# DEPARTMENT OF HEALTH AND HUMAN SERVICES
# PUBLIC HEALTH SERVICE
# NATIONAL CANCER INSTITUTE
# 132nd NATIONAL CANCER ADVISORY BOARD

## Summary of Meeting
## November 30-December 1, 2004

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

**NATIONAL CANCER ADVISORY BOARD**
**BETHESDA, MARYLAND**
**Summary of Meeting**
**November 30-December 1, 2004**

The National Cancer Advisory Board (NCAB) convened for its 132nd regular meeting on Tuesday, November 30, 2004, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, November 30, 2004, from 8:30 a.m. to 4:00 p.m. The meeting was open to the public on Wednesday, December 1, 2004, from 8:30 a.m. until 10:30 a.m. The meeting was closed to the public from 10:30 a.m. until adjournment at noon. NCAB Chair Dr. John E. Niederhuber, Professor, Departments of Oncology and Surgery, University of Wisconsin-Madison, presided during both the open and closed sessions.

**NCAB Members**

Dr. John E. Niederhuber (Chairperson)
Dr. Samir Abu-Ghazaleh
Dr. James O. Armitage
Dr. Moon S. Chen, Jr.
Dr. Kenneth H. Cowan
Dr. Jean B. deKernion
Dr. Ralph S. Freedman
Dr. James H. French (absent)
Ms. Kathryn Giusti
Dr. David Koch (absent)
Dr. Eric S. Lander (absent)
Dr. Diana M. Lopez
Dr. Arthur W. Nienhuis
Ms. Marlys Popma
Dr. Franklyn G. Prendergast
Dr. Carolyn D. Runowicz
Ms. Lydia G. Ryan
Dr. Daniel D. Von Hoff

**President's Cancer Panel**

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

**Alternate *Ex Officio* NCAB Members**

Dr. Michael Babich, CPSC
Dr. Allen Dearry, NIEHS
Dr. Peter Kirchner, DOE
Dr. Raynard Kington, NIH
Dr. John F. Potter, DOD

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

Dr. Andrew von Eschenbach, 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
Mr. David Elizalde, Deputy Director for Management and Executive Officer, Office of the Director
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
Mr. John Hartinger, Acting Director for Management
Dr. Dinah Singer, Director, Division of Cancer Biology
Ms. Sandy Koeneman, Executive Secretary, Office of the Director

## Liaison Representatives

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

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## DAY ONE: TUESDAY, NOVEMBER 30, 2004

### I. INTRODUCTION, WELCOME, AND APPROVAL OF SEPTEMBER 2004 MINUTES—DR. JOHN NIEDERHUBER

Dr. Niederhuber began by asking for a moment of silence to remember patients with cancer and those who have passed away from cancer. He welcomed members and *ex officio* members of the Board; representatives of liaison organizations; members of the President's Cancer Panel (PCP); Dr. Paulette Gray, Acting Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI) and Executive Secretary, NCAB; other NCI staff; and members of the public. He introduced *ex officio* representatives and invited their active participation in the deliberations: Dr. Michael Babich, Directorate for Health Sciences, U.S. Consumer Product Safety Commission; Dr. Alan Dearry, Associate Director for Research Coordination, National Institute of Environmental Health Sciences; Dr. Peter Kirchner, Program Manager, Office of Biological and Environmental Research, Department of Energy; Dr. T.G. Patel, Program Chief, Oncology, Diabetes, and Kidney Diseases, Veterans Health Administration; Dr. Richard Pazdur, Director, Division of Oncology Drugs, Food and Drug Administration (FDA); and Dr. John Potter, Director, U.S. Military Cancer Institute, Department of Defense. 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 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 September 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 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. ANREW von ESCHENBACH

Dr. von Eschenbach, Director, NCI, greeted members and adjunct members of the Board, thanking them and previous members and acknowledging their contributions to the progress that has been made in the National Cancer Program since the passage of the National Cancer Act in 1971. He emphasized that all have an important role in providing guidance, leadership, and a critical interface with the broader community as the NCI continues to move aggressively towards achieving its 2015 challenge goal of eliminating suffering and death from cancer. He then asked for a moment of silence to pay tribute to a friend, supporter of, and collaborator with the NCI, Dr. John LaMontagne, Deputy Director, National Institute of Allergy and Infectious Diseases, who died suddenly on November 2. Before continuing with his report, Dr. von Eschenbach paid tribute to Dr. Hal Moses, retiring Director of the Vanderbilt-Ingram Comprehensive Cancer Center, for his role as a visionary and effective leader who brought together the entire community to create an extraordinary example of transdisciplinary and trans-institute integration within the Vanderbilt community. Dr. Moses also was recognized for his contributions to and leadership in NCI's Cancer Centers Program.

**Staff Appointments and Staffing News**

Dr. von Eschenbach announced that Dr. Ernest Hawk, Chief, Gastrointestinal (GI) and Other Cancers Research Group, Division of Cancer Prevention (DCP), has been appointed Director, Office of Centers, Training, and Resources (OCTR), Office of the Director (OD). Dr. von Eschenbach recognized and thanked Ms. Linda Weiss, who has been serving as Acting Director, OCTR, since January. Dr. Jaye Viner will be serving as Acting Chief, GI and Other Cancers Research Group within the DCP. Dr. Karen Antman, Deputy Director for Translational and Clinical Sciences, OD, will lead the search and recruitment effort for the new Director, DEA. With regard to other personnel actions, NCI individuals and groups were recognized for their accomplishments and the caliber and quality of their service at the annual NCI Award Ceremony on October 28. Finally, Dr. von Eschenbach recognized and congratulated all staff who contributed to the redesign of NCI's Web Site, cancer.gov, which was awarded a "Freddy" at a New York City health communications event. The award recognized cancer.gov as an outstanding Web-based communication vehicle.

Dr. von Eschenbach discussed challenges faced by the NCI in taking advantage of rapidly emerging opportunities in the field of cancer research in a rapidly changing environment. As the single largest organization in support of cancer research and progress, the NCI must apply and direct its force in a way that nurtures and serves the purpose of progress and change, while at the same time maintaining stability and continuity within the National Cancer Program. A portfolio has been defined with which the NCI will conceptualize and focus its efforts to effect the kind of rapid change that will achieve the pace and magnitude of progress needed to achieve the 2015 challenge goal. The portfolio of discovery, development, and delivery will emphasize the culture that must exist within the NCI and the development of its personnel and leadership. To that end, a recent survey of the culture within the NCI was launched to determine how the level of service and commitment that has been demonstrated can be supported in the future. Dr. David Elizalde, Deputy Director for Management, OD, will be working on mentoring strategies, rewards and compensation, and career development opportunities. Elements critical to future success will be emphasized in the NCI portfolio of discovery, development, and delivery. In the area of discovery, they are: (1) maintaining a critical mass of investigators to generate and develop new knowledge, both in terms of numbers and balance across the research continuum; (2) ensuring mechanisms and opportunities for funding; (3) focusing on training to engage young investigators in biomedical research; (4) creating a culture among investigators that moves toward transdisciplinary integration, which will engage investigators in the physical sciences to work in the biomedical arena. Examples of initiatives that exhibit NCI's leadership role in developing a work force suited for future challenges include the Integrated Cancer Biology Program, the Transdisciplinary Tobacco Research Programs, and the transdisciplinary initiative that is being developed in the field of energy balance.

Dr. von Eschenbach noted that many elements of the discovery continuum are vested in areas outside of the NCI but are critical to assuring that interventions are both created and rapidly developed such that they can have applications for patients and for the cancer initiative. Examples are the collaborations and cooperative initiatives such as the NCI-FDA Task Force, the work of NCAB's *Ad Hoc* Subcommittee on Biomedical Technology, the Nanotechnology in Cancer Program in collaboration with the FDA, National Institute for Standards and Technology, and the Department of Commerce. The nanotechnology initiative illustrates the importance of focusing on an area of emerging opportunity, but it was created in a way that defined platforms that will promote collaboration, integration, and transdisciplinary participation. Standards will be uniform and uniformly applied, and the regulatory components of this initiative will be aligned with the discovery components at the outset.

Within the delivery arena, the clinical research infrastructure is a high priority area in the NIH Roadmap Initiative and a critical focus for the NCI. The delivery component presents an opportunity to

apply state-of-the-art interventions to patients, but it also becomes a platform for discovery as it relates to the human biology of cancer, presenting an opportunity to unravel the complexities of human cancer in the clinical arena as well. Other components of NCI's clinical research program include the work of the Clinical Trials Working Group (CTWG), which has assessed the current clinical trials infrastructure with an eye to redesign and recreation that will adapt it to take full advantage of discoveries and developments of the future. The NCI/Center for Medicare and Medicaid Services Task Force is exploring opportunities to collaboratively create a health care infrastructure adapted to the kinds of interventions that are anticipated. This initiative builds on the progress being made in the Division of Cancer Control and Population Sciences' (DCCPS) collaboration with the Centers for Disease Control and Prevention (CDC) and the American Cancer Society to create the infrastructure for state cancer plans and community-based cancer control programs. A key element in the discovery, development, and delivery effort will be the central role played by NCI's intramural program, including resources that exist in the Center for Clinical Research (CCR), the Mark Hatfield Clinical Center, and the research program on the NIH Bethesda Campus and at the Frederick Cancer Research and Development Center. A high priority for the coming year will be a continued focus on opportunities for the intramural program to define its central role of contributing to the entire National Cancer Program, creating opportunities for integrating the intra- and extramural programs so that the whole becomes greater than the sum of its parts.

