

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH  
NATIONAL CANCER INSTITUTE  
157<sup>TH</sup> NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting  
February 8, 2011**

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

**NATIONAL CANCER ADVISORY BOARD**  
**BETHESDA, MARYLAND**  
**Summary of Meeting**  
**February 8, 2011**

The National Cancer Advisory Board (NCAB) convened for its 157<sup>th</sup> regular meeting on 8 February 2011, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, 8 February 2011, from 9:00 a.m. to 1:57 p.m., and closed to the public on Tuesday, 8 February 2011, from 2:00 p.m. to 3:00 p.m. The NCAB Chair, Dr. Bruce A. Chabner, Director of Clinical Research, Massachusetts General Hospital Cancer Center, Massachusetts General Hospital, Boston, MA, presided during both the open and closed sessions.

**NCAB Members**

Dr. Bruce A. Chabner (Chair)  
Dr. Anthony Atala  
Dr. Victoria L. Champion  
Dr. Donald S. Coffey (absent)  
Mr. William H. Goodwin, Jr.  
Dr. Waun Ki Hong  
Mr. Robert A. Ingram (absent)  
Dr. Judith S. Kaur  
Ms. Mary Vaughan Lester (absent)  
Dr. H. Kim Lyerly  
Dr. Karen M. Meneses  
Dr. Jennifer A. Pietenpol

**Ad hoc Participants**

Dr. Marcia R. Cruz-Correa  
Dr. Kevin J. Cullen  
Dr. Olufunmilayo I. Olopade

**President's Cancer Panel**

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

**Alternate Ex Officio NCAB Members**

Dr. Michael A. Babich, CPSC (absent)  
Dr. Patricia Bray, OSHA/DOL  
Dr. Michael Kelley, VA  
Dr. Aubrey Miller, NIEHS  
Dr. Richard Pazdur, FDA (absent)  
Dr. John F. Potter, DOD  
Dr. R. Julian Preston, EPA (absent)  
Dr. Michael Stebbins, OSTP (absent)  
Dr. Marie Sweeney, NIOSH  
Dr. Lawrence Tabak, NIH (absent)  
Dr. Sharlene Weatherwax, DOE

**Members, Scientific Program Leaders, National Cancer Institute, NIH**

Dr. Harold Varmus, Director, National Cancer Institute  
 Dr. Kenneth Buetow, Associate Director, Center for Bioinformatics and Information Technology  
 Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences  
 Mr. John Czajkowski, Deputy Director for Management and Executive Officer  
 Dr. James Doroshow, Director, Division of Cancer Treatment and Diagnosis  
 Dr. Joseph Fraumeni, Director, Division of Cancer Epidemiology and Genetics  
 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. Douglas R. Lowy, Deputy Director, National Cancer Institute  
 Dr. Lori Minasian, Acting Director, Division of Cancer Prevention  
 Dr. Alan Rabson, Deputy Director, National Cancer Institute  
 Dr. Dinah Singer, Director, Division of Cancer Biology  
 Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities  
 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 Wiszneauckas, 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  
 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. Adam Clark, Lance Armstrong Foundation  
 Dr. Yvette Colon, National Cancer Institute, Director's Consumer Liaison Group  
 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. Lovell A. Jones, Intercultural Cancer Council  
 Ms. Rebecca A. Kirch, American Cancer Society  
 Dr. Steven Klein, National Science Foundation  
 Dr. Hal C. Lawrence, III, The American College of Obstetricians and Gynecologists  
 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. Barbara Muth, American Society of Therapeutic Radiology and Oncology  
 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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**TUESDAY, FEBRUARY 8, 2011****I. CALL TO ORDER, OPENING REMARKS, AND CONSIDERATION OF 7 DECEMBER 2010 MINUTES—DR. BRUCE A. CHABNER**

Dr. Chabner called to order the 157<sup>th</sup> NCAB meeting. He welcomed members of the Board, the President's Cancer Panel (PCP, the Panel), *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. Chabner reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Dr. Chabner welcomed three new NCAB members, who attended the meeting *ad hoc*: Drs. Marcia R. Cruz-Correa, Associate Professor of Medicine and Biochemistry, University of Puerto Rico Comprehensive Cancer Center, and Visiting Assistant Professor of Medicine, The Johns Hopkins University; Kevin J. Cullen, Director, Marlene and Stewart Greenebaum Cancer Center, University of Maryland; and Olufunmilayo I. Olopade, Walter L. Palmer Distinguished Service Professor of Medicine and Human Genetics, Director, Center for Clinical Cancer Genetics, and Associate Dean for Global Health, University of Chicago Pritzker School of Medicine.

**Motion.** A motion was made to approve the minutes of the 7 December 2010 NCAB meeting. The motion was seconded, and the Board unanimously approved the minutes.

**II. FUTURE BOARD MEETING DATES—DR. BRUCE A. CHABNER**

Dr. Chabner called Board members' attention to future meeting dates, which have been confirmed through 2012.

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

Dr. Harold Varmus, Director, NCI, welcomed members and described recent news regarding personnel, budgetary, and programmatic changes occurring in the NCI and activities of interest across the NIH. Dr. Varmus informed members that the NCI is awaiting the White House's approval for replacement of the six retired NCAB members and for the appointment of a third member to the PCP. Additionally, Dr. Peter Greenwald is the new Associate Director for Cancer Prevention in the Office of the Director (OD), and recruitment has begun for a Director of the Division of Cancer Prevention (DCP) and other positions. The NCI leadership held a retreat between the Scientific Program Leaders (SPL) and OD staff to discuss NCI activities and direction, including training and activities occurring at the NCI-Frederick campus. An intramural principal investigator (PI) retreat was held and included poster sessions and presentations by intramural investigators and a lecture by Dr. William G. Kaelin, Jr., Dana-Farber Cancer Institute and Harvard Medical School. In addition, Dr. Varmus held the second NCI Town Hall meeting on 10 January 2011.

