

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
155TH NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
September 7–8, 2010**

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

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
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The National Cancer Advisory Board (NCAB) convened for its 155th regular meeting on 7–8 September 2010, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, 7 September 2010, from 4:00 p.m. to 5:37 p.m., and Wednesday, 8 September 2010, from 10:00 a.m. until adjournment at 12:53 p.m., and closed to the public on Wednesday, 8 September 2010, from 8:30 a.m. to 10:00 a.m. The NCAB Acting Chair, Dr. Bruce A. Chabner, Clinical Director, Massachusetts General Hospital Cancer Center, Boston, MA, presided during both the open and closed sessions.

NCAB Members

Dr. Bruce A. Chabner (Acting Chair)
Dr. Anthony Atala
Dr. Victoria L. Champion
Dr. Donald S. Coffey
Dr. Lloyd K. Everson
Ms. Kathryn E. Giusti (absent)
Mr. William H. Goodwin, Jr.
Dr. Waun Ki Hong
Mr. Robert A. Ingram (absent)
Dr. Judith S. Kaur
Mr. David H. Koch
Ms. Mary Vaughan Lester (absent)
Dr. Diana M. Lopez
Dr. H. Kim Lyerly
Dr. Karen M. Meneses
Dr. Jennifer A. Pietenpol
Dr. Carolyn D. Runowicz
Dr. Daniel Von Hoff (absent)

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
Dr. Patricia Bray, OSHA/DOL
Dr. Geoffrey Krystal, VA
Dr. Audrey Miller, NIEHS
Dr. Richard Pazdur, FDA
Dr. John F. Potter, DOD
Dr. R. Julian Preston, EPA (absent)
Dr. Michael Stebbins, OSTP
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
 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, Director, Division of Cancer Prevention
 Dr. Lee Helman, Scientific Director for Clinical Research, Center for Cancer Research
 Dr. Douglas R. Lowy, Deputy Director, National Cancer Institute
 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 Wiszniauskas, 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 Giambaresi, American Urological 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, SEPTEMBER 7, 2010**I. CALL TO ORDER, OPENING REMARKS, AND CONSIDERATION OF 22-23 JUNE 2010 MINUTES—DR. BRUCE A. CHABNER**

Dr. Chabner called to order the 155th NCAB meeting. He welcomed members of the Board, the President's Cancer Panel (PCP), *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.

Motion. A motion was made to approve the minutes of the 22–23 June 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 thanked them for their service on the Board. As the new Director of the NCI, he welcomed the opportunity to obtain advice from the NCAB and indicated his preference to work in a less formal and more collegial manner than is customary with some advisory councils. He recognized the additional service of retired members at this meeting and said that new Board members will be appointed soon. Dr. Varmus discussed his approach to cancer research, challenges facing NCI's cancer research program, and the NCI budget. He informed members that he accepted the NCI Directorship because both the potential for tremendous advances in cancer control and the support from an Administration that recognizes the importance of science in addressing societal issues make this an opportune time to run the NCI and participate in the National Cancer Program (NCP). He also appreciated the opportunity to expunge the "Institute and Center (IC)-envy" that he experienced as the NIH Director when he had little influence over scientific programs and no funds available for trans-NIH initiatives. Lastly, Dr. Varmus expressed a longstanding affection for the NIH as a public institution that embodies the best of America.

Dr. Varmus reported on changes in NCI personnel and organization. Dr. Douglas R. Lowy is a newly appointed Deputy Director and also serves as Acting Director of the Center for Strategic Scientific Initiatives. Dr. Al Rabson remains an NCI Deputy Director. A third Deputy Director, with major responsibilities over clinical and translational research, is being sought. Recruitment is underway for leadership of two new NCI Centers—the Center for Cancer Genomics and the Center for Global Cancer Research—as well as for a Director for the Center for Strategic Scientific Initiatives and an executive officer to serve as the Deputy Director for Management. The Executive Committee (EC) has been separated into two groups: the Scientific Program Leaders (SPLs) and an Office of the Director (OD) staff group.

Dr. Varmus informed members that his approach to cancer research is based on using all available resources to understand and control cancer better without preference for a specific mechanism or specific disease. The cancer domain contains several inherent tensions, including that between individual scientists and scientific teams; both have a place in cancer—high-throughput, complicated multidisciplinary science tends to drive the agenda, but the role of individuals also is important. A concern with scientific teams is that they do not always provide members with the credit they deserve. Another area of tension revolves

around the public health needs that are apparent from accounts of disease burden and scientific opportunities that arise; a balance of these two can help define scientific priorities. These needs and opportunities are delineated in the budget, even though precise quantitation is difficult. Investment in research on rarer diseases, such as retinoblastoma, has provided a window into understanding cancer, including how the cell cycle controls tumor suppressor genes, the way in which cancer genes can be inherited, and the roles of DNA and RNA tumor viruses. Discoveries in developmental biology about fruit flies, worms, and zebrafish have played an important role in studying human disease and stand as a foundation of today's knowledge of oncogenes and tumor suppressor genes. The NCI will continue to support individual investigators in unfettered scientific inquiries through R01 grants as well as centralized mega projects like The Cancer Genome Atlas (TCGA). Dr. Varmus suggested that incentives should not be monetary but rather inspirational and temporary.

Dr. Varmus announced the "Big Questions Initiative," a new effort to advance the progress made against cancer. The initiative will include a small group of scientists who ask questions based on recent scientific discoveries that, if answered, would overcome a significant roadblock in cancer research. Dr. Varmus provided examples of big questions, including "Why do cells die when oncogenes are inhibited or de-induced?" Relying on recent research about oncogene addictions, an answer may be found by employing a metabolic approach to examine cells during anabolic and catabolic phases to enhance understanding of the balance between factors that promote cell survival or death. Another big question draws on research that used synthetic lethality to reveal co-dependencies on serine threonine kinases in the presence of a mutant *ras* oncogene, yielding inherently so-called druggable targets; the kinases were previously known but not perceived as interesting. In addition, Dr. Louis Staudt's work on non-Hodgkin's lymphoma has shown that several elements in the B cell signaling pathway come from mutant antigen receptors, including CAR11, providing new potential targets for therapeutic agents. Other examples include metastatic niches, genotyping, and obesity's role in cancer initiation. Dr. Varmus observed that some NCI activities, such as training, clinical trials for therapeutic testing, and communication efforts, will not be addressed by developing great questions. He expressed his appreciation to NCI staff who have been forthright in their discussions with him about NCI programs, and he said he was impressed with the quality of NCI personnel.

