

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
165th NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
February 27, 2014**

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

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
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The National Cancer Advisory Board (NCAB) convened for its 165th regular meeting on 27 February 2014, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Thursday, 27 February 2014, from 9:00 a.m. to 3:45 p.m., and closed to the public from 3:45 p.m. to 4:45 p.m. The NCAB Chair, Dr. Tyler E. Jacks, Director, Koch Institute for Integrative Cancer Research, David H. Koch Professor of Biology, Massachusetts Institute of Technology, presided during both the open and closed sessions.

NCAB Members

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

Alternate *Ex Officio* NCAB Members

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

President's Cancer Panel

Dr. Barbara K. Rimer
Mr. Hill Harper (absent)
Dr. Owen Witte (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

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

Liaison Representatives

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

Mr. Richard Martin, American Society of Therapeutic Radiology and Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education
Ms. Christy Schmidt, American Cancer Society
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Ms. Pamela Wilcox, American College of Radiology
COL (Ret.) James E. Williams, Jr., Intercultural Cancer Council
LiveStrong Foundation—no representative currently designated

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THURSDAY, FEBRUARY 27, 2014**I. CALL TO ORDER AND OPENING REMARKS—DR. TYLER E. JACKS**

Dr. Tyler E. Jacks called to order the 165th NCAB meeting. Dr. Jacks welcomed members of the Board, *ex officio* members of the Board, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Dr. Jacks reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to approve the minutes of the 10 December 2013 NCAB meeting was seconded and approved unanimously.

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

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

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

Dr. Harold E. Varmus, Director, NCI, welcomed members and reminded them that the next NCAB meeting will be a joint meeting with the Board of Scientific Advisors (BSA). Dr. Varmus reviewed the day's agenda, which focused on cancer research related to tobacco and served partly as a remembrance of the 50th anniversary of the Surgeon General's Report. He informed members about personnel changes, including the upcoming departure of Mr. John Czajkowski, Deputy Director for Management and Executive Officer, to a position at Harvard Medical School. Dr. Varmus introduced new staff, Mr. Peter Garrett, Director of the NCI Office of Communications and Education (OCE), and Ms. Ann Thomas, who will assist the Office of the Director (OD) with press and media issues.

Budget. Members were informed that the FY 2014 Appropriations Bill was approved by the January 15, 2014, deadline, with the result that the NCI received a restoration of \$144 million (M) of the \$255 M reduction from the FY 2013 budget due to sequestration. Final approval is needed from the Office of Management and Budget (OMB) for the FY 2014 budget, but no significant changes are expected in operating plans, and similar levels are expected for FY 2015. Dr. Varmus stated that restrictions on travel and meetings continue to burden investigators as the ability to assemble together is important to the conduct of science and scientific discovery.

Senator Barbara Mikulski (D-MD) recently visited the NIH and advocated for science funding. Dr. Varmus noted that she received accolades during her visit for her efforts in restoring \$1 billion (B) back into the NIH budget. Members were told that several congressmen who have been key NIH proponents are leaving office, including Senator Tom Harkin (D-IA), Reps. Jack Kingston (R-GA), Rush Holt (D-NJ), Henry Waxman (D-CA), and John Dingell (D-MI).

NCI Activities. Dr. Varmus informed members that the NCI leadership retreat in January 2014 discussed diversity issues, including the low number of some minority groups in the intramural research program and more robust representation of African Americans among postdoctoral researchers. Members were told that Dr. Jonathan Wiest, Director, Center for Cancer Training, is leading a group to incorporate ideas for improved training, recruitment, and retention, as well as increase representation of ethnic groups. The launch of the Outstanding Investigator Award (OIA) program has been delayed pending discussions with the U.S. Department of Health and Human Services (DHHS) regarding term length. Additional ideas include awards to facilitate the transition between graduate and postdoctoral years and

the departure of senior scientists, as well as training programs that emphasize the idea of becoming staff scientists. Dr. Varmus stated that the NIH Institutes and Centers (ICs) Directors' retreat focused on the best ways to evaluate and support the scientific workforce, with topics including the early career phase, the peer review process, and the NCI biosketch proposal.

Members were reminded that in response to the Recalcitrant Cancer Act, reports on pancreatic ductal adenocarcinoma (PDAC) and small cell lung cancer (SCLC) have been prepared. Dr. Varmus indicated that the NCI has held productive workshops on certain types of recalcitrant cancers, and he stressed that cancer types should be identified in terms of cell lineage(s) within an organ rather than as organ specific. In addition, members were informed about a campus-wide effort to study the NIH intramural research program. Drs. Robert Wiltrot, Director, Center for Cancer Research (CCR), and Stephen Chanock, Director, Division of Cancer Epidemiology and Genetics (DCEG), are establishing panels with the NCI Board of Scientific Counselors (BSC), with the Institute's emphasis on identifying opportunities that are best suited for intramural research. Dr. Varmus remarked on a similar process used by the NCI Frederick Advisory Committee (NFAC) to vet potential projects for the Frederick National Laboratory for Cancer Research (FNLCR). He noted that the NCI's intramural research program constitutes a disproportionate 40 percent share of research activity at the NIH Clinical Center and that maintaining the viability of the Clinical Center is vital to the NCI's research efforts.

Dr. Varmus said that an annual meeting of cancer research funders from more than 20 countries was held in Paris, France, and included working groups on cervical cancer, tobacco control, and harmonizing clinical trials. Members also were told that all NIH-supported trials in India have been discontinued pending re-evaluation and renegotiation of terms regarding how NIH trials are conducted there. In addition, the Global Alliance for Genomics and Health (Global Alliance), composed of 124 organizations, will meet in London, United Kingdom, in the following week to plan for linking interoperable databases containing genomic information, especially about cancer, rare microbial and rare genomic diseases. The intent is to share the data under politically and ethically acceptable terms.

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

Dr. Barbara K. Rimer, Dean, Gillings School of Global Public Health, Alumni Distinguished Professor of Health Behavior and Health Education, The University of North Carolina at Chapel Hill, summarized the recommendations contained in the President's Cancer Panel (PCP, the Panel) report to the President on accelerating uptake of the human papillomavirus (HPV) vaccine. The recommendations were founded on the substantive discussions that took place at the PCP's 2012–2013 workshop series on epidemiology, behavioral challenges, potential effects of widespread vaccination on screening programs, and global HPV vaccination. Dr. Rimer acknowledged the essential contributions of her fellow PCP members, Hill Harper, J.D., and Dr. Owen N. Witte, Director, Eli and Edy Broad Center of Regenerative Medicine and Stem Cell Research, University of California, Los Angeles, and Investigator, Howard Hughes Medical Institute.

Dr. Rimer described the urgent nature of the challenge of accelerating HPV vaccine uptake. Although there are two effective vaccines for HPV with acceptable side effects, they are underused in the United States, with only 33 percent of age-eligible girls and less than 7 percent of boys having completed the three-dose series in 2012. Compared with other recently approved vaccines for adolescents in the United States, uptake has been slow and has lagged significantly behind that of other countries, such as the United Kingdom and Australia. The need for prioritizing HPV vaccine uptake is evident from Centers for Disease Control and Prevention (CDC) estimates that increasing HPV vaccination rates from current levels to 80 percent would prevent 53,000 future cases of cervical cancer among girls, as well as the growing proportion of HPV-associated cancers, especially oropharyngeal cancers, projected to occur in

males.

