

Board of Scientific Advisors

Meeting Minutes

March 3-4, 2008

Building 31C, Conference Room 10
Bethesda, Maryland

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The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 39th meeting on Monday, 3 March 2008, at 8:00 a.m. in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Robert C. Young, President, Fox Chase Cancer Center, presided as Chair. The meeting was open to the public from 8:00 a.m. until 5:19 p.m. on 3 March for the NCI Director's report; report on NCI Congressional relations; annual ethics training; annual update on the Clinical Trials Working Group (CTWG), Translational Research Working Group (TRWG), and Clinical Trials Advisory Committee (CTAC); and consideration of request for applications (RFA) new and reissuance concepts presented by NCI program staff. The meeting was open to the public from 8:00 a.m. on 4 March until adjournment at 11:35 a.m. for reports on the Early Detection Research Network (EDRN) and Cancer Care Outcomes Research and Surveillance Consortium (CanCORS).

Board Members Present:

Dr. Robert C. Young (Chair)

Dr. Paul M. Allen

Dr. Christine Ambrosone

Dr. Hoda Anton-Culver

Dr. Kirby I. Bland

Dr. Curt I. Civin

Dr. Susan J. Curry

Dr. William S. Dalton

Dr. Kathleen M. Foley

Dr. Sanjiv S. Gambhir

Dr. Todd R. Golub

Dr. James R. Heath

Board Members Present:

Dr. Ellen Sigal

Dr. Bruce W. Stillman

Dr. Victor J. Strecher

Dr. Jean Y. J. Wang

Dr. Jane Weeks

Dr. Irving L. Weissman

Dr. James K. Willson

Dr. Edith A. Perez

Board Members Absent:

Dr. Michael A. Caligiuri (Ad Hoc)

Dr. Mary J. Hendrix	Dr. Joe W. Gray
Dr. Marc A. Kastner	Dr. William N. Hait
Dr. Timothy Kinsella	Dr. Leland H. Hartwell
Dr. Christopher J. Logothetis	Dr. Leroy Hood
Dr. Kathleen H. Mooney	Dr. Richard L. Schilsky
Dr. James L. Omel	Dr. Robert D. Schreiber
	Dr. Stuart L. Schreiber

Others present: Members of NCI's Executive Committee (EC), NCI staff, members of the extramural community, and press representatives.

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Pediatric Brain Tumor Consortium (RFA/Coop. Agr.)
Office of the Director
SBIR Phase IIB Bridge Award Pilot Program (RFA/Coop.
Agr.)

VIII. Informational Update: The Early Detection Research Network (EDRN); Drs. Peter Greenwald, Sudhir Srivastava, Sam Hanash, Dan Chan, Ian Thompson, Mark Thornquist, and Dan Crichton

Introduction; Dr. Peter Greenwald

Translating Biomarker Discovery to Clinical Application;
Dr. Sudhir Srivastava

Clinically Relevant Biomarker Discovery: EDRN
Biomarker Development; Dr. Sam Hanash

Trust, but Verify: EDRN Reference Laboratories; Dr. Dan Chan

Bringing Discoveries to Clinical Application: Clinical Epidemiology and Validation Centers; Dr. Ian Thompson
Statistical Tool and Research Management; Dr. Mark Thornquist

Connecting Biomarker Research Across EDRN; Dr. Dan Crichton

IX. VII. Status Report: Cancer Care Outcomes Research and Surveillance Consortium (CanCORS); Drs. Rachel Ballard-Barbash, John Z. Ayanian, David P. Harrington, and Craig C. Earle

X. Adjournment; Dr. Robert C. Young

I. CALL TO ORDER AND OPENING REMARKS - DR. ROBERT C. YOUNG

Dr. Young called to order the 39th regular meeting of the BSA and welcomed current and new members of the Board, NIH and NCI staff, guests, and members of the public. Dr. Young reminded Board members of the conflict-of-interest guidelines and confidentiality requirements. He called attention to future Board meeting dates through 2010. Members of the public were invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), in writing and within 10 days, comments regarding items discussed during the meeting.

II. CONSIDERATION OF THE 15–16 NOVEMBER 2007, MEETING MINUTES—DR. ROBERT C. YOUNG

Motion: The minutes of the 15–16 November 2007 meeting were approved unanimously.

III. REPORT OF THE NCI DIRECTOR—DR. JOHN NIEDERHUBER

Dr. John Niederhuber, Director, NCI, welcomed new Board members. He described the importance of reducing the human and economic burden of cancer. A recent health policy forum held by House Speaker, Rep. Nancy Pelosi (D-CA), discussed the impact of the cost of health care on the national economy and the importance of investment in biomedical research as one approach to address rising health care costs. In 2007, more than 1.4 million people were diagnosed with cancer, and more than 500,000 Americans died of the disease. The cancer mortality rate per 1,000 people recently has declined but is expected to increase as there is a swell in the population over 60, which constitutes the bulk of the cancer burden. The estimated number of cancer survivors in the United States in 2007 was nearly 12 million. The NCI's challenge is to fund biomedical research with an ongoing flat budget. of \$4.8 B, which represents a 12 percent loss in purchasing power since 2004 due to inflation.

NCI's FY 2008 Operating Budget. Dr. Niederhuber stated that the FY 2008 appropriation is approximately \$4.8 B, a slight increase of \$7.5 M (+0.16%). Members were told that the President's Budget (PB) for FY 2009 includes an increase of \$4 M (+0.1%) from 2008. He described key categories, including NIH taps and assessments, NCI requirements (e.g., mandated salary increases, etc.), and the NCI Director's reserve. The NCI has continued to work through its budgetary process that included a partial restoration of funds to the Cancer Centers, Special Programs of Research Excellence (SPOREs), and Cooperative Groups.

During this process, NCI leaders evaluated programs with the expectation of reduced or flat budgets in the future, planned for a 3 percent reduction for each Division, Office, and Center, and created a pool of funds for NCI-wide mandatory increases and reallocation for specific initiatives. A careful examination of potential recoveries of funds from closed projects resulted in \$55 M available for new initiatives and restoration of funds for ongoing projects.

The NCI established several policies in developing its operating budget, including the decision that there would be 1 percent inflationary adjustments on non-competing grants and no reductions to modular non-competing research project grants (RPGs). In addition, the NCI would award fewer competing RPGs than in FY 2007 (1,283, down from 1,312) while meeting the NIH-provided target for competing new investigator (R01) grants. Other policies are: Type-2 (competing continuing) grants would receive 3 percent above current levels; Type-2 modular grants recommended for seven modules or fewer would be increased by 5 percent; and Type-1 (new competing) grants would be cut by 17 percent from the level requested and approved by peer review. Based on these policies, it is estimated that R01 paylines will be at the 12th percentile with exceptions; new investigator paylines at the 19th percentile; and very large R01s (i.e., those that request more than \$700,000 in direct costs) at the 14th percentile for the first and second rounds. Other RPG projections include R21 grants at the 14th percentile; R03 at a 210 priority score; R33 at a 155 priority score; and, P01 grants selected on a case-by-case basis.