**Budget.** Dr. Varmus reminded members that the NCI is operating conservatively under a Continuing Resolution (CR). The Institute's budget is significantly committed, but reductions to Cancer Center awards, contracts, or noncompetitive awards may be necessary to ensure that funding is available for three priority areas: support for 1,250 new research project grants (RPGs) in fiscal year (FY) 2011; cancer genomics activities; and improvements to the NCI clinical trials system.

The NCI is joining other NIH Institutes and Centers (ICs) in modulating its approach to funding new RPGs, based on peer review evaluation of each application's scientific merit, evaluation by program staff concerning the potential to deliver new and important findings, review by the SPL, and other

considerations related to NCI's portfolio analysis. The NCI anticipates that new investigator-initiated (R01) applications within the 7<sup>th</sup> percentile will be funded in FY 2011 and that it will consider applications between the 8<sup>th</sup> and 15<sup>th</sup> percentile for funding.

Dr. Varmus informed members that the NCI's bypass budget is being prepared and will include a narrative report of the NCI's progress in support of the Nation's efforts in controlling cancer and reducing the morbidity and mortality of cancer by applying basic biology and genetics knowledge to the goals of disease prevention and more effective diagnosis and treatment. He stated that the report highlights six cancers—melanoma, glioblastoma, neuroblastoma, ovarian cancer, lung cancer, and acute myeloid leukemia—that demonstrate significant differences between both types and subtypes of cancers, illustrate the nature and impact of the contributions made by the NCI in recent years, and show the prospects for further progress with continued investment in science both in the United States and around the world. The bypass budget includes a recommendation for a 15 percent budgetary increase. Dr. Varmus expressed appreciation to Mr. Rick Borchelt for his assistance in preparing the report.

**NIH and NCI News.** Dr. Varmus told members that a recent article by *The New York Times* on the National Center for Advancing Translational Sciences (NCATS) misrepresents the Center's purpose. He clarified that the NCATS will manage a number of programs that were overseen by the National Center for Research Resources (NCRR) and will provide more products and diagnostic tools (e.g., imaging) for the benefit of the ICs; programs overseen by the NCATS will not be funded with money taken from other ICs, and the Center will not serve as a pharmaceutical entity for the NIH.

Dr. Varmus highlighted his activities as a leader of the National Cancer Program (NCP), including recent meetings with the Cancer Prevention and Research Institute of Texas (CPRIT) Program and with leaders of the "Dream Team," a group of celebrities serving as a public voice for the Stand Up to Cancer initiative, as well as a teleconference with the board of the American Cancer Society (ACS). In addition, he informed members that the NCI's recruitment for a Director of the Center for Global Health is under way. The first task of the Director of the Center will be to develop a strategy that takes advantage of existing health systems to support research and reduce the cancer burden in poor countries. Research activities in developed countries on virus-related cancers, particularly the Epstein Barr virus (EBV), could be helpful. The NCI and National Institute of Allergy and Infectious Diseases (NIAID) are co-sponsoring a workshop on producing vaccines against EBV, which is implicated in numerous diseases, including mononucleosis, Burkitt lymphoma, nasopharyngeal carcinoma, Hodgkin lymphoma, and post-transplantation lymphoid disorders, as well as some gastric cancers. A collaborative workshop addressing HIV-related malignancies also is under discussion.

The Provocative Questions Initiative is capitalizing on past advances and taking advantage of observations that might not have been explored easily or without the advent of newer technologies. Dr. Varmus reminded members that the initial meeting held in October 2010 resulted in a short list of interesting questions and a Web site that provided a forum for dialogue among a broad set of disciplines. He said that two workshops were held in early February 2011 and solicited input from translational and population science researchers who brought together perspectives from the clinic, behavior, epidemiology, and prevention. A third workshop is planned to bring together basic scientists from oncology, cell biology, physics, chemistry, and other fields. The recent workshops have raised additional provocative questions, including: the use of commonly used drugs (e.g., aspirin) for prevention of colon and other cancers, and the effect of anti-inflammatory and anti-hypertensive agents, statins, and other widespread agents; the best means to evaluate, understand, and better describe primary cancer cells and the malignant potential of disseminated cancer cells; the imaging of smaller tumors through cancer cell targeting and new imaging agents; and the nature of radio resistance, including in combination with chemotherapy or targeting agents.

## Questions and Answers

Dr. Chabner asked about the delay in new NCAB appointments. Dr. Varmus indicated that he has provided candidate suggestions and is awaiting a response from the White House; he also noted the longstanding terms held by the current members of the PCP.

Mr. William H. Goodwin, Jr., Chairman and President, CCA Industries, Inc., suggested that, when the NCI circulates the Bypass Budget report for NCAB review, critical areas requiring review by specific NCAB members or subcommittees could be noted. Dr. Varmus said that the Bypass Budget narrative report has evolved over the years into a more attractive, more readable, and better organ of advocacy for the NCI that includes accounts of how discoveries are made, linkages between activities and ideas, investigators performing the research, and benefits of the work conducted.

