

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE**

3rd Virtual Meeting

BOARD OF SCIENTIFIC ADVISORS

Summary of Meeting

March 20, 2018

**National Cancer Institute
Shady Grove Campus
National Institutes of Health
Bethesda, Maryland**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE**

BOARD OF SCIENTIFIC ADVISORS

MINUTES OF MEETING

March 20, 2018

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 3rd virtual regular meeting on Tuesday, 20 March 2018, at 1:00 p.m. BSA members attended virtually, and NCI staff attended in Conference Room TE406, East Wing, Shady Grove Campus, National Institutes of Health (NIH), Bethesda, MD. Dr. Chi V. Dang, Scientific Director, Ludwig Institute for Cancer Research, Professor, The Wistar Institute, presided as Chair. The meeting was open to the public from 1:00 p.m. until 4:26 p.m. for the consideration of new request for applications (RFAs) and Cooperative Agreements (Coop. Agr.), new and reissue concepts presented by NCI Program staff, the NCI Director's report, and the Legislative report.

BSA Board Members Present:

Dr. Chi V. Dang (Chair)
Dr. Kenneth C. Anderson
Dr. Dafna Bar-Sagi
Dr. Ethan M. Basch
Dr. Michael John Becich
Dr. Melissa Bondy
Dr. Graham A. Colditz
Dr. Christopher M. Counter
Dr. Karen M. Emmons
Dr. Carol E. Ferrans
Dr. James V. Lacey, Jr.
Dr. Maria Elena Martinez
Dr. Luis F. Prada
Dr. Sylvia Katina Plevritis
Dr. Martine F. Roussel
Dr. Robert D. Schreiber

Dr. Victoria L. Seewaldt
Dr. Kevin M. Shannon
Dr. Mary L. Smith
Dr. Ian M. Thompson, Jr.
Dr. David A. Tuveson
Dr. Cheryl L. Walker
Dr. Eileen P. White
Dr. Kevin P. White
Dr. Cheryl L. Willman

Board Members Absent:

Dr. Ariel M. Chinnaiyan
Dr. Joseph M. DeSimone
Dr. Diane Zipursky Quale

Others present: Members of NCI's Scientific Program Leadership Committee, NCI staff, members of the extramural community, and press representatives.

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I. CALL TO ORDER AND OPENING REMARKS—DR. CHI V. DANG

Dr. Dang called to order the 3rd virtual regular meeting of the BSA and welcomed current members of the Board, NIH and NCI staff, guests, and members of the public. Dr. Dang reminded Board members of the conflict-of-interest guidelines and confidentiality requirements. Members of the public were invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities, in writing and within 10 days, comments regarding items discussed during the meeting. Dr. Dang noted future meeting dates were on the agenda and in the Board book.

II. NCI DIRECTOR’S REPORT—DR. NORMAN E. SHARPLESS

Dr. Norman E. Sharpless, Director, NCI, welcomed BSA members and attendees to the 3rd virtual meeting of the BSA and provided an update on the NCI (or Institute) appropriations, intergovernmental affairs, and new and ongoing activities.

NCI Appropriations Outlook. Dr. Sharpless reported that the NCI/NIH is awaiting an approved omnibus spending bill for the fiscal year (FY) 2018 budget appropriations. Members were informed that the NCI regular appropriations have increased for the past 3 consecutive years, and the response from congressional supporters of biomedical research and the NIH suggests a positive outlook for the FY 2019 NIH/NCI appropriations. The NCI is preparing to testify before Congress on the Administration’s FY 2019 budget proposal; the testimony is expected to occur in April 2018. Regarding regular appropriations, Dr. Sharpless updated members on trends in the Research Program Grant (RPG) pool that fund investigator-initiated research (e.g., R01s, P01s, and R21s). The number of R01 applications increased 8 percent between FYs 2016 and 2017. This trend is expected to continue through FY 2018. The number of R01 awards has increased, but not at the pace of the increased rates of the applications. Furthermore, the success rates for established investigators have declined 2 percent. Since FY 2015, the NCI has funded the Noncompeting Continuation (Type 5) awards at 100 percent. Therefore, the total RPG pool required increased allocations annually to support competing (Type 2) and noncompeting awards. The NCI estimates adding \$125 million (M) to the RPG pool to support FY 2018 awards. Although this represents a large commitment of funds, the RPG pool of investigator-initiated research grants is a large part of NCI’s efforts and is too valuable to cut.

NCI Intergovernmental Affairs. Dr. Sharpless remarked on recent visits with U.S. Food and Drug Administration (FDA) Commissioner Dr. Scott Gottlieb, in which key areas for joint NCI–FDA collaborations were identified. The FDA Oncology Center of Excellence, joint training programs, data sharing, and compliance advice on cell culture manufacture were among the topics discussed. Dr. Sharpless will participate in upcoming FDA Grand Rounds.

