Board of Scientific Advisors

Meeting Minutes

November 8-9, 2004

Building 31C, Conference Room 10
Bethesda, Maryland

Quick Links

Members

Agenda & Future Meetings

Meeting Minutes

BSA: Page 1

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 29th meeting on Monday, 8 November 2004, in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Robert Young, President, Fox Chase Cancer Center, presided as Chair.

The meeting was open to the public from 8:00 a.m. until 5:30 p.m. on 8 November for the NCI Director's Report, an update on NCI/ congressional relations, ongoing and new business, presentations on the case for early detection and improving care delivery through translation of evidence-based interventions into practice, the Requests for Applications (RFAs) annual report, presentation of the updated grants report, and new and recompeted or reissued Requests for Proposals (RFPs) and RFAs/Cooperative Agreements. On 9 November, the meeting was open to the public and lasted from 8:30 a.m. until adjournment at 12:15 p.m.; presentations included the National Cancer Advisory Board (NCAB) Working Group's National Advanced Biomedical Technology Interim Report; an update on the Cancer Genome Anatomy Project (CGAP) 2; an analysis of NCI-supported biospecimen resources; and an update on P30/P50 implementation: Specialized Programs of Research Excellence (SPOREs).

Board Members Present:
Dr. Robert Young (Chair)
Dr. David B. Abrams
Dr. Hoda Anton-Culver
Dr. Kirby I. Bland
Dr. Esther Chang
Dr. Neil J. Clendeninn
Dr. Thomas Curran
Dr. Raymond N. DuBois, Jr.
Dr. H. Shelton Earp III
Dr. Kathleen M. Foley
Dr. Sanjiv S. Gambhir
Dr. Patricia A. Ganz
Dr. Joe W. Gray
Dr. William N. Hait
Dr. Mary J.C. Hendrix
Dr. Leroy Hood
Dr. Susan B. Horwitz
Dr. Hedvig Hricak
Dr. Eric Hunter
Dr. William G. Kaelin, Jr.
Ms. Paula Kim

Board Members Present:
Dr. Kenneth W. Kinzler
Dr. Michael P. Link
Dr. Christopher J. Logothetis
Dr. Lynn M. Matrisian
Dr. Christine A. Miaskowski
Dr. Edith Perez
Dr. John Potter
Dr. Richard L. Schilsky
Dr. Ellen V. Sigal
Dr. Margaret R. Spitz
Dr. Jane Weeks

Board Members Absent:
Dr. David S. Alberts
Dr. Stanley J. Korsmeyer
Dr. Mack Roach III

NCAB Liaison:
TBN

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

TABLE OF CONTENTS

VIII. Working Lunch

RFA Annual Report; Dr. Paulette Gray

Updated Grants Report; Dr. Stephen Hazen

IX. RFA/Cooperative Agreement and RFP Concepts; Presented by NCI Program Staff

Office of the Director

NCI's Best Case Series: Developmental Support and Prospective Research Projects (RFP); Dr. Jeffrey White

Division of Cancer Treatment and Diagnosis

Early Therapeutics Development With Phase II Emphasis (RFP Recompetition) 12; Dr. James Zwiebel

AIDS Malignancies Clinical Trials Consortium (RFA/ Cooperative Agreement Re-Issuance); Dr. Jodi Black

Division of Cancer Prevention

Bioengineering Approaches to Energy Balance and Obesity (NHLBI/RFA)

X. NCAB Working Group: National Advanced Biomedical Technology Interim Report; Dr. Eric Lander

XI. Cancer Genome Anatomy Project 2; Drs. Anna Barker and Daniela Gerhard

XII. An Analysis of NCI-Supported Biospecimen Resources; Drs. Anna Barker and Julie Schneider

XIII. P30/P50 Implementation: SPOREs; Dr. Karen Antman

XIV. Adjournment; Dr. Robert Young

I. CALL TO ORDER AND OPENING REMARKS—DR. ROBERT YOUNG

Dr. Young called to order the 29th regular meeting of the BSA and welcomed members of the Board, NIH and NCI staff, guests, and members of the public. He welcomed new Board members: Drs. Kirby Bland, Kathleen Foley, Sanjiv Gambhir, Joe Gray, Mary Hendrix, Leroy Hood, Stanley Korsmeyer, Christopher Logothetis, Edith Perez, John Potter, and Jane Weeks. Board members were reminded of the conflict-of-interest guidelines and future meeting dates through November 2006. Dr. Young invited the public to submit to Dr. Paulette Gray, Acting Director, Division of