Emphasizing the importance of resources to future successes, Dr. von Eschenbach reminded members that even though opportunity, ideas, intellectual capital, and fiscal resources are at an all-time high, personnel and fiscal resources will be under serious restraint and constraint in the coming year. He reported that the entire Fiscal Year (FY) 2004 budget of $4.7 B has been obligated thanks to the last-minute effort of the NCI budget office staff to overcome problems associated with the continuing resolution in effect earlier in the year. More than 5,400 Research Project Grants (RPGs) were funded, including 1,493 competing grants. An RPG success rate of 24 percent was achieved for competing grants, and the R01 payline was maintained at the 20th percentile. The NCI is operating under a continuing resolution (at the FY 2004 level) in the absence of a FY 2005 budget appropriation. On January 11, the NCAB, Board of Scientific Counselors, and Board of Scientific Advisors (BSA) will meet with NCI staff to review the details of what is hoped to be the legislated budget for FY 2005. It is expected that the final NCI budget will not be sufficient to cover what already is committed for FY 2005. Dr. von Eschenbach expressed his commitment to the Board and the community that the NCI will continue to support the growth of new and innovative programs, but with the understanding that when a new investment is approved, something else must end. The difficult decisions will be made with ample consultation and advice, and in the context of a discovery, development, and delivery portfolio that will achieve the 2015 goal.

**Questions and Answers**

Ms. Kathryn Giusti, President, Multiple Myeloma Research Foundation, Inc., asked about NCI plans to address the problem of creating a critical mass of scientists and investigators while having a flat budget. Dr. von Eschenbach outlined strategies being considered by the NCI Training Commission under the leadership of Dr. J. Carl Barrett, Scientific Director, Center for Cancer Research (CCR), and Chief, Laboratory of Biospecimens and Cancer, NCI, including predoctoral initiatives to bring young people into the field, ways to stem the loss of seasoned clinical investigators, and partnering to cofund career development opportunities. The results of Commission deliberations and planning will be brought to the Board. It was suggested that information is needed on graduate student preferences with regard to careers in cancer and on the number who stay in the field after getting the training and degrees. Dr. Barrett noted that the training commission is charged with obtaining that information and meetings are planned to that end; he invited additional input from Board members. Dr. Niederhuber suggested that innovative ways be found to pull seasoned investigators back into training on the new technologies and have them re-enter

the research environment. Additional discussion focused on the role professional organizations can play by providing updates at annual meetings, the critical need for more teachers and more one-on-one mentoring, and the availability of both students and funding sources as a limiting factor in the educational component now that foreign students are increasingly returning home to work or staying home to study.

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

Dr. LaSalle Leffall, Jr., Charles R. Drew Professor of Surgery, Howard University College of Medicine, reminded members that the PCP is conducting a series of meetings on translating research to reduce the burden of cancer, in which barriers to progress are being examined. Results of the August 30 meeting held at the University of California, San Francisco Cancer Center were reported to the Board in September. Since then, meetings were held in Columbus, OH, on September 27, hosted by the Arthur G. James Cancer Hospital and Richard Solove Research Institute; and in Houston, TX, on November 1, hosted by the M.D. Anderson Cancer Center. The final meeting in the series will be held in New York City on January 24, hosted by the Memorial Sloan-Kettering Cancer Center. At these meetings, the Panel will examine the role of academic medical centers (AMCs), NCI-designated Cancer Centers, and Community Cancer Centers in translating research into practice and how these organizations fit into their larger communities. Specific consideration is being given to the peer review process, current and future infrastructure, financing and design of clinical research and clinical trials, and the potential for effective partnerships among academia, government, industry, and other entities. The Panel has heard from leading experts in industry, academia, and government, as well as clinicians, third-party payers, members of the media, and community representatives.

Dr. Leffall presented an update of key points emphasized by participants during their testimony. There was consensus that scientific discoveries are being made at an accelerating pace, but translation of knowledge and practice to clinicians, patients, and communities lags behind. AMCs were regarded as well suited to pursuing basic research, but not as well equipped to move discoveries along the development-delivery continuum. The Panel heard that a new paradigm of team science needs to be developed to address the imbalance that exists in the larger number of basic scientists compared with applied or translational researchers. The new paradigm would promote and reward collaborative study on common development-to-delivery goals. This may require re-evaluation of current grant review criteria, publication peer review processes, and reward structures, including university tenure and increased cross-disciplinary collaborations. The Panel also was reminded that the treatment of cancer is an incremental process, and the impact of discovering individual therapeutic drugs will not be as great as the sum of discovery and application of combination therapies. In this regard, the NCI was urged to continue its role as a public supporter of cancer drug research and development.

The process of moving discoveries from the laboratory into a development phase for possible application to human populations raised another set of issues. It was noted that research development tools need to be updated and improved, including animal toxicology, biomarkers, modeling structures, and surrogate endpoints. The inability to share more resources such as clinical data or tissue specimens was raised as a development barrier. It was suggested that new regulations under the Health Insurance Portability and Accountability Act (HIPAA) impede data sharing among clinical researchers and should be re-examined. Other legal barriers to the development of cancer drugs and therapies include patent law, other intellectual property (IP) issues, and conflict-of-interest (COI) issues. Participants proposed that key stakeholders be convened to consider development of patent research exemptions, IP agreement templates to foster and facilitate academia-industry negotiated collaborations, and clear COI definitions.

Dr. Leffall noted that numerous speakers testified to the need to address barriers to public participation in clinical trials and dispel misunderstanding about the cancer research enterprise.

Suggestions included: (1) better education about the process and complexities of biomedical research along the entire cancer care continuum, (2) involving local communities at early stages in the discovery-development process to alleviate negative perceptions and foster community-based research support, (3) promoting clinical trials as first-line treatments, and (4) addressing the clinical burdens of community physicians and oncologists participating in clinical research studies. It was emphasized at the Ohio meeting that preventing or delaying the onset of cancer is one of the greatest opportunities to reduce the burden of cancer. However, substantial developmental challenges exist in this area, including the length and cost of prevention trials and performing such research in healthy populations. Once promising discoveries have navigated the development process, the challenge of delivery to clinicians and communities remains. The translation of discoveries to all populations is not being achieved in a systematic manner. In particular, large populations of uninsured, medically underserved, and the working poor are not receiving the benefits of cancer discoveries. Participants asked whether there are cancer-related interventions, programs, and cutting-edge interventions that could be provided to these populations now. The question of how Cancer Centers can partner more effectively with community-based organizations to disseminate evidence-based findings also was raised. It was agreed that there must be committed funding and institutional support for Cancer Centers to succeed in and sustain their community outreach efforts. The establishment of partnerships between AMCs and community-based organizations was considered a critical link. The Panel heard from several AMCs that have developed community partnerships successfully. In closing, Dr. Leffall noted that it is the Panel's challenge and goal at the conclusion of these meetings to develop concrete recommendations for improving the way scientific findings are delivered to all of those affected by cancer.

**Questions and Answers**

Dr. Giusti suggested that a concrete plan should be developed for prioritizing the known barriers to translation and take immediate action, recognizing that issues like changing AMC reward systems and removing HIPAA barriers to clinical research will take longer. It was noted that the problem of changing the system of rewards in AMCs is being addressed at the NIH level, and that Web-based approaches to providing training are being explored by the NCI. Dr. James Armitage, Joe Shapiro Professor of Medicine, University of Nebraska, asked whether the Panel considered the effect on translation issues that a fairly dramatic reduction in resources going into the system might have. Dr. Leffall stated that the Panel at its last meeting decided to continue in the coming year to explore translation issues in light of the reduction in resources that is expected.

## V. LEGISLATIVE UPDATE—MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Policy Analysis and Response, OD, reported that the continuing resolution that was passed just before the end of FY 2004 expired on November 20, when Congress convened in a lame duck session. An omnibus bill (HR 4818) was put forward that included the Labor, Health and Human Services (HHS), Education Bill and eight other appropriations bills. The NIH and NCI amounts that appear in the omnibus bill are $28.6 B and $4.865 B, respectively, but these will be subject to a 0.8 percent across-the-board cut and additional taps. The conference report was passed by the House and Senate, and the bill is expected to be signed into law. During negotiations, two provisions were dropped that will have the effect of removing specific limits to attendance at foreign meetings by HHS employees and removing limits to the implementation of the rule shifting federal jobs to the private sector (A-76).

Next, Ms. Erickson reported on the status of health disparities and tobacco legislation of interest to the NCI. The Patient Navigator Outreach and Chronic Disease Prevention Act of 2004 (HR 918) authorizes the Health Resource Services Administration, working closely with the NCI and the Indian

Health Service, to provide grants for model programs to provide individuals of health disparity populations with prevention, early detection, treatment, and appropriate followup services for cancer and chronic diseases. It was passed by the House on October 4, but appeared unlikely to be acted on by the Senate before the 108th Congress adjourns. However, the two-thirds majority vote in the House may make it more likely to move if it is reintroduced in the 109th Congress. Twelve different tobacco bills were introduced in the 108th Congress; some with provisions for FDA regulation of tobacco products, and some authorizing a buyout of tobacco farmers. Late in the season, the tobacco-related provisions were included in the tax bill Jumpstart Our Business Strength, which was signed into law on October 22. The enacted version contained a $10 B buyout for tobacco farmers but left out FDA regulation of tobacco products. Subsequently, the Family Smoking Prevention and Tobacco Control Act was passed by unanimous consent in the Senate. This stand-alone bill providing the authority for FDA regulation of tobacco products appeared unlikely to move in the House before adjournment and will need to be reintroduced in the 109th Congress. The Cooperative Research and Technology Enhancement Act (CREATE) was incorporated into the omnibus appropriations bill and will become law when the omnibus bill is signed. CREATE addresses the issue of team science by making it easier for researchers and inventors to obtain patents for inventions stemming from work by multiple organizations.

