DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
149TH NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
February 3-4, 2009

Building 31C, Conference Room 6
National Institutes of Health
Bethesda, Maryland

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The National Cancer Advisory Board (NCAB) convened for its 149th regular meeting on 3 February 2009, in Conference Room 6, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, 3 February 2009, from 8:00 a.m. to 3:52 p.m., and Wednesday, 4 February 2009, from 8:30 a.m. to 11:24 a.m., and closed to the public on Tuesday, 3 February 2009, from 4:10 p.m. to 5:00 p.m. Dr. Daniel D. Von Hoff, Physician in Chief and Senior Investigator, Translational Genomics Research Institute, and Clinical Professor of Medicine, University of Arizona, Phoenix, AZ, presided during both the open and closed sessions on Tuesday. Dr. Donald S. Coffey, The Catherine Iola and J. Smith Michael Distinguished Professor of Urology, Johns Hopkins University School of Medicine, Baltimore, MD, presided during the open session on Wednesday.

NCAB Members
Dr. Carolyn D. Runowicz (Chair) (absent)
Dr. Anthony Atala
Dr. Bruce A. Chabner (absent)
Dr. Victoria L. Champion
Dr. Donald S. Coffey (Acting Chair on 2/4/09)
Dr. Lloyd K. Everson (absent)
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 (absent)
Dr. Daniel Von Hoff (Acting Chair on 2/3/09)

President's Cancer Panel
Dr. LaSalle D. Leffall, Jr. (Chairperson)
Dr. Margaret L. Kripke
Mr. Joseph P. Torre (absent)

Alternate *Ex Officio* NCAB Members
Dr. Michael A. Babich, CPSC
Dr. Patricia Bray, OSHA/DOL (absent)
Dr. Seth Cohen, OSTP
Dr. Allen Dearry, NIEHS (absent)
Dr. Michael Kelley, VA
Dr. Raynard Kington, NIH (absent)
Dr. Peter Kirchner, DOE
Dr. Richard Pazdur, FDA (absent)
Dr. John F. Potter, DOD
Dr. R. Julian Preston, EPA (absent)
Dr. Dori Reissman, NIOSH (absent)

Members, Executive Committee, National Cancer Institute, NIH

Dr. John Niederhuber, Director, National Cancer Institute
Dr. Anna Barker, Deputy Director for Advanced Technology and Strategic Partnership
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
Ms. Kathy McBrien, Administrative Resource Center Manager
Dr. Alan Rabson, Deputy Director, National Cancer Institute
Mr. Lawrence Ray, Deputy Director for Management and Executive Officer
Dr. Craig Reynolds, Associate Director, NCI-Frederick
Dr. Dinah Singer, Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Robert Wiltrout, Director, Center for Cancer Research
Ms. Joy Wiszneauckas, Executive Secretary, Office of the Director

Liaison Representatives

Ms. Carolyn Aldige, Cancer Research and Prevention Foundation
Ms. Paula Bowen, Kidney Cancer Association
Mr. William Bro, Kidney Cancer Association
Dr. Carol Brown, Society of Gynecologic Oncologists
Ms. Pamela K. Brown, Intercultural Cancer Council
Ms. Suanna Bruinooge, American Society of Clinical Oncology
Dr. Yvette Colon, National Cancer Institute, Director's Consumer Liaison Group
Mr. George Dahlman, Leukemia and Lymphoma Society
Ms. Brenda Nevidjon, Oncology Nursing Society
Dr. Margaret Foti, American Association for Cancer Research
Dr. Robert W. Frelick, Association of Community Cancer Centers
Dr. Leo Giambarresi, 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. David Lofye, Lance Armstrong Foundation
Mr. Richard Martin, American Society of Therapeutic Radiology and Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Ms. Christy Schmidt, American Cancer Society
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Dr. Robyn Lynn Watson, American Society of Therapeutic Radiology and Oncology
COL (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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I. CALL TO ORDER, OPENING REMARKS, AND CONSIDERATION OF 9 DECEMBER 2008 MINUTES-DR. DANIEL D. VON HOFF

Dr. Von Hoff called to order the 149th 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. Von Hoff 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 9 December 2008 NCAB meeting. The motion was seconded, and the Board unanimously approved the minutes.

II. FUTURE BOARD MEETING DATES-DR. DANIEL D. VON HOFF

Dr. Von Hoff called Board members' attention to future meeting dates, which have been confirmed through 2010.

III. NCI DIRECTOR'S REPORT-DR. JOHN NIEDERHUBER

Budget. Dr. John Niederhuber, Director, NCI, welcomed the Board members. He reviewed the closing of the 2008 budget and noted that research project grants (RPGs) were funded at the 14th percentile plus extensive exceptions, for a 20 percent success rate. In addition, new competing grants were funded at the 19th percentile extended payline plus exceptions, for a total of 236 awards. In FY 2008, the NCI funded 1,284 RPGs and added a new cancer center, the Greenebaum Cancer Center, University of Maryland. Dr. Niederhuber congratulated the NCI Budget Office for its work in completing FY 2008 accounting with a balance of $3,302.

Dr. Niederhuber reminded members that the NCI continues to operate under a Continuing Resolution for FY 2009 with a budget of $4.805 B, which reflects a decrease of one-half percent from FY 2008. Accounting for additional expenditures, such as taps or assessments from the NIH, mandated salary increases and other NCI requirements, contract closeouts, and potential project recoveries and redeployments, the FY 2009 budget subtotal is estimated at -$874,000. Foreseeable spendable resources total $109 M and include the RPG RFA pool, the NCI Director's Reserve, and a set aside for facilities.

Members were told that the economic stimulus package currently in Congress emphasizes comparative effectiveness research, other research opportunities called "challenge grants," and NIH facility construction and repairs. Approximately 1,500 challenge grants with a cap of $500,000 each are expected to be awarded for 2 years. In addition, appropriations from the House and Senate could result in a 2.2 percent increase over FY 2008 funding levels. The economic stimulus package could result in an additional $125 M to the NCI; anticipated funds would be highly directed, particularly through challenge grants and additional renovations. The House bill passed on 28 January 2009. The Senate Finance Committee began mark-up of its version on 29 January. Members were informed that Senator Arlen Specter (R-PA) may propose an amendment to the stimulus bill that adds $10 B over 2 years to the NIH. The current bill allocates: $300 M to the National Center for Research Resources (NCRR) for shared instrumentation and capital research equipment; $2.7 B to the NIH for research; $500 M to buildings and facilities; and $1.1 B for comparativeness research, which will be split among the NIH, U.S. Department of Health and Human Services (HHS), and Agency for Healthcare Research and Quality.

NCI News. Dr. Niederhuber reported on news across the NCI and NIH, including the leadership transition at the HHS with the nomination of former Senate majority leader Tom Daschle as the new HHS Secretary and advisor to the President on health, and William Corr's nomination as the HHS Deputy Secretary. Other notable appointments that reflect the emphasis on science include Nobel Laureate Steven Chu as the Energy Secretary, Dr. John Holdren as Assistant to the President for Science and Technology, and Drs. Harold Varmus and Eric Lander as Co-Chairs of the President=s Council of Advisors on Science and Technology. [On 3 February 2009, Mr. Daschle withdrew his nomination as HHS Secretary.]

NCI Division leadership and senior staff in the Office of the Director (OD) have identified topics of importance to the Institute and the National Cancer Program, including clinical research, health information technology (IT), pharmaceutical costs to society, and cancer as a model, as well as quality of cancer care and outcomes research. NCI leadership and staff have written and submitted articles addressing these subjects for peer review and publication in journals such as *The Oncologist* and *Health Affairs*. Through its many networks of cancer centers, community cancer centers, BIG Health™ and caBIG[7], and biology to translation infrastructure, the NCI is addressing issues such as health care coverage and affordability, access and quality of care, innovation through science, and recruitment and training of the next generation of scientists.

Dr. Niederhuber and other NCI leadership met with Dr. Mark McClellan as a follow-on meeting to the 26 September 2008 Brookings Institution Conference on Clinical Cancer Research to continue the dialogue on reducing barriers to clinical research and building a new model for the development of targeted therapies. The discussion centered on cancer as the arena for the investigation of molecular medicine and identified the need to build partnerships, including with the Centers for Medicare and Medicaid Services (CMS), and the exploration of opportunities to co-develop diagnostic and preventive interventions. Members also were referred to the *Nation's Investment in Cancer Research*, NCI's annual budget report, which is required by the 1971 National Cancer Act.

The NCI's Executive Committee (EC) held a Scientific Retreat in late January to discourse about the current direction and future investment in science and cancer research. In a keynote address on "Is Cancer a Disease?", Dr. Robert Austin observed that ordinary Darwinian evolution is unlikely to lead to complex organisms, and that evolution works most efficiently by large-scale genomic changes or rearrangements, rather than through single nucleotide polymorphism (SNP) mutations. He said that the price of high evolution rates is cancer and that, as such, cancer is not a disease. Discussions during the retreat focused on the need to: 1) conduct real-time assays of the stressors and responses that initiate and sustain cancer; 2) model the evolution of cancer with a focus on alterations in the microenvironment; and 3) understand the epigenetic changes that control the type and number of cancer cells.

Dr. Niederhuber updated members on progress made in improving the clinical trials infrastructure to characterize patients and match patient profiles to targeted therapeutic combinations. The NCI has worked with workflow management expert Dr. David Dilts, Vanderbilt University, to help streamline the clinical trials review process. Furthermore, the CEO Roundtable on Cancer, Life Sciences Consortium with representatives from 11 pharmaceutical companies, and representatives from the NCI Cancer Centers has: 1) identified common language, intellectual property, and antitrust as significant issues; and 2) worked during the past year to analyze clinical trial agreements and identify key clauses on intellectual property, study data, subject injury, indemnification, confidentiality, publication rights, and biological samples that need to be managed in each contractual relationship. The U.S. Department of Justice (DOJ) released an announcement that it would not oppose a proposal by the Roundtable regarding model contract language for clinical cancer trials. Future efforts will involve additional stakeholders, such as the U.S. Food and Drug Administration (FDA) and academia, to address common data elements.