Dr. Chabner requested further details about NCI's activities concerning training awards. Dr. Varmus replied that Drs. Jonathan Wiest, Director, Center for Cancer Training, and Sanya Springfield, Director, Center to Reduce Cancer Health Disparities (CRCHD), are overseeing the consolidation of NCI's training (Type K) awards, and that an update report will be presented at a future NCAB meeting. He added that the NCI is involved with training efforts across the NIH, and that NIH ICs have a keen interest in pursuing earlier counseling and training opportunities for graduate students in the biological sciences.

Dr. Chabner asked about NCI's discourse with the U.S. Food and Drug Administration (FDA) to get effective drugs to patients quickly, citing the comparison of active and inactive agents used in a Phase III trial to treat melanoma. Dr. Varmus said that the Institute's interactions with the FDA range from clinical collaboration to the support of regulatory science. In addition, the design of clinical trials of targeted therapies, including which new agents and combination of agents to test, has been raised as an issue during the Provocative Question exercises. Experience with HIV interventions has demonstrated the importance of combination therapies, and the FDA recently issued proposed guidance on the design of multi-drug trials. Dr. Chabner commented on the challenges presented by cellular and molecular resistance to targeted drugs in a variety of mechanisms. Dr. Varmus acknowledged the difficulties in randomized clinical trials across the cancer diseases; the rapid pace of discovery and the mechanisms involving genes other than the B-raf gene in the context of melanoma stand distinctly separate from drug resistance found in the use of erlotinib in lung cancer or in 95 percent of the resistance to Gleevec<sup>®</sup> in the treatment of chronic myelogenous leukemia (CML).

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

Dr. LaSalle D. Leffall, Jr., Chair, PCP, and Charles R. Drew Professor of Surgery, Howard University Hospital, thanked the NCAB and noted that the PCP consisted of himself and Dr. Margaret Kripke; a third panel member will be appointed by the White House. The mission of the PCP is to monitor the development and execution of the NCP and report directly to the President. The PCP should notify the President immediately of any delays or impediments to the NCP's progress.

The PCP's report on its 2009-2010 meeting series, *America's Demographic and Cultural Transformation: Implications for Cancer*, is complete and is expected to be released in March 2011. The 2010-2011 meeting series, *The Future of Cancer Research, Accelerating Scientific Innovation*, also is complete. Meetings were held in Boston, MA; Philadelphia, PA; Bethesda, MD; and Atlanta, GA. The series was inspired by the upcoming 40<sup>th</sup> anniversary of the National Cancer Act and attempted to better define the role of the various stakeholders in the NCP while considering the best direction for the future of cancer research and the NCP. Additionally, the series addressed how the cancer community can use a broad range of scientific, computational, and emerging disciplines to speed the NCP's progress.

At the Bethesda meeting, participants noted emerging models of clinical research that are changing the ways in which research projects are planned and conducted, including the use of Internet-based and other technologies to engage patients. The importance of NCP efforts to promote team science via multi-institutional and cross-disciplinary collaborations, as well as the need for improved coordination of efforts within the NCP, was discussed. Participants at the Atlanta meeting discussed their experiences developing innovative funding models for research and in addressing issues related to clinical research workforce shortages. The topic for the 2011-2012 meeting series has not yet been decided, because the Panel's composition may change. Possible topics include cancer prevention and the global cancer epidemic and research needs, and Dr. Leffall sought input from the Board on topics for the upcoming series. Further information can be found on PCP's Web Site (<http://deainfo.nci.nih.gov/advisory/pcp/pcp.htm>).

## Questions and Answers

Dr. Chabner noted that the topics mentioned were broad, and Dr. Karen M. Meneses, Professor and Associate Dean for Research, University of Alabama at Birmingham School of Nursing, agreed but allowed that the topic of global issues as they relate to cancer would be interesting to explore. Dr. Chabner added that perhaps the PCP could consider some of the "provocative questions" raised by Dr. Varmus.

Dr. Jennifer A. Pietenpol, Director, Vanderbilt-Ingram Cancer Center, B.F. Byrd, Jr. Professor of Oncology, Vanderbilt University Medical Center, suggested that the 2011-2012 series could highlight the six tumor types on which the NCI has chosen to focus.

Dr. Judith S. Kaur, Medical Director, Native American Programs, Mayo Comprehensive Cancer Center, Professor of Oncology, Mayo Clinic, wondered about the public's perception of personalized medicine as well as patients' willingness to participate in research that would require much personal information to be divulged. Dr. Leffall noted that care should be taken when using the term "personalized medicine." Dr. Varmus added that he did not care for the term "personalized medicine," but preferred the term "genetically informed medicine." He noted that this issue is related to the question of how informatics that will be linked to potential identifiers can be constructed. The question of how privacy can be made a respected issue that can be addressed in a way that allows for the use of information from the clinical trials system also must be addressed. Genetic data currently are not being collected or used in an effective manner.

## V. LEGISLATIVE UPDATE—MS. M.K. HOLOHAN

Ms. M.K. Holohan, Deputy Director, Office of Government and Congressional Relations (OGCR), reported on the composition of the new 112<sup>th</sup> Congress, appropriations, legislation of interest, Congressional outreach, and the outlook for the 112<sup>th</sup> Congress.

**The 112<sup>th</sup> Congress.** Ms. Holohan listed the new members of Senate and House committees important to the NCI, including House and Senate leadership; Appropriations Committees; Energy and Commerce; and Senate Health, Education, Labor, and Pensions (HELP).