The Panel identified four primary goals to accelerate HPV vaccine uptake. (1) Reduce missed clinical opportunities for administering the vaccines. The PCP recommended that the CDC lead efforts to disseminate communication strategies to physicians and health professionals; providers strongly encourage HPV vaccination when age-eligible males and females receive other vaccines; electronic health systems be used to coordinate vaccination; measures be taken to ensure that cost is not a barrier to vaccination; the Healthcare Effectiveness Data and Information Set (HEDIS) recommendation for vaccination of adolescent females be extended to males; and a *Healthy People 2020* HPV vaccination goal be set for males. (2) Increase the acceptance of HPV vaccines by parents, caregivers, and adolescents. The Panel recommended that the CDC collaborate with partner organizations to deploy integrated, comprehensive communication strategies that target adolescents in particular. (3) Maximize access to HPV vaccination services. The PCP proposed focusing on pharmacies as alternative vaccination sites, noted that this approach would require changes in the laws that currently prohibit HPV vaccination by pharmacists in 40 percent of all states. (4) Promote global HPV vaccine uptake. The Panel recognized that cervical cancer is a grave problem in less-developed regions, and cervical cancer mortality rates globally are dramatically higher than those of the United States. To facilitate vaccination uptake in low-income countries and encourage low- and middle-income countries to develop cancer control plans, collaborative efforts between the United States and the GAVI Alliance should continue.

Key research needs for advancing prevention of HPV-associated cancers include investigating more convenient dosing schedules, developing next-generation vaccines that offer broader protection as well as easier storage and administration, developing a better understanding of the natural history of oropharyngeal HPV infections, improving communication about HPV-associated diseases and vaccines, and determining the best approaches to integrating vaccination with cervical cancer screening. The PCP suggested that a credible organization such as the National Vaccine Advisory Committee (NVAC) monitor the status of uptake and implementation of the Panel's recommendations. Dr. Rimer heralded the report as a first step toward bridging the gap between the vaccination and cancer communities. She acknowledged the broad support that the PCP had received in drafting its report, including from NCAB members who served as workshop co-leaders, the CDC, the White House Office of Science and Technology Policy, and NCI leadership.

Dr. Rimer introduced the Panel's next topic, which involved cancer communication opportunities in the digital era. The first workshop was scheduled for March 3, 2014, and would provide overall direction for the series, particularly the use of new media (e.g., social and participative media technologies), to improve the control of cancer. Participants in the planning of the series included the Pew Research Center's Internet & American Life Project and principal investigators (PIs) from the Centers of Excellence in Cancer Communications.

Questions and Answers

Dr. Kevin J. Cullen, Director, Marlene and Stewart Greenebaum Cancer Center, Professor of Medicine, University of Maryland, expressed appreciation for the PCP's leadership role regarding HPV vaccination, noted that the American Cancer Society has limited its focus to the vaccine uptake by girls and cervical cancer, and encouraged the NCI to continue research across genders to understand rapid epidemiologic changes related to HPV.

Dr. Beth Y. Karlan, Director, Women's Cancer Program, Samuel Oschin Comprehensive Cancer Institute, Director of Gynecologic Oncology, Department of Obstetrics & Gynecology, and Professor, Obstetrics and Gynecology, David Geffen School of Medicine, University of California, Los Angeles, asked about the efficacy of a school-based approach for HPV vaccination that required uptake prior to

enrollment. Dr. Rimer indicated that this approach had been considered, but that expansion of vaccine providers to pharmacies was deemed the most effective. Dr. Victoria L. Champion, Associate Dean for Research, Mary Margaret Walther Distinguished Professor of Nursing, Center for Research & Scholarship, Indiana University School of Nursing, queried about resistance to retail pharmacy administration and was told that the underlying argument involved economic concerns.

Dr. William R. Sellers, Vice President/Global Head of Oncology, Novartis Institutes for BioMedical Research, Inc., mentioned the recent decision by a national pharmacy chain to cease sale of tobacco products and encouraged the NCI to leverage this event by engaging pharmacy associations and other chains in promoting public health and reducing the burden of cancer and other diseases nationally.

Dr. Sellers noted the number of cervical cancer survivors and suggested that they might serve as a force for education and promotion about the importance of HPV vaccination uptake.

Dr. Douglas R. Lowy, Deputy Director, lauded Dr. Rimer, the PCP, and workshop planners and attendees for their contributions in developing practical and actionable steps that could increase HPV vaccination uptake in the United States. Dr. Varmus also congratulated Dr. Rimer and the Panel for an excellent report.

V. REPORT ON STUDY OF CANCER CENTER BUDGETS—DR. WILLIAM N. HAIT

Dr. William N. Hait, Director, Global Head, Research and Development, Janssen Research & Development, LLC, presented a report of the NCAB Cancer Centers Working Group on Cancer Center support grant funding. Dr. Hait serves as Chair of the Working Group, which is composed of 10 members and was tasked with the goal of considering funding policies for NCI-designated Cancer Centers and with recommending appropriate changes, including providing guidance on policies and metrics regarding funding allocations to the Centers.

Members were told that the NCI leadership and Board recognized the need to examine complex historical funding patterns that influenced the current P30 Cancer Center Support Grant (CCSG) awards. Dr. Hait said that Dr. Varmus tasked the Working Group with answering specific questions, including whether: the 2012 interim funding guidelines were sufficient to address concerns about the current funding distribution; better methods should be used to make funding decisions; and the budget could become more flexible without an increase to the base funding. The Working Group met six times over 1 year, heard presentations from NCI leadership, and reviewed historical and current funding policies and approaches. Working Group members discussed multiple approaches and funding models, and reached consensus on recommendations. Dr. Hait stated that the Working Group concluded that significant disparities exist in the size of CCSG awards, often due to factors other than merit. In addition, the 2012 interim funding guidelines manage award expectations and retain a flat budget. The Centers differ in type, organizational structure, and environmental factors that emphasize certain CCSG characteristics. Additional conclusions were that the Centers should be evaluated on what they do and how well they do it; and components of the CCSG process could be optimized to decrease administrative burden, increase flexible use of funds, and stress the most significant science. The Working Group agreed that underperforming Centers should be reviewed carefully and cessation of funding considered.

Dr. Hait said that the Working Group recognized that the NCI funding has decreased and may remain flat or decrease further in the coming years. In addition, universities have a continuing interest in their Cancer Center attaining NCI designation, and the NCI must be responsive to imperatives to support geographically distributed centers as well as accessibility for underserved populations. Because CCSG awards rarely are terminated, the number of NCI-designated Cancer Centers continues to grow and the budget continues to be stretched.