In conclusion, Dr. Niederhuber identified challenges facing the NCI, including knowing where science and technology is leading cancer research. The NCI also will continue to improve its portfolio,

conduct science at the intersection of disciplines, work across divisions, use resources effectively, and ultimately translate findings to the patient.

Questions and Answers

Mr. David H. Koch, Executive Vice President, Koch Industries, asked about advances in nanotechnology and NCI's investment in the field. Dr. Niederhuber said that nanotechnology has been one of the most successful trans-NCI investments, including in terms of leveraging external resources. Dr. Anna Barker, Deputy Director, Advanced Technologies and Strategic Partnerships, explained that the NCI supports the Nanotechnology Alliance, supports nanotechnology training, and is co-funding a nanotechnology initiative with the National Science Foundation (NSF). She said that, in its initial 3 years, the Alliance has shown proof of concept, particularly through improvements in imaging and new imaging approaches; moreover, the Alliance is responsible for the formation of 30 new companies.

Dr. Anthony Atala, Director, Wake Forest Institute for Regenerative Medicine, and Professor and Chairman, Department of Urology, Wake Forest University School of Medicine, requested that the Web Site URL be provided to Board members to access the standard clauses and other legal language for clinical trial agreements reviewed and agreed to by the Life Sciences Consortium.

IV. PRESIDENT-S CANCER PANEL-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, thanked his colleague on the Panel, Dr. Margaret Kripke, for her passion and commitment to the PCP's mission, and the Panel's Executive Secretary, Dr. Abby Sandler, and her staff for their valuable work. Dr. Leffall noted that the function of the PCP is to advise the President on the activities of the National Cancer Program, particularly the obstacles the Program may face in conducting its work.

Although its efforts are advisory in nature, the PCP has had an impact on the work of the National Cancer Program in a number of areas. For example, the Panel examined barriers to patient navigation, particularly in Indian country, which led to research on patient navigation funded by the NCI Center to Reduce Cancer Health Disparities (CRCHD). Other examples of Panel impact include the development of the NCI Translational Research Working Group and advancing the field of cancer survivorship through recommendations that resulted in the formation of the American Society for Clinical Oncology (ASCO) Survivorship Task Force, the Lance Armstrong Foundation Adult Survivorship Centers of Excellence, and certain Fertile Hope activities. Additionally, the Panel has consistently added its voice to the larger community's call for various tobacco regulations. A study is underway to determine the feasibility of evaluating the impact of panel recommendations. It commenced in October 2008 and will conclude in May 2009. Interviews will be conducted with stakeholders both within and external to the NCI who implement recommendations as well as beneficiaries of the recommendations that were implemented.

The PCP's 2007–2008 Annual Report *Maximizing Our Nation=s Investment in Cancer* was released in October 2008 and is available in print and PDF format. The three crucial actions recommended in this report are: 1) making the prevention and treatment of cancer a national priority; 2) ensuring that all Americans have timely access to necessary health care and prevention measures; and 3) ending the scourge of tobacco in America. The Panel is currently working on its 2008–2009 report, which will examine the role of environmental factors in cancer. Themes covered in this meeting series included: industrial, manufacturing, and agricultural exposures; indoor/outdoor air pollution and water contamination; and nuclear fallout, electromagnetic fields and radiation exposure. The PCP hopes to use the information presented at each of these meetings to determine the status and role of regulatory agencies responsible for monitoring environmental hazards as well as identify research needs and potential new areas of collaboration among federal agencies. The forthcoming report will increase public awareness of

environmental and occupational hazards and cancer risk and will provide recommendations for reducing cancer risk from environmental exposures.

Questions and Answers

Dr. Von Hoff asked if the PCP planned to address obesity, one of the greatest cancer risks, in its future work. Dr. Leffall responded that it would. Dr. Michael A. Babich, Directorate for Epidemiology and Health Sciences, Consumer Product Safety Commission (CPSC), commented that cost/benefit analyses, which Dr. Leffall mentioned in his presentation, are conducted prior to any chemical regulation. Dr. Leffall explained that the point was raised because sometimes a greater emphasis is placed on cost/benefit analysis on human health.

V. LEGISLATIVE UPDATE-MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Government and Congressional Relations (OGCR), reported on the status of appropriations and several new bills that were introduced, and provided information about the upcoming 111th Congress.

Appropriations Status. H.R. 2638 serves as the Continuing Resolution for the FY 2009 appropriations through 6 March 2009. It provides funding for the NIH at the FY 2008 level: approximately $29 B for the NIH and $4.8 B for the NCI. After this date, an Omnibus Appropriation is likely, which might provide a small increase in funding, with additional funds likely becoming available through the economic stimulus package. The official budget for FY 2010 is not expected until April 2009, and the appropriations subcommittees have not determined the number of hearings to be scheduled.

Legislation of Interest. Several bills of interest to the NCAB have been introduced. The Strengthening Our Economy Through Small Business Innovation Research (SBIR) (S. 177) was introduced by Senator Russell Feingold (D-WI) on January 8, 2009, and has been referred to the Senate Committee on Small Business and Entrepreneurship. It increases allocations of federal agency grants for SBIR and Small Business Technology Transfer (STTR) programs, and includes research on water, energy, transportation, and domestic security under topics for special consideration. The National Nanotechnology Program Amendments Act (H.R. 554) was introduced by Representative Bart Gordon (D-TN) and requires: the National Nanotechnology Research Program to develop a strategic plan; the establishment of standard reference materials for environmental health and safety testing; and open access of facilities to companies in development of nonscale product prototypes. The State Children's Health Insurance Program (SCHIP) bills (H.R. 2; S. 275), introduced by Representative Frank Pallone (D-NJ) and Senator Max Baucus (D-MT), contain provisions that would reauthorize SCHIP through 2013 and expand the program using funds from an increase in cigarette taxes. H.R. 2 passed the House on January 14, 2009. The Health Information Technology Act (S. 179), introduced by Senators Debbie Stabenow (D-MI) and Olympia Snowe (R-ME), has been referred to the Senate Committee on Finance. It establishes a grant program to offset the costs incurred from adopting a health informatics system, allows Medicare payments to be adjusted for health information technology enabled services, and requires the development of interoperability standards. The National Childhood Brain Tumor Prevention Network Act, introduced in both the House and the Senate, would require the NCI Director to establish a network to research the causes and risk factors associated with childhood brain tumors, requiring an annual report to Congress and authorizing appropriations of $25 M each year from 2010 through 2014. Several bills considered in the last Congress were reintroduced: The Access to Cancer Clinical Trials Act, the Pancreatic Cancer Research and Education Act, and the National Pain Care Policy Act.

Outlook for the 111th Congress. Ms. Erickson noted that the number of Democrats in each of the committees has increased and referred NCAB members to the report in their notebooks for changes in committee chairs and ranking members. She highlighted a few examples: Representative Henry Waxman (D-CA) will chair the House Energy and Commerce Committee; Representative Edolphus Towns (D-NY) will chair the House Oversight in Government Reform Committee; and Representative Todd Tiahrt (R-KS) will be the ranking member of the House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies. The priorities for the 111th Congress will be the economy, energy, the conflict in Iraq, and health care reform with a particular focus on health IT.

VI. AMERICAN ASSOCIATION FOR CANCER RESEARCH (AACR)-DR. RAYMOND N. DUBOIS

Dr. Raymond N. DuBois, President, American Association for Cancer Research (AACR), described the AACR's conquest of cancer in the new era of science and personalized medicine. AACR's strategic goals are to: foster the highest quality cancer research; maintain standing as an authoritative source and serve as an authoritative voice for cancer research; help plan for the future cancer workforce and fund senior and junior scientists; and develop synergistic national and international partnerships. It has more than 28,000 members from nearly 90 countries, including cancer researchers, physician-scientists, health care professionals, students, cancer survivors, and patient advocates. As a long-standing leader in cancer research, the AACR serves as a collective brain trust for basic, translational, and clinical research and provides a consistent focus on cutting-edge science in cancer etiology, diagnosis, treatment, and prevention. In addition, it emphasizes translational research and innovation to improve patient care and prevention, and it acts as a catalyst for international cross-disciplinary interactions, innovation, and integrative cancer research. The AACR also offers renowned scientific and educational programs and publications and covers the spectrum of cancer research.

AACR=s activities in 2008 involved inception of *Cancer Prevention Research*, a monthly journal encompassing pre-clinical research through clinical trials related to cancer prevention. AACR journals account for approximately 20 percent of the world=s cancer literature. Meetings included: a Think Tank on the future of cancer prevention co-sponsored with the NCI; continuation of a collaborative effort with the FDA and NCI on cancer biomarkers; launch of translational cancer medicine meeting series; San Antonio Breast Cancer Symposium, co-sponsored with the Cancer Therapy & Research Center (CTRC) at the University of Texas Health Science Center; and international conferences held in Jordan and Hong Kong. Other activities included a workshop on the PI3 kinase pathway and planning by the AACR Task Force on Cancer Biostatics for a developing targeted agents workshop. A Clinical Trials Awareness Campaign was initiated based on input from the AACR-Industry Roundtable. The AACR was named the scientific partner of the Love-Avon Army of Women. It also was chosen as the scientific partner of the Stand Up To Cancer initiative, which supports basic science and cutting-edge technologies that are ready to be translated to the clinic; 237 concepts have been received and 8 projects have been selected for review, with final selections to be made in the spring of 2009. The AACR is strengthening its efforts related to science policy and government affairs as well. Along with Susan G. Komen for the Cure, the AACR convened a working group of researchers and advocates to coordinate the community's recommendations to Senate staff on elements of the 21st Century Cancer ALERT Act co-authored by Senators Edward Kennedy (D-MA) and Kay Bailey Hutchison (R-TX).