**Appropriations Status.** There are no budget resolution bills or appropriations bills for FY 2011; a CR is in effect until 4 March 2011. The House will take up an extension of the CR the week of 14 February 2011, but will recess the week of 20 February. The FY 2011 funding levels still must be decided, and there has been discussion about returning to FY 2008 levels, which would mean an approximately \$300 million cut for the NCI. On 3 February, the House Budget Committee released a discretionary spending cap cutting \$34 billion from the FY 2011 CR level. The House plans to take up the CR using "open rule"; this will allow members the chance to target or protect specific agencies and programs. Several members have made public statements that exceptions to budget cuts should be made for biomedical research and/or the NIH budget.

**Legislation of Interest.** Little new health-related legislation is anticipated. A temporary extension (through 31 May 2011) of the Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) programs was signed by President Obama on 31 January 2011. The Breast Cancer Patient Protection Act (H.R. 111), which requires coverage for minimum hospital stays and secondary consultations for mastectomy or other breast surgery, was introduced on 5 January 2011 by Representative Rosa DeLauro (D-CT).

**Congressional Outreach.** The NCI plans to hold a member briefing after the Bypass Budget is released; this also will be an optimum time for NCI to work with advocacy organizations and educate members of Congress about the importance of cancer research and to create new champions in Congress.

**Outlook for the 112<sup>th</sup> Congress.** The Congress has stated that there will be increased oversight of the FDA, the Centers for Disease Control and Prevention (CDC), the Health Resources and Services Administration (HRSA), and the Agency for Healthcare Research and Quality (AHRQ). There is significant controversy within Congress regarding implementation of the Affordable Health Care Act, and various repeal efforts are anticipated. It is unlikely that other health-related issues will receive significant attention, at least in the House.

## **VI. NCI BIENNIAL REPORT: INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH—DRS. PAULETTE S. GRAY AND JEFFREY ABRAMS**

Dr. Gray informed members that the NCI prepares a biennial report on its inclusion of women and minorities in clinical research, which is presented to the NCAB for approval. This activity was initiated by Congress based on a national heart and lung nurse's study in which women were not included. She next introduced Dr. Jeffrey Abrams, Associate Director, Cancer Therapy Evaluation Program (CTEP). Dr. Abrams explained that the NIH policy on the inclusion of women and minorities in all clinical research studies, particularly Phase III clinical trials, was mandated by Congress in 1993 (P.L. 103-43), in espousal of the ethical principle of justice and of the importance of balancing research burdens and benefits. The policy does not allow cost as an acceptable reason for exclusion. The NIH Revitalization Act of 1993 required the preparation of biennial reports that describe the NIH IC's compliance with this requirement.

The NCI has established procedures to implement the NIH policy that encompass institute-wide coordination and communication, input from the NCI Population Tracking Accrual Working Group, training, and the resolution of problems. Important steps in the compilation and dissemination of information about inclusion involve the dissemination of the policy to applicants and peer reviewers, pre- and post-award activities and monitoring, and aggregate reporting to the NIH. In 1997, the Office of Management and Budget (OMB) issued Directive 15, which changed racial and ethnic standards for Federal reporting. Through the Directive, categories were changed to correspond to the 2000 census data collection, and data now are collected about ethnicity in addition to race and sex/gender. The report must describe subject selection criteria and rationale, rationale for exclusions, enrollment dates, outreach plans for recruitment, and proposed composition using new tables. The NCI's data include epidemiological, population-based interventions and therapeutic trials, as well as subset analyses by race, ethnicity, and sex/gender for all Phase III clinical trials with initial funding after 1995. A Phase III clinical trial is defined as a broadly based prospective Phase III clinical investigation that usually involves several hundred or more human subjects to evaluate an experimental intervention or compare two or more existing treatments, often with the aim of providing scientific evidence that can result in a change in health policy or standard of care. The current report cycle covers data reported in FY 2009-2010, which represents subjects enrolled in FY 2008-2009.

Dr. Abrams described overall reporting data and provided data specifically for cancer treatment trials. The U.S. cancer incidence rates estimated for 2003-2007 by race are: American Indian: 0.4 percent;

Asian/Pacific Islander: 5.9 percent; Black: 9.2 percent; White: 83 percent; and Hispanic: 8.9 percent. Dr. Abrams also provided data from Phase III enrollment research studies reported in the older and newer reporting formats, including the change in reporting ethnicities; the data illustrated the complexity of racial composition, cancer incidence rates, and enrollment data for extramural and intramural research studies, ethnic categories, and sex/gender. The percentage of NCI extramural and intramural enrollment shifted slightly between FY 2009 and 2010, with the Division of Cancer Control and Population Sciences (DCCPS) (58.8% in FY 2009 and 64.4% in FY 2010) and the Intramural Research Program (26.9% in FY 2009 and 26.7% in FY 2010) reporting the highest enrollment levels, followed distantly by the Division of Cancer Treatment and Diagnosis (DCTD), DCP, Division of Cancer Biology (DCB), and CRCHD. In addition, enrollment data for CTEP treatment trials for FY 2009 and 2010 were provided by race/ethnicity and gender.