The Working Group discussed approaches to address disparities in funding and reached consensus on the three recommendations. (1) CCSG funding should consist of three components: base award; multipliers of the base predicated on merit and size; and possible supplement. (2) Cancer Center administrators should be involved in planning for implementation of the new approach. Within their Centers, administrators will need to evaluate, prepare for, and communicate potential changes, particularly when there are reductions. Administrators also will need to communicate with the NCI Centers' program staff on the implications of funding changes. (3) Proposed changes should be framed in the context of the NCI and Centers mission: the timeline and mode of communicating changes will determine their acceptability. Members were told that this approach addresses the problem of accretion, as each renewal will re-compete for a predetermined base award applicable to all Centers of the same type. It also negates the need for funding caps as formula-based budgeting levels the playing field. Other advantages of this approach include minimal variations and greater fairness over time, easier integration of funding adjustments and phase-ins, careful monitoring of the impact over time, involvement of leadership within the Centers, as well as advocates, in the implementation and communication process. Dr. Hait remarked on the success of the Cancer Centers Program and its overall importance and impact, and noted that these changes are designed to enhance the Program as a national treasure.

Questions and Answers

Dr. Jacks requested further details about the Working Group's thoughts on non-renewal of designation for underperforming Centers. Dr. Hait acknowledged that there are many reasons why the NCI might want to provide NCI designation to a Cancer Center at a particular geographic location, and he said that the Working Group felt that it could raise issues concerning chronically underperforming Cancer Centers to the NCAB's attention.

Dr. Charles L. Sawyers, Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, Investigator, Howard Hughes Medical Institute, and Professor of Medicine, Weill-Cornell Medical College, expressed appreciation for the Working Group's conclusion to reward Cancer Centers for their strengths and not to penalize them for not being strong in other areas, and he asked for clarification about this idea in terms of requirements. Dr. Hait responded that the Working Group's intent was to emphasize the impact of the science that is ensuing from each of the Cancer Centers.

Dr. Mack Roach III, Professor of Radiation Oncology and Urology, and Chair, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, asked about considerations in maintaining a balance between equitable funding distributions among Cancer Centers and meeting the needs of diverse populations. Dr. Hait agreed that balancing support for geographic areas with special or underserved populations and the mandate to access quality research remains a challenge. Dr. Varmus stated that while providing more funding to those who are underperforming historically has not yielded stellar results, the Working Group's recommendations allows the NCI the flexibility to consider funding adjustments based on other considerations, including the Cancer Center's location, the population served, and the types of research conducted.

Dr. Sellers commented on the NCI Cancer Center Program budget and encouraged the NCI to increase funding and other resources for the Program, and Dr. Jennifer A. Pietenpol, Director, Vanderbilt-Ingram Cancer Center, B.F. Byrd, Jr. Professor of Oncology, Vanderbilt University Medical Center, expressed her support for this idea. Dr. Sellers asked whether a relationship exists between measured merit and real merit and requested clarification on the size calculation for equally meritorious Cancer Centers. Dr. Varmus responded that the score modeling continues to be refined, and a percentile score might be an effective alternate for the impact score. Dr. Hait said that the Working Group considered

quantities within different components, such as the number of shared resources and the number of senior positions, by Centers of various sizes.

Dr. Cullen thanked the NCI for establishing the Working Group and noted that the participants worked together and compromised to reach consensus. He cautioned that implementation will present challenges. Dr. Hait said the Working Group considered approaches to implementation but felt that the NCI should make implementation decisions. Dr. Varmus agreed that it will be important to bring Cancer Center Administrators into the discussion regarding sudden versus gradual funding changes to ensure productivity is not affected.

Dr. Judy E. Garber, Director, Center for Cancer Genetics and Prevention, Dana-Farber Cancer Institute, and Professor of Medicine, Harvard Medical School, encouraged the NCI and the Working Group to help Cancer Centers ensure that their local communities understand that changes to the funding models do not reflect performance funding. Dr. Hait agreed and said that the Working Group discussed the challenges regarding a possible shift in local perception of the Cancer Centers.

Dr. Olufunmilayo F. Olopade, Walter L. Palmer Distinguished Service Professor of Medicine and Human Genetics, Associate Dean for Global Health, and Director, Center for Clinical Cancer Genetics, University of Chicago Pritzker School of Medicine, also expressed appreciation for the Working Group's recommendations and encouraged the NCI to consider providing technical resources to Cancer Centers that serve the NCI's mission in resource-constrained environments. Dr. Varmus said that the NCI provides support to underperforming Centers. Dr. Linda Weiss, Director, NCI Cancer Center Program, described the process and programmatic assistance that the NCI provides to Cancer Centers that face challenging situations, noting that because the NCI designation is highly desired as it brings the ability to leverage many other resources, underperforming Cancer Centers generally make necessary changes swiftly.

Dr. Jacks asked whether extending the length of awards as a means to reduce administrative burden on the Cancer Centers had been considered. Dr. Weiss replied affirmatively but indicated that NIH policies and other factors have resulted in maintaining the 5-year length for awards. She said that the NCI will continue to streamline the grant application. Dr. Varmus added that in his prior role as a Cancer Center Director, he appreciated the 5-year review as a time to evaluate and adjust the Cancer Center.

Dr. Pietenpol encouraged the NCI to continue its supplemental funding mechanism, which enables the rapid mobilization of the workforce and serves as a pivotal role in advancing research. Dr. Jacks summarized the NCAB's general sentiment that the size of the Cancer Centers Program is worthy of further consideration.

VI. ANNUAL DELEGATIONS OF AUTHORITY—DR. PAULETTE S. GRAY

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

The Statement of Understanding with NCI Staff on Operating Principles in Extramural Grants also falls within the Delegations of Authority to the Director, NCI. NCAB operations are conducted in accordance with management and review procedures described in the NIH Manual Issuance 4513. Concurrence of the NCAB with recommendations of initial review groups will be required, except for the

following: (1) Training grants and fellowships and other non-research grant applications are not subject to NCAB review and approval, and without other concerns may be awarded without presentation to the NCAB for concurrence, with the exception of Ruth L. Kirschstein National Research Service Awards. (2) Applications over the 50th percentile will not have summary statements presented to the NCAB unless the Institute is considering an award of such an application or other special consideration is required, requested, or required by NCI or NIH policy or for special consideration by an appointed member of the Board. (3) For applications assigned raw scores that are not percentiled, the cutoff will be a priority impact score of 50 for all mechanisms except R41, R42, R43, and R44 awards; for the latter, all scored applications will be included. Expedited Concurrence: (1) for R01 and R21 applications with percentiled or raw scores that fall within the NCI paylines for that mechanism, a process of expedited concurrence will be used; and (2) the Executive Secretary will alert Board members with responsibility for expedited concurrence when review outcomes for eligible applications are available on the Electronic Expedited Concurrence portion of the Electronic Council Book. Administrative Adjustments: (1) Permission is delegated to the Director, NCI, to allow staff to negotiate appropriate adjustments in dollars or other terms and conditions of grant and cooperative agreement awards. (2) Administrative requests for increases in direct costs that are the result of marked expansion or significant change in the scientific content of a program after formal peer review will be referred to the Board for advice and recommendation. (3) Actions not requiring Board review or advice, such as change of institution, change of PI, phase-out of interim support, or additional support, need not be reported to the Board. (4) NCI staff may restore requested time and support that were deleted by the initial review group when justified by the PI in an appeal letter or when restoration is in the best interest of the NCI and the project is of high NCI programmatic relevance.

In an effort to continue responsible stewardship of public funds, the NIH has instituted a policy of Special Council Review (SCR) of applications from well-funded investigators. Applications from PIs who have \$1 M or more in direct costs from active NIH Research Project Grants (RPGs) must be given additional consideration.