The NCI also had interactions with the Centers for Medicare and Medicaid Services (CMS), including attending and providing support in CMS meetings. NCI Deputy Director Dr. Douglas R. Lowy participated in the CMS Grand Rounds. Dr. Sharpless called attention to two major announcements in recent weeks that are of interest to the NCI. First, CMS finalized the national coverage determination for next-generation sequencing (NGS) of somatic mutations of patients with cancer, which is a major advancement for cancer patients. Second, FDA posted an advanced notice in the *Federal Register* of proposed rulemaking for regulation to establish a tobacco product standard for the nicotine level of combusted cigarettes, which could have a major effect on cancer control in the United States.

Dr. Sharpless attended the Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Network retreat led by Col. Craig D. Shriver, Director, John P. Murtha Cancer Center, Walter Reed National Military Medical Center, Department of Defense (DoD), and was joined by more than 80 participants from the DoD, NCI, U.S. Department of Veterans Affairs (VA), and the Uniformed Services University of the Health Sciences. The DoD and VA have unique capabilities, such as access to the DoD and VA populations (e.g., veterans, active duty military personnel, and their beneficiaries) for cancer studies. The opportunity exists to collaborate on clinical trials that might be a good fit for the NCI, DoD, and VA.

Members were updated on NCI’s interactions with the U.S. Department of Health and Human Services (HHS) leadership. On March 20, 2018, HHS Secretary Mr. Alex M. Azar visited the NIH. Secretary Azar is knowledgeable in NIH-related matters and has expressed interest in being updated on advances in oncology and immunotherapy. Encouraging discussions also have been ongoing with former acting HHS Secretary and current HHS Deputy Secretary, Mr. Eric D. Hargan. Secretary Azar and Deputy Secretary Hargan have spoken on the need for greater efficiency and streamlining within the NCI, such that any dollar amount saved administratively would benefit and support future investigator-initiated research activities.

Dr. Sharpless reported on his ongoing congressional outreach activities, including a visit with House Appropriations Subcommittee Chair, Representative Thomas J. Cole (R) of Oklahoma, and attending a Senate NIH Caucus briefing on November 14, 2017, hosted by co-chairs Senator Dick Durbin (D) of Illinois and Senator Lindsey Graham (R) of South Carolina. At that briefing, Dr. A. Stephen Rosenberg, Chief, Surgery Branch, Center for Cancer Research (CCR) spoke on cancer immunotherapy and was joined by one of his former immunotherapy patients. On January 17, 2018, Dr. Sharpless, more than 20 members of Congress, and members the Pediatric Oncology and Urology Oncology Branches of the CCR attended the Annual Congressional Reception for the Children’s Inn at NIH.

Dr. Sharpless reported that he and Dr. Barbara K. Rimer, Chair of the President’s Cancer Panel, attended a White House Domestic Policy Council (DPC) briefing hosted by DPC Director Mr. Andrew Bremberg to discuss the 2018 President’s Cancer Panel Report entitled “Promoting Value, Affordability, and Innovation in Cancer Drug Treatment.” He noted two other governmental reports that have been released on this topic, the 2017 National Academies of Sciences, Engineering, and Medicine’s “Making Medicines Affordable: A National Imperative” report and the 2018 Council of Economic Advisers’ “Reforming Biopharmaceutical Pricing at Home and Abroad” report. Dr. Sharpless stated that many of the higher priced FDA-approved drugs are used to treat cancer. Drug pricing is one of HHS’s top priorities, as HHS Secretary Azar has remarked.

Method to Extend Research in Time (MERIT) Award (R37) Program. Dr. Sharpless announced NCI's use of the Method to Extend Research in Time (MERIT) Award (R37) as a mechanism to increase funding to Early Stage Investigators (ESIs) that could be implemented in FY 2018 for new competing awards. The MERIT R37 provides critical time for ESIs to launch their careers and become more established before having to submit a grant renewal. ESIs who submit an R01 application that receives a meritorious score within the NCI ESI payline will be considered. After an approval process, an ESI R01 will be converted to an ESI MERIT R37; the same conditions (e.g., budget, reporting requirements, and length of time) as the R01 will apply. An ESI MERIT 37 awardee may, toward the end of the initial award period, apply for a 2-year extension. At some point in the future, the NCI will assess whether the 2 years of additional funding benefitted the MERIT grantees.

NCAB *ad hoc* Working Groups. Members were informed that the newly established NCAB *ad hoc* Global Health, Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR), and Informatics Working Groups member rosters are complete, and meetings are being planned. The Global Health Working Group has been charged to focus on ways to prioritize the diverse requests to participate in global oncology initiatives received by the NCI. The call to determine the SBIR/STTR Working Group's charge is being planned, and the group will focus on evaluating the success of the NCI SBIR program. Dr. Sharpless reported that the NCI soon will begin its search for a new Center for Biomedical Informatics and Information Technology (CBIIT) Director. The Informatics Working Group will provide input on the role of the CBIIT Director as a chief information officer and advise on expanding funding opportunities for data science and bioinformatics research across the NCI.