Extramural Activities (DEA), in writing and within 10 days, comments regarding items discussed during the meeting.

top

II. CONSIDERATION OF THE 24-25 JUNE 2004 MEETING MINUTES AND 12 JULY 2004 SPECIAL SESSION MINUTES—DR. ROBERT YOUNG

Motion: The minutes of the 24-25 June 2004 BSA Meeting and the 12 July 2004 Special Session of the BSA were approved unanimously

top

III. REPORT OF THE DIRECTOR, NCI—DR. ANDREW von ESCHENBACH

Dr. von Eschenbach began by invoking a moment of silence to pay tribute and respect to a friend of the NCI, Dr. John LaMontagne, Deputy Director, National Institute of Allergy and Infectious Diseases (NIAID), who died unexpectedly the previous week on the way to a meeting in Mexico City. D . LaMontagne interacted and collaborated closely with the NCI on many issues over the years and most recently in regard to formulating initiatives and opportunities for the future of Frederick Cancer Research and Development Center.

Dr. von Eschenbach welcomed new members to the Board and expressed gratitude on behalf of the NCI and the overall cancer community to all members for their work in directing the future of the NCI and the National Cancer Program. He recognized the skills, talents, expertise, perspective, and personal qualities that members have brought to bear on the process of assessing NCI’s opportunities and responding to the challenges. He welcomed Dr. Young as the newly appointed BSA Chair and reviewed Dr. Young’s experience with regard to the function and role of the BSA since its inception, his past work in the NCI Intramural Program, and his leadership in the extramural arena as President of both the Fox Chase Cancer Center and the American Cancer

Society. He thanked the Board for its leadership, passion, and willingness to participate in vigorous debate about items with the potential for impact on the future of the cancer agenda, such as developing the recent Nanotechnology in Cancer proposal.

Staff Appointments and Staffing News. Dr. von Eschenbach informed the Board of recent staff changes as the NCI continues to develop expertise and provide career opportunities for those within the organization. Dr. David Elizalde, formerly with the Center for Medicare and Medicaid Services (CMS), has been appointed Deputy Director for Management and Executive Officer, Office of the Director (OD), NCI, with responsibility for the management portfolio, which includes both personnel and budget matters.

Ms. Janice Mullaney, who served as Acting Deputy Director in the Office of Management, has moved to a position within the NIH Foundation. Mr. John Hartinger, Associate Director, Office of Budget and Financial Management, OD, continues to focus on long-range financial planning and fiscal management issues. Dr. Ernest Hawk has been appointed Director, Office of Centers, Training and Resources (OCTR), and will assume that role upon completion of protocols related to COX-2 inhibitors in the Division of Cancer Prevention (DCP). Dr. Jay Viner will serve as Acting Chief, Gastrointestinal and Other Cancer Research Group, DCP, when Dr. Hawk leaves the DCP. Dr. von Eschenbach thanked Dr. Linda Weiss for her commitment and service as Acting Director, OCTR, since the departure of Dr. Brian Kimes. In other activities relating to NCI staff, Dr. von Eschenbach reported that: (1) a recruitment search is underway to fill the position of Director, DEA; (2) new fellows and residents have been brought in over the past few months; and (3) an NCI awards ceremony held the previous week recognized the accomplishments of a number of NCI staff. He emphasized that the NCI will be focusing over the next few years on workforce development to create a culture within the NCI that nurtures individuals and their careers; rewards and recognition will be developed in concert with that focus.