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

VII. OVERVIEW OF NCI TOBACCO CONTROL RESEARCH INVESTMENT AND PARTNERSHIPS—DR. MICHELE BLOCH

Dr. Michele Bloch, Chief, Tobacco Control Research Branch, Division of Cancer Control and Population Sciences (DCCPS), provided an overview of NCI's tobacco control research and collaborative efforts. Dr. Bloch said that tobacco control has been a 20th century success story, as evidenced by research linking tobacco use to disease; the decrease in smoking prevalence from 42 percent to 19 percent between 1965 and 2010; the number of premature deaths (8 million) averted between 1964 and 2012, with an extended mean lifespan of 20 years; and the decrease in adult smoking prevalence from 2010 to 2012. Despite this success, approximately 17.7 million deaths during the past 20 years are attributed to smoking. Members were shown maps of the United States that suggested an association between U.S. adult smoking prevalence in states and lung and bronchus cancer death rates. Tobacco control challenges extend beyond U.S. borders, with global tobacco mortality growing and shifting to the developing world. In 2014, 6 million deaths globally are attributed to annual global tobacco mortality, and the annual number is expected to rise to 8 million by 2030, with 100 million deaths attributed in the 20th century but 1 billion deaths in the 21st century.

Members were informed that the NCI's tobacco research portfolio includes 111 grants that receive an aggregate \$59 M and are focused among cessation, policy, and global issues as well as methodology, epidemiology, secondhand smoke, communication, and other research. The NCI-U.S. Food

and Drug Administration (FDA) tobacco regulatory science portfolio increased from 5 to 33 awards between FY 2010 and FY 2013, with FY 2013 funding at \$39 M, of which \$26 M supports seven new Tobacco Centers of Regulatory Science (TCORS). NCI-supported initiatives work toward a variety of outcomes, including more effective smoking cessation interventions and programs in low-income adult populations; measures and determinants of smokeless tobacco use, prevention, and cessation; and international tobacco and health research and capacity building. Dr. Bloch also described studies focused on state and community tobacco control policy and media as well as research on vulnerable populations and tobacco control monographs. Topics have encompassed method standardization to measure waterpipe smoke emissions and exposure, visual media influences on adolescent smoking behavior, the role of the media in promoting and reducing tobacco use, genetic studies of nicotine use and dependence, and tobacco companies in relation to public policy and global health. Tobacco research underway in the DCEG addresses risk estimates, assessment of smoking patterns, and the characterization of carcinogenic mechanisms.

Dr. Bloch highlighted several NCI partnerships that reflect collaboration across the tobacco control field. The NCI, NIDA, and National Institute on Alcohol Abuse and Alcoholism (NIAAA) work together on the Collaborative Research on Addiction at NIH (CRAN), which focuses on advance substance use, abuse and addiction science research, and public health outcomes. CRAN released a recent funding announcement on using social media to understand and address substance use and addiction. In addition to an NIH-FDA Research Partnership, NIH collaborates with the CDC and World Health Organization (WHO) on tobacco-related activities such as reports, monographs, workshops, and study groups.

The Surgeon General's Report provides several conclusions for cancer patients and survivors, such as that quitting smoking improves prognosis; cigarette smoking increases all-cause mortality, cancer-specific mortality, and risk for second primary cancers; and evidence suggests a relationship between smoking and a risk of recurrence, poorer response to treatment, and increased treatment-related toxicity. Dr. Bloch indicated that research in the cancer treatment setting should be related to tobacco use in cancer patients, and told members that a joint NCI-American Association for Cancer Research (AACR) Task Force is looking at tobacco-related issues. Future research directions include understanding diverse tobacco products and improving cessation and prevention. Key challenges to be addressed are that adolescents and young adults are susceptible to tobacco use, declines in youth prevalence are slowed or stalled, and the proliferation of new tobacco products. Other barriers to improving cessation and prevention include new industry marketing strategies, and the interplay between tobacco, alcohol, and illicit drug use. Dr. Bloch said that states continue to face issues related to tobacco and smoking, such as whether to increase the minimum age for cigarette purchase and marijuana sales. She shared results of a Gallup poll that showed the public primarily blames the smokers, not tobacco companies, for the health problems faced by smokers.

Questions and Answers

Dr. Jacks asked about the movie industry's attitude to changing the inclusion of smoking in films. Dr. Bloch replied that resistance is common for both philosophical and monetary reasons, but progress is being made. She added that one goal is for movies with smoking and alcohol to have an R rating.

VIII. SURGEON GENERAL'S TOBACCO REPORT—DR. JONATHAN M. SAMET

Dr. Jonathan M. Samet, Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine, and Director, Institute for Global Health, University of Southern California, introduced the Surgeon General's reports on tobacco and health, the first of which was written in 1964. Dr. Samet said that these reports were developed at a time when there was controversy about the

effects of tobacco on health, starting with the publication in the 1950s of the first epidemiological reports showing a strong association between tobacco smoking and lung cancer. The tobacco industry's efforts to maintain controversy led to the 1964 Surgeon General's Report, which was requested by President Kennedy in an effort to address the controversy with senators who saw a need for action. The report established criteria for causation that are still in use today and stated that smokers have a 70 percent increased chance of premature death compared to nonsmokers and that smoking causes lung cancer. The report summarized and synthesized scientific evidence and made a comment about the need for action, but did not make specific policy recommendations.

From 1964 onward, the key reports include 1972, which made the first comment about indoor air pollution from tobacco smoke; 1979, which covered every aspect of smoking and health; 1986, which highlighted the effects of secondhand smoke; 1988, which addressed nicotine addiction; 2004, which addressed the health consequences of active smoking; 2006, which addressed passive smoking and caused many states to go smoke-free; and 2012, which addressed the role of media marketing. The reports have always refrained from recommending specific policies. The 2014 report contains several important conclusions, including that the tobacco industry has misled the public. The century-long epidemic of cigarette smoking has caused an enormous avoidable public health tragedy. Since the first Surgeon General's Report in 1964, more than 20 million premature deaths can be attributed to cigarette smoking. The smoking epidemic was initiated and sustained by the aggressive strategies of the tobacco industry, which deliberately misled the public about the risks of cigarette smoking.

Since the 1964 Surgeon General's Report, cigarette smoking has been causally linked to diseases of nearly all organs of the body. Even 50 years after the first Report, research continues to identify diseases caused by smoking, including diabetes, arthritis, and colorectal cancer. Exposure to secondhand tobacco smoke has been linked to cancer and respiratory and cardiovascular diseases, and to adverse effects on the health of infants and children. Although cigarette smoking has declined significantly since 1964, large disparities in tobacco use remain across groups defined by race, ethnicity, education level, and socioeconomic status and across regions of the country.

Comprehensive tobacco control programs and policies in place since the 1964 report have been proven effective in controlling tobacco use. Further gains can be made with the full, forceful, and sustained use of these measures. The burden of death and disease from tobacco use in the United States is overwhelmingly caused by cigarettes and other combusted tobacco products, and rapid elimination of their use will dramatically reduce this burden. The epidemic is heterogeneous, affecting different subpopulations that each requires a plan and a solution. More tobacco-related illnesses are being discovered, and all possible solutions, including e-cigarettes, should be explored to address the problem. Dr. Samet expressed the hope that the 100th Surgeon General's Report would be looking at a never-smoking population and the end of the epidemic.