Dr. Niederhuber provided several examples of downsized and discontinued programs that reflect these policies. He noted that in the Office of Centers, Training, and Resources (OCTR), NCI's support of the co-funded Integrating Aging and Cancer Research project and of the supplements for Imaging Response Assessment Teams in Cancer Centers will not be renewed. In the Division of Cancer Control and Population Sciences (DCCPS), funding is reduced for the Long Term Cancer Survivors Research request for application (RFA), and there is no proposed renewal for the Transdisciplinary Tobacco Use Research Centers (TTURCs) beyond 2008. Instead, the NCI is contributing up to \$4M to a joint NIDA program announcement (PA). Accruals have been reduced over several years in the Division of Cancer Prevention's (DCP) Community Clinical Oncology Program (CCOP) to an estimated

6,100 patients in cancer treatment trials and 4,500 patients in cancer prevention and control trials. In the Division of Cancer Treatment and Diagnosis (DCTD), funds for breast and prostate tissue resources have been eliminated in the Cancer Diagnosis Program and NCI's commitment to the DCTD's Data Resource for Analyzing Blood and Marrow Transplants has also been reduced.

Thoughts About the Future. Dr. Niederhuber announced that Dr. Lynn Matrisian, Vanderbilt University, is working half-time at the NCI to assist with the implementation of the TRWG program to facilitate early translational research progress, including integration with the Coordinating Center for Clinical Trials (CCCT) and plans for the Translational Research Operation Committee (TROC).

In other news in the NCI, changes are occurring in the Office of Centers Training and Resources (OCTR). The Cancer Centers Program will remain in the Office of the Director (OD), but the Organ Systems Branch, which oversees the Specialized Programs of Research Excellence (SPORE) programs, will move to the DCTD. Drs. Niederhuber and James H. Doroshow, Director, DCTD, will oversee the SPOREs and continue monthly teleconference calls with the SPORE Executive Committee. Dr. Toby Tucker Hecht is the acting head during the search for a new SPORE Director. Dr. Jorge Gomez will lead a new initiative to enhance global research and clinical trials participation in Central and South America.

NCI initiatives at the Clinical Research Center include the strengthening of the medical oncology division, recruitment of a new chief for the Laboratory of Pathology, pathology space renovations, and the development of an Oncology Imaging Center. Activities also include the exploration of a satellite center at Suburban Hospital, enhancing fellowship training, and participation in a rare diseases clinic.

An annual translational research meeting will be held during the fall 2008. SPORE investigators and other translational programs will participate in the planning. Dr. Niederhuber also announced plans for the establishment of a Small Business Innovation Research (SBIR) Bridge Award in Drug Development to address the gap between Phase I and II SBIRs, private investment, and subsequent commercialization.

Theoretical Physics Workshop. Dr. Niederhuber informed members that an NCI-sponsored workshop was held in February to explore opportunities to create incentives for collaboration among leaders in physics, chemistry, mathematics, and cancer research. It focused on the complexity of the cancer problem and the cancer micro-environment. Topics included the differences in fibroblasts in connective tissue cells, the diagnosis and prevention of cancer, pharmacogenetics and personalized approach to disease, the effects of new technologies and knowledge on therapy and drug discovery, translation of knowledge from the genome into signal pathways for communication between cells and tissues throughout the body, and, within the body, the effect of chemical gradients, how cells migrate and ultimately transform to disease. Workshop discourses included new conceptual insights into complex systems, experience with modeling computational complexity, the extraction of a signal from confusing noise, salamander limb regeneration, and the adhesion of cells and why metastasized cells come unstuck. He noted that Dr. Paul Davies, Director, Beyond Institute, Arizona State University, a keynote speaker, discussed the technology and complex future of nanotechnology, biotechnology, and quantum technology intersections with cancer. Several small workshops will be organized to further the discussions, and NCI is considering future plans to support research studies in physical sciences in cancer. In closing, a workshop report will be written.

In discussion, the following point was made:

- In response to a member's concern about eliminating the TTURC program, staff commented that the TTURCs may be submitted as program project grants (P01s) in the future and a joint PA with NIDA offers opportunities to continue their research.
- The NCI's new colleagues in mathematics and computer science might be able to assist with mathematical modeling to determine NCI's workforce needs, especially in the area of training. NCI is working with the Health Policy Forum of the Institute of Medicine (IOM) and National Science Foundation (NSF) to look at these issues.
- It is hard to estimate with accuracy the loss of young researchers due to the budget environment and of older researchers in the next 6 to 10 years due to retirement. These losses translate to fewer patients accrued on clinical trials and fewer researchers actively working in the field.

- A copy of the February 2008 NCI Theoretical Physics Workshop report should be disseminated to BSA members when it is available.

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IV. NCI/CONGRESSIONAL RELATIONS - MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Government and Congressional Relation (OGCR), reported on the FY 2008 and 2009 appropriations status, reviewed legislation of interest to the NCI, and described the outlook for the 2nd Session of the 110th Congress. She provided an overview of the Pediatric, Adolescent, and Young Adult Cancer Survivorship Research and Quality of Life Act.

Ms. Erickson referred Board members to the updated OGCR Web Site (<http://legislative.cancer.gov>) for further information on legislative activities.

In discussion, the following point were made:

- A comprehensive health bill is being developed by Sen. Edward Kennedy (D-MA) and Sen. Kay Bailey Hutchinson (R-TX) with plans for hearings next year.

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V. ANNUAL ETHICS TRAINING—DR. MAUREEN WILSON

Dr. Maureen Wilson, Deputy Ethics Counselor, OD, provided an update on ethics issues for Federal Advisory Committee members. Per 18 USC Section 208, Conflict of Interest, committee members may not participate personally and substantially in a particular matter in which the member has a personal or imputed financial interest if the matter will have a direct and predictable effect on that interest. Statutory waivers may be granted under 18 USC Section 208(b)(3) to participate in general matters, but not in matters

affecting their financial interests.

Standards of conduct for Board members include matters that are not statutory conflicts of interest but would raise a question regarding the special government employee's impartiality in the matter. Remedies for conflict of interest issues include waivers, authorization, recusal, and divestiture. There also are limitations on the acceptance of gifts from foreign governments. Compensation is prohibited if the activity relates to official duties.

Dr. Wilson described Board members' responsibilities regarding representation. Dr. Wilson also described other rules under Sections 203, 205, and 207 that clarify matters of compensation, post employment, gifts, testimony, and charity.