## Questions and Answers

Dr. Chabner requested clarification on self-identifying in terms of race, observing that a large number of patients from Central and South America are unsure whether to self-identify as Hispanic, African, or European and self-identify their race as unknown. Dr. Abrams indicated that this is a self-reporting and educational issue. Ms. Gail Blaufarb, DEA, replied that Hispanic was included as a distinct category on the form to allow reporting by race, sex, and ethnicity. She added that another issue is that foreign studies, which do not categorize by these racial categories, are increasing. Dr. Gray said that the NIH created the form based on census categories. Dr. Olopade commented that specific information about ancestral origins would be helpful for genetic and genomic studies but less relevant for enumerating the number of minority patients in studies overall. Dr. Victoria L. Champion, Associate Dean for Research, Mary Margaret Walther Distinguished Professor of Nursing, Center for Research & Scholarship, Indiana University School of Nursing, said that study sections often decide general classifications; the great number of genetic variations within the United States presents self-identification challenges for patients who are enrolling in trials. Dr. Anthony Atala, Director, Wake Forest Institute for Regenerative Medicine, and Professor and Chairman, Department of Urology, Wake Forest University School of Medicine, encouraged the revision of the electronic form to include drop-down menus that increase the number of options available regarding the selection of race. Dr. Atala added that additional ethnicity information may help inform genomic data. Dr. Gray said that these suggestions would be provided to the NIH, which is responsible for the form.

Dr. H. Kim Lyerly, Director, Duke Comprehensive Cancer Center, George Barth Geller Professor of Cancer Research, Duke University Medical Center, asked about policies to increase the enrollment of specific minority populations in high-quality clinical trials. Dr. Abrams replied that individual groups, such as the NCI Clinical Trials Cooperative Group Program, examine enrollment and modify targets according to the perceived incidence in a specific disease as well as the incidence of a group in the U.S. population, but the Biennial Report requires reporting of data that are aggregated, rather than disease specific.

**Motion.** A motion was made to accept the NCI's Biennial Report on the Inclusion of Women and Minorities in Clinical Research. The motion was seconded and approved unanimously.

## VII. CONFLICT OF INTEREST: FACILITATION OF INDUSTRY INTERACTIONS— DR. DOUGLAS LOWY

Dr. Douglas Lowy, Deputy Director, provided an update on NCI interactions with industry relevant to the December 2010 report of the NCAB *Ad hoc* Working Group To Create a Strategic Scientific Vision for the National Cancer Program and To Review Progress of the National Cancer Institute. The report noted that constraints between NCI intramural investigators and the private sector due to conflict-of-interest regulations limit collaboration and exchanges of information, and it encouraged transparent consulting relationships with the private sector as part of NCI investigators' official duties.

Dr. Lowy informed members that consultation with industry is permitted for NIH investigators as part of their regular duties, and that considerable interactions do occur between NCI staff and industry, promoting public health by collaborating on research and clinical trials, sharing research materials, and having substantive discussions regarding the science. However, neither compensation for NIH staff nor exclusivity for industry partners is permitted. The activity usually is conducted with a confidential disclosure agreement (CDA) in place, with confidentiality binding for the entire NIH. Dr. Lowy said that consultative interactions with the private sector often are reduced because of the lack of honorarium and the cost of travel to the NCI.

The NIH employs a variety of agreements in its collaborations with industry. The NIH Office of Technology Transfer handles patenting, licensing, and policy issues. The NCI's Technology Transfer Center oversees transactional agreements related to cancer. In FY 2010, the NCI had 281 new CDAs with industry; 181 new material transfer agreements (MTAs); 19 new and 125 active clinical trial agreements (CTAs); and 216 cooperative research and development agreements (CRADAs), of which 26 were single agreements (regular), 17 were added to existing "umbrella" agreements, and 173 currently were active agreements. Dr. Lowy informed members that CDAs, MTAs, and CTAs do not provide licensing options, whereas CRADAs do.

Challenges to the collaborative process include the time to develop the agreements, particularly the CRADA, which requires multiple, lengthy steps. Nearly all of the NCI's CRADAs are housed within the intramural Center for Cancer Research (CCR) or the extramural DCTD, and efforts are under way to shorten the time needed to effect a CRADA. In addition, the recruitment of senior staff can present a challenge if a key activity of a possible recruit (or that of his/her immediate family) is determined to represent a conflict of interest. Waivers are possible, but they involve a lengthy process and are unlikely.

Dr. Lowy demonstrated the feasibility of successful industry interactions with several examples related to NCI's human papillomavirus (HPV) research activities. CDAs have been formed with companies that manufacture the commercial HPV vaccines and HPV-related technology. In addition, a three-way CRADA is in place to develop a low-cost, second-generation HPV vaccine. Through an MTA, reagents and hands-on instruction are available for a high-throughput HPV neutralization assay. Dr. Lowy said that fair access remains an important component of these agreements.

## Questions and Answers

Dr. Chabner said that he was encouraged to see the extent of the various clinical trial agreements, and that the *Ad hoc* Working Group was most concerned about the greater separation of NCI intramural scientists and clinicians from the newest drugs and treatments for cancer in comparison to their colleagues in academia, which may limit the ability to recruit staff. He observed that industry visits and regularly presents at academic centers about their therapeutics pipeline and asked whether the NCI experience is similar. Dr. Lowy indicated that the NCI and industry interact, although likely on a less regular basis than academic counterparts. Dr. Robert Wiltout, Director, CCR, explained that discussions about potential therapeutics occur between NCI and subsets of pharmaceutical companies through umbrella CRADAs. He acknowledged challenges with NCI investigators serving on scientific advisory boards of industry and noted that several recruited senior candidates have been lost to the CCR because of issues related to patent applications and holdings.

