

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
166th NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
September 9, 2014**

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

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
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The National Cancer Advisory Board (NCAB) convened for its 166th regular meeting on 9 September 2014, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, 9 September 2014, from 9:00 a.m. to 11:40 a.m. and 1:30 p.m. to 5:20 p.m., and closed to the public from 11:40 a.m. to 1:30 p.m. The NCAB Chair, Dr. Tyler E. Jacks, Director, Koch Institute for Integrative Cancer Research, David H. Koch Professor of Biology, Massachusetts Institute of Technology, presided during both the open and closed sessions.

NCAB Members

Dr. Tyler E. Jacks (Chair)
Dr. Victoria L. Champion
Dr. David C. Christiani
Dr. Marcia R. Cruz-Correa
Dr. Kevin J. Cullen
Dr. Judy E. Garber
Mr. William H. Goodwin, Jr.
Dr. Waun Ki Hong
Dr. Elizabeth M. Jaffee
Dr. Beth Y. Karlan
Ms. Mary Vaughan Lester (absent)
Dr. H. Kim Lyerly
Dr. Olufunmilayo I. Olopade
Dr. Jennifer A. Pietenpol
Dr. Mack Roach, III
Dr. Jonathan M. Samet
Dr. Charles L. Sawyers
Dr. William R. Sellers (absent)

Alternate *Ex Officio* NCAB Members

Dr. Michael A. Babich, CPSC (absent)
Dr. Vincent J. Cogliano, EPA (absent)
Dr. Michael Kelley, VA
Dr. Aubrey Miller, NIEHS (absent)
Dr. Richard Pazdur, FDA
Dr. Craig D. Shriver, DoD
Dr. Michael Stebbins, OSTP (absent)
Dr. Marie Sweeney, NIOSH (absent)
Dr. Lawrence Tabak, NIH (absent)
Dr. Richard Thomas, DOL
Dr. Sharlene Weatherwax, DOE (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Harold Varmus, Director, National Cancer Institute
Dr. Jeff Abrams, Co-Director, Division of Cancer Treatment and Diagnosis
Dr. Stephen Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Dr. James Doroshow, Deputy Director for Clinical and Translational Research
Dr. Daniela S. Gerhard, Director, Office of Cancer Genomics
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Peter Greenwald, Associate Director for Prevention
Dr. Ed Harlow, Special Assistant for Science Planning
Dr. Lee Helman, Scientific Director for Clinical Research, Center for Cancer Research
Dr. Warren Kibbe, Director, NCI Center for Bioinformatics and Information Technology
Dr. Barry Kramer, Director, Division of Cancer Prevention
Dr. Douglas R. Lowy, Deputy Director, National Cancer Institute
Mr. Patrick McGarey, Co-Acting Executive Officer
Dr. Alan Rabson, Deputy Director, National Cancer Institute
Ms. Donna Siegle, Co-Acting Executive Officer
Dr. Dinah Singer, Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis Staudt, Director, Center for Cancer Genomics
Dr. Joseph Tomaszewski, Co-Director, Division of Cancer Treatment and Diagnosis
Dr. Ted Trimble, Director, Center for Global Health
Mr. Michael Weingarten, Director, Small Business Innovation Research
Dr. Linda Weiss, Director, Office of Cancer Centers
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Robert Wiltrout, Director, Center for Cancer Research
Ms. Joy Wiszneaukas, Executive Secretary, Office of the Director
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy

Liaison Representatives

Ms. Carolyn Aldige, Cancer Research and Prevention Foundation
Dr. Jeff Allen, National Cancer Institute, Director's Consumer Liaison Group
Ms. Paula Bowen, Kidney Cancer Association
Mr. William Bro, Kidney Cancer Association
Dr. Carlton Brown, Oncology Nursing Society
Dr. Carol Brown, Society of Gynecologic Oncologists
Ms. Pamela K. Brown, Intercultural Cancer Council
Ms. Suanna Bruinooge, American Society of Clinical Oncology
Mr. George Dahlman, Leukemia and Lymphoma Society
Mr. Matthew Farber, Association of Community Cancer Centers
Dr. Margaret Foti, American Association for Cancer Research
Dr. Leo Giambarresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Ms. Christy M.P. Gilmour, American Academy of Orthopaedic Surgeons
Ms. Ruth Hoffman, Candlelighters Childhood Cancer Foundation
Dr. Gerald F. Joseph, Jr., American College of Obstetricians and Gynecologists
Ms. Rebecca A. Kirch, American Cancer Society
Dr. Steven Klein, National Science Foundation
Dr. W. Marston Linehan, Society of Urologic Oncology

Mr. Richard Martin, American Society of Therapeutic Radiology and Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education
Ms. Christy Schmidt, American Cancer Society
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Ms. Pamela Wilcox, American College of Radiology
COL (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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THURSDAY, SEPTEMBER 9, 2014**I. CALL TO ORDER AND OPENING REMARKS—DR. TYLER E. JACKS**

Dr. Tyler E. Jacks called to order the 166th NCAB meeting. Dr. Jacks welcomed members of the Board, *ex officio* members of the Board, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Dr. Jacks reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to approve the minutes of the 23–24 June 2014 Joint Board of Scientific Advisors (BSA)/NCAB meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. TYLER E. JACKS

Dr. Jacks called Board members' attention to future meeting dates listed on the agenda.

III. NCI DIRECTOR'S REPORT—DR. HAROLD E. VARMUS

Dr. Harold E. Varmus, Director, NCI, welcomed members and stated that the next NCAB meeting in December 2014 would be held jointly with the Board of Scientific Advisors (BSA). Dr. Varmus said that the NIH is improving recordkeeping procedures following the recent discovery of an uncatalogued select agent in the U.S. Food and Drug Administration (FDA) laboratory on the NIH campus as well as other select agents in NIH laboratories. Members were told that Drs. Francis S. Collins, NIH Director, and Anthony S. Fauci, Director, National Institute of Allergy and Infectious Diseases (NIAID), are engaged with the Health and Human Services (HHS) Secretary and Dr. Tom Frieden, Director, Centers for Disease Control and Prevention (CDC), regarding the Ebola outbreak in Africa. Dr. Varmus expressed appreciation to Ms. Karen Maurey, NCI Technology Transfer Center, for her leadership during the planning process to decentralize the NIH's technology transfer process. Members were reminded that the NIH is evaluating the intramural research program, and that the meeting's agenda included presentations on NCI's approach to the evaluation.

Budget. Dr. Varmus stated that a Continuing Resolution (CR) at similar levels to fiscal year (FY) 2014 is expected for early FY 2015. Members were informed that in FY 2014, the NCI budget recovered approximately one-half of the 6 percent reduction due to sequestration in 2013. He remarked on shifts in Congress, including the retirement of Senator Tom Harkin (D-IA), and a defeat in primary elections by Representative John (Jack) Kingston (R-GA). He noted that their departures would result in new chairs in January 2015 for Congressional appropriations subcommittees.

Hearings. Dr. Varmus informed members that he had presented testimony at the hearing of the Science Subcommittee of the House Science Congressional Hearing Committee; other presenters included Drs. Jay Keasling, Lawrence Berkeley Laboratory; Marc Tessier-Lavigne, Rockefeller University; and J. Craig Venter, J. Craig Venter Institute. He noted that a recent initiative called 21st Century Cures, led by Representative Fred Upton (R-MI), Chairman of the House Energy and Commerce Committee, is intended to generate white papers, Congressional hearings, and national gatherings on topics related to regulatory and administrative burdens that create difficulties for medical research. Members were told that organizations such as the Office of Science and Technology Policy (OSTP), National Research Council (NRC), and the Association of American Universities (AAU) are conducting relevant studies, and that the AAU found that the calculated administrative tap (26%) for indirect costs is inadequate to cover the average percentage of costs (32-34%).

Grants. Members were informed that the level of FY 2014 grant funding will be similar to FY 2013 levels. In addition, the NCI's Outstanding Investigator Award (OIA) initiative, which provides a 7-year award to outstanding cancer scientists, had been published in the NIH Guide. He noted that many NIH Institutes and Centers (ICs) are supporting similar awards in their respective areas. Dr. Varmus said that Dr. Collins is committed to strengthening NIH expectations concerning grantee reporting behavior as well as service on NIH review panels. Members were informed that the number of NIH-funded investigators under the age of 36 has fallen over the past three decades from 18 percent to 3 percent. He noted that a NCI subcommittee is examining support mechanisms for cancer development, career termination, and making the mid-phase of a career more rewarding.

NCI and NIH News of Interest. Dr. Varmus stated that the NCI-Frederick Advisory Committee (NFAC) will meet in late September and hear about interesting potential initiatives. Other Frederick National Laboratory for Cancer Research (FNLCR) activities include a meeting of the RAS Oversight Subcommittee led by Dr. Levi Garraway, NFAC member, and Associate Professor, Department of Medicine, Harvard Medical School, Assistant Professor of Medicine, Medical Oncology Service, Dana-Farber Cancer Institute. He noted that NCI efforts in pediatric oncology include initiatives to make better use of data resulting from the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) and trial designs similar to the Molecular Analysis for Therapy Choice (NCI-MATCH) trial.

Members were told that Congress and the White House have planned events related to pediatric cancers. Dr. Varmus said that a Specialized Programs of Research Excellence (SPORE) Evaluation Group has been established, with BSA member Dr. Chi Dang, Director, Abramson Cancer Center, serving as chair and including several NCAB members. Members were referred to the Board books for recent reports from The Cancer Genome Atlas (TCGA) on gastric cancer, lung adenocarcinoma, and integrated analysis. He stated that another report of interest was an article in *The New England Journal of Medicine* on the ALB2 gene and germline mutations, and immunotherapy response by Dr. Steven A Rosenberg, Chief, Surgery Branch and Head, Tumor Immunology Section, Center for Cancer Research (CCR), NCI.