Members were told that appropriated funds cannot be used in lobbying. When authorized, they may engage in educational activities relating to a policy or legislative proposal; they also may communicate to members of Congress at the request of Congress. Dr. Wilson asked that all official BSA communications to Congress be coordinated through the NCI's OGCR. She encouraged Board members to contact her with any ethical questions or concerns.

In discussion, the following points were made:

- The regulations govern only those sector funds with a stated policy of investment in health care, devices, and drugs, and affects Board members who discuss or vote on a related topic, such as a specific RFA or the development of a research marker program.
- II. Prior to a BSA meeting, Drs. Wilson and Gray will determine if a member of the Board falls within a category that might preclude that member from the Board's discussion of a topic.

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**COMMITTEE (CTAC)—DRS. SHEILA A. PRINDIVILLE,
KENNETH H. BUETOW, JAMES H. DOROSHOW, AND
LYNN MATRISIAN**

CTAC and Prioritization Update—Dr. Sheila A. Prindiville

Dr. Prindiville introduced the CTAC, which provides the extramural oversight for implementation of CTWG initiatives. Structurally, the CTAC has two active subcommittees (ad hoc Coordination, and ad hoc Public-Private Partnership) and two proposed subcommittees (Evaluation, and Operational Efficiency). The Coordination Subcommittee currently is harmonizing program guidelines among Cancer Centers, SPOREs, and Cooperative Groups to enhance clinical trials collaboration. The Public-Private Partnership Subcommittee provides extramural oversight for the collaborative project – with the Life Sciences Consortium of the CEO Roundtable – to standardize clinical trial agreement terms. The Operational Efficiency Working Group will focus on results, recommendations, and strategies to overcome barriers to the timely activation of Phase III clinical trials.

Dr. Prindiville provided an update on the CTAC steering committees formed for prioritization of clinical trials. The Investigational Drug Steering Committee (IDSC) provides strategic input into NCI's clinical development plans for new agents. Task forces are working in signal transduction, biomarkers, angiogenesis, and clinical trial design. The IDSC has 1) increased transparency in NCI's drug development processes, 2) provided strategic review of NCI's early phase clinical trials, and recommended a Career Development Letter of Interest (LOI) program to engage young clinical investigators in NCI early phase clinical trials.

Disease-Specific Steering Committees (DSSCs) are focused on prioritizing large Phase II trials and all Phase III concepts, convening state-of-the-science (SOTS) meetings, developing Phase II and III concepts for new trials, and reviewing accrual and unforeseen implementation issues. The current committees are: Gastrointestinal (GI) Cancer, Gynecological (GYN) Cancer, Head and Neck (H&N) Cancer, and Symptom Management and Health-

Related QOL (SxQOL). The GI Steering Committee has reviewed 8 concepts, 4 of which are approved or near approval, and convened a pancreas SOTS meeting. The GYN Steering Committee has reviewed 15 concepts, 9 of which are approved or near approval, and convened a cervical cancer SOTS meeting. The H&N Steering Committee has identified four task forces addressing metastatic/recurrent disease, rare tumors, previously untreated and locally advanced, and tumor biology and imaging. The SxQOL Steering Committee has developed a plan to evaluate and prioritize symptom management concepts and developed prioritization criteria for SxQOL studies that are eligible for supplemental funding. Genitourinary and Lung & Mesothelioma Steering Committees will be launched in 2008, and a Patient Advocate Steering Committee is being formed in collaboration with the Office of Advocacy Relations.

Dr. Prindiville described another initiative involving the establishment of a funding mechanism to promote correlative science and QOL studies in association with Phase III trials. Criteria have been developed and the announcement for availability of administrative supplements through the Cooperative Group program as well as the CCOP research bases was made in December 2007. These studies will be reviewed by scientific steering committees, if established, or Cancer Therapy Evaluation Program (CTEP) and DCP staff, who will make recommendations to the CTOC.

In discussion, the following points were made:

- The NCI's efforts in QOL and imaging should include participation from the FDA, particularly regarding the development of endpoints and surrogate endpoints for clinical trials. NCI is working with the FDA in the implementation of biomarker studies linked to clinical trials.
- In addition to the IDSC, the involvement of biologics experts in the IDSCs who understand T-cell therapies would be beneficial to clinical trials and translational research.
- Appropriate individuals focused on surrogate endpoints with imaging agents are necessary during the early developmental stages and on the IDSC. Additionally, representation from the imaging community to link endpoints to clinical trials in earlier phases should be included.

Informatics—Dr. Kenneth H. Buetow

Dr. Kenneth H. Buetow, Director, Center for Biomedical Informatics and Information Technology, NCI, said that informatics initiatives that are relevant to CTWG include: a clinical trials database, interoperability of a National Clinical Trial Information Technology Infrastructure system with caBIG?, standardized case report forms, and an investigator and site credentials repository. The clinical trials database serves as a single source for access to transparent information about NCI-supported trials. The workflow for the database includes the trial submitter registering with the NCI Clinical Trials Data Portal and the registration of the trial. The protocol is abstracted from this information to support querying and reporting, patient-level data are submitted via the web, and comprehensive accrual data are accessible via the clinical data system (CDS) analysis and reporting module. The NCI Clinical Trials Data Portal is in place and is currently in the testing phase.

Next steps are to assemble NCI Policy Implementation Teams to address “legacy” data migration, protocol abstraction, and quality control/quality assurance, as well as to ensure the generation of reports and <http://ClinicalTrials.gov> submissions. Reporting is required for interventional trials only, and registration is not required for trials already reporting to CTEP/DCP. Reporting for NCI-sponsored trials will occur at the PI level, but at the site level for non-NCI-sponsored trials. As of January 1, 2009, all new trials will be reported within 21 days after activation, with all active trials entered by June 2009.

The NCI is creating educational documents and informational Web sites for grantees, and will pilot the process at 5 to 10 sites starting in July 2008. Outcome reporting will be piloted beginning in January 2010. Adverse effects and outcomes must be reported to the NIH as mandated by Public Law 110-85, the FDA Amendments Act. All clinical trials need to be reported as of December 2008 at <http://ClinicalTrials.gov> per statutory requirement.

In the discussion, the following points were made:

- The process of harmonizing clinical trials data management and retrieval is important for the NCI and cancer community. The NCI is committed to dialogue and collaboration with all relevant parties to create national standards that will support oncology clinical trials and will help prevent separate information technology (IT) silos.
- The clinical trials database may be an opportunity to address release of negative results as well as positive results, and productivity issues.
- Early involvement of the Surveillance, Epidemiology, and End Results (SEER) program in this effort is encouraged, as information from cancer registries will be needed in the examination of population-based survivorship. IX. The follow-up of individual patients through time as they are enrolled on different trials will be an important feature while building an informatics capability to collect outcomes.
- EDRN clinical validation studies would be incorporated if they are defined as interventional trials. Most current EDRN validation trials are contained at the level of laboratory validation.
- There will be a linkage and sharing between the clinical database and biospecimen collection and repository at an institutional level. However, NCI cannot share this information without the consent and approval from appropriate institutional review boards (IRBs) and individuals. This would require an upfront consent from the patient.