Dr. Atala encouraged the NCI to continue working with industry to define and commercialize future therapies, recognizing the need for transparency, avoidance of conflict of interest, and the distinct roles of both groups in public-private partnerships. Dr. Varmus agreed, but cautioned that there is resistance to changes in this area based on the idea that government employees may appear to be owned by industry; moreover, true conflict-of-interest issues should not be tolerated.

A discussion ensued about the NCI's policy regarding travel coverage as well as current constraints to the budget. Dr. Varmus reminded members that the NIH with the HHS, not the NCI, has the authority to change the policies. Mr. Goodwin suggested that the Board in tandem with other groups could provide thoughtful recommendations to NIH regarding changes to current policies. Dr. Varmus pointed out that a recent Congressional inquiry of the NCI concerning sponsored travel found no sponsored travel for NCI intramural investigators to industry-sponsored events. Dr. Chabner commented that encouraging this relationship might help discover better treatments or cures for cancer diseases. Dr. Lowy added that these interactions are conducted in the interest of public health.

Dr. Cullen requested details about the total dollar value that comes to the NCI through CRADAs and other mechanisms. Dr. Pietenpol asked whether the amount includes clinical trials. Dr. Lowy indicated \$8-9 M per year are received through CRADAs. Dr. Karen Maurey, Director, Center for Technology Transfer, stated that the CRADA is the only legal authority in technology transfer agreements through which the NCI can receive funding to offset costs related to the specific project defined by the CRADA; she added that clinical trials are supported by CTAs and some CRADAs. Dr. Lowy provided the example of an NCI-supported proteomics initiative that characterizes antibodies that are produced by private sector companies, for which those companies support the endeavor.

In response to a query by Dr. Chabner regarding compensation and the time needed to establish a CRADA versus a CTA, Dr. Maurey clarified that the NCI can negotiate a CRADA that includes funding to offset costs, regardless of the type of research (e.g., basic or clinical) conducted. In conducting a clinical trial, the NCI can receive an agent, information, or data but not funding. There is no notable time savings in developing a specific type of agreement with the NCI's intramural research program. Dr. Varmus said that monetary incentives can support trials that are of lower scientific caliber than desirable.

Dr. Cullen requested clarification about allowable costs under a CRADA. Dr. Maurey explained that the NIH does not permit funding to offset the PI's salary but it can be used to hire a postdoctoral researcher. Dr. Chabner commented that timing is critical in the CRADA process to ensure the agreement is usable for the PI. Dr. Maurey noted that several factors influence the speed in developing the CRADA, including industry priorities and expectations. Dr. James H. Doroshow, Director, DCTD, provided an example of a successful trial conducted under the umbrella CRADA: alveolar soft part sarcoma is a disease with an incidence rate of approximately 100 patients per year; because NCI had an intramural umbrella CRADA in place with a private-sector partner supplying an agent, the protocol for a Phase II trial was prepared in 1 month and the trial already has accrued 30 patients in 1 year's time.

Dr. Kaur stated that the *Ad hoc* Working Group's primary concerns revolved around recruitment challenges caused by the conflict of interest issues and the need for quality work conducted efficiently across the clinical trials system. Dr. Varmus said that the Lasker Scholars Program Award is a recent NIH initiative to recruit junior clinical faculty to the NIH; a symposium is scheduled for March 31.

Dr. Chabner offered the Board's services in advocating for an easier relationship with industry to improve NCI's ability to recruit and retain the best clinical and preclinical investigators. Dr. Varmus suggested that the Board could consider how changes in the NIH's ethical guidance have affected the way that NCI intramural investigators work and whether the policy could be liberalized to allow a richer interface with industry while preserving the NCI's public reputation. Dr. Lowy added that many people have the misperception that NIH investigators are not permitted to work with industry; problems with consulting arose in the past because existing regulations were not followed, rather than because of inadequate regulations. Dr. Atala encouraged involving other ICs in this effort; Dr. Varmus said that the NCAB can address the issue from the NCI's perspective, but that a multi-institute effort would require approaching the Advisory Committee to the NIH Director.

**Motion.** A motion was made to establish a Subcommittee to assist the NCI in interactions with industry, including conflict of interest issues. The motion was seconded and approved with 11 ayes, no nays, and 1 abstention.

The purpose of this *Ad hoc* Subcommittee is to advise the National Cancer Advisory Board (NCAB) and the NCI Director on ways to improve the recruitment and retention of intramural staff and factors that are significantly impeding this effort.

The Subcommittee will evaluate the following:

- 1) Identify recruitment challenges and establish best practices to ensure improved relationships with industry while following conflict of interest policies.
- 2) Consider how changes in NIH's ethical guidance have affected the way NCI intramural investigators work together and whether the policy could be liberalized to allow for a richer interface with industry while preserving NCI's public reputation.
- 3) Advise on how to engage in ethically conducted and fully transparent consulting and collaborative relationships with the private sector *as part of one's official duties*.

### **VIII. ANNUAL DELEGATIONS OF AUTHORITY—DR. PAULETTE S. GRAY**

Dr. Gray requested concurrence by the NCAB on two Delegations of Authority to the Director of the NCI. She described the delegations and the provisions in the Statement of Understanding. Delegation A allows the Director to obtain the services of not more than 151 special experts or consultants who have scientific or professional qualifications. Delegation B specifies that the NCI Director can appoint advisory committees composed of private citizens and officials of Federal, state, and local governments.