NCI Communications. Board members were informed that the NCI had received a Freddie, the top award given in each media category, at the Health Awards Banquet for Media the past weekend. The Freddie was awarded in recognition of NCI's Web site excellence. Dr. von Eschenbach commended Mr. Michael Erhlich and staff in the Office of Communications (OC) for

revising cancer.gov over the past 3 years and bringing it national recognition. Ms. Nelvis Castro, Ms. Mary Ann Wright, and OC staff also were commended for developing the Cancer Bulletin, an electronic publication for communicating NCI initiatives and activities on an ongoing basis.

Selected NCI Activities. Dr. von Eschenbach presented highlights of recent activities. In accord with the recognition of November as Pancreatic Cancer Awareness Month, the NCI is collaborating with the Pancreatic Cancer Action Network to launch the Pancreatic Cancer Research Map. This activity is an example of NCI's continued pursuit of collaborations with the greater cancer community. The NCI Clinical Trials Working Group gathers input from the extramural community and works to ensure that future clinical trials meet emerging challenges and opportunities. Toward the goal of eliminating suffering and death due to cancer, the NCI will continue to pursue programs and initiatives put in place over the past few years. The NCI will work with the BSA to define and develop specific initiatives to address broad, critically important themes. The trajectory of progress in cancer research will be related to the ability to develop and apply emerging technologies, from nanotechnology to information technologies (IT) and bioinformatics. To that end, the National Advanced Technology Initiative has been developed, and the NCI will continue to work with the BSA in the whole area of science and technology integration and application in cancer research. New approaches will be sought to move the scientific endeavor to systems biology, integrated biology, and a transdisciplinary integration of both medical and physical sciences. This movement will involve identifying and implementing strategies, mechanisms, and resources to support those kinds of collaborations and integrations for team science.

Dr. von Eschenbach noted that the NCI will continue to emphasize its leadership role in the cancer research program, especially to create partnerships, alliances, and relationships that foster the acceleration of the entire discovery, development, and delivery continuum. A partnership formed with the Food and Drug Administration (FDA) complements the ongoing relationships with the Centers for Disease Control and Prevention (CDC) and other federal agencies. More recently, the joint CMS/NCI Task Force was formed to address issues such as off-label uses of emerging new cancer drugs. In the area of IT and bioinformatics, the

Electronic Health Record Initiative was established in a collaboration with the Assistant Secretary, Department of Health and Human Services (DHHS). Using cancer as a model, the opportunity exists to create for the DHHS community an IT and bioinformatics infrastructure that will significantly accelerate the pace of progress, especially in the area of clinical research.

NCI Budget Update. Dr. von Eschenbach acknowledged the challenges the NCI faces, including issues related to the budget. Board members were reminded that the fiscal year (FY) 2005 appropriations bill has not yet been enacted and that the NCI is operating under a continuing resolution. However, a variety of initiatives are being pursued in the NCI long-range financial planning effort, including redeployment of resources to address emerging areas of opportunity. In addition, opportunities are being sought for alternative sources of revenue beyond the allocated base. Dr. von Eschenbach noted the number of opportunities regarding the NCI portfolio and infrastructure, such as Cancer Centers and SPOREs. He noted his optimism and enthusiasm about working with the BSA to nurture the extramural community and make progress to reduce suffering and death due to cancer.

In discussion, the following point was raised:

- The NCI continues to model possible budget scenarios in terms of the impact they will have on funding mechanisms. A retreat has been scheduled for January 11, at which the results of the modeling will be reviewed with the help of the BSA, NCAB, and Board of Scientific Counselors (BSC).

top

IV. NCI/CONGRESSIONAL RELATIONS—MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Policy, Analysis, and Response, OD, reviewed the status of FY 2005 budget deliberations. Ms. Erickson noted that a joint resolution passed and signed into law provided funding at the FY 2004 level until November 20 for all government agencies whose appropriations have not been passed. Ms. Erickson reviewed actions of the 108th

and 109th Congress. She also reviewed changes that are expected to occur in the leadership of the full Appropriations Committees in both the House and Senate; the Senate and House Labor, HHS, and Education Subcommittees; and the NCI authorizing committees in both houses (i.e., the Health, Education, Labor and Pension Committee in the Senate and the Energy and Commerce Committee in the House).