Operational Efficiency and CTWG Baseline Evaluation Results —Dr. James H. Doroshov

Operational Efficiency. Dr. Doroshov presented an analysis of the protocol and clinical trial review and approval process using data gathered from Cancer Centers and Cooperative Groups by Drs. David Dilts and Alan Sandler, Vanderbilt University. He stated they observed at three Comprehensive Cancer Centers, and that it takes approximately 200 steps to activate an investigator-initiated trial. For Phase III cooperative group trials, it takes an average of 800 days from the initial study idea to the time that the study is

ready to be initiated, and another 3 to 6 months to begin the trial. A clinical trial might not be relevant if it takes 3 years to open. Another issue is the accrual of patients to clinical trials, with 50 to 60 percent of all the trials at these Cancer Centers accruing fewer than five patients, and one quarter accruing no patients.

Members were informed that the Dilts report recommendations for improvement are to: 1) collect and analyze clinical trials data on activation and accrual; 2) eliminate entitlement culture by refusing to fund some trials; and, 3) allow investigators to make changes after IRB approval. Long-term recommendations are to develop standard administrative processes and use focused Phase III teams. The next step is to charge a CTAC working group to develop recommendations toward cutting clinical trial activation time in half.

CTWG Baseline Evaluation Results. NCI has never previously performed a systematic evaluation of the NCI clinical trials system that integrates qualitative and quantitative information. Dr. Doroshov presented the results of a baseline feasibility analysis using system outcome measures and performance. In addition, an expert panel helped to develop measures and interview guides.

System outcome measures would include the evaluation of the quality of trials through publications, with the recommendation to include a new, publications field in clinical trials databases. To measure the impact of the trials on patient management, the number of plenary session presentations at American Society of Clinical Oncology's (ASCO) annual meetings would be measured or annual Journal of Clinical Oncology (JCO) article publications would assess impact.

Regarding coordination, the baseline study reported almost no incentives to promote collaborations among Cancer Centers and P01 grantees while strong incentives exist for collaborations across Cooperative Groups and SPOREs. Future goals of the IDSC and Scientific Steering Committees include developing recommendations that would enhance transparency and quality of trial concepts.

Dr. Doroshov stated that the accrual efficiency of Phase III trials was low, with two-thirds of all patients coming from 16 percent of

the institutions. Thus, next steps for the evaluation plan include: 1) developing a specific plan for future evaluation; 2) refining baseline measures and developing protocols for future measures; 3) incorporating additional information in clinical trials databases to strengthen future evaluation efforts; 4) preparing initiative-specific timelines for future evaluations; and, 5) formation of a CTAC subcommittee to oversee the evaluation process.

In the discussion, the following points were made:

- Perhaps consideration should be given to alternative designs for cooperative groups. The National Heart, Lung, and Blood Institute (NHLBI), for example, has a model that forms a group around a specific question.
- An update on approved protocols from the Disease Steering Committees, including accrual, should be given at future meetings.
- A timeline for addressing fundamental issues in the clinical trials initiation process should be given at a future meeting.
- Following a discussion of the need for a central agreement that is approved by IRBs, staff indicated that within a year, NCI will have ready for distribution an evaluation of whether central IRBs save money.
- The NCI intends to publish a menu of new Phase II trial designs that are drawn from recommendations of leaders in the field and implement them in NCI-sponsored investigational trials.
- In the focus on specific centers that are able to do more in less time, the NCI should be thoughtful about the characteristics of representative centers so that what is learned can be generalized beyond a small sample of centers.

TRWG Report Implementation—Dr. Lynn Matrisian

Dr. Matrisian informed members that plans based on recommendations in the TRWG report, *Transforming Translation: Harnessing Discovery Research for Patient and Public Benefit*, involve expanding the mission of the CTAC to become the Clinical and Translational Advisory Committee, expanding the mission of the internal NCI clinical trials operating committee to involve

translational research, and building on the resources within the Coordinating Center for Clinical Trials to encompass the duties that were assigned to the translational research support office. Future initiatives include: 1) ascertaining how NCI's coding processes can identify grants as translational; 2) creating a prioritization process to identify those translational ideas that need resources for development; 3) modifying some of the award guidelines to help accelerate the translational research process; and, 4) coordinating core services across award mechanisms and institutions for more efficient use.

In the discussion, the following point was made:

- Concern was expressed about practices of tissue banking that impeded viable cell banks of cancer samples. Staff noted that the concerted efforts have been made during the past 6 years on this issue, such as the development of guidelines and best practices.

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**VII. RFA/COOPERATIVE AGREEMENT CONCEPTS -
PRESENTED BY NCI PROGRAM STAFF**

Division of Cancer Control and Population Sciences

**Increasing Smoking Cessation in Low Income Adult
Populations (RFA)**

Dr. Erik Augustson, Tobacco Control Research Branch (TCRB), NCI, stated that the purpose of the Smoking Cessation RFA is to: 1) promote innovative research to increase smoking cessation in low-income adults; 2) develop and test novel treatment approaches for smoking cessation in low-income adults; and, 3) better understand the impact of barriers to treatment and how to address them. The RFA addresses the problem that high smoking prevalence rates and low rates of successful cessation are directly associated with low socioeconomic status. In addition, observational data indicate a trend toward earlier smoking initiation

and more obstacles to seeking and engaging in treatment among this group.

Potential research questions include novel treatment approaches to increase cessation among low-income smokers, ways to personalize or modify cessation treatments for greater efficacy, what modifications to existing treatment can overcome barriers, and the use of social and other contextual variables to enhance smoking cessation success. Possible evaluation criteria would rely on statistically significant differences between control and experimental conditions to demonstrate the means to improve smoking cessation and the improvement of treatment engagement via interventions funded by the initiative.

The scope of this project will include treatment development and pilot projects, as well as randomized clinical trials, through R01 and R21 mechanisms.

Subcommittee Review. Dr. Susan Curry, Director, Institute for Health Research and Policy, University of Illinois at Chicago, indicated strong support of the concept, and noted its translational focus and commitment to addressing disparities and reducing the cancer burden. The Subcommittee congratulated the team for a well-justified proposal. Dr. Curry stated that Dr. Augustson addressed well how success would be evaluated and how this RFA would interrelate with the RFA on smokeless tobacco use through joint meetings. She informed members that the subcommittee recommendations for the RFA included: emphasizing the importance of development, testing, and particularly the evaluation of interventions that would be both feasible and sustainable in this population; and, giving adequate consideration to more general applications that support smoking cessation as part of a healthier lifestyle.