Dr. Varmus informed members that he attended Dr. Mark Schlissel's installation as President of the University of Michigan where he gave a symposium presentation entitled "Sustaining the Biomedical Research Enterprise." Members were informed that a second presentation was given on privacy, not the issue of privacy regarding protecting patient's medical records, etc., but privacy in a hyperconnected society. There was another meeting of Howard Hughes Medical Institute (HHMI) senior scientists, including him and Drs. Collins, Fauci, as well as Jeremy Berg, former National Institute of General Medical Sciences (NIGMS), and Mary Beckerle, Director, Huntsman Cancer Institute. During this meeting, it was acknowledged that the problems are acute, with no clear indication of what kinds of solutions should be pursued immediately.

Technology Transfer at the NIH. Dr. Douglas R. Lowy, Deputy Director, described changes in technology transfer activities across the NIH. Dr. Lowy informed members that the NIH Technology Transfer Office (TTO) was established 20 years ago to centralize licensing and patents for NIH ICs. A recent decision to decentralize TTO operations was made by NIH leadership. The NCI has a strong transfer technology program that coordinates approximately 40 percent of technology transfer activities across the NIH. As such, the NCI TTO will now serve as a technology transfer service center regarding licensing and patents for 11 other ICs, with the intent to provide services without incurring additional costs by any one institute.

NCI Clinical Trials Programs. Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, told members that the agenda includes presentations on the comprehensive reorganizing of NCI's clinical trials programs, including community programs or early-phase studies, tumor banks, and the NCI Clinical Trails Network (NCTN). Dr. Doroshow expressed appreciation to

Dr. Mack Roach III, Professor of Radiation, Oncology, and Urology, and Chair, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, for his assistance in the meeting program.

Questions and Answers

Dr. Jacks lauded the NCI for launching the OIA, particularly during a fiscally constrained time. Dr. Varmus noted challenges in the OIA approval process and thanked Drs. Dinah Singer, Director, Division of Cancer Biology (DCB), and Gray for their work in moving it forward.

Dr. Jacks referred to the RAS Project as a model of how the NCI shifts research and potential projects and expressed the NCAB's interest in providing early input into future activities of the RAS project.

IV. PRESIDENT'S CANCER PANEL REPORT—DR. BARBARA K. RIMER

Dr. Barbara K. Rimer, Dean, Gillings School of Global Public Health, Alumni Distinguished Professor of Health Behavior and Health Education, The University of North Carolina at Chapel Hill, reminded members that the mission of the President's Cancer Panel (PCP, the Panel) is to monitor the development and execution of the National Cancer Program and to report directly to the President on any delays or blockages in the rapid execution of the Program. Dr. Rimer reminded those in attendance that the likelihood of making actionable recommendations was one of the PCP members' most important criteria in selecting topics for the Panel's focus.

Members were reminded that the report of the 2012–2013 workshop series entitled “Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer” is available online. Dr. Rimer thanked Dr. Lowy for his significant contributions to the HPV series and report. She also thanked Dr. Varmus for the quality of his feedback and guidance. PCP members and staff have presented the HPV report at a variety of venues, including the National Vaccine Advisory Committee, NIH Office of Research on Women's Health (ORWH), American Association for Cancer Research (AACR), and National Foundation for Infectious Diseases (NFID). The PCP HPV report will be presented at a poster session during the November American Public Health Association (APHA) meetings and will be discussed at an upcoming NCI “Research to Reality” cyber-seminar. The Panel used social media tools to promote the HPV report as well as the message about HPV vaccine uptake, and Tweets and Facebook posts revealed strong support for the report. Dr. Rimer presented the latest HPV vaccine uptake data from the CDC, which indicated an increase in three-dose vaccine uptake among boys, from 6.8 percent in 2012 to 13.9 percent in 2013. Uptake in girls increased slightly in 2013 (37.6% received all three doses in 2013, compared to 33.4% in 2012). She mentioned that the NCI announced 1-year grant supplements to promote collaborations between NCI-designated Cancer Centers and state/local cancer coalitions and HPV immunization programs. The CDC also provided funds to develop and administer a national network of cancer prevention organizations to improve HPV vaccination delivery for cancer prevention. Further, the Immunization Action Coalition (IAC) issued a letter to colleagues encouraging strong HPV vaccine recommendations by healthcare providers.

The PCP's 2014–2015 series is on “Connected Health: Improving Patients' Engagement and Activation for Cancer-Related Health Outcomes,” with a focus on examining potential outcomes of enhanced engagement and activation, including improved communication and health care quality, and reduced costs. Dr. Rimer was joined by Dr. Brad Hesse, Division of Cancer Control and Population Sciences (DCCPS), who provided context on digital connectivity among the public and patients/family members in the cancer arena. In accord with meaningful use expectations, Dr. Hesse described increases across the medical industry for adoption of basic and comprehensive electronic health records between

2008 and 2013, as evidenced by an annual report from the Robert Wood Johnson Foundation. Data from the NCI's Health Information National Trends Survey (HINTS) also illustrate the public's move toward increased connectivity as people increasingly use a variety of tools to track their own health, achieve health-related goals and, for those with chronic conditions, to track their symptoms. Studies show that patients who are more actively engaged in their care have lower costs than patients who are less engaged. Dr. Hesse observed that intelligent devices such as remote sensors, wearables, digital cameras, and mobile phone apps are potentially powerful new tools for health. One example is a recent announcement by Apple for its HealthKit app.

Dr. Rimer remarked on the potential ability of sensors, wearables, and other devices to connect individuals' health data to clinical systems, which may enhance adherence to health care regimens. She stated that the "Quantified Self" movement reflects new interest in prevention and healthy behaviors relevant to cancer control. In addition, meaningful use incentives to health care providers focus on the requirement to demonstrate patient engagement through health IT.

Members were told that significant communication challenges exist in cancer care, and a survey of 416 cancer patients found that 47 percent of respondents indicated communication problems when asked about events where an aspect went wrong, or the event could have been prevented or caused significant harm. Dr. Rimer reflected on American Society of Clinical Oncology's (ASCO) response to such problems and others through its cancer LinQ program, which aims to provide real-time data to providers and patients to improve their conversations and health care. In addition, a pilot program at Georgia Tech is using connected health technologies to improve cancer care. Key questions remain about connected health, including such topics as improvements in communication, achievable cancer-related outcomes, the possibility of negative consequences and barriers, the pace of connected health development, the effect of computationally tailored information, effect on diverse patients, and transformative process and technologies.

Dr. Rimer described the planned Connected Health series workshops: Engaging Patients With Connected Health Technologies, in December 2014, in Boston, MA; The Personal Health Data Revolution, Connected Health, and Cancer in March 2015, in San Francisco, CA; and Imagining the Future of the Connected Cancer Patient, date and location to be determined.

Questions and Answers

Dr. Victoria L. Champion, Associate Dean for Research, Mary Margaret Walther Distinguished Professor of Nursing, Center for Research & Scholarship, Indiana University School of Nursing, noted the role of interactive medicine and encouraged reimbursement of communications between patients and health care providers. Dr. Rimer responded that meaningful use incentives have raised this issue and referred to experiments being conducted at a national health maintenance organization (HMO) in which appropriate email contact with patients is reducing in-person visits.

V. INTRAMURAL PROGRAM: REVIEW OF NCI REPORT TO THE NIH— DRS. ROBERT WILTROUT, STEPHEN CHANOCK, LEE J. HELMAN, AND LOUIS WEINER

Dr. Robert Wiltrout, Director, Center for Cancer Research (CCR), introduced the NCI's approach to the NIH's Intramural Research Program (IRP) long-term planning activity. He was joined by Drs. Stephen Chanock, Director, Division of Cancer Epidemiology and Genetics (DCEG), and Lee J. Helman, Scientific Director for Clinical Research, CCR, who described the current state and plans for NCI's IRP. Dr. Louis Weiner, Chair, Board of Scientific Counselors (BSC) for Clinical Sciences and

Epidemiology, and Director, Georgetown Lombardi Comprehensive Cancer Center, provided the BSC perspective.

NCI's Response to NIH IRP Long-Term Planning. Members were informed that Dr. Collins charged the NIH ICs early in 2014 with preparing a long-term plan to develop a 10-year vision for the NIH IRP that included large-scale initiatives capitalizing on IRP distinctive features and a blueprint that maintained scientifically distinctive and outstanding science, including a sustainable Clinical Research Center (CRC). Dr. Wiltout stated that the NCI's perspective is to support its mission by identifying timely projects for broad collaborations across the NCI IRP with potential for trans-NIH collaboration as well as with extramural investigators and industry. He noted the importance of improving the use and fiscal health of the CRC, identifying new organizational elements and cultural features to enhance the distinctiveness of the IRP, and identifying barriers to achieving these goals. Dr. Wiltout reviewed the timeline for the planning process, which commenced on January 31, 2014, and required IC reports by July 31; the IC reports will be integrated, reviewed by *ad hoc* groups, submitted as a draft to the NIH Director in late October, and presented to the full advisory committee and the NIH Director as a final report on December 12.