The AACR's 100th Annual Meeting, which will be held April 18-22, 2009, in Denver, CO, focuses on "Science, Synergy, Success." Other meetings scheduled for 2009 focus on new frontiers in basic cancer research, molecular targets and cancer therapeutics, science of cancer health disparities, and translational cancer research for basic scientists. The AACR is establishing an International Affairs Committee to promote dialogue and research about cancer incidence, mortality, and prevention and to extend worldwide access to AACR programs and resources. Additionally, the first satellite AACR office outside the United States is expected to open in Singapore in 2010. The AACR is providing leadership in

scientific publishing through new scientific journals, electronic products for specific audiences, and additional educational media, as well as improving the public's education about cancer through new outreach materials and a Web site for lay audiences. The AACR also supports increased funding for cancer research, as many researchers pursue alternative careers because of funding concerns. Dr. DuBois expressed sadness at the passing of Jacques Littlefield, a philanthropic supporter of metastatic colon cancer research; Mr. Littlefield established the Jeannik M. Littlefield-AACR Grants to support innovative cancer research projects. A strategic planning meeting is scheduled for March 2009 for *Vision 2012: AACR Strategic Plan*, which will identify scientific priorities and recommend AACR programs and activities to enhance progress against cancer.

Dr. DuBois said that this is an extraordinary time in the historical development of cancer research, noting that basic research now employs a systemic approach to link specific signaling pathways to biologic endpoints, many new technologies have been developed, translational research is working to personalize treatments, and cancer prevention research is seeking safer ways to prevent cancer and discover more effective early detection methods. Following the discovery of DNA and the sequencing of the human genome, the next "revolution" is the integration of emerging technologies, engineering, and the physical sciences with cancer biology. Today=s scientific challenges include the ability to analyze large datasets quickly, integration of chemical biology into projects early, better bioinformatics support, well-annotated biorepositories with high-quality tissues, and training of the next generation of scientists. Dr. DuBois said in conclusion that the AACR continues to foster innovation in science and technology, provide educational opportunities, enhance cross-disciplinary collaborations, encourage international collaborations, and stimulate funding for groundbreaking research.

Questions and Answers

Mr. Koch asked about the AACR's annual budget, whether the AACR funds cancer research directly, and thoughts on substantial annual fundraising efforts for cancer research, particularly high-risk, high-potential projects. Dr. DuBois noted that AACR has some grant programs. Dr. Margaret Foti, CEO, AACR, said that AACR's FY 2009 budget is $80 M. Dr. DuBois also stated that much of AACR's success in public outreach has come through the Stand Up To Cancer initiative, and Dr. Foti confirmed the AACR's intention to increase fundraising.

Dr. Leffall said that Dr. Margaret Kripke, who serves on the President's Cancer Panel, led the AACR in the early 1990s, and she brings the AACR experience with her on the Panel. Dr. DuBois joined in expressing gratitude for Dr. Kripke's service to AACR, as well as that of Dr. Waun Ki Hong, Professor and Head, Division of Cancer Medicine, Department of Thoracic/Head & Neck Medical Oncology, The University of Texas M.D. Anderson Cancer Center, and Dr. Von Hoff, who also led the AACR during times in their career.

Dr. Judith S. Kaur, Medical Director, Native American Programs, Mayo Comprehensive Cancer Center, and Professor of Oncology, Department of Medical Oncology, Mayo Clinic, asked whether the AACR tracks the work and success of students who received support from the AACR. Dr. DuBois replied that specific data are not yet available, as career tracking is a relatively new phenomenon, but there is a definite increase in the membership of underrepresented individuals, minorities, and the medically underserved.

VII. NCI BIENNIAL REPORT: INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH-DRS. PAULETTE S. GRAY AND JEFFREY ABRAMS

Dr. Gray said 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 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 importance of balancing research burdens and benefits. In addition, cost is not allowed as an acceptable reason for exclusion. The NIH Revitalization Act of 1993 required the preparation of biennial reports that describe the NIH Institutes' and Centers' (IC) compliance with this requirement.

The NCI has established procedures to implement the NIH policy that encompass institute-wide coordination and communication, and input from the NCI Population Tracking Accrual Working Group, as well as training and the resolution of problems. Important steps in the compilation and dissemination of information about inclusion involve dissemination of the policy to applicants and peer reviewers, post-award monitoring, collection of data from investigators, 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 (e.g., "Hispanic" shifted from race to an ethnic category), data were now collected about ethnicity as well as race and sex/gender, and a new form created transition changes.

The report about the inclusion of women and minorities 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 the aim of such an investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The current report cycle covers data reported in FY 2007-2008, which represents subjects enrolled in FY 2006-2007.

Dr. Abrams described overall reporting data and provided data specifically for cancer treatment trials. The U.S. cancer incidence rates estimated for 2001-2005 by race are: American Indian-0.4 percent; Asian/Pacific Islander-5.6 percent; Black-9.2 percent; White-83.5 percent; and Hispanic-8.6 percent. He 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 remained relatively consistent between FY 2007 and 2008, with the Division of Cancer Control and Population Sciences (DCCPS) (59.0% in FY 2007 and 57.7% in FY 2008) and the intramural program (31.0% in FY 2007 and 29.3% in FY 2008) reporting the highest enrollment levels, followed distantly by the Division of Cancer Treatment and Diagnosis (DCTD), Division of Cancer Prevention (DCP), Division of Cancer Biology (DCB), and the OD's CRCHD. In addition, enrollment data for CTEP treatment trials for FY 2007 and 2008 were provided by race/ethnicity and gender.

Questions and Answers

Dr. Von Hoff requested clarification about the overall trend in accrual rates to clinical trials. Dr. Abrams replied that patient accrual numbers to both intervention and CTEP-sponsored trials have remained stable.

Dr. H. Kim Lyerly, Director, Duke Comprehensive Cancer Center, George Barth Geller Professor of Cancer Research, Duke University Medical Center, encouraged the NCI to distill the effect that NIH

policies have on enrollment as a compelling argument for states and other organizations to adopt similar policies.

Mr. Koch asked about requirements to match the population category mix in individual trials to the overall national incidence of population categories. Dr. Abrams said that these data are not available, as reporting to the NIH is cumulative across all cancers rather than aggregated by specific disease. In response to Mr. Koch's question about how a cancer center that predominantly serves one racial/ethnic category ensures that its enrollment matches the national incidence, Drs. Abrams and Gray confirmed that requirements are realistic for each cancer center depending on the population patient mix. 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 whether efforts to increase minority accrual into clinical trials have been successful, and Dr. Abrams replied affirmatively.

Dr. Von Hoff asked whether the information has shown large changes in accrual rates. Dr. Abrams said that more work is needed to include the African American and Hispanic populations more in our clinical research. Dr. Champion asked for suggestions on how to recruit the growing Hispanic population, many of whom are undocumented, into the health care system and accrue them into trials. Dr. Abrams acknowledged this difficulty and noted the need for more minority physicians who would have more access to these patient populations. Dr. Kaur commented on the statistics about age differential, noting that the role for prevention may be very strong in younger populations; additionally, there are issues of eligibility and comorbidities for many of populations that dramatically reduce the possibility of enrollment in clinical trials. Dr. Niederhuber said that this population is challenging because of many family and employment responsibilities and added that the undocumented Hispanic population is a different issue because they do not wish to be close to the health care system. He also pointed out that the NCI Community Cancer Centers Pilot (NCCCP) Program and CCOPs program are working to understand and address these issues.

Dr. Von Hoff asked whether anything should be added to or taken away from the monitoring or measuring. Dr. Abrams said that it might be helpful to know how women and minority accrual is performing in individual cancers.

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

VIII. FINAL REPORT AND RECOMMENDATIONS: ENHANCING PEER REVIEW- DR. LAWRENCE TABAK

Dr. Lawrence Tabak, Acting Deputy Director, NIH, and Director, National Institute of Dental and Craniofacial Research (NIDCR), provided an update on the implementation of recommendations to enhance the NIH peer review system. Dr. Tabak informed members that this process has involved three stages: 1) obtaining feedback from numerous stakeholders; 2) designing an implementation plan; and 3) implementing actions, which fall into four priority areas and currently are being guided by the Peer Review Oversight Committee (PROC).

The first priority area focuses on engaging the best reviewers. Reviewer retention will be improved by granting additional flexibility regarding the tour of duty. A toolkit with best practices for recruiting the best reviewers will be issued in 2009. Training that includes changes in peer review will be available to reviewers and Scientific Review Officers in spring of 2009. In addition, pilot projects will be conducted in 2009 on the feasibility of using high bandwidth support for review meetings to provide reviewers with greater flexibility and alternatives for in-person meetings.

Dr. Tabak said that the second priority area is targeted to enhance the quality and transparency of the review process with the goal to improve scoring transparency and scale. Review criteria-based scoring will commence in May 2009. A *Scoring and Review Guide Notice* (NOT-OD-09-024) has been published. There will be a 9-point rating scale for both criterion and overall impact scores. The criterion score will be for significance and the investigator=s innovation, approach, and environment. The overall impact score will describe the expected impact of the proposed work. Differences between the previous and new priority scales include that previous scales had a range from 100 to 500, with 401 possible values, whereas the new scale has a range from 10 to 90, with 81 possible values. The resulting fewer choices for categorizing applications will necessitate careful decisionmaking on the basis of each application. In addition, some "select pay" processes may require revision.

Another improvement of the second priority area is that applications that did not score in the upper half, so-called "streamlined" applications, will not only continue receiving the reviewers' critiques, but also will receive scores for each criterion, thus helping applicants assess whether to resubmit an amended application. Plans include the shortening and restructuring of applications to align with review criteria beginning with the January 2010 receipt dates. For example, a 12-page research plan will be required for a standard NIH RPG (i.e., an R01 grant), with other grant types scaled appropriately. Both applicants and reviewers will be reeducated to focus on major ideas, rather than the details expected in the original peer review process. Regardless of the length of an application, there will be no compromise to human subjects' protection in clinical research. Additionally, the interpretation of what is eligible for the Human Subjects Section E will be expanded; future page limits in this section will be established based on an analysis of current usage patterns.

The third priority area ensures balanced and fair reviews across scientific fields and career stages and reduces the administrative burden. There is a new NIH policy to fund meritorious science earlier. The number of allowed grant resubmissions will be reduced from two to one to increase success rates of new and resubmitted applications. In addition, the NIH has announced new policies to encourage funding of new and early stage investigators. Applications that are alike will be reviewed together whenever possible. In 2009, the NIH will begin clustering applications from new and early stage investigators and will consider this approach for clinical research applications.

