DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
8th VIRTUAL NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
February 13, 2018

Virtual
Conference Room TE406, East Wing, Shady Grove Campus
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
February 13, 2018

The National Cancer Advisory Board (NCAB) convened for its 8th virtual regular meeting on February 13, 2018. NCAB members attended virtually, and National Cancer Institute (NCI) staff attended in Conference Room TE406, East Wing, Shady Grove Campus, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Wednesday, February 13, 2018, from 1:00 p.m. to 2:35 p.m., and closed to the public from 2:45 p.m. to 4:25 p.m. The NCAB Chair, Dr. Elizabeth M. Jaffee, Deputy Director, The Sidney Kimmel Comprehensive Cancer Center, Co-Director, Skip Viragh Center for Pancreas Cancer, The Dana and Albert "Cubby" Broccoli Professor of Oncology, Johns Hopkins University, presided during both the open and closed sessions.

NCAB Members
Dr. Elizabeth M. Jaffee (Chair – attended in person)
Dr. Peter C. Adamson
Dr. Francis Ali-Osman
Dr. Deborah Watkins Bruner
Dr. Yuan Chang
Dr. David C. Christiani
Dr. Judy E. Garber
Mr. Lawrence O. Gostin (absent)
Dr. Scott W. Hiebert
Dr. Beth Y. Karlan (absent)
Dr. Timothy J. Ley
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub
Dr. Mack Roach, III
Dr. Charles L. Sawyers
Dr. Margaret R. Spitz
Dr. Max S. Wicha

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Norman E. Sharpless, Director, National Cancer Institute
Dr. Jeff Abrams, Acting Director for Clinical Research, Division of Cancer Treatment and Diagnosis
Dr. L. Michelle Bennett, Director, Center for Research Strategy
Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Director, Office of Cancer Centers
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Dr. William Dahut, Scientific Director for Clinical Research, Center for Cancer Research
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
Dr. Dan Gallahan, Deputy Director, Division of Cancer Biology
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Ed Harlow, Special Advisor to the Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Tony Kerlavage, Acting Director, Center for Biomedical Informatics and Information Technology
Dr. Kristin Komschlies, Acting Director, Office of Scientific Operations, NCI Campus at Frederick
Dr. Barry Kramer, Director, Division of Cancer Prevention
Dr. Jerry Lee, Deputy Director, Center for Strategic Scientific Initiatives
Dr. Douglas R. Lowy, Deputy Director, National Cancer Institute
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Mr. Jeff Schilling, Acting Chief Information Officer and Chief of Infrastructure and Information Technology Services Branch, Center for Bioinformatics and Information Technology
Ms. Donna Siegle, Acting Executive Officer, and Acting Deputy Director for Management
Dr. Dinah Singer, Acting Deputy Director and Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis M. Staudt, Director, Center for Cancer Genomics
Dr. Ted Trimble, Director, Center for Global Health
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology Transfer Programs
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

Liaison Representatives

Ms. Carolyn Aldige, Prevent Cancer Foundation
Ms. Paula Bowen, Kidney Cancer Association
Mr. William Bro, Kidney Cancer Association
Dr. Carol Brown, Society of Gynecologic Oncologists
Dr. Margaret Foti, American Association for Cancer Research
Dr. Leo Giambarresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society
Dr. Ruth Hoffman, American Childhood Cancer Organization
Dr. Gerald F. Joseph, Jr., American College of Obstetricians and Gynecologists
Dr. Steven L. Klein, National Science Foundation
Ms. Laura Levit, American Society of Clinical Oncology
Dr. W. Marston Linehan, Society of Urologic Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education

Ms. Shelly Fuld Nasso, National Cancer Institute, Council of Research Advocates
Ms. Leah Ralph, Association of Community Cancer Centers
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Christy Schmidt, American Cancer Society
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Dr. Johannes Vieweg, American Urological Association
Dr. Pamela A. Wilcox, American College of Radiology
COL. (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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TUESDAY, 13 FEBRUARY 2018

I. CALL TO ORDER AND OPENING REMARKS— DR. ELIZABETH M. JAFFEE

Dr. Elizabeth M. Jaffee called to order the 8th virtual National Cancer Advisory Board (NCAB) meeting. She welcomed members of the Board, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), NCI, in writing and within 10 days, any comments regarding items discussed during the meeting. Dr. Jaffee reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations. She also thanked NCI Information Technology and DEA Committee Management Office (CMO) staff for setting up the infrastructure for the virtual meeting.