Finally, Ms. Erickson presented an overview of the 109th Congress: (1) Republican majorities increased in both the House and Senate; (2) Senator Harry Reid is the new Minority Leader, and Senator Richard Durbin the new Minority Whip; (3) the Appropriations Committees in both the House and Senate will have new Chairs; (4) Senator Arlen Spector is expected to remain Chair of the Appropriations Labor, HHS, Education Subcommittee; (5) new leadership is expected for the Senate Health, Education, Labor, and Pensions Committee, which is the NCI authorizing committee in the Senate; and (6) in the House, Representative Barton is expected to remain as Chair of the Energy and Commerce Committee, NCI's authorizing committee; Representative Bilirakis is expected to remain as Chair of the Health Subcommittee; and the Oversight and Investigations Subcommittee will have a new Chair.

## VI. REPORT: CANCER BIOMEDICAL INFORMATICS GRID—DR. KENNETH BUETOW

Dr. Kenneth Buetow, Director, NCI Center for Bioinformatics (NCICB), reminded members that as part of its strategic planning, the NCI identified biomedical informatics as one of its key goals—to create a virtual web of interconnected data, individuals, and organizations that redefines how research is conducted, care is provided, and patients/participants interact with the biomedical research enterprise. The Cancer Biomedical Informatics Grid (caBIG) is NCI's first effort to begin the process of constructing this virtual network. It will be based on a common, widely distributed infrastructure and is being constructed using shared vocabulary, common data elements, and common data models to facilitate information exchange. A collection of interoperable (plug-and-play) applications is being developed. There is a commitment in the caBIG activity to make raw, published cancer research data available for mining and integration. Dr. Buetow stated that in its pilot phase, caBIG has the goals of: (1) illustrating that a spectrum of Cancer Centers with varying needs and capabilities can be joined in a common grid of communications, shared data, applications, and technologies; (2) demonstrating that the Cancer Centers, in collaboration with the NCI, will develop new enabling tools and systems that could support multiple Cancer Centers; (3) demonstrating that Cancer Centers will actively use the grid; and (4) creating an extensible infrastructure that will continue to be expanded and extended to members of the cancer research community.

Dr. Buetow reviewed the status of the caBIG pilot with respect to milestones and deliverables established at the outset of the program. In terms of organization, caBIG is organized in five workspaces, areas in which specific development activities take place, specific data contributions are made, and specific infrastructure is built. In addition to the five workspaces, caBIG is organized around three

strategic working groups, one addressing data-sharing and intellectual capital issues; one building training modules and support activities; and one for strategic planning, in which the caBIG community is directly involved in setting priorities, sequencing, and evaluating what needs to be delivered as part of caBIG. Special interest groups constitute the third component and the action-oriented space of the caBIG pilot. The caBIG community has organized itself around 23 special interest groups to work in and around the individual workspaces and focus on specific topics. Dr. Buetow noted that the special interest groups represent the character of the specific workspaces with which they are associated.

Turning next to the status of participation as a milestone and deliverable, Dr. Buetow reported that the pilot as it currently stands is targeted against NCI-designated Cancer Centers, and 44 have executed the base agreement that requires groups to commit to open source, open access, open development, and federation. The multiple roles within individual institutions vary depending on different workspaces and working groups in which the institutions are involved. Participation in the diverse collection of activities is facilitated by the NCI in the form of funding to help defray the costs. To date, there are more than 450 active participants in the caBIG pilot, and 196 teleconferences and 10 meetings have been held. In addition to the members, caBIG participation includes volunteer groups from academic centers and industry, and the management team is working to bring in additional partners and affiliates from other government organizations, NIH Institutes, and NCI programs.

As a measure of progress since the caBIG pilot kickoff in February 2004, products to date include the significant infrastructure already in place to support communication across the diverse and disparate collection of spaces that is the cancer research community. Important components include the caBIG Web Site for sharing products and participation. The site also provides a calendar of teleconferences and other caBIG events and an electronic forum for communication among the workspaces and special interest groups. A variety of electronic newsletters share caBIG activities and events so that the entire community can participate. Dr. Buetow noted that the most important products of caBIG to date may be: (1) the standards that have been developed, including vocabulary and data elements that are shared across the caBIG space; and (2) the creation and codification of caBIG compatibility guidelines, which will serve as templates for building new applications. Dr. Buetow cited other caBIG pilot products, including the significant progress coordinating the community within each of the individual workspaces. Examples of this are the template business processes developed in the Clinical Trials Management Space and the common clinical research information technology infrastructure. Other products are the clinical trials management systems that are being developed in collaborations with a variety of Cancer Centers. A tissue bank and pathology tools model has been developed and most of the architecture and use cases for the Workspace have been completed. The first generation of interfaces and the tissue repository will be available in early 2005 for wide distribution to the broader cancer research community. In the Integrated Cancer Research Workspace, a variety of tools are being created and shared through individual Cancer Centers. Gene annotation tools, data analysis and statistical tools, data management tools, informatics for proteomics, microarray repositories, and tools to manage biological pathways and bioprocesses will become available over the course of 2005.

Projects and components that plug-and-play in the caBIG infrastructure today include electronic data capture for clinical research, the open-source CaARRAY program to support microarrays as a repository and data analytic tool, an image portal that facilitates the sharing of histopathologic images, and a pathway database to permit exploration of multiple biological processes simultaneously. Dr. Buetow observed that although these individual components in isolation will be important in supporting individual bench and clinical researchers, the real success of the caBIG activity will be in bringing the data together and integrating them using the interoperability feature of caBIG. He cited as an example of this type of use the REpository of Molecular BRAin Neoplasia DaTa (REMBRANDT) application, which uses the caBIG infrastructure and the collaborative infrastructure being built by the NCI, NCICB, and

cancer research community to facilitate and empower translational research. The application brings together expression array, SNParray, proteomics, and clinical data in a common representation so that investigators can query across, synthesize, and integrate information from the various domains in an appropriate clinical setting.

As a final example of caBIG infrastructure use, Dr. Buetow described Mission Phoenix, the electronic regulatory submission infrastructure that is being developed in a collaboration among the NCI-FDA Interagency Oncology Task Force, caBIG community, and pharmaceutical manufacturer associations. A collection of modular-based components is being built to facilitate the interface of cancer research and the regulatory infrastructure. Project Firebird, the first activity in Mission Phoenix, is a strategic pilot to test the technical feasibility of automating and centralizing the investigator registration process. The electronic process will continue in parallel with existing processes until feasibility has been demonstrated. Pending the success of Project Firebird, the next steps in Mission Phoenix will be to: (1) develop and test a maturation process for moving from pilot technical feasibility studies into broad community engagement and sustainable production support; and (2) develop and pilot test additional components.

In closing, Dr. Buetow emphasized that caBIG is an open activity with broad participation outside the pilot activities. He issued an invitation for members to participate in and evaluate caBIG through the Web site, by attending open meetings, and by working independently on other applications and to explore how the biomedical informatics infrastructure, CaCORE, can be used.

Dr. Moon Chen, Associate Director, Cancer Prevention and Control, Davis Cancer Center, commended Dr. Buetow on behalf of the *Ad Hoc* Subcommittee on Bioinformatics Vocabulary, for the successful launching of caBIG. Noting that the work of the Subcommittee was thereby ended, he recommended dissolution.

**Motion.** A motion to dissolve the *Ad Hoc* Subcommittee on Bioinformatics Vocabulary was seconded and approved unanimously.

**Questions and Answers**

In response to a question about a reasonable timeline for judging the Firebird Project a success, Dr. Buetow explained that a February launch date is planned, to be followed by a 4-8 week period for evaluating whether feasibility goals have been met. In parallel, the caBIG community will be working to convert the pilot to a sustainable model. Dr. Ralph Freedman, Professor, The University of Texas M.D. Anderson Clinical Center, asked whether the credentialing process would require monitoring systems to ensure that only the best, validated information gets into the database. Dr. Buetow replied that there is great interest in creating uniform credentialing standards and sharing those in a certified fashion across the caBIG infrastructures. Dr. Kenneth Cowan, Director, University of Nebraska Eppley Cancer Center, expressed the view that the deployment of a usable clinical trials management system and provisions for updating, training, and education are high priorities for the clinical research community, and he asked about a projected timeline for that application. Dr. Franklyn Prendergast, Director, Mayo Clinic Comprehensive Cancer Center, agreed with these priorities and emphasized that the issue of intersite interoperability also is critical. He asked about the extent to which all activities are going to be platform independent. Dr. Buetow reiterated that platform independence was a fundamental principle in creating the caBIG infrastructure and will be strictly adhered to in newly built components. However, in recognition of the immediate and acute need for certain tools, some components may be delivered that may not be the ultimate solution but would solve important problems in the near term.