Members were told that the NCI advisory committee contains an equal number of intramural and extramural members, including representatives from the NCAB and BSA, and is led by the two chairs of basic and clinical and epidemiology BSCs and Dr. Lowy. When developing the NCI IRP vision, the advisory committee considered how to balance commitment to the NCI mission with the NIH Director's vision of trans-NIH big science, take advantage of IRP expertise and resources, and create opportunities for collaboration within the NIH across diseases. Specific challenges included how to balance commitments to basic, clinical, and population science in the context of CRC funding difficulties, and ways that the IRP can better utilize the CRC. The evaluation process focused on current staffing and changes during the past decade, including staff reduction by 18 percent based on rigorous review by the BSC, affirmation of the NCI mission and its scientific culture, NCI accomplishments, and current challenges.

Dr. Wiltout stated that the NCI IRP includes a strong cadre of senior, internationally recognized scientists who have been elected to such eminent professional organizations as the National Academy of Sciences (NAS) and the Institute of Medicine (IOM). Its distinctive features include a large program covering basic biology across multiple disciplines and clinical trials, close proximity of basic and clinical researchers that fosters a "culture of the corridors" environment, commitment to patient-based research, and partnership with the FNLCR. The intramural program also supports long-term projects that otherwise would be difficult to fund; provides commitment to study rare diseases or diseases affecting underserved patient populations as well as challenging epidemiological questions; and addresses questions in public health within the Federal Government.

The CCR's research portfolio encompasses topics of cancer biology; immunology; chromosome biology and epigenetics; chemistry, structural biology, and biophysics; cell and developmental biology; and HIV and cancer virology. Basic and clinical achievements include the development of multiple FDA-approved drugs for cancer and HIV as well as technology to enable an HIV vaccine; contributions to treating rare cancers and demonstrating adoptive immunotherapy of cancer; commercialized technology for imaging prostate cancer; and notable contributions regarding interventions for kidney cancer and lymphoma as well as improved understanding of chromatin structure, genome structure, and key regulator proteins. Members were told that 22 of 153 drugs (14%) brought to market before 2008 came from the NIH IRP, with 13 (7%) coming from the NCI. In 2010, the total global net sale of drugs derived from the NIH IRP inventions totaled \$6.9 billion (B), of which \$5.7 B derived from NCI inventions. The NCI IRP represented approximately 40 percent of all NIH IP activity in 2013.

Members were informed about new opportunities to support novel, high risk or distinctive science through a major opportunities program, a rare tumor initiative, and new FLEX programs. The FLEX programs are a series of competitive programs to support methods development and intra-CCR collaborations. He remarked on the distinctive alumni with ties to the NCI, including three Nobel laureates, department chairs for more than 100 U.S. medical centers and universities, and leaders at many biotechnology companies and NCI-designated Cancer Centers. In addition, the NCI IRP has more than 2,000 formal collaborations with extramural academic investigators at 800 institutions in 46 states and 48 foreign countries. The program also partners with more than 180 biotechnology and pharmaceutical organizations. Dr. Wiltrout reviewed the NCI IRP vision statement timeline, noting input and reviews from the scientific community, including intramural PIs and the BSC, and the report submission to the NIH on July 31, 2014.

Questions and Answers

Dr. Jacks reflected on the reduction in the NCI IRP workforce and wondered about the optimal balance for the NCI and NIH's intramural workforce. Dr. Wiltrout explained that the CCR staff reductions were attributable to attrition; BSC review to attain a balance of basic, clinical, and population research and scientists; and the direction of new hires into areas of greater impact. Dr. Varmus added that 16 percent of the NCI's budget supports the IRP, compared to 11 percent across the NIH; the FNLCR is a distinct entity but perceived by many as an extension of the NCI's IRP. He commended Dr. Wiltrout and colleagues for addressing the IRP evaluation seriously and for executing BSC recommendations regarding legacy laboratories.

Dr. Olufunmilayo F. Olopade, Walter L. Palmer Distinguished Service Professor of Medicine and Human Genetics, Associate Dean for Global Health, and Director, Center for Clinical Cancer Genetics, University of Chicago Prizker School of Medicine, asked about the challenges in recruiting translational clinical researchers. Dr. Wiltrout responded that the CCR has been able to recruit junior and mid-level clinical investigators and indicated that the Lasker Clinical Research Scholars Program could be helpful in this area.

Dr. Marcia R. Cruz-Correa, Associate Professor of Medicine and Biochemistry, University of Puerto Rico, Basic and Translational Science Director, University of Puerto Rico Comprehensive Cancer Center, asked about intramural investigators from minority backgrounds and encouraged collaboration with the Center to Reduce Cancer Health Disparities (CRCHD) and other groups. Dr. Wiltrout said that challenges in recruiting underrepresented minorities exist across the NIH, and that the NCI is working with the NIH Office of Minority Activity to develop an effective approach. He noted that the NCI has trainees from underrepresented minorities but an inadequate number at the faculty level, and that the issue will be considered by an NCI committee focused on diversity in the workforce.

Dr. H. Kim Lyerly, Vice President/Global Head of Oncology, George Barth Geller Professor of Cancer Research, Professor of Surgery, Duke University School of Medicine, remarked on the strengths of the CRC, included imaging and cell therapies. Dr. Wiltrout concurred with these strengths and deferred to Dr. Helman's presentation.

Population-based Science in the NCI and Distinctive Contributions to the NIH IRP.

Dr. Chanock informed members that population science research provides a distinctive niche in the IRP, and includes 70 PIs in the DCEG. An upcoming workshop hosted by the Division will bring together population scientists from other ICs to consider shared risk factors such as smoking, obesity, and alcohol. Committee and CRC work comprise other contributions to trans-NIH activities. The CRC is underutilized for population-based studies, and investigations of special populations that enhance understanding of biological mechanisms could have public health implications. The DCEG has a longstanding commitment

to projects that promote public health advances, such as studies of Chernobyl, risk for lung cancer for miners exposed to diesel fuel, high-penetrance mutations in family studies, and Genome-wide Association Studies (GWAS) and cancer risk assessments. Members were told that the DCEG balances PI-driven science with team science; supports excellence in collaborative science involving epidemiologist, biostatisticians, and laboratory science; and has structures in place that encourage PI-driven questions that are reviewed prospectively as well as the pursuit of long-range goals; and responds to emerging opportunities with rapid assembly of expertise from different disciplines. Dr. Chanock said that DCEG employs a variety of cancer risk models and genomic, proteomic, and measurement technologies to conduct descriptive epidemiology, molecular epidemiology, and translational research that provides answers to important public health questions. The challenge for the DCEG portfolio is how to decide which methodological questions and ensuing population-based studies to support and with which tools.

DCEG research balances team science and PI-driven research; emphasizes high-risk, high-reward research; and provides longitudinal resource commitment as well as program-based budget and review. New cross-Branch research programs address such topics as tobacco, translational epidemiology, genetic mosaicism, breast cancer, and microbiomics. Core and special areas of expertise can be leveraged, including radiation exposure in environmental (Chernobyl, radiation-induced thyroid cancer); medical (computed tomography [CT] scans); and occupational (health care workers) settings. Examples of environmental and occupational exposures with risk for cancers are ultrafine particulates and pesticides; the DCEG gathers, analyzes, and publishes information about numerous chemicals that pose cancer risks, such as benzene, formaldehyde, trichloroethylene, and perchloroethylene. Dr. Chanock stated that the DCEG also uses the CRC for mechanistic studies of rare diseases, including rare familial syndromes such as inherited bone marrow failure, Li-Fraumeni syndrome, and *DICER1*, as well as family studies of melanoma, Hodgkin disease, and other common cancers.

Questions and Answers

Dr. Jonathan M. Samet, Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine, and Director, Institute for Global Health, University of Southern California, queried about the DCEG's role in helping to organize the extramural community in GWAS and other areas. Dr. Chanock replied that the DCEG values the involvement of and has actively engaged the extramural community in topics such as genetic susceptibility for GWAS, exomes in families, and microbiomics.

Dr. Olopade asked about the proportion of population scientists and future opportunities for them in the NCI's IRP. Dr. Chanock indicated that the 70 tenure and tenure-track investigators in the NCI's IRP provide a stable cadre of researchers across nine major areas. He stressed the importance of collaboration with the Division of Cancer Prevention (DCP) and DCCPS as translation and prevention research opportunities arise.

Dr. Jacks noted that reviews and renewals of grants provide an opportunity for extramural research to shift as needed and wondered how mid-term corrections are made in long-term projects in intramural research. Dr. Chanock responded that a review of the entire portfolio occurs annually at both the budget and professional levels.

NCI's Identified Areas of Scientific Opportunity: Dependence on Clinical Program and the NIH Clinical Research Center. Dr. Helman stated that the clinical research priorities are to design novel, science-based clinical trials; focus on molecularly-based, tailored medicine; utilize technologies, such as imaging; educate physician scientists; and study rare cancers that are not being studied adequately elsewhere. Members were informed that areas of clinical strength include lymphoma, genitourinary and pediatric malignancies, neuro-oncology, thoracic tumors, marrow transplant, immunotherapy, and rare

cancers. Structural and other changes to NCI's clinical research program during the past few years involved the reorganization of laboratories and branches, the creation of the Medical Oncology Clinical Service, revisions to protocol concepts and review, an accelerated timeline for clinical trial development, and a Protocol Support Office.