The Statement of Understanding with NCI Staff on Operating Principles in Extramural Grants also falls within the Delegations of Authority to the Director, NCI. NCAB operations are conducted in accordance with management and review procedures described in the NIH Manual Issuance 4513. Concurrence of the NCAB with recommendations of initial review groups will be required, except for the following: 1) Training grants and fellowships and other non-research grant applications are not subject to NCAB review and approval, and without other concerns may be awarded without presentation to the NCAB for concurrence, with the exception of Ruth L. Kirschstein National Research Service Awards. 2) Applications over the 50th percentile will not have summary statements presented to the NCAB. 3) For applications assigned raw scores that are not percentiled, the cutoff will be a priority score of 250. Dr. Gray stated that this number, in keeping with the new scoring paradigm, will change to 50 for all mechanisms except R41, R42, R43, and R44 awards; for the latter, all scored applications will be included. Expedited Concurrence: 1) for R01 and R21 applications with percentiled or raw scores that fall within the NCI paylines for that mechanism, a process of expedited concurrence will be used; and 2) the Executive Secretary will alert Board members with responsibility for expedited concurrence when review outcomes for eligible applications are available on the Electronic Expedited Concurrence portion of the Electronic Council Book. Administrative Adjustments: 1) Permission is delegated to the Director, NCI, to allow staff to negotiate appropriate adjustments in dollars or other terms and conditions of grant and cooperative agreement awards. 2) Administrative requests for increases in direct costs that are the result of marked expansion or significant change in scientific content of a program after formal peer review will be referred to the Board for advice and recommendation. 3) Actions not requiring Board review or advice, such as change of institution, change of PI, phase-out or interim support, or additional support, need not be reported to the Board. 4) NCI staff may restore requested time and support that were deleted by the initial review group when justified by the PI in an appeal letter or when restoration is in the best interest of the NCI and the project is of high NCI programmatic relevance.

## Questions and Answers

Dr. Lyerly asked whether members could receive summary statements of grant applications and exceptions in electronic format prior to the Board meeting. Dr. Gray agreed that information about the applications will be included on the electronic Council Board book site, excluding those grants for which members may have conflict-of-interest issues, and that decisions about exceptions are being handled differently than in the past.

**Motion.** A motion was made to approve the NCI's Annual Delegations of Authority. The motion was seconded, and the Board unanimously approved the delegations.

### **IX. STATUS REPORT: IMPLEMENTATION OF THE INSTITUTE OF MEDICINE CLINICAL TRIALS REPORT RECOMMENDATIONS—DR. JAMES H. DOROSHOW**

Dr. Doroshow explained that the NCI's goal is to develop a network of clinical trials groups that will collaborate to co-implement and conduct innovative and practice-changing trials. The NCI must decide how many Cooperative Groups there should be and the nature of the organizing principles and peer review recommendations for the program.

The assumptions underlying the change in the clinical trials system are that the NCI must: rapidly complete large randomized multi-site Phase II and Phase III trials of the highest scientific priority; implement the Institute of Medicine (IOM) recommendations as part of a comprehensive approach to change that alters current incentives; rely on a precisely focused peer review system; and carry out substantial operational, management, and cultural change. Change is necessary because the NCI must be able to prioritize its molecular characterization resources and, given the limitations in resources, prioritize nationally across all diseases. Currently, there are clear disincentives to study less common diseases, which is a major role for the NCI. Additionally, the NCI could more easily implement a shared information technology (IT) infrastructure for clinical data and tissue resource management with fewer independent entities. The NCI must mobilize enough sites to conduct molecular screening on patient populations as well as integrate the resources that have been invested during the past decade in the American College of Radiology and Imaging Network (ACRIN). The Division of Cancer Treatment and Diagnosis could work in better harmony with the Division of Cancer Prevention in creating trials in therapy and cancer prevention. The change will allow the NCI to consider how to develop and access critical tissue specimens from patients by using annotated prospective randomized data. Finally, the NCI must consider how access to a national clinical trials network for clinical and translational investigators.

If the NCI decreases the number of groups and several of those groups still are functioning independently instead of as part of the network, it will have failed in this reorganization. Metrics for success include creating a system that opens and completes trials quickly, provides a unified clinical and translational infrastructure for the extramural community, and is at the forefront of translational cancer discoveries. In the current system, there are 10 funded cooperative groups with their own tumor banks, operations offices, disease committees, and statistics and data-management operations. Ten is too many, but there need to be enough groups to allow a national system of investigators to be engaged. Several multi-disease Adult Groups (not to exceed four) should be ample, and the one pediatric group should remain. The Adult Groups' diseases will be decided based on the integration of specific Group disease committees. This networked system will be better able to perform studies: in less common malignancies, requiring sophisticated imaging modalities, and necessitating rapid molecular characterization of tumors. It also will facilitate studies that involve access to a nationally integrated tissue resource, are initiated by investigators not now involved in current group activities, and are prioritized across all diseases and modalities of care. The current structure will be transformed to support a system that functionally is a network of groups with integrated infrastructure and responsibilities. Any group can generate ideas, manage a trial, be credited by

investigators who belong, and will be required to support and manage studies originated by investigators outside the group if the study is approved by the Steering Committee.