The fourth priority area involves the continuous review of the peer-review process. This activity will be conducted by a recently constituted evaluation group. In addition, there will be ongoing pilot projects and analyses of historical data, and baseline surveys are being developed. In conclusion, Dr. Tabak said that communication and training will be key elements in the success of this project, and he referred members to the NIH's Web site on enhancing peer review for additional information.

Questions and Answers

Dr. Von Hoff expressed appreciation for the efforts made in enhancing the peer review system, particularly in terms of the responsible use of public funds. Mr. Koch requested further clarification regarding the number of reviewers for each application, the identity of reviewers, and computation of the final score. Dr. Tabak responded that there are three reviewers per application, which may increase to four, and that the reviewers participating in a study section are identified, but their assignment to specific applications is not disclosed; in addition, details about the new scoring system are available on the Web site. Dr. Karen M. Meneses, Professor and Associate Dean for Research, University of Alabama at Birmingham School of Nursing, asked whether the new scoring system will be tested in an upcoming review and also about the "select pay" process. Dr. Tabak replied that the scoring system will be tested in a pilot through the RFA mechanism. Dr. Gray explained that the NCI uses the term "exceptions" rather than "select pay." Dr. Champion queried about the page limitation and changes to appendices. Dr. Tabak said that a 12-page limit was selected from the suggested range of 8 to 15 pages, and there will be no appendices.

Dr. Coffey mentioned the difficulty that highly talented cancer researchers have with obtaining a grant and asked whether a study had been conducted regarding the grant handling and the priority scores that the top 10 breakthrough studies received in the past 20 years. Dr. Tabak said that although the NIH has not conducted a formal analysis of this issue, it underscores the shift toward impact and innovation, and away from discussions of minute details and preliminary data. Dr. Coffey also asked about possible correlations between the publication citation index and the priority score, inquired about the definition of "impact," and suggested that the cancer center or other programs should consider assigning a priority score on grant applications to promote brilliant scientists. Dr. Tabak responded that correlations would be true only for exceptional applicants, and he agreed that it will be important to let experts assess whether proposed work could fundamentally change a scientific field. Dr. Gray assured the Board that the NCI welcomes all suggestions, is establishing committees to ascertain how changes will affect review activities, and will continue to update the Board regarding additional changes to the process.

Dr. Atala asked about what systems may be in place for a fair and accurate decision making process to account for the fewer classes available for distributing a similar number of applications. Dr. Kaur wondered if the evaluation path proceeds directly from the study section to program staff. Dr. Tabak explained that the revised approach relies on skilled program staff for decisions rather than on the arbitrary third figure currently in use. He also noted that Advisory Councils perform secondary reviews. Dr. Gray said that the NCAB reviews NCI's portfolio during its closed sessions. Dr. Niederhuber reminded members that multiple layers of review exist in the evaluation process to ensure a fair consideration of all applications and to maintain quality, scientific rigor, and breadth across the cancer continuum in the NCI=s portfolio.

Dr. Seth Cohen, Office of Science and Technology Policy (OSTP), asked about clustering methodology in relation to newer investigators and grant types. Dr. Tabak said that clustering can present logistic problems for program staff and reviewers in concurrent study sections and that, following extensive deliberation, the decision was made not to separate applications by the level of the investigator.

Dr. Champion observed that, in view of a significantly changed grant system, training will be paramount for all parties involved in peer review. Dr. Tabak agreed and explained that training will be provided to the study section leadership and reviewers.

Mr. Koch asked about the extent to which the awarded grant amount is related to an applicant=s proposed budget. Drs. Gray and Niederhuber explained that the NCI EC considers both the requested amount and the dollar level recommended by the peer review panel; most grants are negotiated downward from the original request by approximately 15-17 percent.

Dr. Coffey asked about the tension between funding the best science versus reaching an established payline, as well as the relationship between downward negotiation and the priority score. Dr. Niederhuber said that a survey of the grantee population showed that although most grant recipients felt the pain of downward negotiated grants, they also supported the funding of the highest number of applicants in a legitimate way. Dr. Niederhuber added that peer review recommendations regarding the budget are considered during the negotiation process.

Dr. Baker asked about the efforts to recruit the best people for a grant review process that has a significant workload. Dr. Tabak responded that serving on a review panel should be considered a good and valuable service. The spirit of getting involved apparently got lost, and it needs to be recaptured; he expressed hope that the new system will reduce frustration, foster scientific discussion, and hence entice participation. Dr. Niederhuber said that universities will need to be engaged, requiring participation in a review panel as a part of career development and a prerequisite for climbing the academic ladder.

Dr. Tabak strongly supported this observation. He also confirmed that study sections will be held outside Washington, DC, in western United States.

IX. ANNUAL DELEGATIONS OF AUTHORITY-DR. PAULETTE S. GRAY

Dr. Gray asked for 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. The 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 for all mechanisms except R41, 42, 43, and 44 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 principal investigator (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 restoration is in the best interest of the NCI and the project is of high NCI programmatic relevance.

Questions and Answers

Dr. Lyerly requested clarification about the role of the Board and the efficacy of its input to the NCI regarding expedited approvals; he commented that a periodic summary statement to the Board about the number of exceptions would improve understanding of the level of activity endorsed by the delegation of authorities. Dr. Niederhuber said information about the percent of competing grant applications and payline is provided to the Board in the Director=s Report, and he explained that the exception list is not extensive. Drs. Niederhuber and Gray agreed that a list of those grants that were funded as exceptions could be provided to the Board in a closed session. Dr. Gray said that the Board will be kept informed about NCI's processes to facilitate its future reviews. Dr. Niederhuber reiterated NCI's goal of transparency to the Board and said that all of the concerns raised by members during the meeting are carefully tabulated, assigned to an NCI staff member with responsibility or knowledge for that area, and acted on.

Mr. William H. Goodwin, Chairman and President, CCA Industries, Inc., suggested that, because the guidelines are 15 years old, an *ad hoc* group could review them and potentially recommend updates.

Dr. Coffey expressed support for streamlining the decisionmaking process for NCI staff and noted that a guideline review might facilitate Board reviews and decisions.

Dr. Kaur requested clarification regarding the language about scoring, noting the ongoing peer review pilot that is using a new 50 percent priority score. Dr. Gray confirmed the use of the existing language, as the new impact score has not been implemented.

Motion. A motion was made that the NCAB concur in granting authority to the Director, NCI, as specified in Delegation A and Delegation B and to concur in the Statement of Understanding with NCI Staff on Operating Principles in Extramural Awards. The motion was seconded and approved unanimously.

X. ANNUAL REPORT: IMPLEMENTATION OF CLINICAL TRIALS AND TRANSLATIONAL RESEARCH WORKING GROUP (CTWG/TRWG) RECOMMENDATIONS-DR. JAMES H. DOROSHOW

Dr. James H. Doroshow, Director, DCTD, presented an update on the Clinical Trials Working Group's (CTWG) restructuring initiatives, which focus on five areas: enterprise-wide integrated management; improving prioritization and scientific quality of clinical trials; better coordination of trials; standardization of procedures; and operational efficiency. The Coordination Subcommittee of the new Clinical Trials and Translational Research Advisory Committee (CTAC) has played an important role in fostering improved enterprise-wide/integrated management, especially by acting as a forum for integrating activities and by working with the CMS and FDA. The CTAC has also developed a model for providing additional funds to groups involved in very complex clinical trials.

Improving prioritization and scientific quality is one of the CTWG's major activities. The Investigational Drug Steering Committee (IDSC), which includes content experts and PIs of NCI=s early phase grants and contracts, provides strategic input into clinical development plans for agents for which CTEP holds the Investigational New Drug (IND) Application. The IDSC has enhanced scientific input into the NCI drug development process and identified niches for NCI involvement in areas of drug development unattractive to industry.

Another effort, which focuses on the later stages of the clinical trials process, involves a group of disease-specific steering committees (DSSCs) that prioritize Phase 3 and selected Phase 2 concepts and review accrual and implementation issues. For example, the Gastrointestinal Cancer Committee held a state-of-the-science meeting on pancreatic cancer in December 2007, which resulted in a consensus manuscript emphasizing the need for extensive drug discovery research before large Phase 3 trials on pancreatic cancer are implemented. Other DSSC accomplishments include a state-of-the-science meeting on cervical cancer held by the Gynecologic Cancer Committee and the development of prioritization criteria for symptom management and quality of life studies by the Symptom Management and Health-Related Qualify of Life Committee. Another important step toward prioritization has been the decision to direct a significant amount of money to Aintegral@ studiesCthat is, tests that must be performed so that clinical trials can proceed, even if CMS or insurance will not cover their costs.

CTWG's coordination initiatives involve data sharing and incentives for collaboration. Developing a comprehensive database of NCI-supported clinical trials is an important emphasis. In the area of standardization, efforts are being made to develop a remote data capture system for all cancer centers and a set of standard clinical trials agreement clauses. Finally, to improve operational efficiency, CTAC has established an Operational Efficiency Working Group (OEWG). Its mission includes reducing study activation time by at least 50 percent and ensuring timely study completion.

Dr. Doroshow next presented an update on the implementation of the Translational Research Working Group's (TRWG) recommendations. In its 15 recommendations, the TRWG outlined pathways to achieve clinical goals, particularly the prioritization of promising concepts and acceleration of their translation. To accomplish this, the Translational Research Acceleration Initiative provides a structured means to determine whether a small number of projects are ready for enhanced investment for translation. The project will gather information on translational opportunities, set priorities, and develop a funding and project management plan to accelerate prioritized opportunities. It will not impact discovery research nor replace existing funding mechanisms. The NCI held an NCI-wide Translational Science Meeting in November 2008, that included 513 abstracts and 800 participants as the first step to discovering the best ways to gather information. The CTAC recommended that the NCI establish a process and timeline to accelerate cancer research: gather information, summer 2009; prioritize, fall 2009; and award and manage, 2010. The prioritization of research opportunities will occur through three levels, including recommendations from extramural content experts, followed by advice from the CTAC, with executive decisions provided by the NCI leadership.