Dr. Helman recalled Dr. Collins' thoughts on the importance of the CRC and its contributions during the past 58 years. Some of the CCR's contributions to clinical research include engagement in the development of combination chemotherapy, immunotoxins, gene therapy, and effective anti-retroviral therapies in HIV. CCR's current contributions to CRC infrastructure include surgery, pathology, dermatology, radiation oncology, and urology. The vitality of the CRC could be maintained through a more stable funding strategy, optimal oversight in the decisionmaking process, highest quality clinical research, and mechanisms to facilitate collaborations that allow extramural researchers access to the CRC.

Members were informed about the approach and goals of the five proposals selected from scientific opportunities considered. The precision medicine and prevention initiative will develop strategies tailored to several pediatric and rare cancers as well as tumor types prominent in the IRP portfolio, making use of well-characterized patient populations in the CRC, molecular epidemiological datasets in DCEG, and strong expertise in molecular cancer mechanisms in CCR's basic science laboratories. Combining genome engineering, cell engineering, and immunobiology will support the development of cell-based therapies, such as for cell therapy to common epithelial cancers using antigen identification with personal genomics; the focus will be on approaches and disease types that are not desirable for the current business plans of commercial entities. The microbiome initiative builds on collaborate efforts with the NIAID and will advance the move from descriptive biology to mechanistic insight through a deeper understanding of the interaction between the microbiome and inflammation. The goals are to map the microbiome in health and disease, conduct mechanistic studies of inflammation, signaling, and immune function as related to the microbiome; and apply the deeper understanding to develop more integrated approaches to biomarkers and therapies. The natural products program will aid the discovery for new molecules that target biological processes central to human disease by developing a comprehensive natural products library and establishing a national resource for natural products screening efforts. The human RNA project will allow the IRP to take a leadership role in the development of a comprehensive program for the investigation and therapeutic exploitation of RNA. The project will systematically map the "RNAome" in health and disease, elucidate the RNA structure, and support the development of RNA-based therapeutic approaches and new clinical targets and trials.

Dr. Helman noted barriers to success, including burdensome and complicated travel and meeting policies that limit the exchange of scientific ideas and impair training by imposing quotas on attendance at scientific meetings and conferences, and that often lead to higher airfares and registration costs due to last-minute approval. Members were informed that the NCI has established a Diversity Task Force to address the limited success in recruiting underrepresented minority faculty scientists. The Task Force is charged with developing a culture of minority scientists and trainees, tapping into existing programs such as the Meyerhoff Program, and considering career pathways for minority trainees in bench research, information technology (IT), and clinical research.

Questions and Answers

Dr. Kevin J. Cullen, Director, Marlene and Stewart Greenebaum Cancer Center, and Professor of Medicine, University of Maryland, remarked on the CRC's structure and cost model as a full-service center, noted opportunities to collaborate with external centers, and encouraged the NCI to consider other models, such as renting beds at a local hospital or contracting for professional services in radiation and pathology, to realize greater cost efficiencies. Drs. Helman and Varmus expressed the NCI's interest in

greater clinical research interactions within the NIH and partnerships with regional medical centers that allow the CRC to maintain its strengths.

Dr. Jennifer A. Pietenpol, Director, Vanderbilt-Ingram Cancer Center, B.F. Byrd, Jr. Professor of Oncology, Vanderbilt University Medical Center, asked about the development of a unique vision for the NCI's clinical program that encompasses the multi-disciplinary strengths of the NIH campus. Dr. Helman recognized the challenges of balancing the scale of projects with activities that cannot be conducted elsewhere.

Dr. Waun Ki Hong, Professor, Head, Division of Cancer Medicine, Department of Thoracic/Head & Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, asked how the intramural grant review process (protocol review, approval process, and contracts) compares with the extramural community. Dr. Helman responded that the cycle currently takes an average of 95 days, which is generally better than the extramural review cycle.

Dr. Richard J. Thomas, Deputy Director, Office of Occupational Medicine, Occupational Safety and Health Administration (OSHA), U.S. Department of Labor, asked whether third-party payers can cover clinical care at the CRC. Dr. Helman replied that this is not a possibility. Dr. Varmus explained that a pilot program showed that the cost of setting up and maintaining a third-party payment system would be exorbitant and that required changes in culture might create different classes of patients and have other undesirable effects.

The BSC Perspective. Dr. Weiner said that the NCI intramural program provides a vibrant research culture with fewer academic encumbrances, less time writing grants, and smaller laboratories than the extramural community. Shared resources and access to cutting-edge technology platforms also are advantages. Governmental bureaucracy, however, can be paralyzing, and intramural investigators struggle with such issues as travel restrictions and difficult access to exciting drugs for clinical trials.

Members were told that the BSC advises and supports the CCR and DCEG leadership by conducting periodic review of branches and principal investigators (PIs), evaluating the totality of research programs, and leading rigorous review processes with site visits that consider quality, impact, uniqueness, and mission of a laboratory or program. BSC's typical descriptors are outstanding, excellent, and very good. Opportunities for the intramural program to achieve greater impact include: making better use of the CRC by increasing collaborations trans-NIH and with the extramural community and assuring that CRC priorities can respond rapidly to changing research opportunities; identifying and nurturing key initiatives that leverage the unique intellectual resources and technology available to the intramural program; and supporting an environment that allows the best ideas to rise from the bottom.

BSC representatives attended initial presentations of concepts for the NCI's response. The five proposals selected for NCI's response to the NIH Director's long-term planning request were enthusiastically endorsed because they responded to the goals of the initiative, identified areas for NCI's IRP resource allocation and prioritization, advanced translational science, and capitalized on distinct IRP capabilities. The results were shared with and responses were solicited from the broader BSC community.

Dr. Weiner described key attributes of each initiative as delineated by the BSC. The microbiota initiative represents exciting new science, is multi-institute, and takes advantage of IRP and FNLCR genomics capabilities. The development of cell-based therapies is a home-grown science with a complexity that the IRP and CRC are well suited to address and leverages the IRP's exceptional capabilities in immunology. The natural products discovery program will provide a distinctive resource unavailable elsewhere and facilitate trans-NIH and extramural collaborations. The precision medicine initiative leverages NCI's multi-platform genomics capabilities and fosters connections with the CRC and

Division of Cancer Treatment and Diagnosis (DCTD). The human RNA project provides an area of basic science with new insights that require a comprehensive approach; it also affords trans-NIH and extramural collaborative opportunities.

VI. ONGOING AND NEW BUSINESS—DR. TYLER E. JACKS

Dr. Elizabeth M. Jaffee, The Dana and Albert “Cubby” Broccoli Professor of Oncology, Co-Director of the Gastrointestinal Cancers Program, and Associate Director for Translational Research, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, remarked on the challenges faced by the scientific community when hosting scientific meetings, as government policies hinder NCI staff travel and attendance at extramural meetings. Dr. Jacks stated that the Board could voice its concern in a letter to policymakers that elucidates the policies’ detrimental effect on the biomedical universe. Members agreed, and the Board established an *Ad Hoc* Subcommittee to prepare the letter, led by Dr. Jaffee, with Dr. Gray serving as the Executive Secretary.

Dr. Judy E. Garber, Director, Center for Cancer Genetics and Prevention, Dana-Farber Cancer Institute, and Professor of Medicine, Harvard Medical School, wondered if other groups should be involved in this activity. Dr. Varmus encouraged the NCAB to set an example for others to follow. Dr. Rimer expressed the PCP’s interest in signing the letter. Dr. Olopade suggested that the letter describe the hostile research environment created by restrictive policies, and Dr. Karlan stressed a focus on the culture of science, such as the interactive nature of team science, needed to conduct research most effectively.

VII. CLOSED SESSION—DR. TYLER E. JACKS

This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c)(4), 552b(c)(6), Title 5 U.S. code, and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2).

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

The *en bloc* vote for concurrence with the IRG recommendation was unanimous. During the closed session, a total of 2,119 NCI applications requesting support of \$579,321,836 and 18 FDA applications were reviewed.

VIII. NCI’S EVOLVING CLINICAL TRIALS SYSTEM—DRS. JAMES H. DOROSHOW, MACK ROACH III, MARGARET MOONEY, WORTA MCCASKILL-STEVENSON, SUSAN PERCY IVY, IRINA A. LUBENSKY, AND JEFF ABRAMS

Drs. Roach and Doroshow introduced a panel of presentations on NCI’s evolving clinical trials system, including the NCI programs that comprise the system and extramural perspectives on the impact of the new system. They introduced the presenters for both sessions: Drs. Meg Mooney, Chief, Clinical Investigations Branch, DCTD; Wortá McCaskill-Stevens, Chief, Community Oncology and Prevention Trials Group, DCP; Susan Percy Ivy, Associate Branch Chief, Cancer Therapy Evaluation Program (CTEP), DCTD; Wally J. Curran, Executive Director, Winship Cancer Institute of Emory University, Lawrence W. Davis Professor and Chairman, Emory Department of Radiation Oncology, Group Chairman NRG Oncology (NRG), and Georgia Research Alliance Eminent Scholar and Chair in Cancer Research, Emory University; Nancy E. Davidson, Director, Division of Hematology/Oncology, University of Pittsburgh Cancer Institute, Associate Vice Chancellor for Cancer Research, and Professor

of Medicine, University of Pittsburgh Medical Center (UPMC) Cancer Centers; John A. Ridge, Chief, Head and Neck Surgery, Louis Della Penna Family Chair, Head and Neck Oncology, Fox Chase Cancer Center; Augusto Ochoa, Director, Stanley S. Scott Cancer Center, Al Copeland – Cancer Crusaders Chair, and Professor of Pediatrics, Louisiana State University Health Sciences Center; Geoffrey Shapiro, Director, Early Drug Development Center, Dana-Farber Cancer Institute; and Ms. Nancy Roach, Consumer Advocate, C:3 Colorectal Cancer Coalitions.