Update on the Cancer MoonshotSM. Dr. Sharpless reported that the NCI issued nearly 50 funding opportunity announcements for FYs 2017 and 2018 that support each of the 10 NCAB Blue Ribbon Panel Cancer MoonshotSM recommendations and is supporting six intramural initiatives. The Cancer MoonshotSM RFAs broadly address requirements related to data sharing, health disparities, and underserved populations. He called attention to one initiative being supported by Cancer MoonshotSM funds, the Partnership for Accelerating Cancer Therapies (PACT), a 5-year public-private partnership between the NCI and 12 pharmaceutical companies interested in promoting immuno-oncology. PACT partner investments (\$5 M) and NCI matching funds through the NCI-sponsored Cancer Immune Monitoring and Analysis Centers (CIMACs) and the Cancer Immunologic Data Commons (CIDC) will support the PACT over its initial, 5-year period. The goal of PACT is to develop a precompetitive biomarker validation for immuno-oncology discovery, and CIMAC-CIDC multidisciplinary teams have begun to meet to discuss their ongoing plans. Activities within the network of laboratory centers will include assay development and standardization to support immunotherapy biomarker discovery using state-of-the-art technologies. In addition to funding support, PACT partners are providing guidance and input on the necessary resources and topics to be addressed within the network. PACT leverages other NCI initiatives, including the Immuno-Oncology Translational Network (IOTN) and the Pediatric Immunotherapy Discovery and Development Network (PIDDN).

NCI Experimental Therapeutics (NExT) Program. Members were reminded that the NExT program provides investigators with services that extend from target validation to Phase II and Phase III clinical trials in humans. The program supports drug discovery and development of small molecules and biologics through academic and industry collaborations. Dr. Sharpless reported on several projects that are active in the NExT pipeline, including a high micromolar-potent myeloid cell leukemia 1 (MCL-1) inhibitor of apoptosis developed by Dr. Stephen W. Fesik and his team of investigators at Vanderbilt University. Advancing the discovery and preclinical development of this MCL-1 inhibitor compound through NExT has resulted in the program's first licensing agreement. This is a validation of the success and enabling capability of the NExT program.

Update on Tobacco Control. Dr. Sharpless remarked on a recent study on cigarette use in the United States, which was published in the *JAMA Internal Medicine* and led by Dr. Neal D. Freedman, Senior

Investigator, Metabolic Epidemiology Branch, Division of Cancer Epidemiology and Genetics. The study, which investigated the toxicity associated with the episodic intermittent non-daily smoker (i.e., social smoker), revealed that the mortality risk for light smokers (e.g., less than one cigarette per day) was significantly higher compared to that of nonsmokers and increased with the smoker's age at the time of tobacco cessation. Further studies would be needed to determine whether these findings extrapolate to other tobacco-related products, such as cigars. These data have implications for how the NCI will develop plans to address tobacco control and cessation in the United States.

Update on Rural Cancer Control. Dr. Sharpless informed members that rural cancer control, an effort led by the Division of Cancer Control and Population Sciences (DCCPS), is actively being developed within the NCI. Evidence from population-based and epidemiological studies indicate that the cancer mortality disparity between African American and White men has been decreasing in the United States for more than a decade, whereas the cancer mortality disparity between rural and urban populations has increased steadily since the mid-1990s. The NCI anticipates supporting research to better understand this disparity. Such factors as socioeconomic status, education levels, race/ethnicity, and access to care make it challenging to broadly define what is a rural population. Determining how these factors and behavior-related risk factors affect cancer-related outcomes in rural populations is a challenge the NCI is willing to address. Preliminary planning and engagement efforts have included discussions with rural health experts about potential approaches and convening workshops and meetings on rural cancer control. The NCI will host the first Accelerating Research in Rural Cancer Control Conference on May 30–31, 2018.

NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) Trial. Dr. Sharpless reported that the NCI-MATCH trial, a component of the NCI Precision Medicine Initiative (PMI) in Oncology and the broader national PMI, was supported by 1,100 sites across the United States, including the NCI National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP) sites. This broad dissemination of the NCI-MATCH research speaks to the future of clinical trials in the United States and patient enrollment efforts that are needed for well-designed trials to succeed. One of the fastest accruing trials in NCI history, NCI-MATCH successfully enrolled 6,396 patients, exceeding the accrual goal of 6,000 patients and ending this phase of the trial for rapidly accruing treatment arms. The first NCI-MATCH efficacy data assessing nivolumab in microsatellite instability-high cancers will be released soon. The NCI-MATCH, transitioned to the Rare Variant Initiative in July–August 2017, began enrolling patients with low-frequency mutations and expanded to accept outside-of-the-trial NGS from academic and commercial laboratories to broaden patient enrollment.