The proposed funding strategy is to develop a new process and infrastructure through the Special Translational Research Acceleration Project (STRAP). Through STRAP, which will begin as a pilot project, the NCI faces a number of challenges in its approach to project acceleration, including the development of unique project management capabilities and customized funding strategies that will vary by project, cover a broad range of projects, and require extensive collaboration. The extramural community will need to develop institutional intellectual property strategies, as well as workflow and data sharing models, to facilitate collaborative research. Together, the NCI and extramural community will need to develop milestones, timelines, and commercialization strategies, as well as explore opportunities for participation by industry and foundations. In closing, Dr. Doroshow said that the advancement of translational research requires prioritization, coordination, standardization, and efficiency.

Questions and Answers

Dr. Von Hoff congratulated Dr. Doroshow, noting that this work already has resulted in providing to investigators agents that previously were inaccessible. Dr. Niederhuber complimented Dr. Doroshow on his efforts, and he said that the implementation of CTWG and TRWG strategies is facilitating the NCI's ability to conduct clinical and translational research.

Dr. Hong commented that pathway-driven translational research is extremely important but is expensive and requires infrastructure and personnel, as well as the ability to identify the subset of patients likely to respond to a specific targeted agent.

Dr. Hong asked Dr. Doroshow to address the topic of biomarkers, especially as they relate to rare diseases and the Specialized Program of Research Excellence (SPORE) mechanism. Dr. Doroshow replied that about one-half of the activities in the SPOREs are biomarker related, but that biomarker studies often reach an impasse when the additional work needed to develop the assay to commercial specifications becomes prohibitively expensive. He stated that the NCI needs to provide resources to help bring biomarkers into the clinic. Mr. Koch noted the difficulty for a commercial enterprise to profit from work in biomarkers. Dr. Von Hoff suggested that putting biomarker development out for bid might prove helpful in some instances. Dr. Niederhuber supported work in biomarkers that focus on both diagnostics and therapy, rather than diagnostics alone. Dr. Barker noted that the early development of diagnostics is not very profitable but the wider and broader application of diagnostics can be.

In response to a question from Dr. Diana M. Lopez, Professor, Department of Microbiology and Immunology, University of Miami Miller School of Medicine, about the very poor accrual of patients into

some clinical trials, Dr. Doroshow said that the longer it takes to open a large trial, there is less chance that it will ever finish accrual.

Dr. Lyerly asked about Dr. Doroshow's experience in identifying "productive failures" as part of the prioritization process. Dr. Doroshow replied that, although discontinuing work on a particular agent is never easy, it is important to focus on the most potentially productive areas of research.

Dr. Hong requested clarification about the relationship between the IDSC and DSSCs. Dr. Doroshow replied that liaisons exist in both directions, and that interactions between the committees have led to increases in information sharing.

Dr. Atala asked how resources will be allocated as the number of candidate biomarkers and technologies increases. Dr. Doroshow replied that expert peer review is the only option; a transparent process to assess biomarkers based on expert external input must be developed.

XI. ANNUAL TOBACCO CONTROL UPDATE-DRS. ROBERT CROYLE, K. MICHAEL CUMMINGS, AND CARYN LERMAN

Introduction. Dr. Robert Croyle, DCCPS, introduced Dr. Kathy Backinger, Tobacco Control Research Branch, who provided an overview of the Transdisciplinary Tobacco Use Research Centers (TTURCs). The Centers were cofounded by the National Institute on Drug Abuse (NIDA), the Robert Wood Johnson Foundation (RWJF), and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). They were established by an RFA award in 1999 and re-awarded in 2004. The Centers' purpose is to facilitate a transdisciplinary approach to the full spectrum of basic and applied research on tobacco use to reduce the burden of tobacco use. Seven centers currently receive funding, and 2009 marks the 10th anniversary of the TTURCs, with this being their last year. Dr. Backinger then introduced the speakers: Drs. K. Michael Cummings, Department of Health Behavior, Roswell Park Cancer Institute; and Caryn Lerman, Tobacco Use Research Center, University of Pennsylvania.

Building the Evidence Base for Tobacco Control Policies. Dr. Cummings described translational research on dissemination and policy adoption aimed to build the scientific evidence base for effective tobacco control policies and programs implemented in different countries as part of the Framework Convention on Tobacco Control (FCTC). The TTURC program involves a worldwide network of more than 90 investigators from 35 institutions in 19 countries. To date, NCI's $7.6 M investment has yielded $30 M in funding from sources located primarily outside the United States. Efforts have resulted in more than 100 peer-reviewed scientific papers and more than 200 scientific presentations. The program has been built around three projects and two cores. Common features of the projects have been natural experiments, common data collection protocols, and a common set of measures. When the NCI first began supporting the TTURC in 2004, six countries participated: the United States, Canada, United Kingdom, Australia, Thailand, and Malaysia. By 2009, the program has expanded to include a total of 17 countries, with four new countries in the process of joining.

The policies of the FCTC include: price and tax measures to reduce demand; protection from exposure to tobacco smoke; regulation of the contents of tobacco products; regulation of tobacco product disclosures; packaging and labeling; education, communication, and public awareness; ban of tobacco advertising, sponsorship, and promotion; and dependence and cessation treatments. These policies must be implemented within a certain time period. More than 160 countries, not including the United States, have signed the Treaty. A World Health Organization (WHO) report documents that most countries around the world are at the beginning stages of implementing these policies.

Dr. Cummings discussed how these policies would relate to the United States. Tobacco use has been and continues to be the Nation's leading cause of cancer death. The PCP addressed this issue in two

recent reports. Since 2000, there have been reports from various groups: The Surgeon General's report; an NIH consensus conference; the Centers for Disease Control and Prevention (CDC) Best Practices; Institute of Medicine (IOM); and a report from The Royal College of Physicians. If the FDA is granted the authority to regulate tobacco, the Administration could benefit from research on the effectiveness of FCTC policies implemented in other countries, such as policies regarding warning labels, taxation, product policies, illicit trade, advertising and promotion, smoke-free environments, and light/mild deceptive product descriptors. Many smokers are misled by tobacco product labeling. Misconceptions about "light and mild" cigarettes rank highest in China, Thailand, and the United Kingdom, and are lowest in Mexico and Canada. Cigarette emissions testing and product disclosures have been other study areas in our TTURC. Smoking machines using ISO/FTC protocols produce invalid results, as they do not emulate a smoker's habit of puffing. Those who switch to low yield cigarettes typically puff harder and deeper and often unknowingly cover the invisible vent holes on the tipping paper of the filer to get the necessary dosage of nicotine from the cigarette. Therefore, values for emissions should not be used as consumer information.

One of our projects involves examining 200 cigarette brands from 19 countries tracked over time. One result of this tracking was the observation in the United Kingdom that the establishment of a tar limit on cigarettes based on the ISO/FTC testing machine did not change the consumer's exposure to emissions, whereas filter ventilation increased up to 400 percent. Another subject of study has been the content of lead and cadmium in tobacco obtained from different countries, which is much higher in China than in the United States because of the high level of air pollution in China. This finding is particularly important because, with a 34 percent market share, China is the largest producer of tobacco in the world. Metal content also can be used to detect counterfeit cigarettes from China.

Translating research into practice is challenging, and efforts have been made to compare warnings on packages. Whereas the United States has used text warning messages, much of the rest of the world has employed warning pictures, which have been more effective. As an example that efforts to create a smoke-free environment could be successful, Dr. Cummings showed photographs of public bars in Hungary before and after the smoking ban. He noted that his colleague Dr. Geoffrey Fong had met with the Hungarian Minister of Health in August 2008, during the conduct of air pollution studies there.

Dr. Cummings concluded that good public health practice, similar to clinical medicine, would demand rigorous evaluation to adopt strong evidence-based interventions. The project has been conducting this research and has quickly become the primary source of data for FCTC protocols that are being adopted. They have been synergistic with initiatives conducted by the Bloomberg and Gates Foundations and the CDC Global Tobacco Surveillance System.

Nicotine Dependence Treatment: From Mouse to Man to Medicine. Dr. Lerman described research related to the translational space between basic and clinical research and mentioned that, according to *U.S. News and World Report*, the United States is unlikely to meet its Healthy People 2010 objective of reducing the adult smoking rate to 12 percent or less. Twenty percent of Americans are currently tobacco dependent, and the most effective FDA-approved medications for the treatment of tobacco dependence are successful for only one in three smokers. Therefore, scientists should contribute to the development of new medications. The NCI-funded Transdisciplinary Tobacco Use Research Center at the University of Pennsylvania is identifying novel molecular targets (discovery) for the development of smoking cessation medications through transcriptional profiling and human genetics studies. The program is using initial target validation (development) and proof-of-concept studies in rodents and in humans, including imaging. Two translational research examples from this center include the work to develop medications that target catechol-o-methyltransferase, which regulates dopamine levels in the brain (early phase) and work to develop a biomarker test to tailor smoking cessation therapy.

In one study, the catechol-o-methyltransferase gene, *COMT*, was investigated in relation to nicotine dependence. There is a common functional polymorphism, and one of four people carry the val/val genotype that puts them at three times the risk for relapsing in a smoking cessation trial, whereas other genotype groups are at reduced risk. The val allele is associated with increased enzyme activity, resulting in a decrease of dopamine in the prefrontal cortex, which may cause diminished cognitive functions. The hypothesis developed was that nicotine deprivation would produce cognitive deficits mainly in smokers with val/val genotypes, an effect that might prompt smoking relapse to reduce deficits. This theory was supported by unpublished clinical data indicating that cognitive deficits arising early in nicotine abstinence may predict smoking relapse.

A recently published imaging study demonstrated differences in brain activity. The genotype group with a low risk of smoking relapse, showed absolutely no differences in brain activation while performing a certain task whether they were smoking or abstinent. The high-risk group with val/val genotype, however, failed to recruit the part of the brain required for performing the task. It was apparent that a brain-related biomarker had been discovered for identifying individuals at increased risk of relapse by employing methods of genetics and imaging.

