr. Edwards noted that there has been a long-term increase in incidence followed by a 0.5 percent per year increase since 1987. Mortality rates have declined by more than 2 percent per year since 1990. Survival rates have increased by 13 percent, and more than 60 percent of cases are being diagnosed with localized disease, which is more amenable to treatment. Concerning survival as it relates to stage at diagnosis for the years 1992-2000, the 5-year survival rate for early stage breast cancer is very good, and some 15 percent of breast cancer diagnoses are of *in situ* disease.

Both incidence and mortality have been declining for colorectal cancer in the period of 1975-2001. Incidence declines began in 1985 for women, and in 1986 for men. Small increases were seen during the 1990s, followed by further declines. Dr. Edwards indicated that the variations may be related to screening. Mortality rates for women began to decline before 1975; for men, mortality rates began to

decline in the mid-1980s. With regard to colon cancer, survival rates are linked to stage at diagnosis. For example, 16 percent of cases with Stage 1 disease have 96 percent survival; 27 percent of cases with Stage 2 disease have 84 percent survival; 22 percent of cases with Stage 3 disease have 59 percent survival, and 17 percent of cases with advanced disease have 7 percent survival. A substantial number of cases still are being diagnosed with more advanced disease, pointing to the need for increased application of early detection techniques when possible.

Dr. Edwards then discussed childhood cancer by race/ethnicity. Leukemia, lymphoma, and brain/central nervous system are the most frequent cancers in children, and patterns differ by race/ethnic group. Childhood cancer rates are highest among whites; rates for Hispanics also are high, partly due to high rates of leukemia. In comparing trends in 5-year relative survival rates for male children under 20 years of age during 1975-1979 and 1995-2000, Dr. Edwards noted that the overall survival rate increased by approximately 20 percentage points. Survival rates increased by more than 20 percentage points for bone cancer, leukemia, and NHL. For female children of the same age group during the same time periods, the overall survival rate increased by approximately 13 percentage points. Survival rates increased by more than 20 percentage points for leukemia and NHL. Some of the difference between rate increases for male and female children may be attributed to the cancer sites involved.

In comparing incidence and mortality rates for all cancers among different U.S. ethnic groups during the years 1975-2001, Dr. Edwards noted that rates generally tend to be higher for African Americans and lower for Hispanics, Asian/Pacific Islanders, and American Indians. Differences arise depending on whether incidence or mortality rates are being examined. It is challenging to interpret incidence and mortality rates for the different racial/ethnic groups because patterns differ; more time is needed to explore and understand these differences. Additional information is available by going to http://www.surveillance.cancer.gov and clicking on "Finding Cancer Statistics."

In discussing cancer incidence among males by race/ethnicity for 1992-2001, Dr. Edwards noted that the top three sites were prostate, lung, and colon and rectum. Hispanics were found to have relatively high prostate cancer incidence rates, Asians/Pacific Islanders showed a decline in lung cancer incidence rates, and all groups were found to have relatively high incidence rates for cancer of the colon and rectum. Among females during the same time period, the top three cancer sites were breast, lung, and colon and rectum. For breast cancer, increased rates of incidence were seen for Asians/Pacific Islanders and Hispanics, and white women had the highest rates of incidence. SEER data also showed a higher lung cancer incidence rate among African American women. U.S. mortality data for the women during the same time period, however, indicated that white women had the highest rates for lung cancer. Hispanic women were found to have the lowest rates of lung cancer mortality. Hispanic mortality rates for breast cancer were found to be higher than those for Asians/Pacific Islanders and American Indians/Alaska Natives.

Dr. Edwards indicated that the incidence rates for kidney cancer among both men and women combined increased during 1992-2001, with rates of kidney cancer incidence found to be highest among African Americans. Kidney cancer mortality rates were highest among American Indians and Alaska Natives. For urinary bladder cancer, incidence and mortality rates were highest among whites. Also during 1992-2000, NHL and leukemia incidence and mortality rates were highest among whites, liver cancer was highest among Asians/Pacific Islanders, pancreatic cancer was highest among African Americans, and thyroid cancer was highest among Asians/Pacific Islanders.

The *2004 Annual Report to the Nation* focuses on 5-year relative survival rates for the main cancer sites. Substantial increases in survival rates for men during the period 1992-2000 were seen for several major sites. Among women during the same time period, smaller increases were seen in survival rates for several major cancer sites. In addition, survival rates for both men and women were shown to

vary by race/ethnicity; white, non-Hispanic men and women tended to have better survival rates than did other race/ethnic groups. Dr. Edwards highlighted a new aspect of the current report: the estimation of relative risk among various racial/ethnic groups. A modeling approach was used to estimate how well an individual might fare after being diagnosed with cancer. For males, the relative risk of death versus whites was found to be 1.2 for Hispanics, 1.3 for African Americans and Asians/Pacific Islanders, and 1.7 for American Indians/Alaska Natives. For females, the relative risk of death versus whites was found to be 1.2 for Hispanics, 1.5 for African Americans and American Indians/Alaska Natives, and 1.0 for Asians/Pacific Islanders. These figures were derived from analyses of data by cancer site for the various racial/ethnic groups. Findings showed that although incidence or mortality rates may be higher or lower among various groups, additional disparities exist with regard to prognosis.