Benefits of the reorganization include improvement in the operation of trials, and preservation of the NCI's investment in the current system through maintenance of four Adult Groups. There are risks as well: costs will increase, leadership issues among Groups must be managed, and multiple stakeholders must support the change. To conduct the reorganization, the NCI and Group leadership must: manage the program as a collaborative national program to reach shared goals, share decision making to support the public-private nature of the funding structure, and manage and review the system as both a scientific and operational enterprise, which will require major changes in the peer-review system. Current incentives must be focused away from giving credit to the Group for leading a trial and toward developing trials that will address the most important scientific questions in a timely manner. Assistance in developing priorities will be provided by a cross-disease panel of extramural scientists, Group scientific and statistical co-PIs, Steering Committee Chairs, advocates, and the NCI. Peer review for the new system will include a competitive review of the Groups every 5 years, all conducted in the same year so that the Groups' outcomes can be compared and resources allocated accordingly; these reviews will be briefer than current reviews and limited to Group leadership, and will not be conducted concurrently with Community Clinical Oncology Program (CCOP) reviews. Reviews will focus not only on trials by specific disease committees, but will assess the role of the Group as part of an integrated trials system. Operational efficiency will be reviewed based on implementation of operational frameworks, streamlining of operational processes, development of relevant IT infrastructure, achievement of timeline goals for each step in trial activation, achievement of target accrual goals, effective trial oversight, and data quality. Groups will not be reviewed in isolation, but on their contributions to the national clinical trials system. National specimen banks also must be reorganized to provide prospective collection and storage of specimens, a system for cataloguing and retrieving legacy specimens, an IT tracking system connecting all banks, and connections between banks, statistical centers and the clinical trials system.

The new system will be a network of five groups that interact; Dr. Doroshov hopes to bring this National Clinical Trials Network together with the Cancer Center Network to make the best studies available to all investigators nationally. To implement the change, a new Funding Opportunity Announcement (FOA) will be required. Renewal applications are no longer being accepted for the cooperative groups, which are being maintained through funding supplements. This FOA should be published, tentatively, in July 2012, and come to NCAB for review in May 2013; awards will be presented after October 2013. The next steps in developing the system are to work with stakeholders, provide opportunity for public comment, modify recommendations based on feedback, and simultaneously advance ongoing work on other issues raised by the IOM (e.g., funding, efficiency, tissue banks).

## Questions and Answers

Dr. Champion suggested, based on her involvement in several cooperative groups, that externally funded and purely behavioral studies should be considered.

Dr. Waun Ki Hong, Professor, Head of Division of Cancer Medicine, Department of Thoracic/Head & Neck Medical Oncology, The University of Texas M.D. Anderson Cancer Center, stated his support for the changes, but asked how the existing groups would be dissolved and incorporated into the new groups. Dr. Doroshov answered that the best way to accomplish this would be voluntarily within groups, with facilitation and incentives provided by the NCI. Dr. Chabner asked how specialized modality and surgically oriented groups could join a larger group and still preserve their identities. Dr. Doroshov responded that the NCI was working to facilitate solutions to this issue; for example, if one group is invested in women's cancers and another in brain tumors, the reorganization could put some of those organizations in the lead as opposed to medical oncology dominated groups.

Dr. Atala asked, regarding patient accrual, how the centers that provide patients nationwide can do so in an open manner as in other clinical trials. Dr. Doroshov said that the NCI has considered different reimbursement models that reflect the intrinsic costs of conducting the trials in light of the clearly acknowledged fact that NCI is not supporting institutions at a level that covers their costs.

Dr. Kaur questioned whether any cancer patient nationally might be able to have access to a trial, and if this possibility might both improve the percentage of cancer patients who are placed on a high priority trial and engage a higher percentage of the medical oncology community in high-quality health care. Dr. Doroshov said that the current infrastructure for trials is costly, and that the NCI's work has been progressing in providing the trial sites with a uniform remote data capture IT infrastructure, for example.

Dr. Cullen asked how the NCI envisions affiliations between centers and the new groups if the ultimate goal is an open-access platform. Dr. Doroshov recognized this as a challenge as specialists would accrue to their own specialty trial groups, which would result in piecemeal reimbursement for cases. The NCI must develop a system in which reimbursements help to pay the costs associated with individual patients, whoever is responsible for paying those costs.

Dr. Chabner asked if, after the reorganization, there would be a 50 percent decrease in accrual rates, half the number of trials, and double the funding for cases. Dr. Doroshov answered that a model was in production, but the deciding factor will be accrual rates; it would be helpful if the NCI develops a higher standard for conducting a Phase III trial that follows a randomized Phase II study.

#### **X. ONGOING AND NEW BUSINESS—DR. BRUCE A. CHABNER**

Dr. Chabner invited members to suggest agenda topics for future NCAB meetings. He noted that two matters include: how the FDA handles drug approvals and the NCI's role in that process; and the formation of the NCAB Subcommittee to help the NCI work with industry. Dr. Chabner added that the Subcommittee should plan to meet before the NCAB meeting in June.

#### **Questions and Answers**

Dr. Atala suggested that the first meeting of the new Subcommittee could be held via teleconference.

#### **XI. CLOSED SESSION—DR. BRUCE A. CHABNER**

*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 affirmed by all serving Board members present. During the closed session of the meeting, a total of 4,240 applications were reviewed requesting support of \$1,203,152,723. In addition, 17 FDA applications were reviewed.

**XII. ADJOURNMENT**  
**DR. BRUCE A. CHABNER**

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

There being no further business, the 157<sup>th</sup> regular meeting of the NCAB was adjourned at 1:57 p.m. on Tuesday, 8 February 2011.

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Date

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Bruce A. Chabner, M.D., Chair

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Date

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