top

V. ONGOING AND NEW BUSINESS: BSA AT NATIONAL MEETINGS—BSA MEMBERS

As background, members were reminded that approximately 6 years ago, the BSA suggested a mechanism for a dialogue between the NCI and major cancer-related scientific organizations, with the BSA as a conduit for such conversations. The “NCI Listens” sessions at national meetings were instituted and have been ongoing since then, with varying degrees of success. Some organizations have found they have appropriate access to the NCI and stopped holding these sessions at their meetings. Other organizations, such as the Oncology Nursing Society (ONS), continue to hold successful “NCI Listens” sessions at their meetings.

Dr. Christine Miaskowski, Professor and Chair, Department of Physiological Nursing, University of California at San Francisco, briefly reviewed the report from the ONS “NCI Listens” session at its April 30 meeting. Discussions following the NCI presentations focused on the need for more research in palliative care, access to care, and symptom management; the challenges encountered in obtaining grant review by study sections with appropriate expertise; the need for training opportunities available through the NCI; the importance of providing feedback when requested in the Bypass Budget process; and the need to promote networking between junior and senior members to foster research. BSA members were asked to continue to review the “NCI Listens” mechanism for its utility in getting information of importance to members of professional societies and providing productive feedback to the NCI. Following a brief discussion, a consensus was reached that the “NCI Listens” sessions had value and should be continued. BSA representatives at 2005 meetings are:

- American Society of Preventive Oncology, April, San Francisco, CA - Drs. Hoda Anton-Culver, Patricia Ganz, and Jane Weeks.
- Society of Behavioral Medicine, April, Boston, MA - no volunteers.
- American Association of Cancer Researchers, April 16, Anaheim, CA - Drs. Esther Chang, Joe Gray, William Hait, Susan Horwitz, and Ellen Sigal.
- Oncology Nursing Society, April, Orlando, FL - Dr. Christine Miaskowski.

top

VI. THE CASE FOR EARLY DETECTION—DRS. ANNA BARKER AND LEE HARTWELL

Introduction. Dr. Anna Barker, Deputy Director for Advanced Technologies and Strategic Partnerships, OD, introduced Dr. Lee Hartwell, Dana-Farber Cancer Research Center, to update the BSA on his work and that of the research community in the area of early detection. The goal was to obtain BSA's response to the white paper titled "A Clinical Biomarker Discovery Initiative." As background, members were informed that Dr. Hartwell had been asked to lead an effort to determine the state of science within the community in the emerging field of biomarker discovery and proteomics, evaluate the alignment of resources across the community to optimize research by R01 investigators and others in the next few years, and examine what role the NCI could play in terms of promoting programs to advance this field of research. Following workshops, visits within the community, and interaction with the NCI EC, a white paper was drafted. Two public meetings on the draft have been held, which were attended by a range of investigators from across the cancer community. The BSA was asked, in its advisory capacity, to help direct these kinds of initiatives.

The Case for Early Detection. Dr. Hartwell stated that the consensus at meetings held on both the east and west coasts was that a more organized and systematic approach to discovery would be useful and that an argument can be made for an NCI clinical

proteomics and biomarkers discovery program. One argument for supporting early detection diagnostics is that early detection is estimated to be less costly than the competing strategies (i.e., new drug development or prevention trials) for reducing death from cancer in the next decade. A comparison of the current state of drug development and clinical biomarker development showed that the limiting step in therapeutic or prevention drug development is the relatively expensive clinical trial for each compound at the end of the pipeline. By contrast, clinical biomarker development is constricted at the beginning of the pipeline because it is not yet known how to discover biomarkers effectively.