A new Center for Cancer Genomics is being created to oversee TCGA, which is a collaborative effort between the NCI and the National Human Genome Research Institute (NHGRI). As a signature program of the NCI, TCGA has pilot projects focused on glioblastoma, ovarian cancer, and squamous lung cancer, and early results indicate that the Program will have a significant impact on cancer research. Dr. Varmus described a similar project conducted by the Sanger Center in England as an example of influential genomic studies; that project found that 60 percent of melanomas have mutations in *B-raf*, a serine threonine kinase, and targeting with the agent PLXL4032 in Phase II trials showed an 80 percent response rate, reflecting a monumental breakthrough in treating metastatic melanoma. Recruitment has begun for a Director of the Center who can take advantage of all the opportunities that TCGA and other genomic projects provide across the cancer research spectrum of data collection, diagnostics, prevention strategies, biomarkers, therapeutics, and regulation. Dr. Varmus invited members to recommend names of candidates to direct the Center.

Dr. Varmus next discussed four areas of the NCI that he would like to strengthen. (1) *Improving the clinical trials system*. The Institute of Medicine's (IOM) report identified actions needed, and the NCI has been implementing course corrections. In addition to improving efficiency and organization, this effort is about injecting a new kind of science into the way that the NCI conducts clinical trials. It is a timely activity, given that the basic science of cancer therapeutics is changing and a changed trial system should make better use of TCGA data and other genetic discoveries. (2) *Strengthening clinical research in the intramural arena*. The NCI uses the Mark O. Hatfield Clinical Research Center, but the clinical research effort at the NIH could be strengthened by recruiting great scientists into the program and building the patient base through interactions with the U.S. Department of Defense (DoD) and partnerships with The

Johns Hopkins University (JHU). Approaches include: sharing with JHU the opportunity to accomplish more in oncology than might otherwise be possible, such as the study of pediatric gastrointestinal stromal tumors and other rare cancers that cannot be easily studied elsewhere, and involving extramural investigators who can enrich the cohort of people who conduct clinical research in the intramural program. (3) *Streamlining the research pipeline from basic to translational to clinical and therapeutic research.* Complications include potential overlap between the NCI, NCI-Frederick, or NCI externally and the new Cures Acceleration Network (CAN) initiative; regulatory issues involving the Food and Drug Administration (FDA); and conflict-of-interest issues governing interactions with industry. (4) *Enhancing collaborative activities.* Dr. Varmus expressed support for building bridges between institutions and between the programmatic and clinical sides. Collaborative activities already exist, such as working with the NHGRI on TCGA. Collaboration could be enhanced with other NIH ICs, other Federal agencies (e.g., the FDA and the Centers for Disease Control and Prevention [CDC]), and industry.

The NCI's Center for Global Cancer Research is a new Center that will support the NCI's role in global health. Dr. Varmus said that much work could be done to reduce the growing burden of disease due to cancer in poor countries. For example, cervical cancer is often a major cause of death from cancer in poor countries and is almost always due to human papillomaviruses (HPVs). Dr. Lowy has been instrumental in vaccine development and testing in Costa Rica against the highly implicated HPV strains 16 and 18. Three serial vaccinations have been required, but a recent field study suggests that one vaccination may produce almost the same effect as two or three injections, making the vaccine more affordable to low-income populations and thereby reducing the toll of cervical cancer. The new Center will address a plethora of issues, ranging from the control of tobacco and other carcinogenic substances to the use of vaccines to the development of inexpensive therapeutic modalities. Most deaths from cancer today occur in the poorest areas of the world, and Dr. Varmus affirmed the NCI's responsibility to help address this.

Dr. Varmus informed members about the fiscal year (FY) 2010, 2011, and 2012 budgets. The NCI is expected to close out its FY 2010 budget efficiently and effectively on September 30. The SPLs have been making final funding decisions about requests for applications (RFAs) and other grant programs, and will make several more awards soon. The FY 2010 payline is at the 16th percentile, plus exceptions, and the new investigator payline is at the 20th percentile. A total of 1,250 competing research project grants (RPGs) were awarded in FY 2010, which is slightly higher than in FY 2009. The American Recovery and Reinvestment Act (ARRA) appropriations of \$1.26 B for the NCI will end this year. FY 2011 likely will begin under a Continuing Resolution (CR). The President's Budget (PB) request was presented to both Houses of Congress during the appropriations hearing cycle. The House Subcommittee has marked up a bill, which has not yet been presented to the full Appropriations Committee. The Senate Subcommittee has marked up its bill, which was passed by the full Committee. It remains to be scheduled to the Senate floor for a vote or be incorporated officially into the Health, Education and Labor bill. The Senate's bill reflected the PB request: \$32 B for the NIH and \$5.256 B for the NCI. The Senate bill earmarks \$50 M of the NCI budget for the CAN. The Office of Management and Budget (OMB) asked the NIH to conduct a "5-percent reduction" exercise in preparing its FY 2012 budget. The NCI and other ICs responded with due diligence to this request and await the OMB's response.

Changes in stem cell policy have been prominent this year, most recently with Judge Lamberth's reinterpretation of the Dickey-Wicker Amendment. The Amendment was written when Dr. Varmus served as the NIH Director, and in 1999, he requested Interpretation 15 from the U.S. Department of Health and Human Services (HHS) General Counsel, which stated that stem cells are not embryos and prohibition on use of federal funds for research that would damage or kill embryos does not apply to stem cell research funding. Dr. Varmus expressed his disagreement with Judge Lamberth's ruling, which states that federal funds should not be used for stem cells because creating stem cells does entail damaging embryos, and he noted that the Department of Justice is filing an appeal. A stay has been filed to keep the ruling from going into effect until the Appeals Court has heard the Administration's appeal. Congressional options include

dropping the Amendment this year when the Appropriations bill is passed or again passing a bill to endorse the use of federal funds for stem cell research. Any effect of this policy change on specific grants or grant applications will be discussed during the Board's Closed Session.