Motion. A motion to accept the minutes of the November 29, 2017 Joint Meeting of the Board of Scientific Advisors and the NCAB was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. ELIZABETH M. JAFFEE

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

III. NCI DIRECTOR'S REPORT—DR. NORMAN E. SHARPLESS

Dr. Norman E. Sharpless, Director, NCI, welcomed NCAB members and attendees to the 8th virtual meeting and provided an update on the NCI budget, intergovernmental affairs, new and ongoing activities, and the Research Program Grant (RPG) Pool. Dr. Sharpless informed members that his vision for the NCI, which is forthcoming, should be fully crystalized by the end of the listening tour that he will conclude in March 2018. In his 4 months as NCI Director, Dr. Sharpless observed three clear categories of NCI investment. Category 1 consists of pressing issues that the NCI must do, such as addressing the needs of the NIH Clinical Center and clinical trials infrastructure, both internal and external. Category 2 encompasses additional efforts that the divisions and centers are interested in doing. Category 3 comprises initiatives envisioned for the future and ongoing efforts and commitments, such as multiyear projects that require continued investments. These will be subjects of future discussions with the NCAB.

NCI Budget. Dr. Sharpless reported that the White House Office of Management and Budget (OMB) released the President's proposed appropriations for fiscal year (FY) 2019 and subsequently, an addendum to return $9.2 billion (B) to the NIH. The budget addendum restores NCI funding to the FY 2017 enacted level. Dr. Sharpless reminded members that the release of the President's proposed FY 2019 budget is the first step of the NCI/NIH budget process for the regular appropriations. He noted that Ms. M. K. Holohan, Director, Office of Government and Congressional Relations (OGCR), NCI, will provide details on the FY 2018 budget later in the meeting.

NCI Intergovernmental Affairs. Dr. Sharpless reported on recent visits with U.S. Food and Drug Administration (FDA) Commissioner, Dr. Scott Gottlieb, and Centers for Medicare and Medicaid Services (CMS) Administrator, Ms. Seema Verma. The commitment and interest in data sharing was a crosscutting theme of these meetings, as was both the agencies' enthusiasm for ongoing collaborations with the NCI. The CMS, realizing its strong engagement and long history with the NCI on data sharing, also recognizes a need for enhanced commitments. Dr. Sharpless remarked that the CMS and FDA have accumulated data that are of great interest to the cancer research community and that the NCI is actively discussing with both agencies an appropriately secure mechanism to best make these data publicly available. During his visit to the CMS, Dr. Sharpless also discussed the proposed coverage-related decision regarding next-generation sequencing (NGS) to manage care of cancer patients (i.e., Medicare beneficiaries) with solid tumors of advanced cancer (i.e., metastatic disease). The CMS national coverage

determination process includes a public comment period, after which final results are expected to be released in the coming months.

Dr. Sharpless called attention to ongoing discussions within the NCI on ways to innovatively use manufactured cellular immunotherapy products either at NCI's Frederick National Laboratory for Cancer Research (FNLCR) or within the Intramural Research Program. Cellular immunotherapy biomanufacturing is limited in the extramural community, and the FDA is committed to providing advice to the NCI in the early stages of this process.

Dr. Sharpless informed members of NCI's recent interactions with the U.S. Department of Health and Human Services (HHS) leadership, including Mr. Alex M. Azar, the recently sworn in HHS Secretary; Mr. Eric Hargan, Deputy Secretary; and Dr. Brett Giroir, Assistant Secretary for Health, all of whom have prior experience with cancer research, the NCI, and the NIH. The HHS has expressed interest in and commitment to ensuring that administrative rules and regulations that affect life at the NIH and NCI are not unintentionally burdensome. The NCI is compiling a list of concerns that the HHS might consider addressing.