Proteins were emphasized over DNA or RNA as potential biomarker candidates because they are more numerous and closer to biological function. Two developments that hold promise for improving protein technology are the completion of the human genome sequence, which provides a catalog for proteins and peptides that will be important in current mass spectrometry proteomics technology, and the recent development of improved mass spectrometry instruments to achieve better resolution and throughput. Dr. Hartwell acknowledged that proteomic complexity is a problem because of the many species to be tested with the available tools of mass spectrometry and 2-dimensional gels, and he outlined a “divide and conquer” strategy using current technologies to dramatically increase performance. Through an organized effort similar to that used in the human genome sequencing project, individual laboratories would examine high-probability candidates and coordinate and assemble their information. The proposed clinical biomarker discovery process includes: 1) identifying high-probability candidates in tissue and/or proximal fluid by properties or functions, 2) preparing reagents, and 3) quantitating and comparing in disease versus normal plasma. An important part of organizing an effective activity at the NCI would be the preparation of the necessary reagents for the entire community.

Dr. Hartwell indicated that goals for a coordinated clinical proteomics and biomarker discovery initiative are to: 1) establish the criteria and set up centers for testing biomarker discovery technologies to define an effective pipeline for discovery; 2) develop a publicly available informatics platform that permits data storage, analysis, searching, and comparison; 3) establish a consortia of collaborating laboratories to discover biomarkers in

particular cancer sites and for particular classes of biological molecules; 4) establish repositories of reagents for clinical biomarker discovery; and 5) promote the translation of new imaging agents to clinical trials. Dr. Hartwell presented a diagram of a possible organization for the initiative. He noted that central and facilitating components of the proposed organization are technology, informatics, and reagent cores for technology integration and assessment. Other components are pilot projects and biomarker mines for new technology development and cancer site cores for technology application. In closing, he emphasized that early detection is the major leverage point for such a program in terms of saving lives.

In subsequent discussion, the following points were made:

- This proposed initiative would be integrated with the Early Detection Research Network (EDRN) to accelerate discovery of high-likelihood candidates for validation using processes developed by the EDRN.
- A consolidated listing should be made of all ongoing research in the biomarker field.
- The biomarker initiative should be considered within the larger context of ongoing and planned NCI efforts such as those related to nanotechnology and clinical trials; biostatisticians and epidemiologists should be involved in the planning.
- For screening tests to be useful, they should cause a shift from disease awareness in a way that promotes local intervention through surgery or radiation therapy and cures the disease. For a disease like breast cancer, a serum test would be of limited benefit because of the prevalence of annual or biannual mammography screening. For sufficiently rare cancers (e.g., pancreatic) in which population screening is not carried out, a serum test could make a significant difference. Therefore, real-life issues that could grow out of a program like the proposed biomarker initiative should be considered to ensure that investments are targeted in areas most likely to produce early clinical benefit.
- How ongoing NCI programs, such as the SPOREs, would integrate with the proposed program should be carefully considered.
- New technologies, particularly nanotechnology and

nanowires, should be employed, and biological imaging should be a prominent focus of the proposed initiative.
- A series of metrics for assessment should be adopted early in the project so that data from all participants can be integrated.
- Synergies that exist between the imaging and clinical biomarker arenas suggest that performing imaging studies in parallel with blood proteomic analysis could improve the sensitivity and specificity of the imaging results.
- Internationally, this research field appears ready to coalesce around a set of standards for proteomic software; it also is important that the software be made publicly available.

In closing, Dr. von Eschenbach commented that there is an advantage to viewing this clinical biomarker discovery initiative as cancer-led, not cancer-focused. The initiative will be integrated in larger parts of the national agenda, including the NIH Roadmap Initiative and Department of Energy's microbial proteomics effort. In terms of perspective, cancer is to be viewed as a systems problem that will require a systems solution. Members were told that initiatives such as this are being developed in the construct of the discovery, development, and delivery continuum. In parallel processing, initiatives regarding the larger questions of clinical trials, bioinformatics, IT, imaging, and nanotechnology will dovetail and integrate with the biomarker initiative. The initiative is still in the process of development and will be brought back as a formal proposal with a business plan and funding mechanism for BSA review.

top

VII. IMPROVING CARE DELIVERY THROUGH TRANSLATION OF EVIDENCE-BASED INTERVENTIONS INTO PRACTICE—DRS. MARK CLANTON, JON KERNER, STEPHEN TAPLIN, MOLLA DONALDSON, AND ROBERT CROYLE