NCI's Clinical Trials Program—A Decade of Change: Overview. Dr. Roach reminded members that the primary task of the NCAB is to advise the Secretary of Health and Human Services (HHS), the Director of the NCI, and ultimately the President on a range of issues affecting the Nation's Cancer Program and NCI operations. He stated that the Board's interest in structural and programmatic changes in the Cooperative Group system in March 2014 provided an opportunity to present the topic. Dr. Roach shared potential topics for discussion: improved or weaker areas since the merger of the Cooperative Groups, ways to streamline work to reduce cost and waste, threats to the success of the Cooperative Groups, closer collaboration with the Cancer Centers, strategies to receive credit for unreimbursed expenses, evaluation metrics of the clinical trial enterprise, NCI's evaluation timeline, selection and prioritization of trials, and correlative science in the Cooperative Groups.

Dr. Doroshov provided context for the evolving NCI's clinical trials program. The program underwent numerous extramural reviews during the past decade. Based on reports from the Clinical Trials and Operational Efficiency Working Groups, along with recommendations from an IOM report that emphasized the critical need for a public clinical trials system, the NCI adopted a comprehensive approach to transforming its clinical trials system to create a highly integrated network that can address rapid advances in cancer biology. The rationale for change included that advances in cancer biology offer the potential to improve clinical oncologic practice, opportunities exist for more effective therapies targeting specific characteristics of a tumor, and challenges of evaluating a rising number of highly specific agents in molecularly defined subsets of patients must be addressed. Goals for restructuring the system encompassed coordination, prioritization/scientific quality, standardization, operational efficiency, and integrated management. Dr. Doroshov explained that the evolved system coordinates clinical trials research through data sharing databases and provide incentives for collaboration as a network. In addition, stakeholders design and prioritize clinical trials that address the most important questions through tools of modern cancer biology. The system is standardizing IT infrastructure and clinical research tools as well as using resources most efficiently through improved cost-effectiveness, accrual rates, and more rapid trial initiation. Extramural and intramural oversight of NCI clinical trials has been restructured to ensure that recommendations are implemented in a timely manner.

NCI Clinical Trials Network. Dr. Mooney provided historical context to the NCTN, and referred to NCI's extensive review of its cooperative late-phase clinical trial system with widespread stakeholder input in 2005–2010, with a plan to restructure the system into one pediatric group and four adult groups proposed and approved by the BSA in 2011. The five U.S. groups and Canadian partner are the Alliance for Clinical Trials in Oncology (Alliance), Children's Oncology Group (COG), ECOG-ACRIN Cancer Research Group, NCIC Clinical Trials Group (NCIC-CTG) (Canadian partner), NRG, and SWOG. Dr. Mooney stated that the first NCTN funding opportunity announcements were released in July 2012, and the applications were due in January 2013. The applications were peer-reviewed in July 2013, and the NCTN was launched on March 1, 2014.

The vision for transforming the clinical trials system was to launch trials rapidly and complete accrual through an integrated national network; promote user-friendly, harmonized processes to the extramural community and facilitate collaborations with partners; provide common infrastructure to perform large-scale testing of smaller subsets of molecularly defined cancers; and focus on research questions that are not well-supported in a commercial environment. The previous clinical trials program

consisted of 10 decentralized U.S. groups and one Canadian partner, with infrastructure supported at each site. The NCI decided to eliminate redundancies and increase efficiency. New components of NCTN included awards to 30 lead academic participating sites to provide leadership in the development, accrual, and conduct of clinical trials. Seven integrated translational science awards were made to incorporate translational science into the trials. A radiotherapy and imaging core was created for quality control in the trials. The network has centralized its Institutional Review Board (IRB), data management system, and administrative support.

The NCTN's research agenda emphasizes Phase III trials, practice-changing treatment, and advanced imaging trials, particularly in research areas that are not well-supported in a commercial environment. Public funding allows the NCTN to make contributions in the investigation of combinations of novel and molecularly targeted agents developed by different sponsors; integration of new agents and imaging approaches into standard of care; evaluation of multi-modality regimens; and the development of therapies for pediatric cancers, rare cancers, and uncommon presentation of more common cancers. Dr. Mooney informed members that the NCTN is integrated with the NCI Community Oncology Research Program (NCORP), which is focused on cancer prevention and control trials, cancer care delivery, and comparative effectiveness research. The two programs share infrastructure because the community centers are integral to participation in the NCTN trials and provide ancillary studies on quality of life and symptom control.

Members were told that the NCI has provided \$24 million (M) to consolidate infrastructure and approximately \$40 M to transition to a common data management system called Medidata Rave[®], develop an integrated IT system for the tumor banks, and implement specific precision medicine clinical trials. Savings were realized by removing the separate infrastructures of the decentralized cooperative groups. The average total accrual between FY2007 and FY2013 was 23,670 patients and the average between FY2010 and FY2013 was 20,900 patients. The current projected accrual for the first year of the NCTN Program is between 19,000 and 20,500 patients. Dr. Mooney stated that the new integrated IT system will allow real-time reporting of accrual and management support to help with planning.

NCI Community Oncology Research Program. Dr. McCaskill-Stevens introduced the NCORP, which was approved by the NCI scientific leadership in May 2013 and the BSA in June 2013. The NCORP Funding Opportunity Announcement was released in November 2013 with a due date of January 8, 2014. The applications were peer-reviewed in April and May 2014, and the NCORP was launched on August 1, 2014.

The NCORP conducts clinical trials on cancer prevention and control, health-related quality of life, comparative effectiveness, and screening; cancer care delivery research; and cancer disparities. The Program includes three components: community sites, minority and underserved community sites, and research bases. Five of the NCTN bases also are part of the NCORP. The research bases have their own research foci, which include treatment-related toxicities and comparative effectiveness research. The NCORP community sites, minority and underserved sites, and research bases have a broad geographical reach and organizational diversity.

NCORP clinical trials and studies encompass cancer prevention, cancer control, cancer screening, and health-related quality of life. The centers are interested in identifying interventions to reduce cancer risk and incidence, reducing incidence of comorbidity, evaluating early diagnosis interventions and cancer recurrence, and evaluating health-related quality of life. The trials research agenda is focused on mechanisms of cancer-related symptoms, biomarkers of risk for treatment-related toxicities, molecularly targeted agents, post-treatment surveillance, management of precancerous lesions, and over- and under-diagnosis. In addition, a specific cardiotoxicity task force is charged with prioritizing the cardio-oncology research agenda across the research bases within the NCORP. In the cancer care delivery realm, the

NCORP conducts observational and interventional studies about how care is delivered and how it influences outcomes.

Members were informed that the FY2014 funding for NCORP was \$97.0 M, of which \$91.1 M was allocated for NCORP grants. The NCORP recently received \$2.9 M in supplemental funding for trial accrual. Post-launch activities included a Cancer Care Delivery Research (CCDR) planning meeting held August 25-26, 2014; an investigators and administrators meeting on September 22, 2014; and a natural experiments working group to develop research designs to evaluate natural experiments in the area of policy change and the effects of policies on health care outcomes.

Dr. McCaskill-Stevens said that the CCDR planning meeting held in August began foundational work for CCDR activities. Attendees included Research Base PIs and CCDR leads, including those from Community and Minority/Underserved Sites with enhanced CCDR capabilities. The meeting included four breakout sessions on the following topics: disparities; organization and system science; patient engagement; and “omics” in clinical practice.

The next steps for the CCDR are to assemble initial Coordinating Committee members, determine leadership and additional members of the Coordinating Committee, and determine the structure of the CCDR Steering Committee. The CCDR also will begin the process to identify CCDR research priorities and initiate working groups as well as characterize the health care environments and capacities for the CCDR across the NCORP. Dr. McCaskill-Stevens stated that the NCORP represents the “real world” of oncology practices. It is responsive to extensive stakeholder input and represents an opportunity to evaluate the influence of the current health care system on the successful conduct and implementation of precision cancer therapy.

Experimental Therapeutics Clinical Trials Network (ETCTN). Dr. Ivy described the goals and objectives of the ETCTN, which include: research and development for new treatments; tumor characterization in biomarker-driven studies; enhanced understanding of cancer biology; and education and training for young investigators. The ETCTN faces several challenges, including accrual as molecularly defined diseases result in smaller patient populations; biomarkers, which often require biopsies, validated assays, and functional imaging; and translation, because there is a need for bench to bedside collaborations and better animal models to evaluate tumor heterogeneity. Dr. Ivy described high-priority molecular targets and the drugs that are under development. Most treatments that progress are combination therapies of multiple agents. Clinical translational research involves several steps, beginning with identifying patients eligible for early phase clinical trials through analysis of tumor biomarkers, and then assigning the patient to the trial based on the molecular characterization of the tumor. Patients must be monitored and followed with post-treatment molecular re-analysis of the tumor for response or resistance, so that appropriate combination therapies can be identified.

The ETCTN represents changes from previous trial programs through an emphasis on molecular characterization of tumors and need for team science. The team science aspect means that drug development project teams consist of clinical, translational, and basic science researchers working together with access to centralized support. The Network also includes a drug development plan to tackle critical unanswered questions about biomarkers and drug combinations.