Dr. Sharpless reported on the ongoing congressional outreach and described a visit with the House Appropriations Subcommittee Chair, Representative Thomas J. Cole of Oklahoma. The Senate NIH Caucus briefing, hosted by co-chairs Senator Dick Durban of Illinois and Senator Lindsay Graham of South Carolina, was held on November 14, 2017. At this briefing, Dr. Sharpless spoke to the advances in cancer immunotherapy research and was joined by Dr. Steven A. Rosenberg, Chief, Surgery Branch, Center for Cancer Research (CCR), and one of his former immunotherapy patients. In addition, Dr. Sharpless, members the Pediatric Oncology and Urology Oncology Branches of the CCR, and more than 20 members of Congress attended the Annual Congressional Reception for the Children's Inn at NIH. On February 17, 2018, Dr. Sharpless and Dr. Barbara Rimer, Chair, President's Cancer Panel, will attend a 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," which is expected to be released to the public in March 2018.

Update on NCI Activities. Dr. Sharpless called attention to the proposal to extend funding for Early Stage Investigators (ESIs) who are R01 recipients, for an additional 2 years, which was discussed at the November 29, 2017 Joint Board of Scientific Advisors/NCAB meeting. He announced NCI's use of the Method to Extend Research in Time (MERIT) Award (R37) as a mechanism to increase funding to ESIs to provide critical time (e.g., after the birth of a child or relocating a laboratory) for ESIs to launch their careers and become more established before having to attempt a grant renewal.

The NCI's Center for Strategic Scientific Initiatives (CSSI), is providing expertise and leadership to support the Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Network. APOLLO is a tri-agency collaboration between the Department of Defense (DoD), the U.S. Department of Veterans Affairs (VA) and the NCI, in which cancer patients within the VA and DoD health systems (e.g., veterans, active duty, and their beneficiaries) and civilians in NCI-designated Cancer Centers give their consent to genomic and proteomic analysis via APOLLO's state-of-the art sequencing, data integration, and adaptive learning health care systems, leveraging the existing VA and DoD electronic health records system. The DoD's Murtha Cancer Center at the Uniformed Services University of the Health Sciences is providing sequencing capabilities.

Members were updated on the newly established NCAB *ad hoc* Global Health, Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR), and Informatics Working Groups. Co-chairs have been identified, member rosters are being completed for the Global Health and SBIR/STTR Working Groups, and the NCI has generated a list of sample questions for these groups to begin addressing. Finalizing the Informatics Working Group membership roster and activities will be

done in parallel with NCI's 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, advise on expanding funding opportunities for data science and bioinformatics research across the NCI, and provide guidance for improving data sharing to maximize the impact of cancer research to patients.

Dr. Sharpless reminded NCAB members that the NCI issued 18 Cancer Moonshot℠ Requests for Applications (RFAs) for FY 2018 that support each of the 10 NCAB Blue Ribbon Panel recommendations, and which can be accessed from the NCI website. The new FY 2019 and reissued FY 2018 RFAs will be up for approval at the June 2018 Joint BSA/NCAB meeting and at the August 2018 NCAB meeting. Dr. Sharpless noted that Dr. Dinah Singer, Acting Deputy Director, NCI, would be available to address any questions related to the Cancer Moonshot℠.

Dr. Sharpless announced that the NCI Experimental Therapeutics (NExT) pipeline will see the first licensing of a compound developed in the program, a high micromolar-potent myeloid cell leukemia 1 (MCL-1) inhibitor developed by Dr. Stephen W. Fesik at Vanderbilt University. The NExT program, which provides investigators with services that extend from drug discovery and target validation to Phase II studies, worked with Dr. Fesik and his team of investigators at Vanderbilt in their efforts to discover subnanomolar inhibitors of MCL-1. To date, investigators have generated low-nanomolar and subnanomolar concentration compounds and a lead compound with favorable pharmacokinetics and pharmacodynamics profiles. They also have licensed a series of clinical candidate compounds to pharmaceutical partners for preclinical studies and optimizations prior to the compounds' being tested in humans. Dr. Sharpless noted that Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, would be able to provide additional details on the success of the NExT program.

Dr. Sharpless reminded NCAB members that the Division of Cancer Epidemiology and Genetics (DCEG) has been interested in various aspects of tobacco control, including cigarette use in the United States, especially of the social smoker or non-daily smoker. He called attention to a recent study led by Dr. Neal D. Freedman, Senior Investigator, Metabolic Epidemiology Branch (MEB), DCEG, investigating the toxicity associated with the episodic intermittent non-daily smoker. The study revealed that the mortality risk for light smokers (e.g., less than one cigarette/day) was significantly higher compared to nonsmokers and was not much lower than the risk for active smokers. These data could potentially affect smoking cessation counseling regarding the intermittent use of other tobacco-related products.