In response to another question, Dr. Buetow discussed ongoing interaction of the caBIG community with the NIH Roadmap Initiative, CDC, Veterans Administration, Office of the National Coordinator, National Center for Research Resources, and a variety of other groups to ensure minimal duplication of effort and maximum commonality of purpose and result. In response to the question about a timeline for a clinical trials management system, Dr. Buetow reminded members of the challenge of working with 60 Cancer Centers and their individual business processes. He explained that the template business processes that have been created represent the preliminary step of breaking a hard problem into solvable components. Those components are being built out systematically and will be shared across the community. Dr. von Eschenbach reminded members that the caBIG activity is occurring in conjunction with the work of the CTWG and the Departmental Electronic Health Initiative, and these initiatives ultimately will intersect. He thanked the Board for its ongoing commitment to and support of caBIG and the major investment of intellectual capital and financial resources it represents. In terms of a business model for bioinformatics, he explained that the strategy has been to create a front end that will make caBIG attractive for others to invest in and take on responsibility for downstream events. The actual business model is being developed with full cognizance of the constraints in terms of public-private partnerships.

## VII. ANALYSIS OF NCI-SUPPORTED BIOSPECIMEN RESOURCES— DRS. ANNA BARKER AND JULIE SCHNEIDER

Dr. Anna Barker, Deputy Director for Advanced Technologies and Strategic Partnerships, OD, noted that biomedical research stands at a point where progress toward personalized medicine, made possible by joining the fundamental digital code and human genome code, promises to be unparalleled. A real challenge beyond the connectivity of the community represented by bioinformatics initiatives is the material that will provide the information to drive the issue of personalized medicine. With patients moving into control of the genetic materials that will drive personalized medicine, the issue of biospecimens has become complicated by HIPAA, issues related to patient privacy, the connectivity of the community, and public education. Members were reminded of various national and international initiatives in biospecimen coordination that are attempting to develop best practices to support post-genomics research and of NCI efforts to analyze current resources and develop a strategy for optimizing biospecimen resource quality and access. In response to questions raised by the NCAB and BSA after a series of reports on biospecimen-related issues, NCI-supported biospecimen resources were inventoried with the goals of: (1) providing information on their makeup, quality, responsiveness, cost-effectiveness, and degree of patient protection; and (2) determining the extent to which these resources are aligned to optimize and accelerate the discovery, development, and delivery of genomic- and proteomic-based cancer interventions.

Dr. Julie Schneider, OD, NCI, who led the inventory effort, discussed the overall approach, which included a literature review, analysis of NCI Financial Management Branch data, and analysis of results from a questionnaire disseminated to NCI program staff and followup interviews. After discussing issues and limitations encountered in conducting the inventory and key definitions for standardizing the inquiry, Dr. Schneider presented the raw data and an analysis of the findings: (1) an annual NCI investment in biorepository-related programs of more than $50 M was identified; (2) 125 programs included in this study collected, maintained, and/or stored approximately 4 million biospecimens in FY 2003; (3) most programs collect frozen biospecimens and support genomic and proteomic research; (4) NCI-supported programs do not employ common standard operating procedures (SOPs) or quality control measures; (5) these programs support basic, epidemiologic, translational, and clinical trials research; and (6) these NCI-supported biorepositories are not coordinated to optimize resource value. Key barriers identified were lack of:
(1) common SOPs, standards, and management principles across the programs, which may limit the

ability to manage risks and limit the impact of research programs; (2)common definitions; (3) computerized, common access to information on specimens and cases; and (4) access to information on specimens available from the complete portfolio.

Dr. Barker presented draft recommendations and actions already underway to address the deficiencies that have been identified:

- Create a biorepository/biospecimen oversight and review group (in process).
- Convene a workshop to leverage NCI's prior work and expertise to harness broad input from the community (2005).
- Develop a pilot program to implement best practices-based SOPs and biorepository policies, potentially through the Cancer Centers and caBIG (early 2005).
- Implement a common bioinformatics platform to track and account for biospecimens through caBIG (in process).
- Develop a broadly accessible, comprehensive database inclusive of NCI-supported biospecimen resources (to be derived from the caBIG activity).
- Support a research program in biospecimen banking research to inform the development and refinement of SOPs.
- Facilitate tracking of budget information for human biorepository-related activities through NCI's financial database coding system.

Finally, Dr. Barker reminded members of the components in the National Biospecimen Network (NBN) vision for a new resource for biomedical research, which the NCI collaborated in developing. To accelerate post-genomic progress against cancer, the NCI should take a proactive role to ensure that the highest quality, systematically collected and maintained, privacy-protected biospecimens are provided to the cancer research community, working with the NIH Foundation as it implements the NBN and assuming a leadership role in the emerging international efforts in this area. She reported that a BSA committee has been established to work on the scientific aspects of the problem. The issues of ethics and the availability of genetic information, protection of patient privacy, and access have been identified as areas in which the widest gaps exist.

**Questions and Answers**

Dr. Prendergast identified the following issues of concern: (1) whether the relationship among the NBN, C-Change, and NIH initiatives would be collaborative or competitive; and (2) whether the rules for gaining access to biospecimen resources will be consistent or the same and who will be responsible for adjudication in each case. Dr. Niederhuber suggested that a national resource developed by working with community hospitals and providers in a parallel effort but outside the Cancer Center or academic research community should be considered. Ms. Giusti advised that the patient population should be educated about the biospecimen requirements for research advancement and allowed to become proactively involved in providing biospecimens.

## VIII. CURRENT NCI ETHICS ISSUES—DR. MAUREEN WILSON

Dr. Maureen Wilson, Assistant Director for Ethics, OD, and Deputy Ethics Counselor, NCI, provided an overview on changes in NIH ethics policies and outlook for review of outside activities and awards to NIH employees. She summarized a number of NIH actions to date. The NIH Ethics Program was restructured in January, centralizing the ethics reviews for all senior NIH officials to the office of Dr. Raynard Kington, Deputy Director and Deputy Ethics Counselor, NIH. Each Institute /Center will retain a Deputy Ethics Counselor to convey employee information to the NIH and NIH rulings to the employee as well as to manage activities not handled at the NIH level. The NIH Ethics Advisory Committee (NEAC) was established to provide peer review and assist Dr. Kington in his oversight for outside activities of all senior NIH officials, outside activities involving pharmaceutical or biotechnology industries, and lecture awards valued at $2,500 or greater. At the request of Dr. Zerhouni, a Blue Ribbon Panel of the Advisory Committee to the Director (ACD) was established to review the NIH ethics program and make recommendations to the Director. In addition, a database will be fully implemented to track ethics matters and functions on an NIH-wide basis. The formal training program will be expanded to include every NIH employee, and a random audit process will be initiated to increase oversight and management of potential conflicts of interest (to be conducted by the Assistant General Counsel, HHS). To increase the transparency of the conflict of interest process at the NIH, the number of employees filing public financial disclosure was expanded, NEAC review will continue, and evaluation criteria have been added to performance contracts of every supervisor. In addition, a database will be fully implemented to track ethics matters and functions, the formal training program will be expanded to include every NIH employee, and a random audit will be initiated to increase oversight and management of potential conflict of interest (to be conducted by the Assistant General Counsel, HHS).

Dr. Wilson reported that the NIH has prepared a draft of proposed regulatory changes to existing HHS regulations, as suggested by the Blue Ribbon Panel of the ACD. Three areas of focus in the draft are the nature of prohibited holdings, outside activities, and awards. Dr. Wilson briefed the Board on specific provisions in each of those areas, the implications of proposed changes, and possible issues that will arise and need to be addressed. The draft is under review by the Office of General Counsel, HHS, will be sent to the Office of Government Ethics for final concurrence or further change, and ultimately will require a notice of rule-making in the *Federal Register*. It is likely the draft regulation will be put in place as an interim regulation, to be followed by a period of public discussion. Affected individuals and the extramural community will have an opportunity to request exceptions or provide additional information. Following that 12-18 month period, a final rule would be issued as a supplement to the HHS Standards of Conduct regulation and would reflect what is hoped to be a consistent set of guiding regulations that would apply to the NIH.

## IX. MINISYMPOSIUM: INTEGRATION OF EXTRAMURAL AND INTRAMURAL RESEARCH PROGRAMS—DRS. J. CARL BARRETT, HOWARD FINE, ROBERT HOOVER, EDWARD TRAPIDO, MALCOLM SMITH, LEE HELMAN, DANIEL SULLIVAN, AND KAREN ANTMAN

### Introduction—Dr. J. Carl Barrett

Dr. Barrett noted that there are many interactions between the intramural program and the extramural program. The presentations during this session focused on cancer imaging, pediatric preclinical pharmacology, neuro-oncology, and molecular epidemiology and are representative of the types of interactions that are occurring. Dr. Barrett highlighted new opportunities that are available through the NIH Clinical Center. The intramural clinical program provides broad interaction between basic science, clinical science, and population research. The intramural program generates innovative approaches to cancer and focuses on small trials that test new concepts as opposed to existing therapies. The emphasis is on developing molecular target agents, both biologic and small molecule. Heavy

emphasis also is placed on developing new technologies for early detection, prevention, and therapy delivery. Understudied diseases in cancer also are emphasized, as are preclinical models and methods. This program provides an ideal venue for interdisciplinary and multidisciplinary training.

The NIH Clinical Center is unique because medical care is provided free of charge to each patient enrolled in NIH protocols. This includes coverage of patient travel for minors as well as parents or guardians. The Children's Inn and Edmund J. Safra Family Lodge provide on-Campus housing for families. This allows the Clinical Center to recruit patients from across the country. The Clinical Center includes more than 50 percent of the NIH-funded general clinical research center beds in the United States and enables the NIH to respond quickly to urgent public health needs and to provide long-term, stable funding for high-risk research that takes time to develop.