The ETCTN also represents operational changes to the clinical trials program, which is now organized in an integrated network rather than isolated silos. The new program has a faster timeline for approval from the initiation of a new protocol (15 months vs. 21 months) and provides additional resources for preclinical work (e.g., molecular characterization). Data monitoring reporting systems using Medidata Rave[®] allow Web-based reporting and tabular representations to show enrollment by site. The data in this format will help the ETCTN meet regulatory reporting requirements.

Dr. Ivy told members that the ETCTN will implement a new approach to the development cycle for therapeutics. The NCI project team will meet with program directors about a new drug and identify translational researchers to create an extramural project team to develop a research plan for presentation to an internal investigational drug committee. The process would take approximately 15 months to approval. The ETCTN also has a transformed clinical trials program. The centralized IRB allows a trial to open simultaneously at all sites in the network. The ETCTN will be evaluated to document its implementation, identify course corrections if needed, and provide data to guide decisionmaking for the program's subsequent funding cycle.

NCI's Clinical Trials Tissue Banks. Dr. Lubensky described the NCTN's biospecimen banks, which provide a unique resource to store and provide researchers with well-annotated specimens and clinical data from NCTN Phase III and large Phase II trials. Members were told that biospecimens are associated with detailed clinical data related to therapy, therapeutic response, and clinical outcomes. They are collected by NCTN groups and affiliated institutions (e.g., NCORP) and sent to the NCTN bank of the group conducting the trial. Participants may consent to the use of their biospecimens for additional studies beyond specific trial objectives. Biospecimens collected on NCTN protocols will be used for integral and integrated biomarker studies. Those that remain in excess after clinical trial requirements have been met will become legacy specimens and be distributed to investigators following a defined NCTN access process and approval of the study by expert review. Members were informed that priority for NCTN biospecimens will be given for validation studies of predictive or prognostic biomarkers, with assay development and validation a lower priority. Each NCTN group is associated with a biospecimen bank, which may include such specimens as frozen, formalin-fixed/paraffin-embedded (FFPE), nonmalignant, and tumor tissue; serum and plasma, peripheral blood, urine, bone marrow, RNA and DNA, tissue microarrays, and/or other biofluids. Biospecimen organ sites and types collected are dependent on the specific trial. In the past 5 years, there were 775 papers published and eight patents issued, including studies that spanned leukemia, childhood tumors, and solid tumors of the adults that could not have been conducted without the specimens.

The goals of the new U24 banking RFA are to support NCTN banking operations and infrastructure, and consolidate the biospecimen operation into the NCTN banking network. A total of five U24 awards will be made, providing one banking grant for each new NCTN group, with pathologists or specialists in biospecimen banking serving as the PI. The Web-based NCTN Biospecimen IT Navigator provides a common inventory, specimen-data link, and search engine for researchers. A centralized "Front Door" process will allow access to legacy specimens and facilitate application tracking and timekeeping. Members were told that one bank will be established for early trials, specifically the ETCTN trials.

Dr. Lubensky provided details about the Biospecimen IT Navigator, which aims to consolidate the inventory of biospecimens, connect biospecimens and clinical data, and provide biospecimen access to the research community. An investigator does not need to be associated with an NCTN group to request biospecimens. The Biospecimen IT Navigator will allow investigators to independently query for NCTN bank biospecimens that meet their criteria, and track their request through the review and approval process. The NCTN Front Door Service will guide investigators through biospecimen query, application, and regulatory filing procedures. These tools will improve the efficiency and transparency of the biospecimen request process for the entire cancer research community. If approved, the investigator will be asked to finalize regulatory documentations; the banks will distribute the specimens to the investigator only if such scientific review is successfully done and all the regulatory papers are in order. Dr. Lubensky noted that all related publications can be tracked in the system.

Questions and Answers

Dr. Cruz-Correa queried about the extent of collaboration between the NCTN and NCORP as well as between those programs and the Cancer Centers. Dr. McCaskill-Stevens confirmed interactions between the programs, noting that many NCORP investigators also participate in the NCTN program or Cancer Centers. Dr. Jeff Abrams, Associate Director, CTEP, DCTD, added that collaborative efforts between the DCTD and DCP have strengthened the Cancer Trials Support Unit, which provides an online presence connecting researchers interested in treatment, prevention, cancer control, and other topics.

Dr. Hong wondered if 20,000 project accruals encompassed therapeutic, intervention, and screening trials. Dr. Mooney clarified that the statistic refers to intervention and screening for treatment and advanced imaging.

Dr. Sawyers asked whether consent forms anticipate the use of genomic data resulting from the trials and the possibility of a genomic database that might not be directly linked to clinical outcome but be mineable by the extramural community. He also mentioned that the American College of Radiology (ACR) is supporting a pilot program involving eight sites that have agreed to share genomic data and have compliant consent forms. Dr. Abrams confirmed the intent to facilitate extramural access to data and described a two-pronged approach in which clinical datasets reside in a database and are linked to genomic information. He added that consent forms incorporate questions about sharing genomic data beyond the specific trial.

Dr. Roach asked about the coordination of supply and demand for tissue specimens, and he wondered about the current demand for tissues given that trials are becoming smaller. Drs. Lubensky and Abrams indicated that a review and prioritization process is in place, and that demand is high for specimens from positive trials as the research community seeks prognostic and predictive markers.

IX. IMPACT OF THE NEW SYSTEM—DRS. WALTER J. CURRAN, JR., NANCY E. DAVIDSON, JOHN A. RIDGE, AUGUSTO OCHOA, GEOFFREY SHAPIRO, MS. NANCY ROACH, MACK ROACH III, AND JAMES H. DOROSHOW

NCTN Group Chair Perspective. Dr. Curran provided his perspective as chair of one of the five NCTN Groups regarding reasons to continue the Groups, differences between NCTN Groups and Cooperative Groups, examples of current NCTN trials, and NCTN structure and governance challenges. The primary reasons to continue the NCTN groups include that they have performed practice-defining, paradigm-shifting research for decades; conducted this research in a cost-effective manner, with more than 90 percent of the professional effort in the groups provided on a volunteer basis; achieved alignment with all major U.S. and Canadian Cancer Centers involved in the care of patients; and conducted group trials that would not be possible at single centers or with commercial partners, including trials testing agents from multiple commercial parties, technology trials, surgical trials, and imaging trials. In 2010, the IOM recommended that the Groups increase efficiency, reduce timelines to development and activation, and align more effectively with new science; also recommended were restoring the Groups' funding, reducing oversight by the NCI over Group research, and conducting more trials for patients with rare malignancies. Under the new NCTN system, fewer groups have eased coordination in programs among groups but reduced career opportunities; a more well-defined governance structure is needed, however, that will be comprised of a partnership among CTEP, DCP, and Group leaders. Alignment with new science had already begun and is continuing under the new system. Whether the new system is more cost-effective is unclear, given that the distribution of funding has changed, but promising efficiency efforts are in place. There are more trials for molecular subtypes of common diseases, which can be considered as new diseases, but not for rare malignancies *per se*.

Some of the most exciting NCTN initiatives in precision medicine and biophysical innovation—none of which could have been performed without the scope and capacity to partner with multiple industrial entities of NCTN—are for lung cancer. Current NCTN lung cancer trials are addressing applications of precision medicine, and others involve innovative radiation oncology. LUNG-MAP, an active biomarker-driven trial for patients with squamous cell carcinoma of the lung who are eligible for second-line therapy, will compare the efficacy of standard chemotherapy with biomarker-defined therapy. Thanks to the efforts of the NCI and SWOG, which is administering the trial, LUNG-MAP is able to test agents from multiple industry partners. Another study, called Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST), is underway to determine whether treatment based on genotype can improve the cure rates for patients who have had a resection of nonsquamous lung cancer. Two trials for patients with anaplastic lymphoma kinase (ALK)-defined lung cancer are comparing efficacy of crizotinib or erlotinib versus placebo with standard therapy. A trial scheduled to open in 2014 for patients with Stage III non-small cell lung cancer (NSCLC) will compare individualized response rates for patients to combined modality therapies. In innovative work, lower survival rates for patients with lung cancer were found to be associated with higher radiotherapy doses. In an exploration of the use of individualized dose escalation, positron emission tomography (PET)-CT was used as a basis to guide radiotherapy dose based on response, reducing target volume and normal tissue toxicity. Proton therapy is another approach being considered to reduce normal tissue toxicity. An ongoing study is comparing survival after photon versus proton chemoradiotherapy for patients with Stage IIIB NSCLC. The rationale for the study is that heart dose, which can be reduced with proton therapy, is associated with greater fatality.

Dr. Curran indicated that in addition to lung cancer, such trial strategies might prove applicable for other tumor types if there is a good biologic or biophysical rationale, there are appropriate targets, and NCTN has available resources; candidate disease sites are melanoma, malignant brain tumors, and selected gastrointestinal cancers. Work already is ongoing in the Children's Oncology Group on Philadelphia-positive acute lymphoblastic leukemia (ALL).

The State of Georgia has been a historic underperformer in cooperative group trials, but in 2014, a new Lead Academic Participating Site; a new, multisite minority NCORP; and a new Savannah-based NCORP were added, with most sites in the state enrolling more than one-third of minority patients in trials. The concern is that there is now a tremendously expanded public cancer trials network in Georgia, but it is unclear whether there is a sufficient number of NCTN trials or patient slots in NCTN trials, representing a potential lost opportunity to increase enrollment.

Dr. Curran summarized by recognizing the highly successful adaptation of groups to the new system, the potential for exciting trials in the NCTN that is limited only by available resources, the need to define NCTN governance, the potential for unintended consequences of the transition, and the great need for resources in project development.