The first year cost is estimated at \$3.5 M for 8-10 awards and a total cost of \$17 M for 5 years.

In the discussion, the following points were made:

- Strong consideration should be given to including wording in the RFA that specifies intervention as the focus, rather than validation of the smoking cessation problem.

- Criteria to define the low-income population for this study should be included.
- Criteria to measure the proportion of study subjects who continue treatment to gauge program success should be included in the RFA. A section on feasibility and dissemination should also be required.
- Consideration should be given to establishing collaboration with other federal agencies that currently provide systematic care to low-income populations. Additionally, funding partnerships for this endeavor should be pursued to lessen the burden on NCI or perhaps expand the studies.
- In the future, the RFA concept analysis should include how many applications were submitted, but not funded, as well as those funded.

Motion. A motion to concur on the Division of Cancer Control and Population Sciences' (DCCPS) Request for Application (RFA) entitled "Increasing Smoking Cessation in Low Income Adult Populations" was approved unanimously.

Measures and Determinants of Smokeless Tobacco Use Prevention and Cessation (RFA)

Dr. Mark Parascandola, TCRB, NCI, informed members that the purpose of the Measures and Determinants of Smokeless Tobacco (ST) Use Prevention and Cessation concept is to: 1) understand the progression to ST use and its relationship to other tobacco use; 2) identify and evaluate factors that mediate initiation and use of ST in high-risk populations; 3) develop and apply methods for characterizing the properties of a range of ST products and related behaviors; and, 4) encourage new and experienced tobacco researchers to focus on ST.

The use of ST products is rising among both U.S. adults and high school students. Challenges include aggressive ST product marketing; lack of effective pharmaceuticals for ST cessation; and, limited behavioral counseling methods.

Research has identified more than 28 carcinogens in ST and has shown that ST causes oral and pancreatic cancers. ST use is higher

among adolescents and may occur with the initiation of cigarette smoking. More research is needed to determine the overall public health impact of ST use, determinants of initiation and use in high-risk groups, best measures of ST use and behavior, and impact of new product marketing on prevalence. Evaluation parameters for measuring the success of the RFA could include the number of new applications received, identification of four or more key determinants of ST use in high-risk groups, support of studies to determine whether ST leads to smoking among youth and young adults, and the development of two or more measures of ST use and exposure.

Subcommittee Review. Dr. Christine Ambrosone, Chair, Department of Cancer Prevention and Control, Roswell Park Cancer Institute, told members that the Subcommittee concurred with re-issuance of the concept's intent to explore and identify the extent and impact of the problem with ST use, and suggested incorporating interventions when the evidence base and natural history are established. She noted that there are subgroups, such as Alaskan natives and their use of Iqmik, that warrant study and good interventions. It was suggested that the emphasis be placed on intervention research rather than observational studies.

The first year cost is estimated at \$2.5 M for 8-10 awards and a total cost of \$10 M for 4 years.

In the discussion, the following points were made:

- Evidence from these observational studies will be a critical tool for developing a science base that can inform future policies on tobacco marketing and will be as important as intervention initiatives.
- The RFA scope of work should be carefully written to discourage applications that focus on confirming existing knowledge.
- The NCI may want to consider involving its media relations office to highlight the funds being spent by the tobacco industry to promote ST products.
- This research should also examine the public health impact based on which ST products are being used, how they are being used, and their individual properties.

Motion. A motion to concur with the re-issuance of DCCPS' RFA entitled "Measures and Determinants of Smokeless Tobacco Use Prevention and Cessation" was approved unanimously.

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Division of Cancer Treatment and Diagnosis

Cancer Disparities Research Partnership Program (RFA/Coop. Agr.)

Dr. C. Norman Coleman, Radiation Research Program, NCI, said that the DCTD's Cancer Disparities Research Partnership (CDRP) Program is a pilot program for community-based institutions new to NCI clinical research. Dr. Norman stated that the program's focus is on disparity populations and uses radiotherapy treatment protocols, mentoring/education facilitated through Telesynergy®, community outreach/patient navigation as key components for patient recruitment, and dedicated principal investigators (PIs) at community-based hospitals.

Through September 2007, more than 9,000 patients have been enrolled throughout CDRP sites. Research activities encompass surveys, assessments, evaluations; behavioral interventions, patterns of health care service utilization; patient navigation; and clinical trials. Clinical research includes investigator-initiated trials, as well as Radiation Therapy Oncology Group (RTOG), cooperative groups, and industry trials. Proposed steps to increase clinical trial accrual include: 1) increasing the number of RTOG trials and activating other cooperative group trials; 2) enhancing connectivity to the SPORES program; 3) increasing new patient screening; 4) working with local physicians to define trials of interest, 5) developing a comprehensive, publicly accessible clinical trials database; and, 6) enhancing program infrastructure to encourage physician participation.

Lessons learned thus far indicate a need for target population-appropriate research; a minimum of one radiation oncologist plus

involvement of an additional oncologist; and, additional time for infrastructure development and more formal orientation. In addition, support is needed for patient navigation and community outreach efforts prior to clinical research recruitment, and continued and expanded support is needed for current competing grantees for the next five years.

Subcommittee Review. Dr. Kirby Bland, Deputy Director, Comprehensive Cancer Center, University of Alabama at Birmingham, indicated support on behalf of the subcommittee for re-issuance of a well written letter RFA. Dr. Bland stated that the subcommittee had concerns about differences in accrual rates among the sites and suggested that the use of Telesynergy® be expanded since intra-communication may be efficient in promoting mentorship and reducing disparity for sites located in more remote areas.

The first year cost is estimated at \$4.2 M for 5 awards and a total cost of \$14.5 M for 5 years.

In the discussion, the following points were made:

- A concern was expressed about conducting this study with research dollars when the goals seemed to be more in line with public health activities. The study approach should be modified to clearly state research goals.
- Family physicians should serve as co-PIs in the next phase. Sustained relationships with current mentors and other related groups are needed.
- With one site dropping out of the study and limited success from other sites, consideration should be given to processes that ensure sustainability of the clinical trials programs in the next phase.
- Strategies should be developed for transferring the burden of the patient navigator system to existing community-based delivery systems, such as family physicians and local social services.
- Treatment should be expanded beyond radiation-oncology with this program.
- Accrual benchmarks and more consistent data collection efforts, including measurements of changes in the culture of the physicians and patients and the impact of tele-medicine, should be developed for better evaluations.