Data about the drug tolcapone were also presented. The drug is an inhibitor of *COMT*, it has cognitive enhancing effects, and is FDA-approved for the treatment of Parkinsons disease. The Phase I safety study in smokers indicated that short-term use of the drug was safe and well tolerated; tolcapone (vs. placebo) decreased the correct response time; and the drug had no effect in the met/met genotype group. A Phase II study is underway at this time. It appears likely that a reversal of abstinence-induced cognitive deficits by tolcapone would provide a proof of mechanism and that convergent genetic and pharmacologic evidence would support *COMT* as a therapeutic target for tobacco dependence.

Dr. Lerman also described research involving pharmacogenetics, targeted therapies, and the development of a simple metabolic test. The faster nicotine is metabolized by the CYP2A6 enzyme, the more cigarettes somebody would smoke. The nicotine metabolite ratio in the plasma, saliva, or urine is a stable measure of CYP2A6 activity. Subjects with genetically slow metabolism respond well to transdermal nicotine (patch), whereas those with fast metabolism respond well to bupropion, an antidepressant that is used to treat nicotine addiction. Dr. Lerman also explained the use of an algorithm for personalizing cost-effective smoking cessation treatment based on the nicotine > metabolite ratio. There is a company planning to develop a test for use in a doctor's office to tailor the treatment based on this biomarker. This would be the first evidence of translation to practice of a clinical marker from pharmacogenetics research in tobacco dependence treatment.

Questions and Answers

Mr. Koch asked about the success in using muri models to predict the effectiveness of nicotine therapeutic agents in humans, given that mice generally are lousy predictors in the effectiveness of cancer agents. Dr. Lerman responded that similar translation limitations are generally found, but she noted that some models, such as nicotine self-administration models, provide good validity. Mr. Koch wondered about the extent to which mice are used to test or screen candidate agents. Dr. Lerman explained that transcriptional profiling studies are looking at genes that are expressed to identify some novel molecular targets, and then candidate genes are prioritized for human studies.

Dr. Kaur complimented the presenters on providing excellent presentations and asked whether cofactors had been examined separately from the homozygous situation, as some polymorphisms have shown differences in given populations such as CYP2A6 in metabolism, as well as other drugs that interfere with metabolism. Dr. Lerman stated that in studying CYP2A6, particularly where estrogen actually increases the rate of metabolism, the enzymatic test has been used because it accounts for genetic

and environmental factors; in addition, because there are racial differences in allele frequencies, which can bias genetic studies, the enzymatic test allows the inclusion of all races.

Dr. Meneses expressed her appreciation for the outstanding presentations. She asked about the likelihood of the United States ratifying the FCTC. Dr. Cummings said that this cannot be predicted and reminded members that the PCP had recommended signing last year and that many of the elements in legislation about tobacco and the FDA introduced during the past year are the same as FCTC policies.

Dr. Coffey, noting that personalized medicine is monozygotic, asked whether personalized medicine can be focused on mice, which are identical twins, to find a common denominator for addiction. Dr. Lerman clarified that the animal models have been used in terms of screening compounds based on novel molecular targets, whereas the mice used in the personalized medicine component of the studies are transgenic models rather than standard inbred strains; she added that the pharmacogenetics phase is not relying on animal models.

Dr. Champion wondered whether, in the studies of the val allele, differences in cognition that have been found with nicotine restriction would continue if the deprivation time was extended. Dr. Lerman said that other studies showed that deficits were worst in the first 72 hours, after which the symptoms began to abate. She added that up to 75 percent of people will relapse during the first week.

XII. UPDATE: CENTER FOR CANCER RESEARCH AND INTRAMURAL CLINICAL RESEARCH STEERING COMMITTEE-DRS. LEE HELMAN AND DANIEL KASTNER

Dr. Daniel Kastner, Deputy Director, NIH Intramural Clinical Research, provided an update of the activities of the Intramural Clinical Research Steering Committee (ICRSC), which was established to optimize clinical and translational research in the intramural research program (IRP). Dr. Kastner explained that one high-priority issue for this committee is reengineering the protocol generation and review process to make it more user-friendly, more efficient, and more consistent across the intramural program, while continuing to protect human study participants.

In a series of meetings in late 2008, the ICRSC reached consensus on several aspects of the protocol review process, concluding that: clinical investigators need greater support in the preparation and implementation of human subjects protocols (a conclusion also reached earlier by an Intramural Working Group [IWG] panel chaired by Dr. Cliff Lane); scientific review of human subjects protocols should remain with the specific ICs but should be made more consistent across the IRP; trans-NIH oversight and support for the nomination and training of institutional review board (IRB) chairs and members are needed; and the ethical review process should be streamlined while still ensuring the protection of study participants. The majority of ICRSC members agreed that it would be desirable to transition from the current 11 IC-specific IRBs to six thematic trans-NIH IRBs. This change would have the benefits of making review more efficient and consistent, eliminating potential conflicts of interest, providing specialized expertise, increasing the frequency of IRB meetings, and increasing the pools from which IRB members could be drawn. It would be less drastic, however, than the total centralization of all 11 IRBs into a single structure—an idea that had received a negative reaction when previously proposed. An important aspect of the transition plan proposed by the ICRSC is the creation of six protocol services centers (PSCs) that would include the IRBs and also provide support services to help investigators design protocols and bring them through the review process.

Dr. Kastner also explained that, in the implementation of the ICRSC's proposals, a top priority is the development of training that would change the culture of IRBs to make their relationship with investigators more collaborative and less adversarial. Other opportunities to improve the review process include: creation of a special panel for review of low-risk protocols, harmonizing NIH and FDA policies on adverse event reporting, and selective delegation of some protocols to outside IRBs, such as the

Western IRB. The ICRSC is discussing short- and long-term assessment metrics, including the length of time from scientific clearance to protocol submission and decision and feedback from clinical investigators, as well as the number of new protocols, the number of physicians as PIs, the mean age of PIs, and the quality of the review process.

Dr. Lee Helman, Scientific Director for Clinical Research, Center for Cancer Research (CCR), presented key findings on clinical trials development, based on an evaluation of the intramural program from 2000 through 2007 by Dr. Dilts and colleagues. No differences in the timeline for trials were detected by phase or between high- and low-throughput Branches. Experienced PIs could open trials approximately 2.5 months faster than others. Accrual was low, with 12.5 percent of trials opening and closing with no accrual, and 30 percent not even reaching 20 percent of their stated maximum accrual goals. It required a median of 208 days from the start of scientific review to opening a trial; most of this time was spent on scientific review (64 days), IRB review (96 days), and the delay between the completion of clinical center review and first patient enrollment (50 days).

Dr. Helman reported that Dr. Dilts and his team had made several recommendations for accelerating the timeline of clinical trials development, including giving the Branch responsibility for review of scientific quality; minimizing redundant reviews; practicing quality assurance rather than quality control; and generating protocols from both the bottom up (i.e., from investigators) and the top down (i.e., from CCR leadership). Dr. Dilts' group recommended giving Branch Chiefs responsibility for ensuring that studies are non-competing; ensuring consistent quality across branches; and developing and maintaining the vision, portfolio, and priorities of trials. Other recommendations included the creation of tools—including training, metrics, and visibility—to assist in the achievement of goals. The ultimate goal is to reduce the time between the initiation of scientific protocol review and the opening of a trial from 200+ days to 60 days.

On the basis of the findings from Dr. Dilts' investigation and discussions at a retreat in September 2008, the Protocol Review and Monitoring Committee (PRMC) has been disbanded, with responsibility for scientific review given to the Branches. Implementation teams have been formed to establish standard operating procedures for scientific review and provide guidance in protocol development.

Questions and Answers

Mr. Koch asked about the FDA's engagement in efforts to streamline approval of new drugs. Dr. Niederhuber said that the NCI and FDA meet regularly. Dr. Helman observed that the NCI would be in a better position to encourage the FDA to expedite its process if the NCI first streamlined its own process, and Dr. Goodwin expressed his agreement with this idea. Dr. Lyerly said that he has been working with Dr. Richard Pazdur, FDA, to organize a workshop on accelerating drug approval, which is held on the FDA campus every spring. He also pointed out that the FDA approval process occurs in a relatively short time period, but that it may take as long as 8 years to obtain the necessary data before the process can take place. Dr. Barker said that she has been pleased with the NCI's and FDA's progress in improving their processes and noted that agreement had been obtained on the exploratory IND and on improving the approval path through FDA for biomarkers, once they become available. Dr. Coffey observed that there was no representation from the FDA at today's NCAB meeting and expressed the hope that the FDA would be represented at future meetings to facilitate communication.

In response to a question from Dr. Hong about the time to complete a trial, Dr. Helman reported that the data indicate that 57 percent of NCI's intramural trials meet their accrual goals and that 12.5 percent never accrue anyone. It is possible to ascertain within 3 months whether a protocol will not meet its accrual goals.

Dr. Kaur commented on the importance of public trust in the research enterprise and noted that IRBs play an important role in developing that trust. Dr. Helman agreed that public trust is crucial. He added that the current informed consent process is not ideal. Dr. Atala queried about steps that are being taken in conjunction with the Office of Human Subjects Research (OHSR) to simplify both the review process and the consent form. Dr. Kastner replied that the ICRSC includes a representative from the OHSR and that the ICRSC plans to have a dialogue with the OHSR about how to make the consent process more efficient. Dr. Coffey suggested approaching the advocacy community to form a group, including members of both genders and different ethnicities, to approve an understandable consent form written in plain English.

XIII. CLOSED SESSION-DR. DANIEL D. VON HOFF

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 IRG recommendation was affirmed by all serving Board members present. During the closed session of the meeting, a total of 1,964 applications were reviewed requesting support of $ 606,099,558.