Improvements have been made in the estimation of cancer prevalence in the *2004 Annual Report to the Nation*. Cancer prevalence is defined as the "number of people or the proportion of people alive who have been previously diagnosed with cancer." The new estimate for 2001 is 9.8 million. This is the most popular statistic among the cancer survivorship community. In closing, Dr. Edwards noted that the new report contains much "good news," although there still are areas that need improvement. All of the data contained in the report are important and may serve various purposes. For example, comparing cancer mortality data for all sites together in 1992 and 2001 shows a 6 percent increase in cancer deaths in the United States during this period. Accounting for the facts that the population both grew (by 11 percent) and aged during this period, however, shows that the population size increased much more than did cancer deaths. In fact, the crude mortality rate declined by 4 percent. Accounting for the aging of the population during the 10-year period indicates an overall 8 percent reduction in age-adjusted cancer mortality rates. Overall, the picture is favorable, though there are areas in which the incidence of cancer and/or cancer mortality are increasing, and there are survival rate differences among racial/ethnic groups.

Dr. Edwards noted that the SEER Web Site (http://www.seer.cancer.gov) contains material from the Annual Report, as does NCI's Intranet. She also will respond to e-mail inquiries for additional information. Dr. Edwards closed her presentation by recognizing Dr. Constance Lebair Percy, who enjoyed a long and productive career and had been a pioneer in identifying smoking as a risk factor in cancer. She passed away this year at the age of 89.

Questions and Answers

Dr. Ramirez characterized the Annual Report as "excellent" and thanked Dr. Edwards for having incorporated the race/ethnic data. Dr. Edwards responded that more such data will be forthcoming and that the data will be refined in the future.

XVII. SUBCOMMITTEE REPORTS—DR. JOHN E. NIEDERHUBER

Dr. Niederhuber explained that the two active NCAB Committees met jointly on the first day of the meeting; therefore, there were no Subcommittee reports at this time.

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

Dr. Niederhuber asked Board members if there was any new business or if they had any future agenda items to suggest. Dr. Chen suggested that a future NCAB meeting include a presentation on future NCI-, NIH-, and DHHS-level activities related to the Cancer Health Disparities Progress Review Group, and what the Board can do to help accelerate the Group's recommendations. Dr. Clanton noted that such a presentation will be prepared and given at a future Board meeting. He added that the Secretary's Trans-HHS Disparity Council will hold a meeting on the next steps for the Cancer Health Disparity Progress Report. Results from that meeting also will be presented to the Board. Additional

possible future agenda items identified during the meeting include updates on: (1) NCI/NIAID activities focused on responding to radiological/nuclear terrorist attacks, (2) Center for Strategic Dissemination Initiatives, and (3) plans and progress of initiatives resulting from the NIH Roadmap.

Dr. deKernion asked about agenda setting and planning for future NCAB meetings. Dr. Niederhuber assured Board members that efforts will be made to incorporate more of the Board members' input in helping to set future agendas. He reminded members that a great deal of time was spent on agenda planning at NCAB's Strategic Planning Retreat. A template was developed to give some guidance to the NCI about certain reports that should be brought to the Board on a regular basis. Other presentations at Board meetings were timed for certain parts of the year (e.g., Bypass budget planning, etc.). He suggested that the summary report from this process be distributed to NCAB members in the week following this meeting. He also noted that adjustments in the approach taken to set the agenda for NCAB meetings can be made based on members' input. He asked that Board members submit any suggestions to himself or Dr. Gray.

Dr. Niederhuber also explained that within the month following this meeting, new NCAB members will be announced and their orientation process will begin. A meeting is planned in conjunction with the September NCAB Meeting to bring current and new members of the Board together for an orientation process. There also is the possibility of holding a brief meeting on the evening prior to Board meetings to discuss and review with NCI staff the agenda items and what each of those items might be seeking from the Board in terms of information exchange, comments, recommendations, and so on. Another approach may be to send a summary document to Board members 1 or 2 weeks before each NCAB meeting with information on the agenda items.

XIX. ADJOURNMENT—DR. JOHN E. NIEDERHUBER

Before adjourning the meeting, Dr. Niederhuber recognized and thanked Board members who were attending their last meeting. The 130th meeting of the National Cancer Advisory Board was adjourned at 11:37 a.m. on Thursday, June 3, 2004.

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Date John E. Niederhuber, M.D., Chair

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Date Paulette S. Gray, Ph.D., Executive Secretary