Motion. A motion to concur on the re-issuance of the Division of Cancer Treatment and Diagnosis' (DCTD) RFA/Cooperative Agreement entitled "Cancer Disparities Research Partnership Program" was amended in discussion to defer approval and form a BSA Subcommittee (Dr. Kirby Bland (chair), Kathleen Mooney, Timothy Kinsella, and James Willson) to work with staff to resolve issues about the concept's structure and goals. The motion was approved with 20 yeas, 4 nays, and no abstentions.

Pediatric Brain Tumor Consortium (PBTC) (RFA/Coop. Agr. Reissuance)

Dr. Malcolm A. Smith, CTEP, NCI, informed members that the PBTC includes 10 academic centers and children's hospitals, with a focus on novel treatment strategies for children with brain tumors through Phase I and II clinical trials. The Operations and Biostatistics Center at St. Jude Children's Research Hospital coordinates the PBTC's research efforts, and a relationship with the Children's Oncology Group (COG) is maintained to ensure that promising results can be further developed through COG. Challenges include devastating neuropsychological sequelae in some survivors; poor outcome for children with ependymoma; and guarded outcome for children with disseminated medulloblastoma and for infants/young children with nondesmoplastic medulloblastoma.

Dr. Smith noted that PBTC progress includes meeting accrual benchmarks; spearheading efforts at directed therapies and intraventricular and intrathecal therapies; developing signal transduction inhibitor agents, and, setting antiangiogenesis agents in the brain tumor population. The Neuroimaging Center has completed 2,300 brain Magnetic resonance imaging (MRI) studies, 1,500 MR perfusion studies, 1,600 MR diffusion studies, 1,200 MR spectroscopy studies, 895 spine MRI studies, and 409 PET studies. PBTC has been involved in caBIGTM imaging workspace meetings and also completed a pilot project to begin integrating its images into the National Cancer Image Archive (NCIA) system.

The PBTC's future plans are to: 1) identify specific populations

and design targeted therapies and an expanded focus on molecular biology and the treatment of brain stem gliomas; and, 2) cover the budget deficit with a co-sponsorship approved by the National Institute of Neurological Disorders and Stroke (NINDS) (\$200,000 per year), and a potential decrease in work scope.

Proposed evaluation criteria include: 1) adequate clinical trial development, with appropriate protocol development timelines and patient accrual; 2) appropriate incorporation of pharmacokinetic (PK) and translational biology studies into Consortium trials; 3) incorporation of state-of-the-art imaging studies and neurosurgical expertise; and, 4) the use of caBIG™ -compatible systems for the management of PBTC clinical and imaging data.

Subcommittee Review. Dr. Curt Civin, Professor of Pediatrics, The Johns Hopkins University School of Medicine, indicated strong support for continuation of this RFA and felt that the PBTC will make unique use of new molecular medicine and apply it in the next phase. The Subcommittee concurred with the re-issuance's focus on molecular biology and advocated the benefit of pursuing molecular biology synergies with other NCI programs.

The first year cost is estimated at \$2 M for and a total cost of \$10.8 M for 5 years.

In the discussion, the following points were made:

- The process of recompetition through the letter RFA mechanism among a limited number of eligible institutions is a concern. Consideration should be given to allowing both new domestic and international institutions to compete.
- Alternative funding mechanisms, such as P01s or through the cooperative group mechanism to support the PBTC should be considered.
- NCI is encouraged to restructure the program approach to allow for increased molecularly targeted studies, collaborations and data- and specimen-sharing with other institutions and investigators, and the review of research ideas from outside investigators for possible inclusion in PBTC studies.
- A national repository for distribution of rare tumor tissues, including viable frozen cell suspensions, is needed. The

COG may be appropriate for pediatric tumors since they see newly diagnosis patients.

Motion. A motion to concur on the re-issuance of DCTD’s RFA/ Cooperative Agreement entitled “Pediatric Brain Tumor Consortium” was approved unanimously.

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Office of the Director

SBIR Phase IIB Bridge Award Pilot Program (RFA/Coop. Agr.)

Mr. Michael Weingarten, SBIR Program Director, provided an informational overview of Small Business Innovation Research (SBIR) program enhancements at the NCI. Mr. Weingarten informed members that the SBIR and Small Business Technology Transfer (STTR) programs are major NIH resources for technology commercialization of research tools, medical devices, and therapeutics with a set aside of \$650 M across NIH. He stated that SBIR recommendations for program enhancements include: 1) establishing the NCI SBIR Development Center; 2) focusing solicitations on commercially viable technologies; 3) co-investing with the private sector to bridge SBIR projects toward commercialization; and 4) assembling an external SBIR Advisory Committee. NCI is proceeding with these recommendations and collaborating with interested Institutes and Centers (ICs).

Members were told that the management of the SBIR program would be overseen within the new Development Center, i.e., one center organized around new teams with appropriate scientific and business expertise. Center activities will include 1) marketing the program to attract the best companies; 2) integrating all NCI SBIR initiatives; 3) building relationships with stakeholders; and, 4) focusing solicitations on commercially viable technologies with a strategic shift towards focused contract topics.

He stated that the SBIR Phase IIB Bridge Award is a follow-on award to the SBIR Phase II award and the goal is to co-invest with the private sector by facilitating partnerships. The Phase IIB pilot will focus on cancer therapeutics and cancer imaging. Costs will be covered by NCI SBIR set-aside dollars and a minimum one-to-one match from the investor(s). Third-party investors are expected to provide rigorous commercialization due diligence and guidance during the award, and additional financing beyond the initial matching funds.

The initial RFA will use the cooperative agreement mechanism and fund up to 10 awards in FY08/09 with a \$10 M set-aside, and projected cost of \$30 M over 3 years. The NCI intends to fund 20 additional awards in FY10 and FY11 with a comprehensive outcomes assessment conducted after 3 years.

Subcommittee Review. Dr. Sanjiv Gambhir, Director, Stanford Molecular Imaging Program, indicated that the subcommittee agreed with the intent of the program's goals. Dr. Gambhir reported that the subcommittee wondered whether the NIH might capture a partial return on intellectual property (IP) developed through the program.

In the discussion, the following points were made:

- The NCI was encouraged to consider not requiring matching funds until the application is approved for funding. Instead, awards would be dependent upon receipt of proof of matching funds. A reverse site visit should also be considered as part of the review process.
- The study sections reviewing applications should have the appropriate technology development and small business commercialization expertise.