The intramural program has emphasized the development of technologies that are being applied to the molecular diagnosis of cancer, including imaging, proteomics, genomics, specialized therapeutic deliveries, pharmacokinetics, and pharmacodynamics. Imaging activities are an excellent example of interdisciplinary research because they involve clinicians working with such specialists as physicists, pathologists, molecular biologists, and chemists. With regard to genomics and proteomics, recent work has enabled the understanding of individualized cancers at the molecular level via signal network profiling and other techniques. In addition, laser capture microdissection was developed at the NIH. Other recent advances include the development of a centralized resource (infrastructure) for medical oncology, the collaboration between the NCI and FDA that has enabled medical oncologists to be trained in molecular oncology as well as regulatory issues relating to new therapies, and clinical bioinformatics activities.

Possible models for involving the NIH Clinical Center in additional collaborative studies with extramural investigators include accommodating clinical investigators while on sabbatical, developing collaborative studies for limited highly specialized procedures, protocol development and standardization efforts, and developing partnerships for multi-institute and multicenter efforts.

**The Glioma Molecular Diagnostic Initiative: A Cooperative Effort by the Extramural and Intramural Neuro-Oncology Community—Dr. Howard Fine**

Dr. Howard Fine, Chief, Neuro-Oncology Branch, CCR, NCI, highlighted the Glioma Molecular Diagnostic Initiative (GMDI) as an example of collaboration between various NCI components, including the intramural and extramural programs. He noted that the Neuro-Oncology Branch is a collaborative effort between the NCI, NIH's National Institute of Neurological Diseases and Stroke, the extramural community, the private sector, and patient advocates to develop novel diagnostic and therapeutic modalities.

Primary brain tumors are now the leading cause of cancer death in children and a leading cause of cancer death in people under the age of 54. The incidence of this disease in those over the age of 60 also has increased significantly. Glioblastoma is the most common of these diseases, and no significant improvement has been made in its survival in the last 20 years. Median survival is less than 1 year, and the few long-term survivors (especially children) face significant, lifelong neurocognitive effects. Thus, novel diagnostic and therapeutic approaches for this disease are needed desperately. Glioma classification represents a significant need. The current system is not consistently predictive of prognosis or biologically based, provides little insight into pathogenesis, and rarely is predictive of responsiveness to specific therapies. The solution may be to develop a publicly accessible, data-rich, biologically and clinically oriented molecular database that would address these limitations. The GMDI is an attempt to address this need.

The GMDI is a national study that is being conducted through two NCI-funded extramural brain tumor consortia and will accrue more than 1,000 patients with gliomas. Extensive prospective clinical data will be correlated with molecular data. The objectives of the study are to develop a biologically significant pathological classification system for gliomas that will enable prognostication and more informed decisionmaking, define new molecular targets, and produce a publicly accessible database that contains the analysis tools needed by all elements of the research spectrum. The database will be generated in two phases. The first phase involves a retrospective study of approximately 300 banked glioma specimens with a historical clinical database that will allow model building. The second phase will be a prospective study through NCI's Cancer Therapy Evaluation Program (CTEP) collaborative groups and select institutions that will accrue 1,000 to 1,500 gliomas with extensive clinical and molecular/genetic data and enable model validation. The prospective study will allow uniform collection of specimens and more accurate collection of clinical data. In addition, patients will be accrued to Phase I and Phase II studies of new molecular-targeted therapies such as epidermal growth factor receptor inhibitors. The GMDI will accrue data from tumor, blood, and plasma samples as well as clinical data. Samples will be analyzed for DNA, RNA, tumor core punch, and proteins. Both study phases are well underway.

Dr. Fine introduced REMBRANDT, a data warehouse that will encompass GMDI-generated data as well as data generated by extramural investigators funded to perform genomic profiling of brain tumors. REMBRANDT goals include producing a national molecular/genetic/clinical database of several thousand primary brain tumors that is fully open and accessible to all investigators, and providing informatics support to molecularly characterize adult and pediatric primary brain tumors and correlate these data with extensive retrospective and prospective clinical data. REMBRANDT leverages and is compatible with NCI's NCICB and caBIG infrastructure components and principles. It will be accessible to translation by users who are sophisticated in bioinformatics techniques and by those who are not, will allow the user to move easily between diverse data sets, and will allow simultaneous visualization of both clinical and genomics data. REMBRANDT will contain features designed to enable clinicians to enter a secure Web site and search for answers to specific questions with relative ease. Queries will result in user-friendly reports and graphs. Currently, the project is in the proof-of-concept stage, and the first data version, which will include a search and retrieval portal, is due for release soon. Full release is anticipated by next summer.

**Molecular Epidemiology Consortia—Drs. Robert Hoover and Edward Trapido**

Dr. Robert Hoover, Director of Epidemiology and Biostatistics in the Division of Cancer Epidemiology and Genetics, NCI, stated that NCI's extramural epidemiology program has a long history of extensive collaboration on etiologic studies of different cancer sites with many institutions. Recent advances in molecular science and technology have increased these collaborative efforts and have focused on the development of transdisciplinary consortia. These advances have led to extraordinary opportunities throughout the research enterprise in cancer and in basic, clinical, and population sciences, specifically in the area of molecular epidemiology, which is the incorporation of genomic and other molecular biomarkers into formal, robust epidemiologic research designs to promote understanding of the causes, natural history, prevention, and control of disease. Goals of molecular epidemiology include identifying susceptibility genes, identifying previously unrecognized exposures that are carcinogenic, examining the interaction of multiple genes in cancer causation, and exploring the relationship between genes and exposures in gene-environment interactions in cancer causation.

A formidable list of scientific and practical challenges accompanies these opportunities. The NCI has established several principles in an attempt to address these challenges in gene-environment studies.

These principles emphasize that studies be large and collaborative; employ rigorous methods of design, conduct, and analysis; incorporate validation in more than one study, ideally in diverse groups; and provide resources for the entire biomedical research community. These principles should be achieved through the development of consortia. Epidemiology is particularly suited to consortia because it is a highly collaborative discipline. The NCI is well positioned to develop and coordinate large-scale national and international collaborations and has been investing in three major types of consortia: (1) family-based,
(2) case-control, and (3) cohort. Family-based consortia have been in existence for some time and attempt to identify highly penetrant genes responsible for familial excesses and the genetic and environmental modifiers of these genes. Cohort and case-control consortia have been developed more recently.

The cohort consortium was established approximately 5 years ago and contains 23 population-based cohorts that involve more than 1 million individuals. Information exists for these individuals on risk factors, exposures, DNA, and other biologic specimens. Cohorts afford the opportunity to follow large groups of individuals over time and are especially suited for the study of common tumors such as breast and prostate. Multiple outcomes can be studied, as can mechanisms that may apply to more than one tumor type. The consortium's first study is of breast and prostate cancers and has been operating for 16 months. The study is comprehensively surveying 56 candidate genes that are in the steroid hormone pathway and in the insulin growth factor pathway. Results are expected to become available early in 2005.

Case-control consortia are well suited for studying intermediate- and lower-incidence tumors. They often are clinically based studies that involve large numbers of cases, identification of appropriate controls, and collection of biologic specimens and information. Case-control consortia have been formed or are forming in lymphoma, bladder, brain, breast, esophagus, oral, and lung cancers as well as for multiple myeloma.

Dr. Edward Trapido, Associate Director of the Epidemiology and Genetics Research Program, DCCPS, NCI, noted that the NCI has been providing funding above and beyond what each of the cohorts had on its own. Dr. Trapido indicated that the consortia have been scientifically interesting and stimulating to investigators; demonstrated the feasibility of studying gene-environment interactions by systematically collecting and pooling data from existing cohort studies; and promoted collaborations between population geneticists, biostatisticians, and epidemiologists. Other lessons learned from the consortia are that team processes inherently are more cumbersome; larger cohorts that already have developed separate studies may jeopardize their own funding or scientific investment; younger, nontenured investigators may be invisible in team science, thereby harming their career advancement; costs can be reduced within existing cohorts through collective purchasing of laboratory reagents; resources are produced that can be used by other investigators; increased collaboration with funders can be helpful; and such initiatives require extensive bioinformatics support.

Key issues to be addressed include how to allocate credit for publications to ensure that young investigators are not overlooked; funding for consortia development and for the consortia themselves, including the review of applications and funding mechanisms for awards; membership issues, including whether membership should be open or closed; and the availability of consortia resources to other investigators.

In response to a question about the development of metrics for assessing transdisciplinary research initiatives, Dr. Robert Croyle, Director, DCCPS, stated that work is progressing in this area. Efforts began with the development of evaluation measures for the Centers' initiatives and have

progressed to a second phase involving the development of draft instruments to assess collaboration and its effectiveness. It may be appropriate to include the issue of nontenured investigators in this assessment.

**Pediatric Preclinical Testing Program—Drs. Malcolm Smith and Lee Helman**

Dr. Malcolm Smith, Associate Branch Chief for Pediatrics, CTEP, Division of Cancer Treatment and Diagnosis (DCTD), NCI, stated that the Pediatric Preclinical Testing Program (PPTP) was announced in November in the *NCI Cancer Bulletin* under the headline of "Improving the Efficacy of Pediatric Cancer Trials." The purpose of the Program is to improve the efficiency with which more effective treatment is identified for children with cancer through clinical trials supported by the NCI. This is a collaborative effort that involves multiple extramural programs and Divisions, intramural researchers, and extramural researchers.