Dr. Sharpless remarked that the NCI Children's Oncology Group Pediatric MATCH trial opened in July 2017 with eight treatment arms. To date, 131 patients in the 1–21 years old age range have been enrolled, of whom 35 percent are adolescents and young adults. Each treatment arm has at least one patient enrolled, and genomic sequencing analyses have been completed on 94 patient tumors.

National Cryo-EM Facility (NCEF). Dr. Sharpless reported that the NCEF became operational on May 15, 2017, at the Frederick National Laboratory for Cancer Research (FNLRC) campus with one Titan™ Krios microscope. A second Krios microscope will be operational in fall 2018, and a third will be added in 2019 if demand increases. More than 70 extramural cancer-related projects from 20 different institutions across the United States have been completed by the NCEF, and user feedback has been positive. The first NCEF user project data were recently published in *Nature Communications*. NCEF key personnel who are responsible for daily operations include Program Adviser, Dr. Sriram Subramaniam, Senior Investigator, CCR, NCI; NCEF-dedicated staff; and FNLRC leadership.

NCI Vision. Dr. Sharpless informed members that his vision for the NCI is being shaped by a 4-month listening and learning tour of the Institute, including visits to internal divisions and offices, extramural institutions, industry partners, and advocacy groups to firmly grasp the operations and directions of the NCI. Three key focus areas are envisioned: Focus Area 1 prioritizes what the NCI must do to achieve its

mission; Focus Area 2 encompasses what research and activities the NCI must continue supporting; and Focus Area 3 outlines what the NCI will do as the Nation's leader in cancer research.

In the discussion, the following points were made:

- The NCI indicated that guidelines to significantly lower the nicotine levels in combustible cigarettes, which the proposed FDA rulemaking is designed to do, should expand to decrease the use of unregulated tobacco products, such as electronic cigarettes (e-cigarettes).
- Program staff clarified that the NIH's Office of Disease Prevention, through the Tobacco Regulatory Science Program, coordinates trans-NIH tobacco-related research in collaboration with the FDA Center for Tobacco Products. In FY 2017, 12 new grants were funded to support e-cigarette-related research. The FDA needs new evidence from this research to develop regulatory guidelines.
- The NCI acknowledged that connecting implementation of rural health programs to the NCI Surveillance, Epidemiology, and End Results (SEER) Program and including new data elements, such as complete treatment data, would be good ideas to consider after the SEER recompetition period ends in May 2018. Scaling up surveillance to include risk factor behavior data also could be considered.
- BSA Members emphasized that although data analysis showed similar outcomes for women and underrepresented minority R01 applicants, the opportunity exists to consider whether the MERIT R37 mechanism could be used to boost participation in these and other groups (e.g., clinicians).
- Dr. Sharpless explained that the MERIT R37 mechanism is NCI's first, but not only, step to increase support for ESIs. Discussions are ongoing within the NIH to determine other measures (complex metrics) in the long term. The 21st Century Cures Act directs the NIH Director to address ESI support broadly. The Advisory Committee to the NIH Director's Next-Generation Researchers Initiative Working Group has been established to fulfill that requirement.
- The Research to Accelerate Cures and Equity (RACE) for Children Act of 2017, which requires companies developing targeted cancer drugs for adults to develop those drugs for children, is at the forefront of NCI's attention. The NCI is prepared to provide subject-matter expertise regarding targets for adult and pediatric cancers.
- Members encouraged the NCI to consider ways that the Office of Communications and Public Liaison could communicate the success and updates on NCI's research and programs to internal and external investigators to leverage existing large-scale efforts.
- Members suggested that the NCI include requirements to review its data sharing rules in program renewals.
- Given the collaborations with the Veterans Administration (VA), the opportunity exists to increase partnerships in extramural projects focused on precision medicine. Such partnerships could enhance the NCI R01 portfolio of funded investigators. The NCI and VA Interagency Group to Accelerate Trials Enrollment (NAVIGATE) is one such collaboration to leverage.

III. LEGISLATIVE REPORT—MS. M. K. HOLOHAN

Ms. M. K. Holohan, Director, Office of Government and Congressional Relations, reported on the budget process, appropriations, congressional visits, and other legislation of interest. Ms. Holohan called attention to the detailed legislative report contained in the Board's meeting book. She informed members that the NCI is working closely with the FDA to implement the provisions of the RACE for Children Act. Representatives from the FDA, NCI Division of Cancer Treatment and Diagnosis (DCTD), academia, patient advocacy groups, and industry participated in an informal public meeting on February 20, 2018, to consider approaches to develop a list of molecular targets relevant to pediatric cancer. The FDA will convene a public meeting on April 20, 2018, to review such a list.