IX. PATHOPHYSIOLOGY OF TOBACCO-INDUCED CANCERS—DR. ROY HERBST

Dr. Roy Herbst, Ensign Professor of Medicine and Professor of Pharmacology, Chief of Medical Oncology, Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven, described the pathogenesis of tobacco-induced cancer, joint AACR-NCI efforts related to tobacco control in patients receiving cancer treatment and the implications of patients' tobacco use for clinical trials, and new approaches to the treatment of tobacco-induced disease. Dr. Herbst informed members that more than 18 types of cancer are related to tobacco use, and approximately one-third of all cancer cases in the United States are tobacco related, including liver disease and colorectal cancers. In addition, tobacco causes approximately 85 percent of lung cancers. He stated that inhaling the mix of more than 7,000 compounds found in cigarette smoke, of which 60 are known carcinogens, induces tissue injury and changes the cellular environment, thus fostering the proliferation of cells and transformation into cancer.

Mutations result in loss of normal growth control, silencing of tumor suppressor genes, and activation of oncogenes. Patients who smoke often develop multiple cancers; even if the first one is treated, second cancers are common. Cancer risk remains elevated for former smokers.

The molecular and cellular carcinogenesis of lung cancer follows a progression characterized first by patches of cells and premalignant lesions that evolve into early stage lung cancer. Dr. Herbst stated that major efforts in lung cancer screening have helped to identify cases before they become advanced, because advanced stage lung cancer is very difficult to treat. Similar to lung cancer, head and neck cancer progresses by well-defined phenotypic and genetic changes. Tobacco-related carcinogenesis is a complex, multistep process involving many cellular and molecular changes, and specific mutations have been studied, including P53 mutations in lung cancer, epidermal growth factor receptor (EGFR) mutations in adenocarcinoma, and Kirsten rat sarcoma (KRAS) mutations in smoking-related cancers. A better understanding of the mechanisms of pathogenesis would lead to more effective therapies.

Members were told that joint AACR and NCI efforts related to tobacco control have examined tobacco use for patients being treated for cancer, and the impact of their tobacco use on the outcomes of clinical trials. Assessing tobacco use by cancer patients and facilitating cessation is important for both the patient's health and evaluation of the confounding effects of tobacco use on cancer treatment, disease progression, comorbid events, and survival. Cancer patients who smoke have worse outcomes, including higher all-cause and cancer-specific mortality, and risk of tobacco-related second primary cancers. Smokers also have a higher risk of recurrence, poorer response to treatment, and increased toxicity. In addition, many small-molecule tyrosine kinase inhibitors can be ineffective in patients who smoke because of their altered metabolism.

Dr. Herbst said that despite an impetus to help patients with smoking cessation, smoking by patients who are receiving cancer therapy is not widely being addressed; tobacco use assessment methods are inconsistent, and there is little follow-up during and after treatment. Members were told that fewer than 50 percent of NCI-designated Cancer Centers include tobacco use in their patients' medical records. Of all NCI-funded Phase III Cooperative Group trials, only 22 percent record cigarette smoking status at enrollment and 4 percent during follow-up. To address this problem, the AACR and NCI formed a combined task force in March 2013 to develop recommendations for assessing and documenting tobacco use in clinical trials and to identify research priorities. Recommended measures include: smoking 100 or more cigarettes in a lifetime, the length of time since one smoked, the number of smoking years, and the average number of cigarettes smoked per day.

Dr. Herbst told members that the AACR has raised awareness of the issue. All AACR journals have articles commemorating the 50th anniversary of the Surgeon General's Report this year, and the AACR 2014 spring meeting will have two sessions on tobacco control. The first will honor the 50th anniversary of the Surgeon General's Report, and the second will focus on advancing tobacco regulatory science. In addition, a joint AACR-American Society of Clinical Oncology (ASCO) subcommittee will be tasked with developing recommendations for the regulation of e-cigarettes. Dr. Herbst encouraged the development of new approaches to the treatment of tobacco-induced disease, as former smokers retain a higher risk of developing cancer. Efforts at Yale now focus on understanding the changes in the immune system and microRNAs of past-smokers. A trans-institution Master Protocol is being developed by the NCI, FDA, Foundation for NIH (FNIH), Southwest Oncology Group, and others to conduct clinical trials that screen patients based on biomarkers and treat them accordingly. Finding the appropriate therapy for each patient is a challenge that requires coordination across multiple institutions.

Questions and Answers

Dr. Samet asked about analyzing the levels of cotinine in serum biospecimens to better understand the scope of the pathophysiological issues. Dr. Herbst replied that new clinical trials are often developed based on the design of old clinical trials. He added that the Master Protocol being developed breaks this mold and represents efforts to make progress in personalized or precision medicine.

X. NEW DIRECTIONS IN CESSATION OF TOBACCO USES: A 2014 UPDATE— DR. MICHAEL FIORE

Dr. Michael Fiore, Director, Center for Tobacco Research and Intervention, University of Wisconsin, shared new directions in the cessation of tobacco uses. Dr. Fiore explained that the scientific, public health, and clinical response to 20th century epidemic in tobacco use remain unrivalled, including a remarkable improvement in the reduction of tobacco use. The prevalence of tobacco use has shifted from 44 percent in 1964 to 18 percent in 2014. He credited the Surgeon General's Reports on tobacco and health as largely responsible for this response and told members that the 2014 Report provides a vision for ending the tobacco epidemic. Approximately 50 million individuals still use tobacco, and they are concentrated among segments of the population that are particularly vulnerable. Evidence-based cessation interventions have poor population penetrance. Thus, there are three core scientific information needs: first, to develop better approaches to treat and reach underserved populations; second, to develop population-based cessation interventions with better penetrance; and third, to seize the health care visit with the primary care doctor as an opportunity for cessation intervention.

Rates of tobacco use among the poor, the least educated, the mentally ill, and substance abusers are at least twice the current overall adult prevalence rate of 18 percent. The poor report the desire to quit but there is an extraordinary amount of misconception about cessation treatments. For example, individuals from the poorest neighborhoods reported that using nicotine patches posed a greater risk to their health than smoking. Those with mental health diagnoses account for almost half of all cigarettes smoked and have lower rates of cessation success. They live on average 25 years less than those without mental health diagnoses due to tobacco-related illnesses. This poses a challenge because the cessation interventions needed for these individuals are not known. The settings in which mental health patients receive health care used to condone tobacco use; cigarettes often were used as a reward for good behavior.

Telephone cessation quitlines are a success story in the United States, and approximately 500,000 smokers call each year. However, unstable budgets across states lead to a patchwork of available services. There is a need to deliver information in a more consistent way. eHealth and mHealth approaches to cessation have the greatest penetrance of any initiative thus far. Led by the NCI, the initiative reaches teens, Spanish-speakers, pregnant women, and other at-risk populations.