There is a need to prioritize the testing of new agents for children with cancer. Dozens of new agents and hundreds of combinations of agents potentially are applicable to the treatment of childhood cancers. Only a small subset of these agents, however, can be evaluated in Phase I studies, and even fewer can be evaluated in Phase II and III studies. More effective prioritization should enhance efficiency by increasing the discovery of more effective therapies for children with cancer. It is anticipated that a systematic approach to pediatric preclinical testing will result in increased selection of "active" agents.

Another key component of the PPTP will be to focus on pharmacokinetics and compare systemic exposures that are required for antitumor activity in mice for a particular agent with those that are achievable in humans. This will allow the elimination of trivial explanations for false-positive predictions from xenograft models. For targeted agents, the relationship between target modulation and activity will be evaluated to bring those agents into more rational clinical evaluations.

The PPTP is a research contract that builds upon past work by Dr. Peter Houghton at St. Jude's Children's Research Hospital. Other institutes that participate via subcontracts include the Children's Hospital of Philadelphia, Albert Einstein College of Medicine, Duke University Medical Center, Children's Cancer Institute Australia, and Children's Hospital of Los Angeles. The program will use an *in vivo* panel with 44 xenograft lines and an *in vitro* panel with 24 cell lines. The plan is to test 10-15 agents per year against childhood cancer panels for rhabdomyosarcoma and Ewing sarcoma, neuroblastoma, osteosarcoma, acute lymphoblastic leukemia, glioblastoma and non-glioblastoma, and kidney cancers.

The Pediatric Drug Development Group (PedDDG) advises Dr. Smith, PPTP Project Officer, on all aspects of PPTP performance, including technical issues related to *in vitro* and *in vivo* testing, regulatory and IP issues related to obtaining new agents for testing, identification of candidate agents for the PPTP to consider for testing, and prioritization of agents for PPTP testing. Members of the PedDDG include representatives from CTEP's Investigational Drug Branch, Clinical Investigations Branch, and Regulatory Affairs Branch; and NCI's Developmental Therapeutics Program and Pediatric Oncology Branch representatives.

IP issues associated with preclinical testing of proprietary agents are a key area being addressed in collaboration with NCI's Technology Transfer Branch. A model Material Transfer Agreement (MTA) was developed with pharmaceutical sponsors and academic institutions for use in agent testing. This model has been accepted by all of the institutions that will participate in the preclinical testing program. Dr. Sherry Ansher is CTEP's contact for inquiries about the MTA.

With regard to the molecular characterization of the xenograft and cell lines that will be part of the PPTP, this process is now underway through a collaboration with the intramural program and the Pediatric Oncology Preclinical Protein-Tissue Array Project. Dr. Lee Helman, Chief of the Pediatric Oncology Branch, CCR, explained that the aims of the program are to transcriptionally define preclinical pediatric xenograft models, determine the extent of similarity and difference between primary tumor tissue and the xenografts, and address the recurring problem in high-throughput transcriptional studies in which identified transcripts often do not correlate with protein levels. Findings to date indicate that the xenografts closely reflect primary tumor biology and that the tissue microarrays are performing as expected with diagnostic markers.

Dr. Helman concluded that well-founded prioritization decisions are key to future treatment advances in childhood cancer. In addition, the NCI is committed to testing the premise that systematic preclinical testing will allow validation and optimization of pediatric preclinical tumor panels useful for prioritization decisions.

**Cancer Imaging—Dr. Daniel Sullivan**

Dr. Daniel Sullivan, Associate Director, DCTD, NCI, and head of DCTD's Cancer Imaging Program, defined imaging as the *in vivo* characterization and measurement of biological processes at the cellular and molecular levels. Key aspects of the use of biomedical imaging to improve the development of cancer therapies include the use of imaging as an *in vivo* assay to select patients with the appropriate molecular phenotype for targeted drugs being tested (e.g., to enrich the trial population and promote a higher response rate), the potential to give therapy in the optimum biologic dose as opposed to the maximum tolerated dose (although this area is at the outer edge of current research), and the use of imaging to assess appropriate biologic endpoints to enable more timely changes in therapy if warranted. Potentially, these steps could lead to smaller clinical trials with fewer patients, early "go/no" decisions in Phase I and Phase II trials, as well as faster regulatory approval and shorter time to market.

The first step is to develop novel imaging probes. Ideally, these would be targeted probes. This is a major activity of the intramural program's new CCR Molecular Imaging Program. After an agent has shown feasibility, the next step is to accomplish the testing needed to acquire an investigational new drug (IND) application, including toxicity and mutagenicity testing. The Development of Contrast Imaging Drugs and Enhancers (DCIDE) Program was established to assist investigators in accomplishing the required testing. Under this Program, contractors conduct tests and the data are provided to the investigator for use in applying for an IND. Once an IND is available, Phase I and II clinical trials must be performed on the imaging agent. This is distinct from using the imaging agent in Phase I and II drug trials. Phase I trials of the imaging agent primarily show safety, and Phase II trials show that the imaging agent provides the information claimed. The NIH Clinical Center is an ideal facility in which to conduct many of these early studies.

Next, the agent is evaluated as a potential biomarker for use in drug trials. This implies the need to evaluate issues of standardization, reproducibility, and validation. The NCI is well suited to performing these types of studies because radiologists and others in imaging traditionally have limited experience with them. Some of this validation can be accomplished in animal models. After animal validation, there is an interest in evaluating some of the imaging tests in what might be called "Phase 0" therapy trials. These are early, pre-Phase I trials in which optimization of image acquisition parameters is the goal. Small numbers of patients, for example, could be brought to the NIH Clinical Center for multiple functional imaging studies at no cost to the patient and at little incremental or no cost to the Clinical Center. Such studies would enable determination of the most useful imaging methods and optimal parameters for subsequent Phase I or II clinical trials that could be conducted at the Clinical

Center or in CTEP-funded cooperative groups. Phase I and II therapy trials then would be conducted to validate whether the imaging method, in fact, is a useful biomarker for pharacodynamic, prognostic, or predictive information or perhaps as a surrogate marker. Ideally, those images subsequently could be used to develop image archives for secondary analysis.

Dr. Sullivan concluded that a sophisticated imaging informatics infrastructure is being established to support imaging in clinical trials groups and clinical centers, including the NIH Clinical Center. Images can be transferred to central archives operated by the NCICB and, with the agreement of investigators, to an archive that can be accessed by the general public. The advantages of these interactions between extramural and intramural programs include the exchange of expertise and advice among groups with different perspectives and backgrounds.

**Questions and Answers**

In response to a question, Dr. Sullivan noted that the NCI-FDA Interagency Oncology Task Force has been in existence for more than 1 year. Some of its subcommittees have been exploring various imaging techniques as surrogate markers. A January workshop also will focus on specific imaging techniques as surrogate markers. Dr. Antman asked the group for advice on overcoming the extramural community's apparent lack of knowledge about the new NIH Clinical Center and the resources available there. She noted that Dr. Barrett previously had mentioned the possibility of sabbaticals.

Dr. Prendergast highlighted the importance of defining the capacity of the Clinical Center to collaborate in a realistic way so as not to create a demand that is too large to be responded to properly. Dr. Armitage raised the issue of intramural and extramural groups competing for shrinking amounts of funding. Dr. Antman noted that a Blue Ribbon Panel had reported recently on the nature of Clinical Center research and had reached the consensus that the Clinical Center should conduct research that is cutting edge but not necessarily unique. She raised the issue of patients who come to the NIH for clinical trials and who suffer a disruption when they are sent back to their referring physicians. Dr. Barrett noted that although the intramural program has a strong record of success, there is a need to avoid duplication with the extramural world. He added that the Clinical Center no longer is divided into Institute-based programs, but is divided into program-based patient care units to enable more rapid shifting of resources among Institutes.

Dr. Sullivan noted that the NCI recently began developing new imaging agents. In addition, the DCIDE Program provides the opportunity for the NCI to bring in radiopharmaceuticals from a variety of investigators that are in the public domain and could be made available to others. The issue is complicated by the fact that the substances must be synthesized onsite. Once the INDs are received, such substances can be made available. Synthetic module boxes have been another limiting factor, and a Request for Proposals recently was issued under the Small Business Innovation Research (SBIR) Program to stimulate small businesses to create such boxes.

Dr. Niederhuber raised the issue of the need to stimulate imaging research in radiology departments across the country because radiologists traditionally have not been involved in laboratory research or translational research to a great extent. Dr. Sullivan indicated that efforts are underway to stimulate such interest among radiologists. Dr. Antman urged the group to consider collaborative efforts that might be established with the extramural community in the area of uncommon tumors. Although uncommon tumors account for about 50 percent of all cancer deaths, collaborative efforts in this area are lacking.

After the presentations on Day 1 of the meeting, NCAB members were given a tour of the NIH

Clinical Center.

## DAY 2: WEDNESDAY, DECEMBER 1, 2004

## X. INITIATIVE FOR DISCOVERY OF CLINICAL BIOMARKERS— DR. LELAND HARTWELL

Dr. Hartwell, President and Director, Fred Hutchinson Cancer Research Center, presented a plan for a program in clinical biomarker discovery. He began by explaining that for 30 years as a basic scientist, he had assumed that a better understanding of cancer would lead to better cures. However, as a Cancer Center Director for the past 8 years, Dr. Hartwell has been involved more closely with patient care and cancer outcomes and has been frustrated with slow progress in attaining our shared goal of reducing the burden of cancer and deaths from cancer. He has come to believe that the simplest and fastest way to reduce death from cancer is to detect cancer at an earlier stage, when a cure with current therapy often is possible. Over the past 2 years, Dr. Hartwell has worked at the request of Dr. von Eschenbach to determine whether recent advances in proteomics technology can be used more effectively to reveal biomarkers for the early detection of cancer.