Ms. Holohan noted that the main legislative concern for the NCI and NIH is the FY 2018 appropriations. The federal government is operating under a continuing resolution (CR) that funds the government through March 23, 2018. Congress has until midnight March 23 to pass an omnibus spending bill to fund the government for the remainder of FY 2018. Such policy issues as provisions for family planning and establishing a border wall have delayed the Appropriations Subcommittees on Labor, Health and Human Services, Education, and Related Agencies spending bills.

Members were reminded that, the NCI/NIH budget process for the regular appropriations begins with the release of the President's proposed budget, which appropriation committees consider as they prepare their legislation. Congress reconciles and finalizes the appropriations, the President signs the appropriations bill into law, and funds are made available to the NIH and NCI. The FY 2018 process is still pending completion. Concurrently, congressional appropriations committees are considering the President's FY 2019 budget proposal, which was released on February 12, 2018. The Labor, HHS, and Education Subcommittee held its third Secretary-level budget hearing. On March 15, 2018, HHS Secretary Azar testified in support of the FY 2019 HHS budget proposal. The NIH and other agency-level budget hearings are to be determined.

To date, there have been five CRs in FY 2018 and two government shutdowns, which are not uncommon or historical outliers. The fifth CR included a 2-year budget agreement (H.R. 1892) that raised the debt limit; increased the budget spending cap; and provided funding for certain priority areas during the next two years, including a \$2 billion (B) increase for the NIH. Ms. Holohan noted that this preserves, but does not cap, the NIH budget increases. Other priority allocations include \$6 B for opioid treatment research and \$20 B for infrastructure. Appropriators modified their proposed FY 2018 spending bills that considered the new budget caps and priorities, including adjustments to the 302(b) allocations. The next steps for Congress are to finalize and approve the omnibus spending bill. Despite the challenges in finalizing the FY 2018 omnibus spending bill, the NCI remains hopeful, given the recent appropriations trend.

Ms. Holohan also provided an update on congressional visits. Members were informed that on February 16, 2018, Senator Maggie Hassan of New Hampshire visited the NIH and met with IC directors and pediatric oncology patients, and visited several research laboratories. Dr. Sharpless met members of the newly formed Congressional Cancer Survivors Caucus (Representatives Mark DeSaulnier, Ted Poe, and Rick Nolan) at the March 14, 2018, Association of Community Cancer Center's Luncheon. Dr. Lowy delivered the luncheon keynote address. Continuing the tradition of prior NCI directors, Dr. Sharpless met with Representative Nita Lowey, ranking member of the House Appropriations Committee, to discuss support for the NIH and the upcoming omnibus spending bill.

IV. RFA/COOP. AGR. CONCEPTS—NCI PROGRAM STAFF

DCCPS

Improving the Reach and Quality of Cancer Care in Rural Populations (New RFA) —Dr. Robert T. Croyle

Dr. Robert Croyle, Director, DCCPS, presented a concept on improving the reach and quality of cancer care in rural populations. Dr. Croyle informed members that health disparities in the United States have been largely viewed as a function of race and ethnicity. Such observations have been the driver of health disparity-related research supported by the NCI and NIH. However, recent reports from the Centers for Disease Control and Prevention (CDC) on the U.S. death rates for all cancers for the period 1992–2014 revealed that disparity trends in minority populations have been converging. Population and health scientists who monitor health disparities have been sensitized to the geography of incidences of cancer and other diseases. Similar to those of other chronic diseases, cancer incidences and mortality rates are influenced by geographical factors. At the county level, reports on health disparities in the United States showed that from 1999 to 2013, the cancer mortality rates varied significantly across the country, were higher in certain regions of the country, and persisted in mostly rural and lower income populations. Trends in cancer mortality by locality and within a rural region reveal that the rural disparity is greater in the southern United States and is most severe among ethnic minorities who live in rural areas. The trend in cancer mortality rates in rural versus urban populations is diverging rather than converging. During the past two years, the NCI, through outreach and planning efforts, has engaged the rural health community to develop ideas on how best to address this issue. Dr. Croyle acknowledged that the Federal Office of Rural Health Policy and the Health Resources and Services Administration are helping to shape the NCI rural cancer control program.

The RFA will support observational research and pilot testing of interventions to identify, understand, and address predictors of low-quality cancer care in rural, low-income, or underserved populations and cancer control intervention research to address such predictors.