Dr. Varmus reported other news of interest. The NCI leadership will meet with representatives from the OMB to discuss clinical trials and other issues; Mr. Jack Lew is being appointed as the OMB Director. Dr. Varmus will speak at a caucus meeting arranged by the American Association for Cancer Research (AACR) that several members of the House are expected to attend. He also noted that the NCI held a ground-breaking ceremony on 1 September 2010 at the Shady Grove site for the new buildings that will house 2,200 NCI employees.

Questions and Answers

Dr. Chabner asked how the NCI might expedite the new approach to treating cancer disease, particularly in terms of sophisticated processing of clinical specimens. Dr. Varmus recognized the difficulties in proper specimen collection and handling and described NCI's role as a convener and communicator in the interactions between genetic testing organizations, Cancer Centers and other NCI-supported laboratories, and clinical research groups.

Dr. Aubrey Miller, National Institute of Environmental Health Sciences (NIEHS), asked about NCI's approach to the interplay between environmental exposures and genetics in cancer research. Dr. Varmus replied that environmental contributions to oncogenesis are important, and scientific investigations on tobacco use, for example, indicate that genotyping may help identify carcinogenic agents in the environment.

Dr. Jennifer A. Pietenpol, Director, Vanderbilt-Ingram Cancer Center, and B.F. Byrd, Jr. Professor of Oncology, Professor of Biochemistry, Vanderbilt University Medical Center, asked Dr. Varmus to share his thoughts on extramural activities, such as training and recruitment of individuals into cancer-based research. Dr. Varmus answered that training is important, but a greater concern is having trained investigators focus on important and interesting questions. He added that novel means of streamlining academic training and recruiting students to become cancer disease-focused investigators and physicians include a Ph.D. graduate curriculum in cancer biology with clinical experience.

Dr. Carolyn D. Runowicz, Director, The Carole and Ray Neag Comprehensive Cancer Center, Northeast Utilities Chair in Experimental Oncology, and Professor of Obstetrics and Gynecology, University of Connecticut Health Center, requested further details about how Dr. Varmus envisioned working with the NCAB. Dr. Varmus proposed an approach similar to the one he used when he was NIH Director, namely that his advisory board held general discussions on matters of interest, and members were assigned to deal with specific problems in the extramural or intramural scientific communities; external experts were consulted to assist with finding solutions.

Dr. Chabner indicated that the December 2010 meeting would include a report from the NCAB *Ad hoc* Working Group To Create a Strategic Scientific Vision for the National Cancer Program and Review of the National Cancer Institute.

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

Dr. LaSalle D. Leffall, Jr., Chair, President's Cancer Panel (PCP, the Panel) and Charles R. Drew Professor of Surgery, Howard University Hospital, reminded members that the Panel currently consists of Dr. Leffall and Dr. Margaret L. Kripke. The White House appointment of a third Panel member is pending. Dr. Leffall stated that the mission of the Panel is to monitor the development and execution of the activities

of the National Cancer Program (NCP) and to report any delays or blockages in the rapid execution of the NCP directly to the President.

The 2009–2010 meeting series covered the topic “America’s Demographic and Cultural Transformation: Implications for the Cancer Enterprise.” Meetings were held in Seattle, WA; Los Angeles, CA; Wilmington, DE; and Miami, FL, and statements and summaries of the meetings are available on the PCP Web site (<http://deainfo.nci.nih.gov/advisory/pcp/>). The Panel has begun preparing the 2009–2010 report and anticipates its release in January 2011.

Dr. Leffall informed members that the 2010–2011 meeting series “The Future of Cancer Research: Accelerating Scientific Innovation” is inspired by the 40th anniversary of the 1971 National Cancer Act. The meetings will attempt to better define the role of various stakeholders in the NCP and will reflect on past progress and consider the best direction for the future of cancer research and the NCP. The series also will consider how the cancer community can utilize a broad array of scientific, computational, and emerging disciplines to accelerate progress of the NCP. The meetings are scheduled for 22 September 2010 in Boston, MA; 26 October 2010 in Philadelphia, PA; 14 December 2010 in Bethesda, MD; and 1 February 2011 in Atlanta, GA. The meeting in Boston will include speakers from across federal agencies, the public and private sectors, and nonprofit and academic organizations, who will discuss how their organizations define the NCP and their role and responsibilities within the NCP. Subsequent meetings may explore topics related to technologies applicable to research on cancer prevention, causation, and care; collaborations needed to apply such technologies to cancer research; medical, ethical, and legal issues; and barriers to advancing to a new era of cancer research.

Questions and Answers

Dr. Runowicz expressed support for filling the vacant seat on the Panel, noting the tremendous inspiration that former member Mr. Lance Armstrong provided in keeping the cancer problem visible and in serving as an inspiration to young people. Dr. Leffall affirmed Mr. Armstrong’s impressive story as a cancer survivor and powerful role as a PCP member; he indicated that the PCP is awaiting response from the White House concerning the appointment of the third Panel member.

Dr. Chabner asked about the public availability of the Panel’s meeting agendas, the level of effort that Dr. Leffall expends on the meetings, and the impact of the PCP’s work on the White House. Dr. Leffall confirmed that the meeting agendas are available to the public on the PCP Web site and said that he spends a significant amount of time on the Panel’s meetings and related activities. He confirmed that the White House is aware of the PCP’s activities.

V. LEGISLATIVE UPDATE—MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Government and Congressional Relations (OGCR), reported on appropriations and legislation of interest. The PB was announced on 1 February 2010, allocating to the NIH and NCI \$32.09 B and \$5.26 B, respectively. In the House, the Labor, HHS, Education Appropriations Subcommittee passed a bill, but it was not considered by the full Committee. In the Senate, the Labor, HHS, Education Appropriations bill and report were passed by both the Subcommittee and the full Committee in July 2010.