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VIII. UPDATE: THE EARLY DETECTION RESEARCH NETWORK (EDRN)—DRS. PETER GREENWALD, SUDHIR SRIVASTAVA, SAM HANASH, DAN CHAN, IAN THOMPSON, MARK THORNQUIST, AND DAN

CRICHTON

Introduction—Dr. Peter Greenwald

Dr. Greenwald, Director, DCP, NCI, opened the EDRN session and stated that the focus would be on discovery and validation of biomarkers. Dr. Sudhir Srivastava, Chief, Cancer Biomarkers Research Group, introduced the speakers: Drs. Sam Hanash, Fred Hutchinson Cancer Research Center; Daniel W. Chan, Johns Hopkins University; Ian Thompson, University of Texas Health Science Center; Mark Thornquist, Fred Hutchinson Cancer Research and Daniel Crichton, Jet Propulsion Laboratory, California Institute of Technology.

Translating Biomarker Discovery to Clinical Application—Dr. Sudhir Srivastava

Dr. Srivastava described the goals of the EDRN, which are to: 1) discover, develop, and validate biomarkers for cancer detection, diagnosis, and risk assessment; 2) conduct correlative studies/trials to validate biomarkers as indicators of early cancer, pre-invasive cancer, risk, or as surrogate endpoints; 3) develop quality assurance programs for biomarker testing and evaluation; and, 4) forge public-private partnerships. The EDRN is an investigator-driven consortium with a unique infrastructure for supporting collaborative research on molecular, genetic, and other biomarkers in human cancer detection and risk assessment. The management structure contains collaborative groups organized around organ sites.

Seminal discovery examples include: gene fusion in prostate cancer; translocation in bladder cancer; epigenomics as biomarkers for lung, pancreatic, ovarian, and prostate cancers; foundational studies on proteomics as diagnostic markers; and, mitochondrial mutations as cancer biomarkers. The EDRN has more than 127 biomarkers in Phase I and II studies; 15 biomarkers will be transitioning to Phase III, and 5 are in Phase III. TRWG-supported Risk Device Pathways are already being supported by the EDRN, and a number of

biomarker tests will be ready for submission to the FDA.

Clinically Relevant Biomarker Discovery: EDRN Biomarker Development—Dr. Sam Hanash

Dr. Hanash described EDRN's biomarker development activities, which include collaborative work within and outside EDRN laboratories. He outlined the challenges involved with developing clinically relevant biomarkers and discussed two studies that have progressed from discovery to blinded validation in the context of early detection.

The first study is based on auto antibodies, which occur early during tumor development and may provide a means to early cancer detection. A blinded validation study was developed to test whether annexin had utility for early diagnosis of lung cancer. Samples from the Beta Carotene and Retinol Efficacy Trial (CARET) study were microarrayed and initial results showed auto antibodies in 30 percent of cases collected one year prior to diagnosis of lung cancer. The next step is to augment computed tomography (CT) scans with blood tests for these same antigens in a Phase II blinded validation study.

A second study used a mouse pancreatic cancer model with K-ras activation and Ink/Arf inactivation to isolate 54 potential markers by proteomic analysis. A panel of these markers were compared to CA19.9, the standard pancreatic marker in humans, using 13 matched controls from the CARET study and showed improvement in specificity and sensitivity between cancer and controls.

Dr. Hanash also described a discovery study with the NHLBI and the Women's Health Initiative (WHI) to identify colon cancer markers with a 10-member consortium. The findings showed that the identified proteins that were upregulated approximately one year prior to diagnosis of colon cancer were associated with the cancer disease process, including the TGF beta pathway. The next step in this research is to conduct validation studies with an independent set of samples from the WHI cohort.

EDRN has leveraged resources from the Lustgarten Foundation to

fund antibody development using the most promising pancreatic cancer markers from the mouse model study. In addition, the Avon Foundation, and the Canary Foundation are collaborating with EDRN on lung and breast cancer.

In the discussion, the following points were made:

- EDRN takes steps to canvass the field on existing biomarkers to avoid duplication of efforts and encourages investigators to work with EDRN towards validation.

Trust, but Verify: EDRN Reference Laboratories—Dr. Dan Chan

Dr. Chan explained that the EDRN biomarker reference laboratories serve as a resource for clinical and laboratory validation of biomarkers, including technology development and standardization of assay methods and refinement. Many potential biomarkers exist, but challenges include identifying those for translation to the clinical setting and selecting the right technologies to validate them. Dr. Chan described the method for selection of biomarkers for prevalidation studies. An EDRN committee met and classified biomarkers in terms of discovery phase, validation phase, or clinical trial phase, with the top five markers are selected for blinded prevalidation studies. Validation of a pro-form of prostate-specific antigen (PSA), which is one molecular form of free-PSA, led to a public-private partnership between the EDRN and Beckman-Coulter to begin multicenter clinical trials in March 2008. Another biomarker, PCA3, is also being validated for prostate cancer diagnosis.

EDRN reference laboratories have set up proteomic standards to achieve high accuracy and consistent results, and to diagnose clinical conditions correctly. Dr. Chan presented reference standards that were developed using a complex mixture of serum and plasma enriched with cancer biomarkers. He noted that multiplexing will be important in the future, and that the EDRN is exploring and developing new technologies, working together with industry, and is in a unique position to make significant impacts on biomarker discovery, validation, and the rapid translation of cancer

biomarkers into clinical practices.

In the discussion, the following points were made:

- Clarification is needed as to whether serum proteomics has been demonstrated as a good source for biomarker discovery in cancer research.
- Behavioral indicators, including diet, could be explored for possible links to some of the cancer markers.

Bringing Discoveries to Clinical Application: Clinical Epidemiology and Validation Centers—Dr. Ian Thompson

Dr. Thompson, in an overview of the Clinical Epidemiology and Validations Centers, stated that epidemiologists and biostatisticians are needed to fully translate analysis findings, mitigate bias, and select appropriate populations for discovery and validation. He presented examples that showed how the genitourinary (GU) group functions within the EDRN including the investigation of surface-enhanced laser desorption ionization (SELDI) technology, and the prioritization process for selecting biomarkers and developing standard reference sets. Dr. Thompson also reviewed the lessons learned from their studies. He noted that control samples must be carefully selected and fully ascertained to include other cancers and/or inflammation (nonspecific markers of disease). Sample size must be sufficient to reach clinically meaningful decisions, and biological issues related to the tumor diagnosed should be included in the analysis.

Dr. Thompson described the development of a standardized reference set for use in GU studies. Members were told that a risk assessment tool for physicians was developed that integrated available biomarkers with other factors to predict the likelihood of cancer. The promising new biomarker, PCA3, increases the ability of the tool to determine risk. Other validation studies in ovarian cancer, lung cancer, and colorectal cancer are in progress or planned.