Subcommittee Review. Dr. Carol E. Ferrans, Professor and Associate Dean for Research, Director, University of Illinois at Chicago (UIC) Center of Excellence in Eliminating Health Disparities, Department of Biobehavioral Health Sciences, College of Nursing, UIC, expressed the Subcommittee's strong enthusiasm for the concept and noted that focusing on the reach and quality of cancer care in rural areas fulfills a critical need. Dr. Ferrans anticipates that the insights gained from this work will extend to the urban and suburban areas that also may be challenged to deliver quality cancer to their communities. The Subcommittee thinks that broadly addressing cancer disparities in rural populations is a clear strength. The fact that the RFA concept will support observational and interventional studies, requires pilot studies, and consists of scientific teams that meet regularly are strengths. The Subcommittee encouraged the NCI to establish productive boundaries so that ideas are translatable to address the problem and to leverage such existing efforts, such as the Cancer Center Support Grants (P30s) for NCI-designated Cancer Centers.

In the discussion, the following points were made:

- Members lauded the NCI's efforts for bringing the issue of rural cancer control to the forefront of research.
- Members encouraged the NCI to consider ways to address sustainability and community engagement in the long term for any programs that would be developed in the community. Engaging experts (e.g., National Rural Health Policy Institute) for advice on ideas for developing community-based sustainable programs, and fostering relationships between NCI-designated

Cancer Centers and state rural health offices where there are staff dedicated to resolving rural health issues will be critical.

- One possibility to explore is establishing new partnerships between NCI-designated Cancer Center researchers and health provider organizations that are strategically located in rural areas and are experts in providing care to rural populations. Forging such partnerships would greatly accelerate NCI's rural cancer control efforts.

The first year's cost for the one-time issuance is estimated at \$7 M for 10 R01 awards, with a total cost of \$35 M for 5 years.

Motion. A motion to concur with the DCCPS's RFA entitled "Improving the Reach and Quality of Cancer Care in Rural Populations" was approved unanimously.

**Tobacco Cessation Interventions Among People Living with HIV/AIDS (New RFA/Coop. Agr.)
—Dr. Annette Kaufman**

Dr. Annette Kaufman, Program Director, DCCPS, presented a concept to support studies to improve tobacco cessation treatment among people living with HIV/AIDS (PLWH), with an emphasis on those studies that adapt existing evidence-based cessation interventions for application to this population. Dr. Kaufman informed members that this research aligns with the Office of AIDS Research (OAR) FY 2018 Strategic Plan and was prioritized by the OAR as high-priority AIDS research. PLWH are a heterogeneous population composed of people from diverse backgrounds, demographics, life circumstances, and cultures. The CDC reported that in 2016, sexual transmission accounted for most new HIV diagnoses (67% male-to-male transmission and 24% heterosexual transmission). African Americans (44%) had the highest rate of diagnoses compared to Whites (26%) and Hispanics (25%) in the United States. In addition, youth between the ages of 13 and 24 accounted for 22 percent of new U.S. HIV diagnoses in 2015. The advent of novel therapies, such as antiretroviral therapy, has led to a decline in AIDS-related mortality and has increased the life expectancy of PLWH. Today, HIV is considered a chronic health condition. Non-AIDS defining cancers, particularly lung cancers, are the leading cause of death not related to AIDS. It is estimated that 94 percent of lung cancers among PLWH could be prevented by eliminating cigarette use.

An estimated 40 percent of the 1.1 million PLWH in the United States smoke cigarettes, whereas only 15 percent of the general population smoke. Furthermore, PLWH who use tobacco experience increased morbidity, and their life expectancy is reduced by at least 16 years compared to the 11- to 12-year reduction seen in the general population. Given the diverse PLWH population, tailoring approaches to deliver the best tobacco cessation intervention to this multifaceted and unique group is challenging. The 2008 Clinical Practice Guideline for Treating Tobacco Use and Dependence recommends randomized clinical trials to assess the effectiveness of medications and behavioral interventions, motivational interviews and educational approaches, and social support networks among PLWH. Studies assessing the efficacy of tobacco cessation are limited and lack rigorous methods, suggesting a need to build the science in this area.

Dr. Kaufman stated this RFA will support research examining the effectiveness of evidence-based tobacco cessation interventions that can be tailored and adapted for PLWH and research that seeks to understand the barriers and how best to integrate these interventions in diverse health care settings. The NCI-appropriated AIDS funds, as established by the OAR, will support this research. The National Institute Drug Abuse also has committed funds to this effort.

Subcommittee Review. Dr. Graham A. Colditz, Niess-Gain Professor of Surgery, Professor of Medicine and Associate Director Prevention and Control, Alvin J. Siteman Cancer Center, Deputy Director,

Institute for Public Health, Chief, Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, expressed the Subcommittee's enthusiasm and support for the concept. Dr. Colditz stated that the Subcommittee appreciates NCI staff responses to their requests to consider the implementation science aspect, the diverse and unique needs of the PLWH population, and the potential synergistic relationship between HIV treatment adherence and smoking cessation.