Ms. Erickson informed members that the Patient Protection and Affordable Care Act (P.L. 111-148) included provisions relevant to the NIH. It authorized the CAN within the NIH OD to provide grant and partnership funding to bridge the gap between laboratory discoveries and life-saving therapies; the Appropriations bill included \$50 M for CAN. The Act also addressed comparative effectiveness research (CER) by establishing the Patient-Centered Outcomes Research Institute (PCORI), which will include the Directors of the NIH and the Agency for Healthcare Research and Quality (AHRQ) and will fund research

that evaluates and compares health outcomes and clinical effectiveness, risks, and benefits of medical treatments and services.

WEDNESDAY, SEPTEMBER 8, 2010

VI. 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.

En bloc Appropriated: The en bloc vote for concurrence with IRG recommendations was affirmed by all serving Board members present. During the closed session of the meeting, a total of 3,866 NCI applications were reviewed requesting support of \$1,044,654,687 and 34 FDA applications were reviewed requesting support of \$25,413,815.

En bloc ARRA: The en bloc vote for concurrence with IRG recommendations was affirmed by all serving Board members present. During the closed session of the meeting, a total of 2 applications were reviewed requesting support of \$8,082,117.

The Special Action Subcommittee meeting adjourned at 9:45 a.m.

VII. STATUS REPORT: THE CANCER GENOME ATLAS (TCGA)—DRS. MARK GUYER AND LYNDA CHIN

Drs. Mark Guyer, Director, Division of Extramural Research, and Acting Deputy Director, NHGRI, and Lynda Chin, Professor, Dana-Farber Cancer Institute, provided an update on TCGA activities. Dr. Guyer reminded members that TCGA is a collaborative effort between the NCI and NHGRI which began as a pilot program to explore the processes required to perform a high-throughput, large-scale, disease-focused genome characterization. These processes involve: the acquisition of biospecimens; large-scale genome characterization and sequencing; the integration of data, laboratories and teams; and the development of uniform policies on the execution of the research. The pilot has focused on glioblastoma and ovarian cancer, and has demonstrated that the process is feasible, as these efforts have enabled the discovery of new cancer-related genes and demonstrated that integrated research teams can be organized and function in a productive manner to generate clinically relevant data.

Phase II of the Program has been supported by funds from the ARRA for the first and second years of the 5-year program. This phase aims to complete the characterization of 10 tumor types, which entails the analysis of 200 cases per tumor type. Of these 200, 90 percent (180 samples) will undergo exome (coding region) sequencing, and 10 percent (20 samples) will undergo whole genome sequencing using next-generation sequencing technologies. Another 10 tumor types will be partially characterized (100 cases per type).

TCGA's "project pipeline," that is, the various steps and centers involved with the data analysis, involves a system in which uniform categories of data are generated for each tumor type. Currently, 2 cancer types (glioblastoma and ovarian cancer) have comprehensive data available, 6 cancer types have considerable progress made toward achieving a comprehensive database, and 12 others are in the preliminary stages of data acquisition. TCGA is a member of the recently formed International Cancer

Genomics Consortium (ICGC), along with many similar genomic projects under way around the world. An initial goal of the ICGC is to establish data standards to ensure that data are collected and analyzed in a consistent manner worldwide.

Sample accrual is a major obstacle facing the project. All samples are subjected to TCGA-defined criteria which are stringent, thus, only 40 to 50 percent of samples ultimately qualify. The initial sample criteria developed for the pilot program were highly stringent to reduce the probability of problematic samples interfering with the goal of the pilot program, which was to demonstrate feasibility. However, the criteria for tissue samples accrual into the project now are far flexible due to improving technologies, enabling inclusion of potentially clinically important biospecimens, such as tumor specimens that have been exposed to treatments or have lower purity due to the biology. The TCGA principal investigator (PI) heading each tumor project team will organize a disease working group to develop tumor-specific sample criteria.

Dr. Chin described TCGA's scientific progress and challenges. TCGA is the first truly integrated cancer genome project, simultaneously analyzing multiple genome dimensions that could be involved in cancer, such as point mutations, copy number alterations, promoter methylations, and coding and non-coding RNA expression deregulation. The pilot has demonstrated that novel mutations can be identified (e.g., p85, PIK3R1) and can resolve outstanding controversies, such as NF1 involvement in glioblastoma. It also has the added benefit of being unbiased, which can produce unexpected discoveries, such as temozolomide resistance in glioblastoma patients. The multi-dimensionality of the TCGA dataset has yielded notable discoveries and been highly informative to the scientific community. For example, while, among the the four molecular subtypes (proneural, neural, classical, and mesenchymal) of glioblastoma, the proneural subtype has a very slightly increased survival. When integrated with promoter methylation profiles, it was revealed that the survival advantage of the proneural subtype is driven by those patients with G-CIMP phenotype within this group. The initial publication of the glioblastoma dataset in 2008 has now been cited in 225 publications covering a variety of topics, including comparisons to mouse models, novel gene discovery, and the development of new analytic tools, which speaks to the impact of such a reference catalogue.

An important objective of TCGA is to generate a high-quality public reference on the cancer genome that is comprehensive, thus it needs to stay course on using large sample cohort for statistical power. Because new sequencing technologies that permit high-powered statistical analyses (e.g., resulting in key discoveries like the p85 α mutation) are needed, TCGA has moved towards transformative technology—next-generation massively parallel sequencing, which can discover not only point mutations and indels, but also translocations and copy number alterations. Library construction for such sequencing platforms has been improving; for example, initial input requirement was 10-20 microgram of DNA for whole-genome sequencing and current optimized protocol requires as little as several hundreds nanograms. A major challenge now is development and improvement of mutation calling algorithms, which require validation of somatic mutations identified by a second methodology. This is not a small task as these massively parallel sequencing methods are uncovering thousands of mutations in each tumor genome.