The health care visit represents an unequalled opportunity to intervene with smokers. More than 80 percent of smokers visit a primary care clinic each year, but only 40 percent of them receive any assistance in quitting. Electronic medical records provide a way to document tobacco use and treatment. Institutional changes also are important and necessary. Because the poor and mentally ill often receive health care in nontraditional settings, alternative methods of outreach and intervention may be needed to reach these populations. There also is a need to support patients in maintaining cessation, and to develop policies such as taxes, clean indoor air laws, and media campaigns to promote cessation. It currently is unknown whether e-cigarettes are an effective cessation tool. Although there has been a stable decline in tobacco use in the United States during the past 50 years, the collective challenge is to accelerate the end of the tobacco use epidemic.

Questions and Answers

Dr. Varmus shared a comment made by Dr. Sellers about the possibility of applying “defensive medicine” practices in the context of cervical, oropharyngeal, or lung cancers as a means of preventing lawsuits by patients who develop cancer. For patients who smoke, this could be accomplished by a signed statement from them certifying that they were informed about risks and evidence-based cessation methods. Dr. Pietenpol commented that the meaningful use rule has started this process, and Dr. Fiore pointed out that the Affordable Care Act (ACA) contains specific language that all Task Force Recommendations A and B must be covered without copay, limits, or barriers.

Dr. Jacks asked about medical interventions such as vaccinations in this area. Dr. Fiore replied that attempts by the NIDA and private sector organizations to develop vaccines against nicotine addiction have been largely unsuccessful, although the idea is conceptually appealing.

Dr. Jacks asked about coordination with the American Cancer Society (ACS). Dr. Fiore answered that the ACS has been an important partner in tobacco cessation, including through its Great American Smokeout campaign, and that the ACS, NIH, and other organizations can effect systems-level changes. Dr. Cullen added that the ACS has focused on working with individual state legislatures to develop anti-tobacco policies, particularly through increases in tobacco taxes.

XI. E-CIGARETTES: UNANSWERED QUESTIONS—DR. PAMELA CLARK

Dr. Pamela Clark, Research Professor, School of Public Health, University of Maryland, College Park, presented the state of research and opportunities to study the health effects of e-cigarettes. Dr. Clark described the increase in advertising for e-cigarettes and said that approximately 200 manufacturers exist, with traditional cigarette companies working on absorbing the independent market. E-cigarette companies employ the same political and public relations strategies as for traditional cigarettes and are not likely to allow cannibalization of their cigarette sales.

Members were informed that e-cigarettes use an electronic nicotine delivery system (ENDS) composed of a housing, a tip that is sucked on by the user, a batter, an atomizer that heats the liquid and vaporizes it, and a cartomizer, which is a tank that holds the e-juice and atomizer. The e-juice ingredients are propylene glycol or vegetable glycerine, nicotine (0–36 mg/mL), flavorings, and additives to mimic “throat grab.” Multiple generations of e-cigarettes have been produced, with the third generation incorporating advanced personal vaporizers and control of battery voltage.

The vaping population includes those who are younger, have a higher income, and are better educated; and encompasses both genders as well as dual users. Dr. Clark said that a vaping subculture has arisen among those who believe that their addiction can save the lives of millions of smokers of traditional cigarettes, disdain “cigalikes,” and are obsessed with the customizable technology; they may spend thousands of dollars each year for accessories, colors, and flavors. Vapefests have become popular as highly sponsored, multi-day events, with the vaping culture forming powerful special interest groups with industry backing.

Dr. Clark presented the state of the research on the efficacy of e-cigarettes in terms of nicotine delivery, craving or withdrawal symptoms, and smoking cessation. Studies have examined the P3 and N2 components of cortical ERP with inconclusive results to date. Research on blood nicotine levels has yielded mixed results, with some studies finding that only tobacco smoking raised blood nicotine levels, and others that ENDS reached a maximum blood level of 1.2 ng/mL in 20 minutes. Dr. Clark noted the early stage of research and cautioned that studies may have recruited naïve users or focused on ineffective first-generation devices. She observed that e-cigarettes appear to be moderately effective at alleviating

tobacco cravings and that randomized controlled trials using cigalike ENDS suggest that cessation rates are comparable to nonrandomized trials.

Dr. Clark discussed the implications of FDA regulation of ENDS, which ultimately would provide a definition of harm. An adverse effect is that such regulation would require an investigative new drug (IND) application if testing for efficacy for cessation and likely would ensure that no independent randomized controlled trials for cessation are conducted. Other concerns about expanding the definition of harm include that traditional smoking could be renormalized, and youth might be encouraged to increase use or maintain dual use behavior. Discussions continue among tobacco researchers regarding e-cigarette use, particularly as a possible tool for quitting among some cigarette smokers, but weighted with findings that disease risk is only modestly affected in dual users and passive exposure results in cotinine levels that are similar to those of passive smokers.

Questions and Answers

Drs. Cullen, Karlan, and Champion requested further details about the vape population and vape events. Dr. Clarke explained that the number of those using vape products doubled between 2010 and 2012 and there has been a large increase in the number of vape shops. She added that tobacco control experts have significant concerns that people who would not start smoking traditional products will start vaping and then shift into smoking analog products.

Dr. Sellers observed that some forms of nicotine, such as Nicorette gum and patches, are sold as over-the-counter products, whereas e-cigarettes and other forms of nicotine delivery can be sold more openly. Dr. Samet said that the nicotine dosage contained within the products is variable, with dose and deposition highly dependent on particle size distribution and content. Dr. Pietenpol commented that research on whether various devices offer different levels of appetite suppression would have important implications for teenage users.

XII. GLOBAL TOBACCO CONTROL

Global Tobacco Use: Current Status and Challenges. Dr. Thomas J. Glynn, Director, Cancer Science and Trends, and Director, International Cancer Control, American Cancer Society (ACS), presented the ACS's approach to global tobacco use, describing the current status and highlighting challenges. Dr. Glynn said that the disease consequences of tobacco use are universal, as all forms of tobacco products—such as cigarettes, pipes, cigars, bidis, hookahs, e-cigarettes, and other forms of smokeless tobacco—are sold throughout the world. He informed members that global smoking prevalence rates are expected to rise during the next decade from 1.3 billion to 1.7 billion smokers in the world. Asia has the highest smoking rates, with overall country rates of up to 40 percent, and one-third of the global population age 15 and older smokes. Cigarette smoking is a 20th century phenomenon, with global cigarette consumption in that one century having increased more than 100 times. In addition, deaths caused by tobacco use during the 21st century are projected to total 1 billion.

Cigarette consumption varies by global region, and public health organizations and tobacco cancer researchers have noted consumption shifting significantly between 1990 and 2009 from the western hemisphere, which saw a 26 percent decrease, to the Middle East and Africa, which have experienced a 57 percent increase. Approximately two-thirds of the world's smokers live in 10 countries, with 40 percent living in China and India. Dr. Glynn reviewed lung cancer incidence rates for males and females by world region and said that approximately one-third of deaths globally due to tobacco are cancers, with the remaining two-thirds primarily comprised of respiratory and cardiovascular diseases. Secondhand smoke is a concern, as it results in 600,000 deaths annually; furthermore, more than 50 percent of the people in the Western Pacific region are exposed to secondhand smoke.

Dr. Glynn said that by 2015, the WHO estimates that the annual global cost of tobacco will be \$500 B, and smoking-related costs can contribute up to 15 percent of total health care costs in developed countries. Members were told that as much as 10 percent of family income in some parts of the world is spent on tobacco. According to the WHO, tobacco represents a unique threat to global health as it has a significant lobby force and employs multinational public relations firms (*WHO Zeltner Report, 2000*). Tobacco is a big business, with its global market valued at almost \$0.5 T, and approximately 6 trillion cigarettes manufactured annually.