Dr. Sharpless updated members on one of NCI's newer projects: rural cancer control. Recognizing that 14–19 percent of the U.S. population resides in rural (i.e., non-metropolitan) areas and the notable challenges this presents to health care, the NCI and the Division of Cancer Control and Population Sciences (DCCPS) became interested in investigating the disparity of cancer control in rural versus urban patient settings. The research questions being considered are whether living in a rural area is a risk factor for poor outcomes in cancer and what the implications of this cancer disparity are for science, broadly. The NCI is eager to address these questions, has engaged with experts, and has planned and convened several meetings on rural cancer control, including the upcoming Accelerating Research in Rural Cancer Control Conference to be held on May 30–31, 2018, at the NIH. Discussions are ongoing regarding the best use of NCI resources to address cancer disparities in rural areas.

RPG Pool. Dr. Sharpless reported that the RPG pool of investigator-initiated research grants (i.e., R01s, P01s, R21s), which provides the NCI with innovative meritorious science leading to translational discoveries and cures, comprised roughly $2 B of NCI's FY 2017 budget. He called attention to the R01 payline and application trends. The number of unsolicited R01 applications increased from 4,000 in FY 2015 to 5,200 in FY 2017, a trend that is expected to continue in FY 2018. Conversely, the number of R01 awards has remained stable and the funding success rate declined in FY 2017. In addition,

the average R01 award amount has steadily increased in this same period such that the $300 million (M) allotted for new R01s in FY 2017 comprised 60 percent of the RPG pool funding. The NCI has had to increase funding for new (Type 1) and competing (Type 2) awards annually in the RPG pool to support investigator-initiated research, which required concomitant increases to fund the Noncompeting Continuation (Type 5) awards at 100 percent. To continue funding Type 5 awards at 100 percent, maintain favorable paylines, and maintain comparable success rates for new R01s would necessitate the NCI adding $125 M to the RPG pool in FY 2018. Noting that the RPG pool is unlikely to decrease, this investment would limit the flexibility of the NCI to support new ideas. One alternative to increasing RPG funding is to consider a prior practice of reducing the Type 5 awards by 3 to 5 percent, which could make any further decreases in the long-term challenging. The NCI welcomes input from the NCAB on these next steps regarding scientific investments as well as fiscal implications that would be beneficial for the Institute in the current budget climate.

Questions and Answers

Dr. Electra D. Paskett, Marion N. Rowley Professor of Cancer Research, Director, Division of Cancer Prevention and Control, Department of Internal Medicine, College of Medicine, The Ohio State University, pointed out that, per the NCI funding policy, the current reduction in an investigator's R01 award can range up to 20 percent, which places a burden on researchers to complete the proposed work with less staff. She recommended that any decision to discontinue funding the RPG pool awards at 100 percent not be considered in the same timeframe as the current reductions.

IV. LEGISLATIVE REPORT—Ms. M. K. HOLOHAN

Ms. Holohan reported on the federal budget and appropriations process and other legislation of interest. The Senate Committee on Energy and Commerce passed the federal Right to Try legislation, which allows patients with a terminal illness or life-threatening disease or condition to request access to non-FDA-approved experimental treatments, out of committee in August 2017. The House Committee on Energy and Commerce is working with the FDA to resolve differences in opinion. Concerns over patient safety have been voiced by the public and medical and academic groups that opposed to such a legislation have issued precautionary statements.

Ms. Holohan informed members that the NCI/NIH budget process for the regular appropriations process is currently between steps two and three of the four-step process for both the FY 2018 and FY 2019 budgets. The FY 2018 Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies allowance increases funding to the NIH by $2 B and to the NCI by $169 M. The NCI is allotted $400 M through the 21st Century Cures Bill funding, which also is subjected to annual appropriations. Congress is in the process of reconciling and finalizing appropriations for the FY 2018 budget to be sent to the President. Congressional appropriations committees are considering the President's FY 2019 budget proposal, released on February 12, 2018, and OMB is scheduling budget hearings to begin drafting legislation.