Despite the technical and scientific challenges and obstacles associated with transitioning to these new technologies, TCGA continues to produce useful data and generate new insights. For example, TCGA characterization has revealed that p53 mutations occur in 96.5 percent of ovarian cancer cases, and pathway analysis has shown that defective homologous recombination is observed in almost 30 percent of the ovarian cancers in addition to germline and somatic mutation in *BRCA1/BRCA2*, the latter known to predict sensitivity to PARP inhibitor in the clinic. RNA sequencing has detected transcript fusions in acute myelogenous leukemia. Rearrangements also have been observed with colorectal cancers.

The broader cancer community, external to TCGA, needs to perform downstream biological experimentation based on these data to gain understanding of what these genetic alterations mean

biologically. Therefore, dissemination of the data to the general cancer research community through publication and data release is a major goal of TCGA and a major challenge. To enhance this, the Genome Data Analysis Center (GDAC) has been added to Phase II. The GDAC is tasked with developing new analytic tools to integrate multiple dimensions of data and make such integrative analysis results available to the greater scientific community. To address the challenge of generating and making available such analysis results rapidly, GDACs are building an automated analysis pipeline that can run a set of pre-defined integrated analysis on all TCGA data and present such results in a format that is “usable” to the general community. Using such pipeline, it is anticipated that a set of integrative analysis results can be generated within 1-2 days automatically, enabling frequent and multiple iterations of the analyses without long delay. Furthermore, multiple tumor project data sets can be analyzed simultaneously in parallel. It is the hope that this system will increase the speed of publication and data/results dissemination.

Questions and Answers

Mr. David H. Koch, Executive Vice President, Koch Industries, requested additional details about the tumor types that were selected. Dr. Guyer replied that the tumor types initially were chosen based on characteristics that would simplify the pilot study, such as yielding high tumor purity and quantity, to ensure that the approach employed was feasible. The criteria have expanded with the next Phase and include characteristics such as prevalence, lethality, and availability. He added that tumors with a significant amount of previously documented genomic information were not specifically included or excluded.

Dr. Lloyd K. Everson, Vice Chairman and Member of the Board of Directors, US Oncology Incorporated, asked about the tissue sources. Dr. Guyer answered that the Program has used retrospective samples bought from commercial sources and individual Cancer Centers; a prospective sample accrual network is planned that will involve community cancer groups and any other available sources.

Dr. Chabner inquired about the verification of sample collections, including pretreatment and assurance that the specimen is the correct tissue. Dr. Guyer responded that researchers rely on the tissue source sites for clinical data collection, including the case quality control form that confirms no history of pretreatment and the accompanying pathology report from the surgery; a second pathology review is performed, independent of the primary institution that supplied the sample.

Dr. Judith S. Kaur, Medical Director, Native American Programs, Mayo Comprehensive Cancer Center, and Professor of Oncology, Mayo Clinic, wondered why Australia’s ICGC projects do not include melanoma, given that the country has the highest world prevalence of the disease. Dr. Guyer noted that some of the melanoma samples being accrued for TCGA are coming from Australia. Dr. Chabner asked about the collection of information regarding the ethnic/racial backgrounds of patients to address racial differences. Dr. Guyer answered that the information was being collected and could be studied.

Mr. Koch asked about the rejection rate of the samples and if the rate was related to the increased training of personnel handling the specimens. Dr. Guyer said 50 to 60 percent were rejected at the BCR (Biospecimen Core Resources) for various reasons, including failure to pass the pathology report, insufficient collection of DNA/RNA from the samples, or quality control standards not being met for molecular analytes. The major significant factor of rejection at the Tissue Source Site is missing matched normal for the tumor samples stored in the retrospective banks.

Dr. H. Kim Lyerly, Director, Duke Comprehensive Cancer Center, George Barth Geller Professor of Cancer Research, Duke University Medical Center, asked about eliminating the analysis of less common cancer types, such as thyroid cancer, and expanding the analysis of more prevalent cancers with a large multitude of subtypes, such as breast cancer. Dr. Guyer acknowledged the ongoing debate regarding

the breadth to make these databases as comprehensive as possible across cancer diseases versus achieving deep analysis of several cancers and their subtypes.

Dr. Chabner asked whether the research groups have used free DNA from blood fluids or DNA from tumor cells circulating in the blood to perform these analyses. Dr. Chin responded that although this approach is beyond the current scope of TCGA, the technology is improving such that in the near future, such small amount of input materials may be sufficient for the multi-dimensional nature (i.e. requiring sufficient materials for DNA/RNA/methylation) of TCGA study.

Dr. Donald S. Coffey, The Iola and J. Smith Michael Distinguished Professor of Urology, and Professor of Urology/Oncology/Pathology/Pharmacology and Molecular Science, JHU, asked about what DNA elements are undetected by these analyses, such as small repetitive DNA elements and transposons, and further inquired about functional elements within the genome, such as DNA loops in higher order chromatin structures. Dr. Chin estimated that approximately 80 percent coverage is obtained, with GC-rich regions being more challenging; sequencing centers are examining this through complementary Sanger-based sequencing and are working hard at addressing these technical issues. She added that although TCGA is not performing analyses concerning chromatin structure, it is hoped that the data TCGA does generate will enable outside researchers to execute on those investigations. Dr. Coffey cautioned cancer researchers not to repeat the mistakes of the past by underestimating the potential role of methylation in cancer. Dr. Guyer mentioned the NHGRI's Encyclopedia of DNA Elements (ENCODE) Program, which is identifying functional elements within a genome on a large scale and also remarked that TCGA's large-scale approach will take advantage of the 100 times more mutations in non-coding regions of the genome.

Dr. Everson asked about TCGA plans to prospectively access naïve tumors in the community, where 80 to 90 percent of all cancer is in that state. NCI program staff said that TCGA would be announcing the official sites for prospective collection networks, and two currently are in place—Christiana Care and Catholic Health Initiatives. Seven additional sites are planned, including community hospitals working in collaboration with academic institutions where the primary samples are untreated tissue. Dr. Chin added that it is important to study post-treatment tumors as well as to obtain untreated tumor samples.