Dr. Mark Clanton, Deputy Director for Cancer Care and Delivery Systems, OD, informed members that the objective for this mini-symposium was to begin a dialogue with the BSA about the science of quality measurement, particularly quality of care and improvement. If the 2015 goal is to be achieved, the public impact

of cancer can change only if the performance of the health care system can be enhanced. Three forces that affect the overall performance of the system are how to pay for health care, how quality of care measurement and improvement is perceived, and how access to care is enhanced. Quality of care research involves understanding how the system performs and what can be done to enhance performance. Three themes are: (1) quality of care significantly defines the public health impact of the health care system, (2) health systems change is necessary to improve the overall performance of the health system, and (3) collaborations among independent actors in the health care system are required to improve the performance of the system.

Translating Research into Public Health Practice. Dr. Jon Kerner, Assistant Director for Research Dissemination and Diffusion, Division of Cancer Control and Population Sciences (DCCPS), reminded BSA members that the CDC has been supporting states to develop comprehensive cancer control (CCC) plans since the late 1990s and envisioned the development of a series of Comprehensive Cancer Control Leadership Institutes (CCCLIs). The NCI became involved in phase I of that effort in the summer of 2001. Phase I focused on establishing teams of leaders in the state, building partnerships, and enhancing infrastructure to move the CCC process forward and develop state plans. NCI's role was to bring a research perspective to the effort by engaging cancer prevention and control researchers funded by the NCI and other agencies in the process. In phase II, which began in 2004, a series of four regional CCCLIs were held, and leadership training focused on eight action modules with the goal of moving beyond planning toward action and implementation. NCI staff were involved in the PLANET and Health Disparities modules, the latter to focus on applying the science of cancer control and health disparities to influence practice. Staff from NCI's Cancer Information Service also have been providing Planning Assistant Teams to support the states in the area of implementation. In 2005, CCCLIs will be held for U.S. territories and Native American tribes to involve the entire American population in this activity. Dr. Kerner indicated that NCI-sponsored Cancer Centers have played an important role in comprehensive cancer control planning. As part of NCI's leadership and partnership through C-Change, the goal of having every state implement CCC plans by the end of 2005 is well on the way to being achieved.

Dr. Kerner discussed resources that the NCI brings to CCC support at the state level. Cancer Control PLANET was developed by the NCI, CDC, Substance Abuse and Mental Health Services Administration, Agency for Healthcare Research and Quality, and American Cancer Society (ACS) to address the need for a Web-based tool to provide access to data and resources that can help design, implement, and evaluate evidence-based cancer control programs in a unified way. Since the site was launched in April 2003, the average number of unique PLANET visitors has increased by 39 percent. More than 800 public health providers and practitioners have been trained to use the PLANET, and the uptake and utilization of evidence-based interventions in cancer control are being tracked to determine the impact of making this resource available. Clinicians Linking Information to Patients (Cancer CLIPS), another NCI-sponsored resource, is being developed to deliver pertinent and up-to-date information right at the point of care. Cancer CLIPS will leverage existing and evolving electronic health records and systems to enhance consistency and reduce costs of updating software. Dr. Kerner emphasized that the systems and interventions are being developed to work in resource-limited health care settings as well cutting-edge and state-of-the-art centers.

Finally, Dr. Kerner discussed partnership opportunities and challenges associated with NCI's leadership role, which focuses on strategic investment, convening partners, and acting as a catalyst for collaboration. He noted that challenges for translating research into action were: (1) researchers are more comfortable with efficacy than dissemination and implementation, (2) process measures to evaluate dissemination and implementation are hard to find or agree on, and (3) experience usually trumps evidence when evidence-based approaches conflict with practitioner experience.

Improving the Quality of Primary Care Practice. Moving from public health practice to primary care practice, Dr. Stephen Taplan, Applied Research Program (ARP), DCCPS, presented two examples of delivery, one in the area of breast, colon, and cervical cancer screening and the other in mammography implementation. Board members were reminded that: (1) screening rates for breast, colon, and cervical cancer have increased but could be improved, particularly in low-income populations; (2) screening is a complicated process, with many opportunities to fail; and (3) failures in the process may be associated with poor outcomes.