Members were reminded that, to date, there have been five continuing resolutions (CR) in FY 2018 and two government shutdowns. Operating under a CR, the NCI remains at the FY 2017 funding level. On February 9, 2018, the President signed into law a 2-year budget agreement that included a CR that funds the government through March 23, 2018. This agreement raises the debt limit; increases the budget spending cap; and during the next 2 years provides funding for certain priority areas, including a $2 B increase for the NIH. This guarantees, but does not cap, the NIH $1 B increases for FY 2018 and FY 2019. The next steps for Congress will be to finalize an FY 2018 omnibus spending bill that considers the new budget caps and priorities.

V. 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 authority to the NCI Director to appoint one or more advisory committees composed of private citizens and officials of Federal, state, and local governments to advise the Director with respect to his or her 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 20th 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 principal investigator (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.

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 RPGs must be given additional consideration.

Motion. A motion to approve the NCI Annual Delegations of Authority was approved unanimously.

VI. NEXT STEPS IN STUDYING THE HUMAN MICROBIOME IN EPIDEMIOLOGIC STUDIES—DR. CHRISTIAN C. ABNET

Dr. Christian C. Abnet, Branch Chief and Senior Investigator, MEB, DCEG, presented DCEG's efforts to optimize biosample collection and standardize protocols to investigate the human microbiome in epidemiological studies. Pre-clinical and clinical studies of the human microbiome have benefited from the advent of such improved methodologies as Next-Generation Sequencing that allowed for new methods of microbial community characterization that previously were limited to culture-based methods.

To facilitate studying the human microbiome in epidemiologic studies, which primarily involves healthy people, development of specific methods is needed, including biosample collection, quality control standards, and new statistical methods. Techniques used in collecting biological samples must be reliable and stable and provide accurate measurement of the microbiome. Methods also should be cost efficient, suitable for multiple platforms, and acceptable for healthy persons' use. Quality control methods will be needed that can evaluate reproducibility across and between studies and facilitate data pooling. Epidemiologists should engage biostatisticians who have experience and that are familiar with compositional data.

Dr. Abnet described a study conducted in collaboration with the Mayo Clinic, Rochester, Minnesota, to optimize fecal sample collection. Fecal samples were collected from study participants in a hospital setting using different collection methods, including freezing them to -80°C without a solution, which was used as the gold standard, or stored in a solution such as RNA*later*® or different concentrations of ethanol. Two methods often used in colorectal cancer screening, the fecal occult blood test (FOBT) card and fecal immunological test (FIT) tube also were evaluated. Evaluation of the technical reproducibility of sample replicates, specimen stability, and concordance/accuracy were calculated for common microbiome metrics from 16S ribosomal RNA (rRNA) gene profiling, which showed that the samples collected in no solution or 75 percent ethanol were the least stable. Sample collection methods were further evaluated using shotgun DNA sequencing and metabolomics, while transcriptomics analyses are in progress. MEB used these studies to develop a plan for collecting and storing reliable fecal and oral samples.

Recognizing that a certified microbiome quality control (QC) standard was not available at the National Institute of Standards and Technology (NIST) or elsewhere, MEB focused on developing such a standard. Three types of QC standards were developed—a synthetic fecal sample generated by a Robogut (i.e., chemostat); generous specimen donors; and an artificial microbial community generated from a single culture of multiple bacterial strains of known quantities—to generate thousands of aliquots for sharing with the epidemiologic community.

Dr. Abnet, Dr. Rashmi Sinha (DCEG, NCI), Dr. Owen White (University of Maryland), Dr. Rob Knight (University of California San Diego), and Dr. Curtis Huttenhower (Harvard University) initiated the Microbiome Quality Control Project (MBQC) to investigate the impact of DNA extraction, PCR amplification, sequencing, and bioinformatics on microbial results. Within the MBQC workflow, fecal samples, chemostat, artificial community, and blanks either were sent raw or were centrally extracted. These samples were randomized, blinded to the end user, and shipped to 15 participating laboratories. Data were uploaded to the NIH Human Microbiome Project data portal and processed by nine bioinformatics laboratories, integrated data analyses were performed, and such data visualizations as ordination plots stratified by specimen type and relative phyla abundance maps were generated. The artificial community samples, which allow an exact read standard, were assessed across participating laboratories using the 16S rRNA assay. Few of the groups reported data that were below the acceptable range, suggesting that this problem could be related to their internal protocols. The baseline study design of the MBQC was published in the December 2015 issue of *Genome Biology*, and final results were published in the November 2017 issue of *Nature Biotechnology*. Findings showed interlaboratory variations, which could be linked to the DNA extraction methods used in each laboratory's protocol, which, if controlled, could improve measurement consistency across labs.