Dr. Lyerly requested further details about the detection of non-human DNA and the role of pathogens. Dr. Chin responded that TCGA is generating whole-genome sequencing data, and some preliminary studies by TCGA investigators have shown that detection of pathogen DNA is possible from whole-genome sequencing data. Thus, going forward, as TCGA begins to generate more and more whole-genome data, detection of non-human DNA and their possible roles in cancers and interaction with other environmental factors will likely be emphasized.

Dr. Geoffrey Krystal, VA, asked about the Program's plan for prospective collection of serial specimens from patients. Dr. Chin said that such collection has not begun, but the collection network and plan are being put in place. Thus far, pre- and post-treatment samples have been collected from ovarian cancer and glioblastoma patients.

Dr. Chabner questioned the need to collect samples from community centers when large Cancer Centers, such as Massachusetts General Hospital and Dana-Farber Cancer Institute, are conducting sequential biopsies and sophisticated cancer trials. NCI program staff said that the small size of the biopsied tumors represents a significant limitation for TCGA, as it is less conducive to rapid analysis. Dr. Varmus noted that the utility of the samples depends on the questions being asked; TCGA can compare metastases and primary tumors, examining tumors from patients who have been treated with conventional therapy to ask what predicts response. Dr. Guyer added that the range of questions that can be addressed using this approach will grow rapidly as TCGA expands into other cancers.

VIII. STATUS REPORT: CANCER BIOMEDICAL INFORMATICS GRID (caBIG) ACCOMPLISHMENTS—DR. KEN BUETOW

Dr. Ken Buetow, Director, Center for Bioinformatics, provided an update regarding cancer Biomedical Informatics Grid (caBIG[®]) accomplishments that have occurred over the course of the project. Since the June 2010 NCAB meeting, substantial increases in participants in the program, community support, caBIG[®] capabilities, and caBIG[®] content have been realized. Since caBIG[®]'s establishment in 2004, a number of NCI programs with broad cancer interests have been added to caBIG[®]; they all desired similar key core uses or capabilities, such as clinical data management and distributed data sharing. An open community of participants was encouraged, and interconnection of data with open source programs, rather than data centralization, was chosen. Furthermore, leveraging of existing academic and commercial software reduces expenses and saves time.

Domain work spaces were created to allow the development of common infrastructure and capabilities across the cancer community. Participation in weekly teleconferences has increased. Attendance at annual meetings has increased from 169 in 2004 to more than 1,050 in 2009. Knowledge Centers and Support Service Providers (SSPs) have been established. SSPs consist of 19 licensed groups, ranging from small start-up information technology (IT) companies to academic centers to large government contractors.

To interconnect the community and overcome any disconnect of data among individual programs and institutions, caBIG[®] has created a framework of common cancer data language based on common data elements, vocabularies and ontologies, and information models that results in caBIG[®] as a whole community being more valuable than the sum of the individual components. An example of a capability is electronic data capture (EDC): 194 sites, representing more than 1,000 users, use C3D (an EDC tool); 1 million case report forms have been entered, and 342 trials use C3D, from which 59 publications have been generated.

Although individual organizations and centers have different needs, they exhibit a common theme: they all utilize some component of the caBIG[®] infrastructure while leveraging their own pieces in an integrated fashion. For example, different capabilities supporting molecular analysis generated and owned by other organizations are available to the cancer research community through caBIG[®]. Multiple universities are using caBIG[®] to interconnect their research programs, including Washington University, Ohio State University, and the University of Alabama–Birmingham.

caBIG's[®] potency lies in its ability to cross-connect the cancer community, bridging different institutions and organizations by utilizing a “common cancer language,” creating an infrastructure that interconnects them to one another. It makes complex biomedical data available to various groups without the need to install and learn complex IT infrastructures. The Glioma Molecular Diagnostic Initiative, the Duke Multi-Center Vaccine Study, the Director's Challenge Lung Study, and the Cancer Genetic Markers of Susceptibility (CGEMS) study all operate using caBIG[®] to share data and capabilities. caBIG[®] has resulted in 25 publications generated from data mining within the CGEMS project. caBIG[®] is used to manage more than 4 million medical images and 2 million biospecimens. It also helps support a breast cancer data mart containing data from 54 studies collected by six cooperative groups, which includes more than 65,000 patient records.

The Cancer Molecular Analysis Portal is one activity that leverages the caBIG[®] resources and provides access to data across the cancer research spectrum. Users are able to integrate genomic data with corresponding clinical information, find novel correlations that were difficult or impossible to find using conventional methods, and provide access and analytic capabilities to a variety of other research studies (e.g., Repository of Molecular Brain Neoplasm Database [REMBRANDT], and Therapeutically Applicable Research to Generate Effective Treatments [TARGET]). A similar scenario has been

established with the Cancer Genome Workbench for Integrated Cancer Data, for which the user can access a variety of data for a specific gene or genome segment and view them in an integrated manner.

Dr. Buetow described the broadening use of caBIG[®]. Fifteen countries are associated with caBIG[®] technologies. The 2.0 framework facilitates interconnection with the health care delivery system to create a seamless connection between the research environment and the care environment to mediate the transaction of information between the domains to support next-generation clinical trials, population research, and novel clinical investigations. The efforts concerning caBIG[®] involvement in the facilitation of clinical research are exemplified by the I-SPY TRIAL (Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And molecular Analysis).

Questions and Answers

Dr. Chabner asked about caBIG's[®] budget and how much is used to develop local IT infrastructure. Dr. Buetow answered that the budget is approximately \$40 M per year, which includes core engagements with the Cancer Centers, and that the majority of funds is spent in the community and under the operation of NCI-Frederick. He added that Knowledge Centers are operated by the academic centers whereas development efforts commonly are managed in partnership between commercial and academic developers.

Mr. Koch asked about the level of participation with caBIG[®] by medical centers internationally. Dr. Buetow explained that the ability to measure adoption rates is limited; however, more than 9,000 unique users have accessed the Workbench, and most Cancer Centers (56 out of 60) use caBIG[®]. In addition, the complexity of the system can overwhelm small laboratories, and rewards (e.g., top-tier publications and grants) in the academic setting are not awarded to research performed using and re-using large datasets.