WEDNESDAY, FEBRUARY 4, 2009

XIV. NATIONAL EFFORTS IN BLOOD AND MARROW TRANSPLANTATION- DRS. JAMES H. DOROSHOW, ROY WU, ROBERT BAITTY, MARY M. HOROWITZ, AND DENNIS L. CONFER

Introduction. Drs. Doroshow and Roy S. Wu, Chief, Clinical Grants and Contracts Branch, NCI, provided an overview of NIH's support of hematopoietic stem cell transplantation (HCT) research. Dr. Wu explained that, in contrast to the limited involvement in HCT research by large pharmaceutical companies in the private sector, a large Federal investment ensures that HCT therapy is available through the C.W. Bill Young Transplantation Program and the National Cord Blood Inventory (P.L. 109-219). The NCI's successful support of blood and marrow transfer (BMT) research is evidenced by the awards of a Nobel Prize and a GM Prize to Dr. Donnell Thomas and Dr. George Santos, respectively. In 2008, the NCI and National Heart, Lung and Blood Institute (NHLBI) provided more than $69 M in clinical funding for BMT, including providing support for the Blood and Marrow Transplant Clinical Trials Network (BMTCTN) and the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR maintains a registry of transplant outcomes data that many organizations use for cost effectiveness, quality of life, and other health care research. Dr. Wu next introduced the speakers: Drs. Dennis Confer, National Marrow Donor Program (NMDP); Robert Baitty, Blood Stem Cell Transplantation Program, Health Resources and Services Administration (HRSA); and Mary Horowitz, CIBMTR, Medical College of Wisconsin.

Worldwide Growth and Development of HCT. Dr. Confer said that HCTs continue to increase for both types of transplants that use blood or marrow either from a patient (autologous) or from another person (allogeneic); the potential for further growth is high. Estimates for current worldwide activity indicate that 37,000 autologous and 22,000 allogeneic transplants are performed every year, with more

than 14 million donors registered. The world's inventory of unrelated donor (i.e., public) umbilical cord blood units currently exceeds 400,000.

Whereas bone marrow transplants were used almost exclusively in the NMDP until 1998, the number of peripheral blood stem cells (PBSC) and cord blood transfers has steadily and significantly increased since then. PBSC and cord blood transplants combined have outnumbered bone marrow transplants since 2003; PBSC transplants now are used most frequently. From 1988 through January 2009, the NMDP included 7,435,426 adult marrow donors; from 2000 to January 2009, the cord blood units totaled 94,604. The percentage of NMDP recipients 55 years and older has grown significantly since 2000. It approached 900 in 2007, which is approximately 27 percent of first NMDP transplants.

HCT transplants are used most frequently in North America for the following indications: multiple myeloma–5,100 transplants annually; non-Hodgkin's lymphoma (NHL)-4,300; acute myeloid leukemia (AML)-3,100; Hodgkin's disease-1,500; acute lymphoblastic leukemia (ALL)-1300; and myelodysplastic syndrome/myeloproliferative disorders (MDS/MPD)-1,000. Autologous transplants are typically used for multiple myeloma, NHL, and Hodgkin's disease. Allogeneic transplants are used predominantly for AML and exclusively for ALL and MDS/MPD.

More than one-half of allogeneic transplants use products from unrelated donors. Outcomes with related and unrelated donors have improved over time, and results obtained with both types of transplants are now comparable. The 1-year survival rate was 70 percent in 2005. Continued clinical research is necessary, however, to optimize outcomes.

HRSA's Role in Blood and Marrow Transplantation. Dr. Baitty explained that the purpose of the National Bone Marrow Donor Registry is to facilitate unrelated donor transplantation. The Registry, which was preceded by the National Organ Transplant Act in 1984, was established in 1986 and supported by a grant from the U.S. Department of the Navy (hereafter referred to as Navy). Oversight was provided by the NHLBI as a research activity, but in 1994 supervision was transferred to HRSA. The Registry has been operated by the NMDP since its inception under HHS's contracts. Both the HHS and Navy have provided significant financial support for more than 20 years.

Improvements to the Registry followed the Reauthorization Act of 1998. The Act: increased the number of minorities in the Registry; provided patient advocacy services; implemented quality standards and procedures; gathered outcomes data on unrelated-donor transplants that were facilitated by the Registry; and maintained transplant center-specific survival analyses to aid transplant center quality improvement and to provide patients and referring physicians with data to help guide the choice of transplant center.

The Stem Cell Therapeutics and Research Act of 2005 (P.L. 109-129) expanded access to HCT. It aimed to increase: 1) the number of blood stem cell transplants using unrelated adult donor sources or umbilical cord blood grafts, and 2) the number of cord units available for research. It also established the National Cord Blood Inventory and the C.W. Bill Young Cell Transplantation Program, a successor to the National Bone Marrow Donor Registry, with an authorized budget of $38 M per year and a FY 2009 Continuing Resolution of approximately $23.5 M. Other initiatives that were established include the Secretary=s Advisory Council on Blood Stem Cell Transplantation (BCT); the Bone Marrow and Cord Blood Coordinating Centers; the Office of Patient Advocacy (OPA) that provides case management; the Single Point of Access (SPA) that provides electronic searches for patients and physicians; the Stem Cell Therapeutic (SCT) Outcomes Database that collects basic scientific data on transplant recipients; and a program that collects additional comprehensive research data on HCT through other mechanisms.

Dr. Baitty presented a schematic overview of the C.W. Bill Young Cell Transplantation Program contracting structure that illustrated NMDP's relation to the Cord Blood Coordinating Center, the OPA/SPA, and the Bone Marrow Coordinating Center.

Multicenter Networks for HCT Research: CIBMTR and Blood and Marrow Transplant Clinical Trials Network (BMTCTN). Dr. Horowitz said that the CIBMTR was established in 2004 to support clinical research in HCT and related fields. It developed from an affiliation with the NMDP and the International Bone Marrow Transplant Registry (IBMTR). The centers that participate in the CIBMTR are located on five continents; the centers are distributed most densely in the United States, Europe, and Japan.

Dr. Horowitz further described the CIBMTR Observational Database and the current and future data flow. The role of the Observational Database in clinical research is to analyze trends; pursue descriptive studies; identify trends associated with outcome; assess treatments and strategies; study late effects; analyze access and utilization; and design, interpret, and facilitate clinical trials.

The BMTCTN was established as an NIH-funded initiative in September 2001, and renewed in October 2006. It has 16 core center cooperative agreements and 1 data coordinating center cooperative agreement with the CIBMTR, including subcontracts with the NMDP and the EMMES Corporation. The goal of the program is to provide the infrastructure needed to allow promising HCT therapies to be developed and evaluated in high-quality multicenter studies. Since 2003, more than 70 centers have enrolled patients; 25 percent of enrollment comes from Affiliate Centers. Statistics demonstrate that 80 percent of BMTCTN transplants are allogeneic, and more than 5 percent of U.S. transplants are autologous. In addition, more than 900 transplants are from unrelated donors, which is approximately 10 percent. Both the BMTCTN and CIBMTR have roles in human studies of safety and efficacy. CIBMTR also is involved with facilitating better access to BMT, improving HCT outcomes, exploring new HCT drugs and strategies, furthering optimal HCT treatment, achieving greater transplant success, and examining and improving discrepancies in patient HCT.

Questions and Answers

Dr. Coffey expressed his congratulations on the research accomplishments in BMT and heralded the field as an area with great potential for research and discovery. He suggested that the NCI examine closely what has been learned about stem cell properties and consider the use of circulating tumor cells as research and diagnostic tools, and he encouraged the Navy to publicize its efforts in BMT and stem cell transport broadly to the scientific community.

Dr. Hong asked for further information about the improvement of supportive care, cost effectiveness, and quality of life. Dr. Confer answered that many factors have contributed to the improvement, such as the improved ability to manage *graft-versus-host* disease, the greater awareness about immune reconstitution, and new knowledge about allele-level matching has resulted in better matches and higher survival rates; he also noted that many transplant recipients experience excellent quality of life, but patients disabled by chronic *graft-versus-host* disease face many challenges. Dr. Horowitz added that an ongoing study looking at longitudinal changes in quality of life in a variety of populations is yielding interesting findings.

Dr. Kaur congratulated the researchers on the wealth of data accumulated and wondered about issues of access, particularly for racial and ethnic minority populations. Dr. Confer replied that access remains an important component of the program, but that difficulty remains in finding matches in the registry for African Americans; he noted that umbilical cord blood is a promising graft source because it does not have to be as closely HLA matched as adult products. Dr. Horowitz observed that significant disparity in utilization of related HLA identical sibling donor transplants and autologous transplants,

which is not affected by HLA issues, persists as an access issue. Dr. Baitty said that the HRSA, which is funding cord blood banks to collect units for the national inventory, is interested in the potential that cord blood has to improve access for minority populations, especially African Americans.

Dr. Coffey suggested that PIs should consider the other types of stem cells present in cord blood. Dr. Baitty confirmed that the number of these cells currently is unknown.

Dr. Atala was impressed by the research and requested information about the cost overall per unit transplanted. Dr. Confer said that the cost of searching to find a donor or an umbilical cord blood unit ranges from $5,000 to 10,000 per transplant, and adult products are approximately $24,000 delivered. Umbilical cord blood varies by bank, and many of the banks have an FDA cost recovery and cord blood ranging from $22,000 to $35,000 per unit.

Dr. Meneses asked whether the data collected from international sources, particularly Asians, showed differences for outcomes related to either access or survival. Dr. Horowitz responded that data from island populations, such as Japan and Ireland, show in populations that have less HLA heterogeneity a decreased risk of *graft-versus-host* disease. Additionally, an International Studies Working Committee, recently established, is working with Asian Pacific and Middle East blood and marrow transplant groups on the topic.

XV. STATUS REPORT: OFFICE OF COMMUNICATIONS AND EDUCATION- MS. LENORA JOHNSON

Ms. Lenora Johnson, Director, Office of Communications and Education (OCE), reported on changes to the OCE and its future direction. Ms. Johnson said that the NCI is mandated to provide information to the public, patients, and physicians on cancer treatment and clinical trials using information systems available to the public. In addition, the NCI must maintain a database to store and disseminate information on cancer research and the results of clinical trials. The OCE is working to transfer the registration of trials to one central NCI database (CTRP) to further its mission of disseminating research results, which involves creating tools, programs, and opportunities by which people can understand and interpret these results to change their behaviors.