Dr. Abnet called attention to the May 16–17, 2017, workshop entitled "Next Steps in Studying the Human Microbiome and Health in Prospective Studies," sponsored by MEB, DCEG, and the DCCPS's Epidemiology and Genomics Research Program, which brought together epidemiologists interested in studying the human microbiome to discuss the state of the science. A meeting report of the conclusions and recommendations is being finalized. The next step for the MEB, DCEG will be to collect fecal and oral samples in existing cohorts. Dr. Abnet stressed the importance of including QC standards

and method blanks routinely; continuing work on standardizing DNA processing, bioinformatics, and metabolomics platforms; and fostering deeper collaborations and engagements with biostatisticians. Dr. Abnet highlighted DCEG's research portfolio and ongoing projects, including collaborations with the Centers for Disease Control and Prevention on using the National Health and Nutrition Examination Survey data, Yunnan Tin Miners Cohort Study data, Oral Microbiome Case-Cohort Study data, and the meta-analyses of shotgun sequence data for colorectal cancer from five case-control studies.

Questions and Answers

Dr. Deborah Watkins Bruner, Robert W. Woodruff Chair of Nursing, Nell Hodgson Woodruff School of Nursing, Associate Director for Outcomes Research, Winship Cancer Institute, Emory University, noted the concerns regarding QC and the comments in the microbiome research community to use only one laboratory in the United States; she asked whether there would be any guidance forthcoming that would affect the way science in this field is currently conducted. Dr. Abnet recognizes that the community should be made aware of the challenges and understand the role of QC and validation in these types of studies. The DCEG, NCI is not advocating for specific laboratories, but if commercial laboratories offered these services, it would provide an alternative for some groups to obtain benchmarked data. The MBQC data are publicly available, and investigators can request QC standards, samples, and other resources when needed.

Dr. Margaret R. Spitz, Professor, Department of Medicine, Dan L. Duncan Cancer Center, Baylor College of Medicine, wondered whether any thought had been given to studying the metabolites that represent microbiome function and absorption to leverage existing large-scale specimen repositories. Dr. Abnet pointed out that studies addressing microbiome function would be complementary to the current work and that the laboratory is pursing both approaches. Dr. Spitz also asked about the prospects of publishing guidelines on sample collection methods. Dr. Abnet remarked that the MBQC project was a natural history study not designed to validate a single protocol for the 16S rRNA assay. A larger scale study involving multiple different protocols and laboratories would be necessary to establish a consensus protocol and guidelines.

VII. ADJOURNMENT OF OPEN SESSION— DR. ELIZABETH M. JAFFEE

Dr. Jaffee adjourned the open session. Only Board members and designated NCI staff remained for the closed session.

VIII. CLOSED SESSION— DR. ELIZABETH M. JAFFEE

"This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c) (4) 552b(c) (6), Title 5 U.S. code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2)."

The Board was informed that a comprehensive listing of all grant applications to be included in the **en bloc** vote was in the Special Actions package. Those grant applications, as well as those announced during the closed session, could be considered for funding by the Institute.

The NCAB **en bloc** motion to concur with IRG recommendations was unanimously approved. During the closed session, a total of 2,578 NCI applications were reviewed requesting direct cost support of $887,837,814 and 2 FDA applications requesting direct cost support of $292,490.

IX. ADJOURNMENT— DR. DR. ELIZABETH M. JAFFEE

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

There being no further business, the 8th virtual meeting of the NCAB was adjourned at 4:25 p.m. on Tuesday, February 13, 2018.

Date	Elizabeth M. Jaffee, Ph.D., Chair
Date	Paulette S. Gray, Ph.D., Executive Secretary