Dr. Coffey asked about the quality control of input data and the use of instructional workshops to train researchers and IT staff on how to use the caBIG[®] infrastructure in their institutions. Dr. Buetow responded that caBIG[®] is present at American Society of Clinical Oncology (ASCO) and AACR annual meetings with interactive booths designed to teach how to use the tools; these booths are usually well-attended by meeting participants.

Dr. Coffey noted that 15 countries are using caBIG[®], and the United States represents 5 percent of the world population. Given this, he asked about the level of funding that comes from these other countries, particularly the wealthy countries, to support this endeavor. Dr. Buetow replied that the United Kingdom and The Netherlands are full partners. India is leveraging U.S. information and in return is providing access to its advanced IT systems; for instance, the country has one of the fastest supercomputers in the world and has expressed the desire to connect it into the caBIG[®] framework to offer its capabilities in exchange. Dr. Lyerly referenced collaborations with China and how the standards set forth by caBIG[®] have resulted in China harmonizing its infrastructure with caBIG[®], thereby allowing meaningful data from Chinese trials to be obtained.

Dr. Kaur asked where Iceland's genetic database and annotated biology of cancer and other chronic diseases fit in with caBIG[®] with regard to environmental and gene interactions. Dr. Buetow mentioned that the National Library of Medicine's data definitions are leveraged throughout caBIG[®]. Anyone using national standards for any other studies can interconnect their information using the electronic interfaces.

Dr. Chabner asked whether the Cooperative Groups are using caBIG[®] to consolidate activities, such as patient registration and data management. Dr. Buetow replied that the NCI is working on a large-

scale program to deploy the next-generation clinical trial data management system, and a common information representation tool will be created within the next year to assist with consolidation efforts.

IX. NEW NCI FACILITIES: SHADY GROVE, RIVERSIDE, AND OTHER NEW FACILITIES—MR. DARYL PAUNIL

Mr. Daryl Paunil, Director, NCI Office of Space and Facilities Management, described NCI's selection of a new, expanded administrative and program campus and the planned facilities. The NCI held a ground-breaking ceremony at the new Shady Grove Campus (Shady Grove, the new site) on 1 September 2010. The site selection process began in January 2007 and involved the U.S. General Services Administration (GSA), with the selection made in November 2009 based on the best overall value. JHU is providing a ground lease for the site, and the developer JBG will build the \$200 M facility through private debt and equity, with HOK as the architect. GSA awarded the 10-year lease in February 2010, with lease commencement anticipated in January 2013. The NCI signed the occupancy agreement with GSA in July 2010 to lease 574,614 rentable square feet.

Mr. Paunil explained that the NCI is moving because its current lease expires in 2012 without the possibility of a simple renewal. The current facilities also are aged and do not meet today's HHS security requirements. The new "build-to-suit" facilities will provide additional space to accommodate NCI programs' changing needs. The Shady Grove site provides 1-year rent abatement, an estimated 8.5 percent reduction in annual rent, lower energy and operating costs than current facilities, and a Leadership in Energy & Environmental Design (LEED)-certified facility. The buildings will include collaborative spaces for employees and guests via video conference rooms and an onsite auditorium, natural light and daylight harvesting to conserve energy, and water-saving fixtures, as well as outside green space and convenient amenities. The site also provides additional building capacity to accommodate any future needs.

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, asked about the design of the cubicle offices and the design effect on holding private conversations. Mr. Paunil said that the cubicles are designed to be 5-6 feet high. Three or four small meeting rooms will be located in the interior of each floor to accommodate private conversations. Two large conference rooms plus a third larger conference room will be located on each floor to provide places for additional meetings.

Mr. William H. Goodwin, Jr., Chairman and President, CCA Industries, Inc., encouraged a longer lease term than 10 years for economic thrift. Mr. Paunil said that 10-year leases are a government standard. Dr. Chabner asked whether it was legislated. Mr. Paunil confirmed that the authority for the lease comes through GSA from Congress and noted that there is not a renewable clause.

Mr. Koch asked about the buildings being vacated. Mr. Paunil said that the NCI had leased four buildings owned by three separate owners; two of the buildings will be re-leased in whole or part by the NCI, and the two larger buildings will be vacated by the NCI.

Dr. Michael A. Babich, CPSC, asked about the indoor air quality considerations for the new site. Mr. Paunil indicated that the LEED has a standard; to maintain LEED certification, a number of air changes per hour must be demonstrated and a percentage of air from the outside and cleanliness of that air must be maintained.

Dr. Chabner asked about the proximity to Shady Grove Hospital. Mr. Paunil replied that the new site is approximately one-half mile away from Shady Grove Hospital, which is an independent facility and not associated with JHU.

X. THE INSTITUTE OF MEDICINE (IOM) CLINICAL TRIALS IMPLEMENTATION: REPORT CARD DATA FORMAT—DR. JAMES H. DOROSHOW

Dr. James H. Doroshow, Director, Division of Cancer Treatment and Diagnosis (DCTD), presented an update regarding the Operational Efficiency Working Group (OEWG) and issues related to the lack of timeliness and activation of clinical trials. Data collected from 2006 to 2008 demonstrated that nearly 60 percent of Phase III clinical trials took more than 2 years to open. In response, the OEWG has developed a new timeline that results in a 60 percent improvement in activation time and requires funding cessation for any trials that are not opened or institutional review board (IRB) approved within 2 years. A similar process, but limited to a 7-month timeline, was developed for Phase I and II trials; trials not activated after 18 months are terminated.

Following the implementation of the OEWG timelines on April 1, 18 concept proposals for Phase III trials were received. Three were approved, six were in review on or hold due to issues related to obtaining/using the drugs involved, five were disapproved or withdrawn, and four are awaiting Steering Committee review. It was noted that the three that were approved are well within the prescribed timelines proposed by OEWG, with none having exceeded the 90-day target for review.