In the discussion, the following points were made:

- Focus on enhancement of existing strategies is a concern. The EDRN should focus on exploring new biomarkers for unmet needs; however, integrating other biomeasures may be necessary to refine individualized risk assessments.
- A process is in place for progressing from discovery to validation, which includes the entire EDRN structure, not just validation laboratories.
- Members indicated that it is not clear what the EDRN is doing to understand the variance in the “normal” population. Staff noted that the EDRN, in partnership with several NIH Institutes, has identified 900 plasma proteins associated with variances in the normal population and is examining others (e.g., age, ethnicity, and obesity) that may impact them.

Statistical Tool and Research Management—Dr. Mark Thornquist

Dr. Thornquist discussed areas of emphasis at the Data Management and Coordinating Center (DMCC), which include the design and analysis of validation studies, censored event time outcomes, issues in risk prediction, quantitative proteomics methods, biomarker discovery, and dissemination of DMCC statistical techniques. He stated that the DMCC had developed a checklist for performing rigorous validation studies. The checklists account for clinical context, marker measurement, marker performance, and sample size and power.

Members were told that the Validation Study Information Management System (VSIMS) is EDRN’s Web-based data management system to promote consistent study execution and high-quality data collection using common data elements (CDEs). The system is used for data entry, confirmation of eligibility, issue tracking, specimen tracking, study reports, and study information. VSIMS can be used to support studies intended for submission to the FDA.

Connecting Biomarker Research Across EDRN—Dr. Dan Crichton

Dr. Crichton discussed the development of a comprehensive informatics infrastructure for biomarkers research, and noted that distributed informatics environments are being developed to support the capture and dissemination of scientific results across the EDRN. The EDRN knowledge portal is connected via integration with the ERNE (the EDRN Resource Network Exchange), caBIGTM, caDSR, caTissue, VSIMS, and eSIS. EDRN informatics has met with and shared its architecture and success with other groups outside the NCI, such as the FDA, AACR, and National Biospecimen Network. New bioinformatics tools can be developed for use with this infrastructure, which has provided a foundation for access, management, and sharing of biomarker information.

In the discussion, the following points were raised:

- An alternate approach would be the discovery of biomarkers in advanced disease, rather than using prediagnosis specimens.
- The productivity and direction of EDRN is unclear. The next EDRN BSA presentation should focus on the selection of markers, the ability to bring in new marker strategies, and the analysis of new markers.

A subcommittee (Dr. Todd Golub, Timothy Kinsella, Jane Weeks, and Stillman) was formed to establish a dialogue between the Board and the EDRN concerning future directions and presentations.

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IX. STATUS REPORT: CANCER CARE OUTCOMES RESEARCH AND SURVEILLANCE CONSORTIUM (CanCORS)—

DRS. RACHEL BALLARD-BARBASH, JOHN Z. AYANIAN, DAVID P. HARRINGTON, AND CRAIG C. EARLE

Dr. Rachel Ballard-Barbash introduced a collaborative NCI effort in cancer health services and delivery research involving a consortium of more than 50 investigators at seven sites around the country. The longitudinal study began in 2001 and involves 10,189

patients with lung or colon cancer. Dr. Ballard-Barbash introduced the speakers: Drs. John Z. Ayanian, Harvard Medical School; David P. Harrington, Dana-Farber Cancer Institute; and Craig C. Earle, Dana-Farber Cancer Institute.

Dr. Ayanian stated that the quality of cancer care varies by patient age, race and ethnicity, education and income, and geography. Studies to date have not explained why disparities arise. Possible explanations include patients' lack of information, personal preferences, physicians' inadequate knowledge base, and personal biases. System factors such as inadequate facilities and access to care, poor coordination or fragmentation of care, and inadequate reimbursement also are considerations. Real-world outcome data are needed on cancer and the affect of cancer treatment on patients and their families.

The scientific goals in CanCORS are to: 1) examine treatment choices with a special focus on why certain groups receive lower quality care; 2) characterize the outcomes of treatment; 3), and develop state-of-the-art methods for outcomes research. Dr. Harrington described the prospective data collection that was completed in September, 2007 which included patient interviews, medical records, physician and caregivers surveys, and Medicare claims.

Dr. Ayanian presented results concerning racial and age disparities. He noted that the study found fewer racial disparities for adjuvant chemotherapy in stage III colon cancer, while they still exist for early-stage lung cancer surgery. Additionally, pervasive age-related disparities also continue despite approximately 40 percent of all patients diagnosed with colon cancer being age 75 or older. Studies suggest that elderly patients who receive chemotherapy gain similar survival benefits as younger patients, yet fewer than half of elderly patients who are potential candidates receive adjuvant chemotherapy. There was substantial variation in treatment decisions for older and sicker patients; younger physicians, those involved in teaching, and physicians working at cancer centers are more likely to recommend chemotherapy. Enhanced information and decision support regarding the benefits and risks of chemotherapy for the elderly are needed as well as randomized trials with inclusive eligibility criteria for older populations.

Dr. Earle presented a study on the dissemination of bevacizumab

(Avastin®) into routine practice for metastatic colorectal cancer patients. Overall, 22 percent of patients received first-line bevacizumab in the year following drug approval. Twice as many patients received the drug in SEER registry population-based sites, than the integrated health network HMO types of sites. Women were twice as likely as men to receive bevacizumab, and there was an inverse age gradient. There was no effect of race, education, or comorbidity.

CanCORS has examined the impact of cancer on employment. Many patients must quit or curtail their work, which may lead to a change in insurance status. Several factors are associated with higher rates of workforce departure, such as lung cancer versus colon cancer, stage III disease versus stages I-II, and increased age. Additional factors include race/ethnicity, lower education levels, and lower income. Married men were less likely than unmarried men to stop working, whereas married women were more likely than unmarried women.

The study found that cancer caregiving has shifted from the hospital to the outpatient and home setting, which has increased family involvement in day-to-day care. “High need” required approximately 26 hours per week of caregiving, while other patients required approximately 15 hours per week of care. At least 25 percent, and up to 62 percent, of caregivers perform clinical tasks (i.e., administering medications, managing symptoms such as nausea and pain, changing bandages) with no clinical training. More than half of surveyed caregivers also must balance work, child care, and caregiving tasks.

Early results from the CanCORS study suggest that physician recommendations drive patterns of care. Disparities in cancer care that need to be addressed include optimizing treatment for older patients, better access to new therapeutics, and increased support for caregivers.

In discussion, the following points were made:

- The CanCORS study offers the best health services oncology study data to date.
- Consideration should be given to addressing “why” some patients do not receive chemotherapy.

- Collaborating with the caBIG? investigators to ensure that key data elements and measurements are captured for the entire cancer community is encouraged.
- As molecular diagnostic tests become available, it will be important to understand how they can be adopted on a population basis.

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X. ADJOURNMENT—DR. ROBERT C. YOUNG

There being no further business, the 39th regular meeting of the Board of Scientific Advisors was adjourned at 11:35 a.m. on Tuesday, 4 March 2008.

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