Many countries require graphic warnings on cigarette packaging and are now shifting toward plain packaging; in response, tobacco companies have tried to use economic agreements to block legislation about packaging and continue selling cigarettes. The Framework Convention on Tobacco Control has been a critical element in tobacco control around the world. It is the world's first treaty to address a public health issue, offers the best chance to address tobacco control globally, and affects every country in the world. Dr. Glynn said that the effects of significantly reducing global tobacco use could include: avoidance of 200 million premature deaths during the next 50 years; the disappearance of lung cancer as a public health menace; the reduction of global heart disease risks by 25 percent; the rise of global life expectancy by 3–5 years; and significant savings in terms of health care expenditures.

Dr. Glynn described tobacco control research criteria, needs, and topics in the international arena. Research is needed on the ability to influence population-level prevention and cessation, to address specific country needs, and attract support for political and policy changes. Broad international research needs involve capacity building, funding, political will, and awareness about the enormity of tobacco's effects. Additionally, the tobacco control research field could be advanced by a new generation of research leaders, greater prominence on global health and development agendas, strategic alliances, and integration of modern communications technology into global research efforts. Dr. Glynn informed members about a proposal for a Global Consortium for Tobacco Control Research (GCTCR) among cancer centers globally, which could provide a structure for collaborations, help develop research and communications networks, and facilitate information exchange and dissemination. The GCTCR also could serve a vital role in promoting common measures, increasing research capacity and infrastructure, and promoting tobacco control research as an essential element for developing countries.

Questions and Answers

Dr. Cullen asked about the possibility of the United States ratifying the Framework Convention on Tobacco Control. Dr. Glynn responded that this is unlikely because the Senate has insufficient votes for passage.

Perspectives on Global Tobacco Control from NCI. Dr. Ted Trimble, Director, Center for Global Health (CGH), provided the NCI's perspective on global tobacco control. Dr. Trimble said that during its establishment, the CGH identified common risk factors for tobacco and other noncommunicable diseases as a priority. Members were told that much of the research that supported The WHO Framework was sponsored by the NCI. The Institute works closely with the WHO and CDC to develop reports and action plans related to tobacco and noncommunicable diseases. Global health diplomacy is an important component in communicating effective health messages, and Dr. Trimble provided examples of visits by Dr. Varmus, Dr. Mark Parascandola, and other U.S. tobacco control ambassadors to China and Indonesia to assist with tobacco control research, analysis, and partnerships. In addition, NCI staff have leadership roles in the mHealth Global Partnership, which focuses on international behavioral intervention projects, including developing smoking cessation text messages based on NCI's SmokefreeTXT libraries. Current mHealthText Projects include reducing secondhand smoke exposure in infants in China, strategizing about adding physical activity messages to the

SmokefreeTXT in South Africa, and implementation of SmokefreeTXT in Portuguese in Brazil. He also referred members to a forthcoming publication on smokeless tobacco and mentioned a joint U.S. Agency for International Development (USAID)-NIH Partnerships for Enhanced Engagement in Research (PEER) Health project to support developing country researchers on implementation science. Questions on global tobacco control span topics such as variations in risks of smoking, the effects of socioeconomic transitions on tobacco use, effective cessation interventions for underserved populations, and the effects of price, poverty, and health outcomes on tobacco use. Members were told that expanding tobacco control research and research capacity in the developing world is important to understanding the impact of policies in different environments and crucial to reducing the disproportionate burden of tobacco use and cancer.

Dr. Trimble reviewed the major research areas of NCI's global tobacco control grants, which have totaled 56 since FY 2002, addressing areas of capacity building, epidemiology, intervention, policy, and laboratories. The NCI's portfolio currently includes 21 active grants in low- and middle-income countries, including a P01 grant to study the effectiveness of tobacco control policies in high- and low-income countries, as well as work on the Fogarty International Center's (Fogarty) Framework Programs for Global Health (FRAME), and a joint RFA with Fogarty and the National Institute on Drug Abuse (NIDA) that is focused on international tobacco and health research capacity building and currently supports eight projects in 13 countries. Dr. Trimble also informed members about the NCI's participation in the 1st International Conference on Public Health in the 21st Century in 2013 on tobacco and ancillary activities, as well as the World Conference on Tobacco or Health in 2009, 2012, and the upcoming conference in 2015.

Questions and Answers

Dr. Olopade asked about opportunities for collaboration with the Bill and Melinda Gates Foundation (Gates Foundation). Dr. Trimble replied that Dr. Collins, Director, NIH, asked the ICs to suggest topics to explore with the Gates Foundation, and the NCI submitted tobacco control research, particularly secondhand smoke affecting childhood diseases, on its list of topics. He added that the NCI intends to propose tobacco control as a topic for the Global Alliance for Chronic Diseases to undertake. Dr. Glynn indicated that the ACS has an international commitment and currently has a grant from the Gates Foundation to help organize a consortium in Africa to work toward policy change in tobacco control, as well as support from the Bloomberg Initiative.

XIII. FDA REGULATIONS AND THE FDA-NIH REGULATORY SCIENCE PARTNERSHIP—MR. MITCHELL ZELLER

Mr. Mitchell Zeller, Director, Center for Tobacco Products, FDA, discussed issues related to regulatory science at FDA, programmatic priorities, and the beneficial collaboration with the NIH. Mr. Zeller said that the FDA launched the first investigation into the role of nicotine in the design and manufacture of cigarettes and smokeless tobacco products 20 years ago, and Congress granted the Agency the ability to regulate tobacco products in 2009 through the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act).

The FDA's public health objective is to use the tool of regulation to reduce death and disease from the use of tobacco products. The Agency will regulate tobacco products by employing a standard that is appropriate for the protection of the public health. Mr. Zeller informed members that the Surgeon General's 2014 report, which marks the 50th anniversary of the first Surgeon General's report, reported more than 480,000 annual deaths from tobacco use, resulting in up to 18 million preventable deaths in the United States between now and midcentury. A population-level public health standard will allow the FDA to assess the risks and benefits to the population as a whole, determining the impacts on users and

nonusers. Members were told that the FDA is applying the tool of regulation in an unprecedented manner to accomplish eight objectives: (1) understand the regulated products; (2) restrict product changes; (3) prohibit modified risk claims that state or imply reduced exposure or risk; (4) restrict marketing and distribution; (5) decrease the harms of tobacco products; (6) ensure industry compliance with FDA regulation through education, inspections, and enforcement; (7) educate the public about FDA's regulatory actions; and (8) expand the science base for regulatory action and evaluation. An adequate science foundation is required for all policies to protect against litigation, and a strong evidence base developed through regulatory science is necessary to inform how the FDA interprets and applies the Agency's regulatory authority.

The fruitful collaboration between the FDA and NIH was established in 2010 with the Joint NIH-FDA Leadership Council for Regulatory Science, which spawned the Tobacco Regulatory Science Program (TRSP) in 2013. TRSP encompasses the best contributions of each organization to determine how to use the tools in the Tobacco Control Act to independently reduce the death and disease toll from tobacco use. The FDA contributes expertise in tobacco regulatory science as well as the statutory authority and funds to support the research. The NIH possesses expertise in tobacco research and administrative infrastructure mechanisms that can be leveraged to advance the program. The TRSP partnership enables the FDA to work with the relevant Institutes to accomplish the research necessary to create the regulatory science foundation for product regulation.