Since the timeline implementation, 21 letters of intent (LOIs) have been received for Phase II trials. Five LOIs have been approved with two protocols submitted, 4 LOIs are in review or in time-out, and 12 have been disapproved, withdrawn, or declined by the pharmaceutical company involved; those approved are meeting the 60-day target. Similarly, U01/N01 Phase I/II trial LOIs are also meeting the new guideline target dates.

To facilitate these changes, a kickoff meeting was held in late March that included relevant investigators from both the Cooperative Groups and NCI-designated Cancer Centers to establish a common understanding of the procedures. Using funds from the ARRA, project managers were hired to oversee the program implementation. To save time, effort, and money, Cancer Therapy Evaluation Program (CTEP) reviews have been modified to use “Track Changes,” which allows changes to be made to the protocols and then be rapidly accepted. Further modifications include streamlining the internal standard operating procedures and improving communication. Phase I and Phase II investigators have been contacted about their protocols at risk of being discontinued if not opened by 1 January 2011. Requests for extensions have been received and denied; it is critical to maintain established deadlines.

Two critical accomplishments have had a large impact on the program. The first is the development of a Web portal, through which intramural and extramural investigators can track the status of their protocols. It provides an easy-to-use tool for receiving information about the protocol and does so in a totally transparent matter. Although it is still in beta-testing, the portal is advanced and will be demonstrated to the Board at a future NCAB meeting. The second involves OEWG conference calls between the study team and the NCI to clarify comments in the Consensus Review and hasten the approval process. Since 1 April 2010, 80 calls have been conducted. Nearly 100 percent of the time, the lead reviewer and site statistician have participated in these calls, decreasing the time required to respond to questions and achieve protocol approval. Dr. Doroshow closed his presentation by reminding the group that the goal is a 60 percent increase in efficiency. It was critical to understand that the only way to achieve this increase in efficiency was not only to implement aggressive deadlines but also to maintain strict adherence to those deadlines.

Questions and Answers

Dr. Chabner asked if the online portal includes the status of LOIs. He also inquired about other changes recommended in the IOM report that were substantive and long-term. Dr. Doroshow replied that

the online clinical trials data management program covers Phase I applications and includes all LOIs. It includes everything that involves CTEP but does not include Cancer Center trials for which the NCI does not hold the investigational new drug application (IND). Dr. Doroshov offered to provide a demonstration of the portal at the next NCAB meeting and make a presentation related to the long-term changes recommended in the IOM report.

Dr. Chabner asked whether the NCI's review is necessary for trials in which the Institute is not the acting sponsor. Dr. Doroshov responded that the NCI still participates and offers its opinions. However, the Institute does not have the ultimate decision-making authority; the extramural community still makes decisions about the concept and the NCI serves in an advisory role.

Dr. Diana M. Lopez, Professor, Department of Microbiology and Immunology, University of Miami, Leonard M. Miller School of Medicine, asked about the plan regarding trials that currently are open but have low accrual rates. Dr. Doroshov replied that Centers have been encouraged to be careful with opening trials, as lack of patient accrual in trials wastes money. The NCI is primarily interested in studies that finish, and accrual rate is very important. He indicated that there are defined guidelines in place to terminate trials that are open but fail to accrue patients.

Dr. Anthony Atala, Director, Wake Forest Institute for Regenerative Medicine, and Professor and Chairman, Department of Urology, Wake Forest University School of Medicine, observed that the IOM encouraged an increase in IND filings, and that the NCI now has the Therapeutics Group; he wondered how these goals mesh with the work under way. Dr. Doroshov replied that having one pipeline for early phase investigations allows for the handling of regulatory aspects to be performed in a consistent fashion and noted the financial burden in filing INDs. The NCI would like to provide expert advice and assistance to individuals working with early phase molecules, particularly those with little to no regulatory experience.

Dr. Chabner asked about the progress made during the past 6 months. Dr. Doroshov replied that the timeline implementation has definitely provided forward progress and a large group of extramural investigators now recognizes that an 800-day activation period is unacceptable.

XI. NCAB ONGOING AND NEW BUSINESS—DR. BRUCE A. CHABNER

Dr. Chabner reviewed the Board's request at the June 2010 NCAB meeting for a regular report card on the status of NCI's implementation of the IOM report on Clinical Trials. The report recommendations were to monitor progress and implementation, improve efficiencies of the clinical trials system, advise the NCI on a system that will eliminate duplication, provide appropriate oversight in advising the NCI about fund allocation regarding national clinical trials, and track progress in shifting some resources to per case reimbursement. The intentions of the report card are to encourage performance and allow NCAB monitoring of this important aspect of clinical research.

Following Dr. Varmus' suggestion that a request for frequent reports is adequate and a formal motion for updates unnecessary, Dr. Chabner said that the request had been formed as a potential motion to express the Board's recognition of and support to the NCI in solving the problem. Members agreed to request regular updates at reasonable time intervals and quantitative assessment of the NCI's activities in response to the IOM report rather than a motion. Dr. Chabner stated that the overall yearly analysis of accrual and group activities in Centers and clinical trials will begin at the December 2010 NCAB meeting, and regular updates will occur throughout the year.

Dr. Kaur asked about the appointment of new members to the Board. Dr. Gray explained that the new member roster is being developed, and the new members are expected to attend the December NCAB meeting.

Dr. Kim Lyerly expressed the Board's enthusiasm for NCI's efforts on global health associated with cancer, and he observed that the NCAB *Ad hoc* Subcommittee on Global Cancer Research needs a chairperson. Dr. Gray said that membership on all NCAB Subcommittees will be re-addressed once the new members are appointed.

Dr. Chabner encouraged members to send to him or to Drs. Gray or Varmus additional agenda items for the December meeting. The December meeting will include the NCAB *Ad hoc* Working Group To Create a Strategic Scientific Vision for the National Cancer Program and Review of the National Cancer Institute (Strategic Working Group) report. Retired NCAB members who served on the Strategic Working Group are welcome to attend the December meeting as public attendees.

XII. ADJOURNMENT **CDR. 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 155th regular meeting of the NCAB was adjourned at 12:53 p.m. on Wednesday, 8 September 2010.

Date

Bruce A. Chabner, M.D., Acting Chair

Date

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