Members were informed that the NCI has started working with Bureau of Primary Healthcare Centers (BPHCs), CDC, ACS, and Institute for Healthcare Improvement on a cancer collaborative to foster improvement in the area of risk assessment through conscious planning by physicians and health care providers before they are in the middle of care. A chronic care model is being developed to guide the planning process. The NCI and its partners are planning for the next phase, which will extend the impact to reach 800 practice facilities and the 16 million people served by the BPHCs, many of whom are under- or uninsured and are at the highest risk. By implementing the chronic care model initiative with the BPHCs, a model and experience will be provided for systems change in other populations. Discussions with the CMS and CDC have initiated planning for a colorectal cancer screening effort based on this chronic care model.

In the area of detection as part of the screening process, the NCI is building on the work of the Breast Cancer Surveillance Consortium (BCSC), which has been linking mammograms and cancer registries for 10 years and is providing new information about factors affecting mammography performance variations in interpretation. Partnerships established with primary care physicians, practicing radiologists, the American College of Radiology (ACR), and software vendors have led to change. Data collection in the course of care led to the development of Breast Imaging and Reporting Data Systems (BI-RADS®) to clarify clinical care. BCSC investigators identified problems with use of BI-RADS®, worked to standardize terminology, and developed a tool to address the problems encountered by BCSC investigators. The tool subsequently was offered to the ACR and is now incorporated in the Fifth Edition of BI-RADS®.

Improving the Quality of Cancer Care. Dr. Molla Donaldson, Outcomes Research Branch, ARP, DCCPS, described two examples of NCI projects to understand and improve cancer treatment and palliative care. Both involved the NCI as a catalyst working within the public and private sectors to improve patient outcomes. The first project was a study to improve care for patients with ovarian cancer. Findings from the 1991 NCI Patterns of Care/ Quality of Care (QOC) Ovarian Cancer Study showed that women with early stage ovarian cancer were likely to be understaged and not receive appropriate therapy because of the lack of nodal sampling. This problem was found to be greater for older, African

American, and Hispanic women. These results were presented at a special session of the American Society for Clinical Oncology and received national news coverage. A 1994 Consensus Development Conference sponsored by the NIH Office of Medical Applications of Research affirmed the need for nodal sampling for all stages. The NCI then worked with professional organizations to develop training programs for gynecologic surgeons. Since then, the NCI has been monitoring change. In a repeat study conducted in 1996, it was found that the number of patients receiving optimal care increased, and the greatest increase was found in groups that had the lowest rates of optimal care in 1991. Another repeat study begun in 2002 will determine whether the improvement continues. Along the way, partnerships have been fostered for monitoring change, for example, a Surveillance Epidemiology and End Results Program-Medicare study of the over-65 population and a partnership involving the Society of Gynecologic Oncology, extramural research experts, and NCI staff to evaluate the outcomes following surgical treatment.

In the second example of NCI-supported initiatives, the transagency Quality of Cancer Care Committee (QCCC) has been developing a series of collaborative initiatives with the Veterans Administration (VA), HRSA, CDC, and CMS. A new NCI-sponsored project is the CCC Collaborative on Palliative Care, whose purpose is to improve palliative care for American Indian and Alaska Natives from the time of cancer diagnosis onward. The NCI is working in a partnership with the IHS, Sovereign Nations and Tribes, Rochester Mayo Clinic, and university-based Native American Research Centers for Health. Dr. Donaldson noted that a needs assessment has been completed on the basis of information gathered in three pilot studies and a Spirit of Eagles Conference. A summary paper is nearing completion and will be used to devise targeted, evidence-based interventions at the clinician, patient, and systems levels. This project has generated interest from a number of other agencies and organizations, including the HRSA for information that can be used in its telehealth program and the VA for application in the care of rural veterans and Native American patients. The NCI also plans to evaluate these interventions for their effectiveness, sustainability, and generalizability.