Lead Academic Site/Cancer Center Perspective. Dr. Davidson provided a view of the NCTN from the perspective of an academic site and Cancer Center. Her university, UPMC, includes 320 faculty members across 42 academic departments. Clinical research and care is provided through UPMC hospitals and cancer centers, and a thriving cancer center network serves as a unifying hub for UPMC medical facilities and activities. The network encompasses 40 sites in 29 counties in western Pennsylvania; many sites are engaged in clinical research, and all the sites are managed by a single IRB. Members were told that integrating clinical trials in the new system will be challenging. Many Cancer Centers have participated actively in clinical trials during the past 10 years, and the UPMC had approximately 1,000 interventional trial accruals in a given year. Dr. Davidson reflected on a decrease in accruals to the National Group trials, likely attributable to the reengineering of the Cooperative Groups.

Under the new system, the UPMC hosts the NRG Biostatistical Center, led by Dr. Joe Constantino; an ETCTN site, led by Dr. Ed Chu; and a lead academic participating site (LAPS), led by Dr. Adam Brufsky. Prior to the reorganization, the UPMC participated in eight of 10 Cooperative Groups; now it participates in four of five Cooperative Groups, which has led to significant integration within the UPMC and streamlined financial and administrative functions. Dr. Davidson observed that enthusiasm for using the NCI central IRB previously was not robust, but the NCTN system has provided institutions the opportunity to streamline the IRB process. It also spurred the UPMC to assemble a Steering Committee to consider the design of future UPMC clinical trials, accrual strategies, and resource allocations.

Challenges for the UPMC include shifting focus and loyalty from legacy groups and disease areas to new cooperative groups, maintaining engagement of LAPS leaders with the scientific leadership of new Cooperative Groups, encouraging NCTN involvement for young investigators given the lack of opportunity to lead, and financial penalty for over-accrual of patients. Considerations for the future include the impact of a more centrally directed NCTN in the field, how a goal of smaller biologically based trials will be implemented in the community, and interactions between and roles of the component parts to advance the clinical trials agenda.

Disease Committee Perspective. Dr. Ridge provided the perspective as a surgical oncologist and co-chair of the Disease Committee on the new clinical trials system. He reminded members that in 2005, the Clinical Trials Working Group prioritization scientific initiatives requested the establishment of an investigational drug steering committee and a network of steering committees to address design and prioritization of Phase III trials that would involve the Cooperative Groups, SPOREs, Cancer Centers, and the broader oncology community. The goals of the scientific Steering Committees (SCs) were to increase the transparency and openness of the trial design and prioritization process; enhance patient advocate and community oncologist involvement in design and prioritization; and convene clinical trials planning meetings to identify questions and unmet needs, and prioritize key strategies. The five scientific SCs were: Disease-Specific, Investigational Drugs, Symptom Management and Health-Related Quality of Life, Patient Advocate, and Clinical Imaging. The first Disease-Specific SCs were established in 2006–2007 and included gastrointestinal, gynecologic, and head and neck, with nine other committees following.

The roles of the Disease-Specific SCs are to increase information exchange in the early stage of trial development; increase the efficiency of trial collaboration; reduce redundancy; develop, evaluate, and prioritize concepts for Phase III and large Phase II trials; and conduct clinical trials planning meetings, which replaced state-of-the-science meetings. The aims of clinical trials planning meetings are to identify directions of clinical trials for the field, reach consensus on important trials to conduct, identify gaps, identify innovative trial design opportunities, and facilitate collaboration.

Members were informed that Disease-Specific SC members include the committee co-chairs, NCI staff, and representatives from the Cooperative Groups, SPOREs, community oncologists, biostatisticians, pathologists, and patient advocates. Disease-Specific SC mission statements address functions to harmonize an efficient, cost-effective, science-driven, and transparent process that identifies and promotes the best science in the respective field. At inception, Disease-Specific SCs had uncertain roles, were broadly based, and involved a variable number of Cooperative Groups. Dr. Ridge stated that the process has evolved, with experiences varying by disease site and year of initiation. In addition, PIs face additional levels of review and task force roles remain undefined. Clinical trials planning meetings, however, provide opportunities.

Dr. Ridge reflected on the Disease-Specific SCs' experiences, observing that the Disease-Specific SCs do not all function in identical ways and are vulnerable to misunderstandings. He noted that Cooperative Groups demand autonomy and should be enlisted rather than managed. In addition,

conflicting incentives, such as efficiency versus broad representation, have presented challenges. Issues also exist regarding academic competition and industry sponsorship. The Disease-Specific SCs have increased information exchange at early stages of trial development, evaluated and prioritized trial concepts, and conducted clinical trials planning meetings successfully. However, it is not clear that the efficiency of clinical trial collaboration has been increased by the Steering Committee process, and it is unlikely that trial redundancy has been reduced as there was not much redundancy beforehand. The Disease-Specific SCs are vulnerable to “one-size-fits-all” prescriptions.

Dr. Ridge provided observations on the new system from his perspective as a surgeon. Individual surgeons occupy leadership positions in several of the Groups, but many feel disenfranchised by the new structure as groups under the previous system are no longer independent and the number of co-chairs may be reduced. There is a unique suitability of trials for the NCTN program, such as a focus on understudied diseases or populations; use of radiotherapy, surgery, or imaging techniques; and conduct of combination trials or therapy optimization trials. In addition, trials unlikely to be undertaken by the industry could be conducted. The NCTN also provides important specimen and data resources for public use. Members were told that opportunities for advancement in the Groups are likely to decline with the change in the organizational structure and the decline in number of trials performed. Concerns remain among surgical oncologists, particularly for Groups with strong surgical traditions. The challenge is to maintain and encourage engagement by junior faculty and community oncologists from all disciplines, and address declines in morale on the part of surgical oncologists in the establishment at all levels.

NCORP Principal Investigator: Community Investigator Perspective. Dr. Ochoa said that the Gulf South experiences the highest cancer mortality rates in the United States and unique challenges in terms of the biology, the disease and how it presents. The region has high rates of triple-negative breast cancer and familial prostate cancer, and notable health disparities and co-morbidity issues with a large community of minority and underserved patients. More than 90 percent of adult cancer patients in the Gulf South do not participate in clinical trials, and most clinical oncologists in this region are not located within 100 miles of a comprehensive Cancer Center. In addition, many patients cannot afford an extended period of time to travel to an NCI-designated Cancer Center, and options are more dismal for patients belonging to a minority underserved community. Community oncologists have several choices, such as using standard of care, enrolling patients on a pharmaceutical trial, referring patients to the closest academic center; many will participate in structured clinical trials if provided the opportunity.

In 2005, Hurricane Katrina forced oncologists and cancer researchers in the Gulf South to change perspective on clinical trials as patients dispersed throughout the state and country; the city of New Orleans was under mandatory evacuation and the public Charity hospital was closed permanently. A meeting with 35 groups of oncologists in September 2006 solicited their interest in participating in a clinical trials program. Many expressed interest and declined to charge for participation in exchange for help in developing the programs, which prior to the NCTN required regulatory auditing and data monitoring that many deemed too complex to manage. Their condition was that participation not detract from their bottom financial line. Rules were established for the Community Clinical Trials Program, in which an academic center would manage and compete for the clinical trial and provide centralized regulatory and data management support; the community oncologists agreed to provide their own research nursing, use electronic medical records provided by the academic center, accrue a minimum number of enrollments, and participate in monthly meetings.

The NCTN brought positive changes, including fewer contracts and audits, streamlined regulatory affairs through the central IRB and data management, and access to biology and genomics-driven trials as well as multi-drug clinical trials. The NCORP provided the stimulus to consolidate smaller Community Clinical Oncology Programs (CCOPs) into more effective oncology programs. In addition, the NCORP Cancer Care Delivery Research and Health Disparities programs demonstrated to community

oncologists that cancer care also involves understanding cancer in the region. Dr. Ochoa described changes in the region, including integration of the tumor registry into the clinical trials program, development of health disparities programs, and several community-based participatory research programs. He noted that the health information exchange (HIE) programs are helping to identify patients early in the process.

In the Gulf South, the NCORP incorporated two minority-based CCOPs and the NCI Community Cancer Centers Program (NCCCP) and expanded to cover 26 sites across Louisiana and southern Mississippi. Community oncologists have increasing interest in access to biology and genomics trials, referring patients without “losing” them, and joint management of complex cases. Members were told that new initiatives include collaborations with three statewide health disparities research programs and a Patient-Centered Outcomes Research Institute (PCORI) program tasked with starting more smoking cessation education. Training initiatives involve minority research nurses and navigators, as well as a state-wide course on new billing practices for clinical trials.

Dr. Ochoa described preliminary outcomes, including a shortened time for protocol approval, increased referrals from community oncologists and new requests from community practices to participate in the NCORP. The NCORP sites face challenges of funding, staying engaged, incentivizing community oncologists and community participation, and keeping the community informed. Challenges for the Cooperative Groups include funding, trial prioritization based on scientific rationale, and potentially competitive pharmaceutical trials. Dr. Ochoa reiterated that the Gulf South represents a unique opportunity to demonstrate the efficacy of the NCTN and NCORP to effect positive change.