In the discussion, the following points were made:

- Members recognize that studies investigating smoking cessations are limited and that science in this area is needed, but there is a concern that the R21 funding mechanism might not provide investigators sufficient time to capture the translational aspects of the research.
- Such interventions as pharmacotherapy have worked to shift the scale in tobacco cessation.

The first year's cost for the one-time re-issuance is estimated at \$2.5 M for three R01 awards and three R21 awards, with a total cost of \$11 M for 2–5 years.

Motion. A motion to concur with DCCPS's RFA/Coop. Agr. entitled "Tobacco Cessation Interventions Among People Living with HIV/AIDS" was approved unanimously.

Division of Cancer Prevention

**Cancer Preventive Agent Development Program: Early Phase Clinical Research
(New RFA/Coop. Agr.)—Dr. Eva Szabo**

Dr. Eva Szabo, Program Manager, Division of Cancer Prevention (DCP), presented a concept on early phase clinical research for the Cancer Preventive Agent Development Program. Dr. Szabo informed members that the DCP drug development program uses a systematic, multipronged approach to drug development consisting of three critical components—preclinical toxicology studies, early phase clinical trials, and Phase III efficacy trails—which are supported by programs within DCP. The preclinical studies are conducted in the Prevent Cancer Preclinical Drug Development Program (or PREVENT). Specifically, the Phase 0/I/II Cancer Prevention Clinical Trials Program (or Early Phase Prevention Trials Consortia) supports early phase trials, and Phase III definitive efficacy trials are conducted by NCORP. The PREVENT and NCORP have been recommended by the BSA for continuation. This concept focuses on the Early Phase Clinical Trials Consortia, which aims to qualify cancer preventive agents for further clinical development in Phase 0, I, and II trials. The goals are to optimize trial designs, develop surrogate or intermediate endpoint biomarkers, test novel imaging technologies, and develop further insights into mechanisms of action of the cancer preventative agents. This research will leverage the NCI Cancer MoonshotSM and existing NCI activities.

The current program structure consists of five contract companies that coordinate more than 100 member sites to conduct Phase 0 microdosing biomarker modulation trials, Phase I pharmacokinetic safety trials, and Phase II preliminary efficacy trials. From FY 2013 to FY 2017, the program received 67 concepts and approved 43 protocols for 30 preventative agents, including eight vaccines, one of which is FDA approved and seven that are experimental. During this period, the program enrolled 1,210 participants into 31 clinical trials, approved a central institutional review board (IRB), developed an Accrual Quality Improvement Program, and developed a biospecimen repository. Key scientific successes include expanding a new immunoprevention portfolio, progressively moving several agents through the drug development pipeline, and optimizing the risk-to-benefit equation for promising agents using topical approaches and alternative dosing regimens. A 2017 program evaluation by an external review committee identified key strengths and recognized that the program was unique and filled an unmet need. The evaluation concluded that the program was successful in achieving its goals in accrual, opening new

trials, and identifying promising cancer prevention strategies. Proposed recommendations (e.g., increase funding) and endorsements from the evaluation have informed modifications to the program.

This RFA will support a proposed new structure for the DCP Early Phase Clinical Trials Consortia consisting of lead organizations and a coordinating center to monitor the activities of the consortia. Key program changes will include a shift from a contract to a grant funding mechanism, centralized coordination, a data management system, and restricted funds for interconsortia studies and high-priority new scientific areas. The consortia will continue to develop new scientific areas, focus on strategies to optimize risk, and repurpose drugs for cancer prevention, with an emphasis on drugs that affect multiple chronic diseases in addition to cancer.

Subcommittee Review. Dr. Kenneth C. Anderson, Kraft Family Professor Medicine, Harvard Medical School, Director, Lebow Institute for Myeloma Therapeutics, Dana-Farber Cancer Institute, expressed the Subcommittee’s support for the concept, which addresses an unmet need and is a good investment for the NCI. Dr. Anderson stated that the Subcommittee agrees with the program’s external review report and noted that this work is not likely to be funded by industry. The Subcommittee suggested including metrics of success, adopting immune-related prevention strategies, increasing rigor in the RFA, and moving studies into Phase III trials more rapidly.

In the discussion, the following point was made:

- Accrual numbers reflect the types of studies that are open at the time, rather than a drop in the program’s enrollment.

The first year’s cost for this one-time issuance is estimated at \$5 M in year 1 for six UG1 awards, \$2 M for one U24 award, and \$13 M in years 2–5, with a total cost of \$59 M for 5 years.

Motion. A motion to concur with the DCP’s RFA/Coop. Agr. entitled “Cancer Preventive Agent Development Program: Early Phase Clinical Research” was approved with 23 ayes, 0 nays, and 1 abstention.