The OCE has a number of opportunities to pursue, including the use of social networking Internet sites and a new Administration that is skilled in communication and has developed new plans to combat cancer. However, the need to centralize and coordinate communication efforts across the Institute, serving a wide array of audiences, and strengthening public education outreach efforts are challenges that the OCE must meet when considering a public awareness campaign to change impressions and perceptions about the NCI and cancer in general. The OCE was formed in 2007 by merging the Office of Communications and the Office of Education and Special Initiatives, which resulted in a return of $14 M to research efforts through efficiencies gained in the reorganization. Based on reviews from an NCI EC subcommittee and MITRE operations analyses, the Cancer.gov Web Council and Web Operations Team were launched, and a transition plan was developed to move information technology services from the OCE to the Center for Biomedical Informatics and Information Technology (CBIIT). The OCE provides numerous other functions at the NCI, including the engagement of technologies, operations, attention to information content accuracy and integrity, and the provision of support to NCI divisions, offices, and centers.

Ms. Johnson said that the OCE serves a diverse audience of consumers, researchers, health care providers, advocates, partners, media, policymakers, and program planners. Forty percent of cancer patients with Internet access visit Cancer.gov, and of these, 42 percent expressed satisfaction with their visits. However, OCE uses numerous channels to distribute information, including publications for patients, Cancer Information Services (CIS), direct responses to e-mails, minority media outlets, the

biweekly *Cancer Bulletin*, exhibits at national conferences, and Cancer.gov in English and Spanish. A computer-animated video presentation to the NCAB demonstrated the OCE=s ability to use current technologies to reach diverse audiences.

The NCI has decided to continue to fund the 1-800 CIS service, but to consolidate it into one contract. The OCE plans to link the CIS service more closely with the scientific activities of the NCI. The CIS partnership program consists of approximately 750 partners, 300 of whom are involved in cancer control activities at the state, tribal, and territorial levels, and has served as a bridge between the NCI and the community for almost 30 years. The current partnership contracts continue through January 2010; NCI's EC has decided not to move forward in procuring another contract to operate the partnership program when the contract ends, because the NCI needs to reevaluate the approaches through which audiences receive information. The Institute must better position itself to engage in research dissemination efforts to quickly transfer information to targeted audiences. In addition, the NCI plans to expand partnerships with clinicians and care-delivery settings to shift research discoveries into clinical practice. The NCI itself offers programs that meet the needs of the medically underserved and minority communities, and these should be coordinated and reinforced. The public provided feedback to the decision through more than 100 letters (including members of Congress), media coverage, and high participation in the Office of Advocacy Relations teleconferences. The public recommends that the NCI: reconsider the decision; extend current contracts until a new concept is in place; employ a transparent process and stakeholder input for developing the new concept; and/or focus efforts on populations with higher than average cancer rates. To move forward, the areas that NCI should consider a priority must be determined. Ms. Johnson asked the NCAB for its input to assist in identifying organizations to serve as partners so that resources may be combined, and in carrying forth NCI=s intention to engage the public in innovative ways.

Questions and Answers

Dr. Coffey stated that it was important to note the NCI's mission and responsibility as defined by law and history, because one third of Americans will develop cancer. It must be determined where the delivery of information fits in with the delivery of medical care and with cancer research. Dr. Champion asked what would happen until a new plan to replace the partnership program is in place. Ms. Johnson responded that although there may be a gap in contracts, a transition plan will be in place. Dr. Lopez stated that although the NCI's primary mission is to conduct research, the public has come to expect direct communication such as that conducted through the partners program, and asked if there was a way to maintain such a program through 2015. Ms. Johnson responded that the NCI would continue to engage in partnership efforts, but not at the same level; the focus will be on areas with the greatest need. Dr. Meneses asked if those areas had been identified, and if public comment had been greatest from these areas. Ms. Johnson stated that the public response indicated the program is important to all areas, but part of the assessment will be an examination of where the need is the greatest in terms of resources available within communities.

Dr. Kaur asked whether the OCE had received assurances from nonprofit organizations that they would assume some of the outreach activity for the NCI, and also asked how the OCE would address the issue of the "digital divide" that persists between those who are comfortable with online communications and those who are not. Ms. Johnson said that outreach activities would be a point of discussion with partners. She added that the OCE recognizes that not every home contains a computer, and that, while the NCI is not situated to be direct-to-consumer, in many cases, the NCI can use technology to transfer information to intermediaries and build capacity at the community level.

Dr. Champion asked if the partners understand that their input will be sought during the transition. Ms. Johnson responded that she is aware that the partners want to and will be engaged in the planning process. Dr. Atala noted that NCI=s cancer centers, including the new community cancer

centers, may serve as a good resource for future information dissemination. Ms. Johnson explained that the OCE plans to capture, organize, and coordinate NCI=s programs in the field in a way that supports the Institute's outreach needs.

XVI. SUBCOMMITTEE REPORTS AND FUTURE AGENDA ITEMS-DR. DONALD S. COFFEY

Biomedical Technology *Ad Hoc* Subcommittee. Dr. Coffey referred the Board to the minutes of the subcommittee meeting held in December 2008.

Motion. A motion to accept the minutes of the 8 December 2008 NCAB *Ad Hoc* Subcommittee on Biomedical Technology Meeting was seconded and approved unanimously.

Global Cancer Research *Ad Hoc* Subcommittee. Dr. Coffey said that the Board=s concurrence has been requested to establish a new NCAB *Ad Hoc* Subcommittee on Global Cancer Research. He read the functional statement:

> The purpose of this *ad hoc* subcommittee is to advise the National Cancer Advisory Board (NCAB) and the NCI Director on strategic approaches and opportunities to enhance NCI=s contribution to global cancer research. This group will provide leadership and expertise with the intention of offering input on proposed initiative, concepts, and partnerships or provide information to help determine prioritization of new prospects for NCI global cancer research. In addition, this subcommittee may search for those opportunities whereby the NCI can contribute internationally, such as the advancing clinical cancer research, building and bridging technology and research capacity, or promoting innovative training programs.

Questions and Answers

Dr. Barker said that the establishment of the Subcommittee will provide an opportunity for some NCI advisory groups to report to the Board and for the NCAB to provide additional advice on NCI's strategic direction. Dr. Gray said that, if the Subcommittee is approved, that Drs. Niederhuber, Gray, and Carolyn D. Runowicz, Director, The Carole and Ray Neag Comprehensive Cancer Center, University of Connecticut Health Center, will discuss the membership of the Subcommittee and identify a chairperson.

Dr. Hong expressed his full support for creating this Subcommittee. He also asked Dr. Gray about the number of existing NCAB subcommittees. Dr. Gray said that there are eight NCAB subcommittees in addition to the Subcommittee on Special Actions, which acts in closed session only.

Dr. Lyerly expressed his strong endorsement and enthusiasm for the Subcommittee, pointing out that the increasing recognition that the impact of cancer is global and solutions for cancer research and cancer patients will emanate from interactions on a global scale.

Dr. Coffey voiced his personal support for the creation of the Subcommittee but cautioned that this would mean allocating American taxpayers' money to fund cancer research projects around the world. Dr. Lopez requested further clarification about supporting global programs. Dr. Barker said that the NCI currently funds a large number of global programs and provided several examples, including the Division of Cancer Epidemiology and Genetics' (DCEG) seminal work in epidemiology, as well as solutions around leukemia and benzene that resulted from studies conducted outside the United States. She added that, because many countries are further advanced in areas such as genomics, the NCI can double or triple its investment through these partnerships that will expand its resource base significantly.

Dr. Lopez asked whether these partnerships mean that the NCI is expected to increase its help substantially from the current levels. Dr. Coffey said that such is his understanding. Dr. Gray reiterated that the NCAB subcommittee will be advisory to both the NCI and the Board, thus providing another venue for the NCAB to interact and provide additional definitive advice to the Institute. Dr. Champion said that this Subcommittee will provide the Board with a chance to solidify views that impact the global community; what affects the rest of the world affects the United States. Dr. Barker said that there are great opportunities as well as issues that should be addressed cautiously, and this is a reason for establishing the Subcommittee. In addition, the bringing of resources by philanthropic groups and countries to build partnerships is new to the NCI. Dr. Coffey agreed that there is no doubt that science has a responsibility to humankind. He observed that conflicts on resources that may result from the dual responsibilities to the United States and humankind will need to be worked out carefully by the Subcommittee.

Motion. A motion to establish an NCAB *Ad Hoc* Subcommittee on Global Cancer Research was seconded and approved unanimously.

Future Agenda Items. Dr. Coffey asked members to identify topics to be covered at future meetings. Suggested topics included: training and career development; followup regarding the transition for the Office of Cancer Communications and Education; the role of the NCAB and development of an agenda to meet those objectives; and a roadmap to personalized cancer therapy and medicine in general by understanding the biology and the transitional research. Drs. Gray and Barker said that a retreat with the NCAB might be an appropriate venue to discuss NCAB functions.

In closing, Dr. Coffey shared a thought about personalized medicine that Dr. Joseph F. Fraumeni, Jr., Director, DCEG, expressed during a meeting on cancer biology and the physical sciences. The country one lives in, such as China or the United States, is an important factor in what happens to an individual medically. Dr. Fraumeni had further explained that approximately 7 percent of the energy and mass in the universe currently is understood, and that Adark matter@ comprises the remaining 93 percent. The genome work reported by researchers comprises about 7 percent or less of the genome, so 90 percent could be termed “dark genome.” The public perception about advances in genomic discoveries and level of progress toward personalized medicine, however, may not accurately reflect the real situation. Dr. Coffey said that the public often is led to believe that the science fields sometimes are more knowledgeable than is actually the case. He expressed the view that leaders in scientific research fields have responsibility in this area, and he encouraged them to publicize the human genome project in the proper context from the research and scientific aspects.

XVII. ADJOURNMENT-DR. DONALD S. COFFEY

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

There being no further business, the 149th regular meeting of the NCAB was adjourned at 11:24 a.m. on Wednesday, 4 February 2009.