The future of tobacco product regulation is captured in the numerous tobacco regulatory research funding opportunities offered by the TRSP since its creation. One example of the many successful collaborative research projects is the Population Assessment of Tobacco and Health (PATH) Study, which is a longitudinal cohort study of tobacco use and health-related outcomes that was initiated in September 2013. The study is collecting data from more than 60,000 adults and children to begin to ascertain who is using tobacco products, including e-cigarettes, and to correlate behavioral patterns with biomarkers. The NCI's input was critical to study design, instrument development, and implementation. Similarly, the Health Information National Trend Survey (HINTS) and Tobacco Use Supplement to the Current Population Survey (TUS-CPS) represent beneficial collaborations designed to inform the FDA and NIH about important trends related to perceptions and use of tobacco products. The TCORS are multidisciplinary programs funded to inform the FDA's Center for Tobacco Products' (CTP) regulatory activities. With a budget of \$273 M over 5 years, the TCORS will conduct rapid-response research to ensure that tobacco-related data are current and that policies are based on up-to-date information.

Mr. Zeller stated that the CTP's priorities are substantial equivalence, menthol, deeming, public education campaigns, and product standards. Tobacco products can be reviewed via the substantial equivalence pathway to allow a manufacturer to demonstrate that its product is similar to a predicate product to receive FDA approval; in February 2014, for the first time, FDA banned currently sold tobacco products because it was determined that the products were not substantially equivalent. The Tobacco Control Act excluded menthol from the ban on characterizing flavors in cigarettes and required the FDA to convene a Tobacco Products Scientific Advisory Committee (TPSAC), which has issued a report detailing a series of actions related to menthol, including a preliminary scientific evaluation of menthol cigarettes and a public education campaign. Members were told that the deeming mechanism enables the FDA to assert jurisdiction over products that meet the statutory definition of a tobacco product through rulemaking; in 2009, the FDA took enforcement action against e-cigarettes, declaring them to be unapproved drugs and devices, but resulting litigation ruled that the FDA prohibition was inappropriate based on the definition of a tobacco product. In addition, the FDA recently launched a national youth education campaign aimed at vulnerable 12- to 17-year-olds to prevent tobacco use initiation and experimentation. The FDA also is supporting research and exploring the potential to use product standards—designed to prohibit or restrict the allowable levels of substances delivered to the user—to reduce nicotine product addictiveness, toxicity, and appeal.

Members were told that the FDA has the opportunity to develop and promulgate a comprehensive nicotine regulatory policy throughout HHS across the spectrum of all nicotine-delivery products. Mr. Zeller said that policy is made at a population level, and net behaviors will be considered in evaluating new tobacco regulations.

Questions and Answers

A discussion ensued about the Framework Convention on Tobacco Control. Although the U.S. Government has not ratified the convention, the government and the tobacco control community is heavily involved in its work, playing a critical role in informing two WHO committees: Committee on Tobacco Product Regulation, and the Global Network of Tobacco Testing Laboratories. Mr. Zeller said that the FDA is close to an agreement with WHO to convene all regulators, regardless of the signing of the Framework Convention.

Dr. Sellers queried about the FDA's ability to confirm that e-cigarettes, patches, and lozenges contain only nicotine and not additional substances. Mr. Zeller replied that the FDA has not validated whether the nicotine in e-cigarettes is identical to the nicotine from tobacco. He added that products that are not currently on the market must be reviewed through a substantial equivalence or broader public health safety pathway. In either case, the manufacturer must disclose all of the materials within the product.

Dr. Pietenpol asked about the role of menthol, noting that a recent study from the Southern Community Cohort demonstrated that individuals who smoke menthol cigarettes have a lower incidence of lung cancer. Mr. Zeller replied that menthol is a complex subject, and its study should not be limited to direct health effects as menthol clearly has a role in smoking initiation. He also said that the FDA has included menthol in its public education campaign and is funding research to investigate menthol cigarettes.

XIII. DISCUSSION

Dr. Samet suggested that lessons from the shift between types of lung cancer during the past 40 years, specifically the decline of squamous cell and the rise of adenocarcinoma tumors, can inform an effective research agenda. Dr. Varmus commented that molecular signatures found in different types of lung cancer have garnered interest and mentioned that clinicians are attending to the distinctions between tumors arising in smokers versus never-smokers. He referred members to an article by Dr. Prabhat Jha on the benefits of cessation, particularly the effects of reduction in cancer that occur when people cease smoking at different stages (*NEJM* 2013). Dr. Hong emphasized the importance of screening, early detection, and prevention, pointing out that former smokers comprise one-half of lung cancer patients, followed by current smokers (30%), and never-smokers (15%). Dr. Varmus agreed and pointed out that the accumulated benefit from cessation is noteworthy, even for those who have smoked for 20 to 30 years.

Dr. Cullen asked about tax policies on e-cigarettes compared to conventional tobacco products. Mr. Zeller indicated that the tobacco control community is debating whether excise tax policy should be based on principles of harm reduction, specifically whether the less harmful products should be taxed at a lower rate as an incentive to use them. He added that the majority opinion is that e-cigarettes should be treated the same as conventional combusting products for tax and clean indoor air law purposes, and said that the CDC's Office of Smoking and Health is serving as a technical resource for states on this topic.

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

Subcommittee on Planning and Budget. Mr. William Goodwin, Chairman and President, CCA Industries, Inc., informed members that the Subcommittee on Planning and Budget met on 26 February 2014. Mr. Goodwin reminded members that the Subcommittee heard from U.S. Senate staff during its meeting in December 2013. He said that the Subcommittee wanted to obtain a deeper perspective on planning and budget concerns, and Dr. Varmus joined the Subcommittee in a closed session during its February meeting and provided his reflection on NCI's budgetary reductions and future plans. Mr. Goodwin provided a report on the NCI's FY 2014 budget, which is \$4.9 B, including a 2.8 percent increase (\$144 M) from the FY 2013 levels. He pointed out that one-half of that increase is allocated to mandatory budget items. Mr. Goodwin also showed a graphic representation of the consequences of inflation and the Budget Control Act on funding for NCI research as of February 2014.

Motion. A motion was made to accept the reports of the 26 February 2014 NCAB Subcommittee on Planning and Budget meeting. The motion was seconded, and the Board unanimously approved the report.

Future Agenda Items. Dr. Jacks asked members of the committee for potential agenda topics. No topics were suggested.

XVI. CLOSED SESSION— DR. TYLER E. JACKS

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

The NCAB *en bloc* vote for concurrence with IRG recommendations was unanimous. During the closed session, a total of 2,301 NCI applications requesting support of \$964,444,128 and 5 FDA applications were reviewed.

XVII. ADJOURNMENT— DR. TYLER E. JACKS

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

There being no further business, the 165th regular meeting of the NCAB was adjourned at 4:45 p.m. on Thursday, 27 February 2014.

 Date

 Tyler E. Jacks, M.D., Chair

 Date

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