Division of Cancer Treatment and Diagnosis

**Cooperative Human Tissue Network (Re-Issue RFA/Coop. Agr.)
—Dr. Rodrigo Chuaqui**

Dr. Rodrigo Chuaqui, Program Director, DCTD, presented a reissue concept for the Cooperative Human Tissue Network (CHTN), which is a resource to procure high-quality samples for basic and early translational research. Dr. Chuaqui informed members that the CHTN consists of five adult divisions—Eastern (The University of Pennsylvania), Mid-Atlantic (The University of Virginia), Midwestern (The Ohio State University), Southern (The University of Alabama at Birmingham), and Western (Vanderbilt University)—that distribute samples geographically according to the location of the investigator, as well as one pediatric division at the Nationwide Children’s Hospital that distributes samples across all geographical areas. Each of the adult divisions works with two to six remote-site hospitals to increase the procurement capacity. The pediatric division procures samples from 90 percent of pediatric hospitals in the United States.

The CHTN is a unique public biospecimen resource available to the broader scientific community that prospectively procures samples, mostly during primary surgeries, in response to a researcher’s questions. Samples are distributed immediately upon procurement, include a redacted pathology report, and include deidentified data collected under a waiver of consent by the IRB at each institution. The CHTN supports early discovery and translational research and assay development, and nearly 100 percent of procured

samples are distributed and used.

From 2012 to 2016, the CHTN distributed 250,000 samples to 1,125 individual researchers. Of the 1,125 researchers, 77 percent were academic investigators, two-thirds were R01 grantees, 18 percent were from industry, and 5 percent were government researchers. During this period, CHTN participants produced 854 publications and 103 patents. The CHTN division principal investigators, who also are board-certified pathologists and leaders in biospecimen organizations, contributed to improving the state of the science and establishing biobanking best practices.

This re-issuance RFA will support: 1) a 20 percent increase in funding to continue supplying high-quality samples to the research community at large; 2) establishing a dedicated central information technology (IT) capability; and, 3) hosting, maintaining, and upgrading the existing IT system.

Subcommittee Review. Dr. Cheryl Willman, The Maurice and Margaret Liberman, Distinguished and Endowed Chair in Cancer Research, University of New Mexico (UNM) Distinguished Professor of Pathology, UNM School of Medicine, Director and CEO, UNM Comprehensive Cancer Center, UNM, expressed the Subcommittee's strong support for the concept reissuance. Dr. Willman remarked that the Subcommittee observes that the CHTN has been a productive resource, provides a unique service that tailors sample acquisition to the researcher's needs, and has been a successful initiative for the NCI. In addition, the CHTN is an important source of tissue specimens for academic and pharmaceutical investigators, responds rapidly to meet the needs of researchers, enhances collaborations, and has resulted in numerous publications and patents during this funding period. Furthermore, the biobanking purpose of the CHTN differs from the significant activities ongoing in the NCTN, the Specialized Programs of Research Excellence (SPORE), and NCI-designated Cancer Centers. Dr. Willman voiced the Subcommittee's concerns that the CHTN: 1) has been somewhat siloed from other NCI biobanking activities within the SPOREs and NCTN; 2) has not incorporated state-of-the-art banking approaches over time regarding sample annotation and IT infrastructure; and, 3) sample collections may not fully represent the racial and ethnic diversity of the U.S. population. The Subcommittee suggested that the NCI consider strategies to improve siloed biobanking activities across the NCI programs, collect clinical data to annotate samples, and consider developing other sites in the United States in areas not currently represented in the CHTN, especially new sites within the Western Division.

In the discussion, the following points were made:

- The CHTN should be broadened geographically to increase racial and ethnic representation in the sample collections to reflect the diversity of the U.S. population.
- Members supported the re-issuance concept in general, but encouraged the NCI to consider an in-depth review of tissue banking activities across the NCI and devise strategies to standardize sample annotation and data collections and improve the IT infrastructure in large-scale efforts.
- The costs of a standard annotation model, patient consent at the institutional level, and availability of clinical data for samples collected and distributed in real-time would need to be addressed.
- NCI will consider a report on tissue banking activities across the NCI, including the approaches and reach to the cancer research community, at a future BSA meeting.

The first year's cost for the one-time re-issuance is estimated at \$5.8 M for six UM1 awards, with a total cost of \$29 M for 5 years.

Motion. A motion to concur with the re-issuance of the DCTD’s RFA/Coop. Agr. entitled “Cooperative Human Tissue Network (CHTN)” was approved with 22 ayes, 0 nays, and 2 abstentions, with the consideration to broaden the CHTN geographically to increase racial and ethnic representation in the samples that reflect the diversity of the U.S. population.

V. ADJOURNMENT—DR. CHI V. DANG

There being no further business, the 3rd virtual regular meeting of the BSA was adjourned at 4:26 p.m. on Tuesday, 20 March 2018.

Date

Chi V. Dang, M.D.
Chair, Board of Scientific Advisors

Date

Paulette S. Gray, Ph.D.
Executive Secretary, Board of Scientific Advisors