Early Phase Therapy/Translational Scientist. Dr. Shapiro provided a clinical translational researcher’s perspective on the ETCTN. Participation in the ETCTN is essential for the vitality of early drug development (Phase I) programs. The creation of drug-specific project teams provides an opportunity to contribute to a collaborative network with substantial input into drug development plans that includes junior investigators. In addition, the ability of NCI-CTEP to foster the development of novel drug combinations facilitates the leveraging of preclinical results that otherwise might not be translated to clinical trials. In the prior system, NCI-CTEP procured an agent and solicited letters of intent (LOIs) that required extensive preclinical data; the process had a high failure rate and resulted in substantial investigator frustration, particularly at the junior level. The new system involves applications for team membership from basic and clinical investigators, including junior researchers, a project team is assembled and leaders designated, and members confer with NCI-CTEP staff. The project teams are tasked with preparing a pre-clinical/translational plan that addresses critical questions to inform drug development and to propose innovative disease- or biomarker-based clinical trials incorporating safety, pharmacokinetic, pharmacodynamics, and efficacy endpoints. The drug development plan is presented to the Investigational Drug Steering Committee (IDSC), after which full LOIs are prepared.

Dr. Shapiro described the first ETCTN project team’s experience, which concerned HSP90 inhibitor AT13387, a novel second-generation resorcinol compound developed by the pharmaceutical company Astex. The NCI’s interest in the compound included study in lymphomas, triple-negative breast cancer, EGFR-mutated lung cancer, and DNA damage and repair proteins. The large project team was assembled, led by Dr. Len Neckers in basic science and Dr. Shapiro in translational research; the team included junior investigators with mentors, and SPORE researchers, as well as radiation oncologists, biostatisticians, and imaging specialists. He explained that the team discussed proposals for specific studies during 13 teleconferences over 4 weeks and culminated into four proposals presented to the IDSC: a monotherapy Phase II study of lymphomas; Phase I/Ib monotherapy study of triple-negative breast cancer; Phase Ib study of Erlotinib/AT13387 for NSCLC; and Phase I study of AT13387 with standard dose chemoradiation for squamous cell carcinoma of the head and neck. Biomarker prioritizations included proof of mechanism, genomics, and noninvasive assessments. Additional safety work, such as

cisplatin and AT13387 in preclinical head and neck models, was recommended. Challenges facing the project team model included the large size or selectiveness of the project team, heavy time investment required, and varied priorities of team members.

Dr. Shapiro shared examples of several ETCTN studies at the Dana-Farber/Harvard Cancer Center, including Trametinib/Navitoclax in KRAS mutated cancers based on synthetic lethal interaction of MEK and Bcl-xL inhibition; Dinaciclib/Veliparib based on CDK inhibitor-mediated disruption of HR repair and sensitization to PARP inhibition; and several studies of Cediranib/Olaparib, which include recent findings of greatest benefit of the combination for epithelial ovarian cancer in non-BRCA carriers. He emphasized that these studies could not be conducted outside of CTEP. Two ETCTN molecular characterization hubs have been established to support genomic results and ensure harmonization of results.

Members were told that the project team model facilitates a highly collaborative and interactive process for proposing a drug development plan. It is superior to the legacy system in which there was far less engagement of U01 sites in trial prioritization and design for particular agents. In addition, it is highly advantageous for ETCTN to draw on a multi-disciplinary team of senior leaders and junior investigators early in the process. The NCI-CTEP portfolio is poised to promote development of innovative combinations from different pharmaceutical companies based on strong preclinical rationale. Moreover, NCI-CTEP operational improvements, such as the central IRB, patient registration, and data management, will facilitate more rapid activation of studies and engagement of the network when required for robust accrual.

Patient Advocate. Ms. Roach provided her perspective as a patient advocate on clinical trials. Ms. Roach indicated that most patient advocates become involved in advocacy because they were ill or someone whom they care about became ill. In Ms. Roach's case, her mother-in-law was diagnosed in 1996 with Stage II rectal cancer and treated at a regional hospital; participation in a clinical trial was not presented as an option. In 1999, her mother-in-law was diagnosed with a rare form of uterine cancer; there was no clinical trial open for her because of the rarity of her cancer and because she had been treated previously for cancer. Ms. Roach also served as a patient advocate for a family friend who participated in clinical trials; his name was Andrew, and he was diagnosed with ALL at 13 years of age. These experiences provided Ms. Roach with direct involvement in the new and old clinical trials systems.

Ms. Roach obtained feedback regarding what the community wants from the NCTN by surveying many other advocates. The advocacy community wants immediate action to ensure that the clinical trials network collaborates well, responds to the patient community, and works quickly. To achieve these goals, the advocacy community suggests conducting scientifically driven trials, assessing feasibility before opening trials, and attending to the feedback from patients and community oncologists about the ways in which patients are willing to participate in trials. In addition, the advocates cited strategic planning as being important. Also key is the evaluation of individual trials, comparing trial components to reward productive and collaborative behavior. One advocate suggested that review panels should be comprised of members who were not part of the U.S. research community to avoid potential conflicts of interest. This suggestion reflects concern about the lack of transparency of the clinical trial system. Real-time feedback was mentioned as being critical. An advocate proposed that PIs be surveyed at the beginning of each protocol to learn about problems, issues, and frustrations. Immediate course corrections are vital to fix these problems. There needs to be more emphasis on other modality trials. In addition, Ms. Roach called for providing leadership opportunities to train advocates. Looking at the system systematically to identify opportunities for consolidation and collaboration is important as well.

Members were told that respondents provided disparate views when asked for their opinions of the NCTN, ranging from those who felt highly engaged to those who doubted that they were being attended to at all. The community, therefore, is highly polarized about the NCTN. She noted that there are

Steering Committee and Cooperative Group advocates, but the majority of the community is not engaged. To ensure effectiveness of advocates, there needs to be better training so that advocates understand the entire system, not just their areas of specialization. The role of advocates also should be clarified for researchers. Regarding governance, Ms. Roach stressed that the NCTN is a multi-stakeholder system, and as such, needs multi-stakeholder governance rather than governance by the NCI and the Group Chairs.

Ms. Roach concluded by reporting that her mother-in-law and Andrew are doing well. One of Ms. Roach's staff members, however, has Stage IV metastatic rectal cancer and is in search of a clinical trial. Ms. Roach recognized that these patients represent the reason that the work of the NCTN is important. They also are the inspiration for the patient advocacy community to try to help the clinical trials system and campaign for change when it is not working well.

Questions and Answers

In response to a query by Dr. Cruz-Correa, Dr. Doroshow acknowledged the challenges in providing opportunities for junior investigators in Phase III studies as a mature understanding of the national cancer landscape that is needed to ensure successful investigations. Dr. Curran recalled 2-day training programs for new investigators that were effective in previous groups. Dr. Doroshow said that mentoring of junior investigators might be incentivized. Dr. Peter Adamson, COG, stressed the importance of supporting young investigators and encouraged the review process to identify unsuccessful applications sooner in the process. Dr. Olopade asked whether existing training grants (T32, K12, Paul Calabresi Career Development Award) could be integrated into the NCTN process.

Mr. Carl Schwartz, patient advocate, suggested that consensus reviews include the number of reviewers who shared the same areas of disagreement during the review of NCTN study applications. He expressed appreciation for the clinical trials planning meetings in moving disease-specific committees forward.

Ms. Barbara LeStage, patient advocate, expressed concern about accrual rates and encouraged the NCI to change LOI and other forms to require further research that indicates likelihood of reaching proposed accrual rates.

Mr. Rick Bangs, patient advocate and Chair, SWOG Patient Advocate Committee, asked how real advances against cancer might be achieved in a fiscally constrained environment in which the NCI's budget is reduced in terms of inflation-adjusted dollars. Dr. Varmus acknowledged the challenges in supporting critical work such as the NCTN and referred to the NCI's emphasis on designing trials with a stronger science base. He added that the intent of adjusting the accrual rate is to fill trials while obtaining adequate results. Mr. William H. Goodwin, Jr., Chairman and President, CCA Industries, Inc., commented on the lobbying role of patient advocates and the need for the general population to become active in influencing Congress about the need for increased funding for medical research. Mr. Bangs reflected that the NCI is one stakeholder among many, and encouraged all stakeholders, including industry, to collectively collaborate around the budget issue. Dr. Jacks added that disease-specific foundations also should be coordinated in support. Dr. Robert Comus, ECOG-ACRIN, stated that in a time of constrained resources, increased flexibility can facilitate interactions with other organizations. Dr. Lowy said that the NCI is open to hearing from groups that are interested in working closely with the Institute.

Dr. Roach referred to an idea by Dr. Garber and invited feedback on whether the focused presentations on the NCI clinical trials system served as a useful exercise and might help improve the dialogue between the NCI and Cooperative Groups. Drs. Jaffee and Jacks wondered about how the NCI might best support, accelerate, and measure the best science, noting that science decisions can be

influenced by the local environment. Dr. Doroshow commented on the importance of engaging various communities to help make decisions. Dr. Varmus said that the discussion model is useful for some topics. A participant suggested that standards should be raised for Phase III trial designs and lowered for Phase II trials.

Dr. Deb Bruner, NRG, encouraged the NCI to consider the advantages of conducting large portfolio reviews (e.g., cross-study comparison of all disease sites in a portfolio vs. a study-by-study or organ-specific basis) for some mechanisms. Dr. Ridge reflected on the continued utility of disease-specific studies and other traditional modalities, pointing out that feasibility issues can arise with newer approaches.

X. ADJOURNMENT— DR. TYLER E. JACKS

Dr. Jacks thanked all of the Board members, as well as all of the visitors and observers, for attending.

There being no further business, the 166th regular meeting of the NCAB was adjourned at 5:20 p.m. on Tuesday, 9 September 2014.

Date

Tyler E. Jacks, M.D., Chair

Date

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