Early detection can dramatically improve cancer outcomes. The 5-year survival rates for colorectal cancer, breast cancer, and most other solid tumors if detected localized or regionally are very high compared with disease that has metastasized. It is established that early detection can save lives. Screening through a colonoscopy, for example, can result in a 70 to 80 percent reduction in mortality from colon cancer. Competing strategies to reduce death from cancer in the next decade include new drugs or therapeutics and prevention trials, but both of these activities are very expensive compared with long time lines compared to the potential for early detection through biomarkers. Bringing a new drug to clinical use takes about $800 M and more than a decade, and prevention trials often cost $100 M. If there were a better way to discover biomarkers for early cancer detection, their validation can piggy-back on samples from previously conducted prevention trials like CARET and WHI. Moreover, diagnostic biomarkers can be multiplexed (unlike drug trials or prevention trials), dramatically reducing the cost for each biomarker tested.

The biomarker pipeline is currently limited by lack of knowledge about how to effectively use available technologies for their discovery. The Early Detection Research Network (EDRN) is capable of carrying markers through the validation steps, but the problem is that the pipeline is constricted at the discovery phase. It is reasonable but unproven to assume that biomarkers exist for early stage cancer. For example, in thyroid cancer and ovarian cancer, biomarkers exhibit high sensitivity and specificity. For heart disease, there are reliable markers of cardiac problems, and pregnancy is assayed through protein blood markers. Because tumor cells undergo necrosis, they must release their contents into blood. Also, new blood vessels around tumors are leaky and as a result, tumor DNA and other molecules enter the blood. The challenge is whether these markers can be detected sensitively and specifically.

Proteins are probably the most promising biomarkers. The information content increases from DNA to protein because the diversity increases by at least 10-fold and because proteins are the functional entities of the cell. For example, when a cell receives a single double-strand break, which would be very difficult to detect by any DNA technology, all of the proteins of the DNA damage response are phosphorylated so that dramatic amplification occurs at the protein level. The best technology for molecular biology is in analyzing the DNA level. Transcript analysis also is fairly sophisticated, but protein analysis is still in its infancy in terms of technology.

Several things are needed to use existing protein technology to detect biomarkers for early cancer

detection more effectively. First, because of technology limitations, a credible job in any single cancer site will require teams of investigators dividing up the large number of potential approaches. Collaboration among teams will require the development of a proteomics informatics platform that facilitates data storage, analysis, and sharing. It is likely that effective biomarkers will be at too low a concentration in blood to detect by direct screening with current technologies, but rather will require that candidate biomarkers first be discovered in the disease tissue. Candidates must be identified and quantitated. To quantitate and compare candidate levels in blood, a large number of antibody and peptide reagents will be needed that can be shared among investigators. Implementing these needs will greatly improve the potential for biomarker discovery. In addition, it is likely that technology advances will occur rapidly in proteomics and a program should incorporate mechanisms to identify and incorporate new technology improvements. Such a program would benefit therapeutics as well as early detection because therapy trials can be faster and more specific if biomarkers that reveal prognosis and therapeutic response are available.

The technological challenges include resolution (many species) and sensitivity (dynamic range). The major tools are mass spectrometry and two-dimensional gels. The best mass spectrometry technology can resolve individual peptides with very high mass accuracy and reproducibility and can identify the proteins that those peptides come from by tandem mass spectrometry. Nevertheless, a single analytical analysis can identify only about 100 proteins. The question is whether there is a rational way to apply this technical capacity to the problem.

By using a systematic "divide and conquer" strategy, current technologies can examine 1,000 biomarker candidates and 10,000 random proteins. No single laboratory will be able to do so effectively in any disease site; instead, a collaboration of many laboratories will be required to divide the problem and pool the data. With current technology, an analysis of 1,000 to 2,000 candidate biomarkers can be achieved. The steps in clinical biomarker discovery are to: (1) identify candidates in tissue and/or proximal fluids, (2) prepare reagents, and (3) quantitate and compare in disease versus normal plasma. Proteomic techniques must be used to identify informative proteins in the tissue. Reagents are needed to proceed from this first step to the serum or blood to compare cancer and noncancer tissue. Limitations in collaborations and reagents decrease the likelihood of significant discoveries.

Categories of proteins in cancer tissue that are very likely to be informative are differentially expressed, cell surface, prominent, secreted, glycosylated, processed by the proteases in the tumor environment, and phosphorylated. Angiogenesis is necessary for any solid tumor to grow beyond a few millimeters in size. Lymphogenesis—changes in the lymph system—occur very early in tumorigenesis. Proteins are involved in metastases, DNA replication, mitosis, proteases, and wound healing. The most common transcription signature of all tumors is a wound-healing signature. A reasonable approach to the problem would involve identifying 100 proteins using proteomic techniques for some of the categories and bioinformatics approaches for others to arrive at 1,000 proteins. Current technology can identify 1,000 candidates and determine whether they are biomarkers for early disease detection in the blood. The analysis requires an investment in reagents at different stages in the process. The major reagents are: (1) antibodies that recognize either proteins or peptides, and (2) reagents that can be used for mass spectrometry. These reagents are critical to the process. The discovery process is floundering at the present time because the community does not have these reagents at hand. The cost of this protocol is about $18-20 M. The major portion of the cost is producing the reagents. Because the reagents are a reusable resource, the cost decreases to approximately $4 M at the next cancer site.

The goals for a coordinated clinical proteomics and biomarker discovery initiative are to: (1) develop a publicly available informatics platform that permits data storage, analysis, searching, and gene comparison; (2) establish a consortia of collaborating laboratories to discover biomarkers in

particular cancer sites and for particular classes of biological molecules; and (3) establish repositories of reagents for clinical biomarker discovery. Other goals include developing a technology assessment site to compare competing technologies head-to-head on identical samples from mouse models of cancer; identifying technology innovations through pilot grant funding and NCI programs; encouraging academic and industry collaborations; and encouraging engineering to improve reproducibility, throughput, and automation. The following needs exist: (1) an informatics core, a technology core, and a reagents core for technology integration and assessment; (2) a consortia of investigators working on specific cancer sites for technology application; and (3) pilot projects and biomarker mines for new technology development.

Translating discovery to clinical applications starts with identifying markers of cancer from relatively advanced cancer and testing them to determine their usefulness for early detection. For example, frozen blood samples taken before clinical symptoms of a disease appeared are valuable for validating early detection markers. The pharmaceutical industry then could be convinced to support analysis of the same group of biomarkers for therapeutic response in well-designed therapeutic trials. After more biomarkers flow into the pipeline, the EDRN is well prepared to validate those biomarkers. Protein biomarkers will be useful for early detection to save lives, and they will be very useful for molecular-targeted imaging and therapy.

**Questions and Answers**

Dr. Giusti asked whether industry has expressed an interest in the area of reagents and whether any group is currently acting as a consortium to look at a specific disease. Dr. Hartwell responded that he has just begun to look at potential sources that could provide reagents on a contract basis, and academic activities in other countries show some progress in this area. He also explained that he has been working with a variety of groups, both nationally and internationally, to study specific diseases. He mentioned that the NCI has an opportunity to lead an international program by providing informatics support and reagents.

Dr. Daniel von Hoff, Director, Translational Genomics Research Institute, asked whether amplification techniques have been explored. Dr. Hartwell replied that a number of amplification techniques have been used recently, including nucleic acid amplification and proximity-based amplification. A variety of amplification methods should be tested head-to-head, but there is every reason to expect that it would be possible to obtain a signal from very small numbers of proteins. In response to a question about pancreatic cancer, Dr. Hartwell called for vetting different cancers to determine where to start as a proof of principle.

Dr. Freedman asked whether NCI's intramural program is well positioned to advance the field or provide some of the needed components. Dr. Barker responded that work on early detection is underway in the clinical arena for diffuse B-cell lymphoma. In addition, extensive interactions are ongoing between the intramural and extramural communities. These interactions tend to leverage the intramural community's strong foundation in basic science and translational science. An advanced research technology program exists on the Frederick Campus that enhances the basic discoveries made in proteomics and applies them on a larger scale. The resources developed in association with the intramural program can play a value-added role in this endeavor. A large contract on the Frederick Campus can be tasked with specific types of technology development and translational options that historically have supported both the intramural and extramural communities and can be further tasked to address expanded options or initiatives. There is great flexibility and a real desire on the part of the intramural community to leverage some of these platforms in basic science, clinical science, and technology with some

components of the extramural community.

Dr. Arthur Nienhuis, St. Jude's Research Hospital's Department of Hematology and Oncology, asked about the use of the Human Genome Project model, which relied on establishing centers for sequencing the genome versus R01 funding mechanisms for individual investigators. He also asked whether early detection will necessarily result in improvement. Dr. Hartwell responded that a great deal of coordination is needed for this activity; therefore, an R01 mechanism is not appropriate. He noted that the potential impact is great compared with the relatively modest investment; therefore, it is worth the effort. Cervical, colon, and breast cancers reveal that early detection can save lives, and protein markers are potentially as informative as imaging technologies. Dr. Jean deKernion, Professor and Chairman, Department of Urology, University of California, Los Angeles School of Medicine, noted the importance of investing in technology. Dr. Hartwell responded that technology development will occur rapidly and that existing technology is worthwhile right now. Dr. deKernion asked whether enough laboratories are dedicated to proteomics to launch the effort or whether a great deal of further seeding and grant-type funding is needed to stimulate the effort. Dr. Hartwell noted that most institutions now have a proteomics expert and machines that perform very well. The technology is even disseminated broadly internationally, and the manpower also is sufficient to the task.

Dr. Niederhuber asked Dr. Hartwell to comment on the possible integration with nanotechnology efforts. Dr. Hartwell remarked that nanotechnology is very broad based. The most directly relevant application is in developing agents for imaging and for delivery of therapeutic agents to tumors. This type of initiative would provide the agents that the nanotechnologists need to carry to the next step.

Dr. Prendergast asked whether the development phase can take place within the academic sector or whether it will be an industry responsibility. Dr. Hartwell responded that the technologies used for discovery of biomarkers are very likely to be different from the technologies used in clinical laboratories to apply those discoveries. The discovery process can be carried out in academic laboratories, but the ultimate development of more effective technology platforms for clinical applications of proteomics likely will occur in the industrial sector. Dr. Prendergast agreed that the academic sector will play a major role in the areas of discovery and validation, and the development phase will occur in industry. He also asked whether the approach will be detection and quantitation or pattern recognition. Dr. Hartwell responded that most of the useful prognostic information coming out of transcript arrays is pattern recognition because the relative differences are small. Proteins change qualitatively when physiology changes; a half-dozen proteins are likely to be very informative about a particular type of cancer.

Dr. Armitage noted that successful completion of this project will help to answer important clinical questions regarding when the proteins appear. Dr. Barker announced that 8-10 centers around the country are moving in the right direction in terms of proteomics, and this initiative will be successful in terms of discovery expertise. Some very unusual mechanisms will be pursued for this program. Technology development will take place in the private sector once sufficient numbers of robust biomarkers are identified and validated for a business model.

Dr. von Eschenbach noted that the NCI will look to its boards for advice, guidance, advocacy, and support during the implementation phases of the initiative. Implementation of the initiative will require a realignment of restricted resources, and tough implementation strategies will require the expenditure of political capital. He explained that the NCI must not simply provide resources; it must exercise leadership to create components and drive the coordination and integration of the components. The Institute has experience in creating consortia and collaborative relationships across different Centers of Excellence and will amplify and expand those efforts. Dr. von Eschenbach explained that examining opportunities in prevention, early detection, and elimination of disease at its earliest possible stages of

development is essential to the 2015 goal.

Dr. Niederhuber thanked Dr. John Gallin, the Director of the NIH Clinical Center, for the previous day's tour and its resulting insights into the clinical research developments at the NIH.

## XI. P30/P50 IMPLEMENTATION PLAN: SPOREs—DR. KAREN ANTMAN

The Specialized Programs of Research Excellence (SPORE) Program began in 1991, with $20 M from Congress. The Program has expanded a number of times since its inception. Current funding is approximately $130 M. SPOREs support interdisciplinary teams dedicated to translational research focused on a specific human cancer or group of cancers. In 2003, the P30/P50 Working Group recommended program changes, and the SPORE Program guidelines currently are under review. At present, SPORE programs include approximately 300 translational, 230 developmental, and 115 career development projects, for a total of more than 640 projects that represent 21 thematic categories. Clinical orientation includes 347 therapy and treatment projects, 65 prevention programs, and 527 biomarkers projects. The SPOREs are integrated with other NCI programs.

The P30/P50 Working Group recommended various SPORE changes, including the following:

- *Slow SPORE growth to the rate of R01s.* In 2004, no cost-of-living adjustments were made for the first time because of the budgetary situation. This is expected to continue in 2005. Only program announcements (PAs) that already had been published were acted on, and eight new SPOREs were funded for a total of an additional $5 M. The budget for 2005 is expected to be flat, and PAs will be issued only for renewals. Funding for new programs will be based on paylines and programmatic needs, particularly priority scores and balancing the burden of disease. In an effort to control costs, new SPOREs will be capped at $2.5 M instead of $2.75 M as in the past. The same number of research projects (four) has been accessioned. Prevention and population science projects have been changed to "highly encouraged" for less common tumors.

- *Allow SPOREs to focus on pathways, mechanisms, and population research.* Although there are many mechanisms for pathways, mechanisms, and population research, SPOREs are the only disease-associated mechanism, so it was decided to continue the organ/disease orientation for SPOREs. Programmatic coordination will be encouraged among researchers working on the same pathway or disease mechanism.

- *Fuse cores and check for overlaps with Cancer Centers.* The SPOREs program will encourage highly specialized, cutting-edge cores. Cancer Center and SPORE cores that are similar will have to be justified.

- *Develop a SPORE parent committee to review applications across sites.* A standing Special Emphasis Panel (SEP) is being established, along with a two-tier review process. The SEP will meet three times per year, and members will serve 4-year terms. Initial members will be appointed for 1- to 3-year terms so that balanced rotations can begin. Two members will be appointed from each organ site, yielding a broad range of scientific expertise. At least 50 percent will be SPORE investigators, especially senior investigators with multidisciplinary expertise, including translational science.

- *Use a science priority score rather than the number of slots for a particular disease.* The burden of disease (e.g., mortality, incidence, years of life lost) also will be considered, along with other NCI funding.

- *Create a national clinical research and informatics system.* This system should be integrated appropriately with Cancer Centers, industry, and other interested parties. Collaboration with caBIG is underway, as is collaboration with the Clinical Trials Committee.

Other changes include the fact that the NCI now is emphasizing data sharing, as is all of the NIH, and applicants will need to develop a plan for data sharing across SPOREs and with other mechanisms. Applicants also will need to develop an IP management plan. In addition, more credit will be given for collaborations when projects are evaluated, and the pathology and specimen banking cores will be strengthened with tissue annotation and clinical data and parameters. A final recommendation was to describe and quantitate the contributions of the P30/P50 programs annually. This process is underway.

**Questions and Answers**

Dr. Nienhuis, one of the Chairs of the P30/P50 Working Group, asked about measuring the impact of the Program, perhaps by assessing the number of projects that achieve the goal of translating research into clinical application during the 5-year funding period. Dr. Jorge Gomez, Chief of NCI's Organ Systems Branch, responded that a recent review of SPOREs shows that the Program is meeting these goals. This will continue to be assessed annually. Dr. Barker noted that many of the interventions have resulted in partnerships with industry. She also indicated that more thought should be given to developing the infrastructure needed to support this process. In the future, increased development of partnerships may be the way to address this issue. Scale-up and validation are two of the areas to be addressed. Dr. von Hoff suggested an open auction process as a way to involve industry in this effort. Dr. Barker suggested the cofunding of some SPOREs and establishing an SBIR-like mechanism as possible approaches that may enhance the auction concept.

Dr. Prendergast noted the difficulties involved for institutions in adhering to current Good Manufacturing Practices (GMPs) requirements and the hidden costs that often are involved. He cited good tissue practices and good laboratory practices for cellular-based therapies as examples of items that academic institutions can accomplish that are not likely to be fundable through industry. He suggested holding a workshop on this subject to include participants from the biotechnology, biopharmaceutical, and academic communities, along with groups that have successful GMP efforts. Dr. Barker said that such a workshop has been planned for next March and will be announced shortly.

## XII. NCAB SUBCOMMITTEE DISCUSSION—DR. JOHN NIEDERHUBER

Dr. Niederhuber drew the members' attention to handouts including a tentative list of NCAB Subcommittee assignments and descriptions of each Subcommittee. Currently, members are assigned to at least two Subcommittees. He asked members to review the materials to be sure that they are comfortable with their assignments. Members should contact Dr. Gray regarding any changes. The Subcommittees are important to the activities of the Board and often are used in creating work groups and task forces that expand the Board's ability to reach out to the scientific community. Board members are free to attend meetings of Subcommittees other than those to which they are assigned, and also may participate in Subcommittee presentations that are made before the Board as a whole.

Dr. Niederhuber commented that the Subcommittee structure and activities are heavily dependent on the Executive Secretaries who are assigned to each Subcommittee from NCI staff. He expressed his appreciation for the time and effort these staff extend to the Subcommittees. Dr. Gray noted that in the past, Subcommittee meetings generally were scheduled on the evening or night before a Board meeting.

That did not work well, and Subcommittee meetings now are scheduled during the first regular day of the Board meeting. Subcommittee assignments were made with the idea that two or three Subcommittee meetings could be scheduled at the same time.

Dr. Niederhuber encouraged night-before meetings as the best time to accomplish the needed work. They require traveling so as to be at the meeting by 7:30 p.m. on the prior day. Conference calls may be another option. Dr. Prendergast emphasized the importance of making the work of the Subcommittees substantive. He also encouraged the use of e-mail and conference calls to the extent possible.

The open session was adjourned at 10:37 a.m.

## XIII. 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.

There was a review of intramural site visits and tenured appointments, committee discussions, and recommendations. There also was a discussion of personnel and proprietary issues. Members absented themselves from the meeting during discussions for which there was potential conflict of interest, real or apparent.

## XIV. ADJOURNMENT—DR. JOHN NIEDERHUBER

There being no further business, Dr. Niederhuber thanked Board members for attending and participating in the meeting. The 132nd meeting of the National Cancer Advisory Board was adjourned at noon on Wednesday, December 1, 2004.