Questions for Discussion. Dr. Robert Croyle, Director, DCCPS, asked Board members to provide advice and guidance on key questions that have been encountered in the course of planning for

dissemination and delivery initiatives. What is the NCI's appropriate role in evidence synthesis and dissemination, provider training, developing and facilitating the use of standard measures of outcomes and quality, and shaping health care program decisions and policy? How can NCI-supported research infrastructures be used most effectively to test strategies for overcoming barriers to the delivery of quality cancer care? What key partnerships remain to be developed to maximize NCI's impact on improving the quality of cancer care?

In discussion, the following points were raised:

- The NCI can play an important role in setting research priorities toward the goal of improving the health care system, for example, working with the CMS to get payment for colorectal screening approved in the population older than age 65, thereby clearing the way for third-party payers to follow suit. Financial incentives and QOC monitoring are needed to ensure improved QOC in the area of treatment as well as detection, for example, identifying and eliminating barriers in the patient, doctor, and system to ensure that adjuvant therapy for individuals with Stage 3 colorectal or breast cancer is administered. An NIH Consensus Development Conference should be convened in the area of quality of cancer care.
- Good data are needed to determine which interventions are effective to change the multiple systems that make up the health care trenches; the interventions may need to be different depending on whether the care is taking place in a comprehensive cancer center or a primary care physician's office in a rural community. Another critical aspect of the process is the need for standard outcome measures.
- Health service researchers seem to be lacking at the cancer control level; training in this area of research should be emphasized.
- To achieve a mainstream delivery of care and make a population impact, a transdisciplinary effort or business plan is needed to learn more about the metrics of efficiency, which combines quality and cost effectiveness, and to maximize both in a realistic way that could be adopted and integrated by third-party insurers. The plan should drive and guide research and how research questions are framed so that the issues of health services, economics, and efficiency

metrics are built in at the very beginning of study design. The idea would be that the NCI could fund what could be called leveraged research, in which the outcome would be in the currency and language that would be readily adopted in the policy environment and permanently integrated into the health care system.

top

VIII. WORKING LUNCH

RFA Annual Report. Dr. Gray presented the annual BSA Concept Review Report. She briefly reviewed how the report was organized and informed members of a new feature, i.e., inclusion of abstracts on CDs. Board members were asked to decide whether 1996, 1997, and possibly 1998 grants should be dropped because many of those no longer are on the table, or whether they should be retained as a historical record. Following a description of the various sections and clarification of information in several of the sections as requested, Board members were asked to continue their review and bring suggestions to the February BSA Meeting for making the Report more useful.

Updated Grants Report. Mr. Stephen Hazen, Chief of NIH's Extramural Financial Data Branch, reminded members that at its June meeting they reviewed a draft version of a new report on success rates and award levels for several grant mechanisms. He stated that the current report included BSA requested revisions, i.e., a comparison of P01s and SPOREs and several more years of history. Members were asked for input as to whether the new tables display the information that the BSA wishes to see at each meeting and, if not, what should be added or deleted. This report will compare the current year (FY 2005) and the 2 prior years (FY 2003 and 2004) at each meeting, with the 5-year trends reported at the end of the year (each November). Members were asked to comment on whether that meets the needs of the Board.

The following comments were made during the presentation:

- R01 applications received in FY 2004 increased, and expectations are that FY 2005 will see a continuation in the

trend, presenting difficulties in trying to maintain the success rate and payline for those grants.

- The total number of NCI-funded grants is expected to increase in FY 2005 and probably into FY 2006.
- The number of funded R21s increased, but the approximately 50 percent increase in applications submitted resulted in a decreased success rate. The NCI is funding more R21 grants than ever before.
- The overall number of RPGs is increasing at a greater rate than the number of R01s over the past 2 years, reflecting the bounce in numbers of R21s funded.
- Looking at the history of the success rate, the numbers for all mechanisms are decreasing in the face of the fact that the NCI has funded more competing grants in the past few years than ever before and the number funded in each mechanism continues to increase.

top

IX. RFA/COOPERATIVE AGREEMENT AND RFP CONCEPTS—PRESENTED BY NCI PROGRAM STAFF

Office of the Director

NCI's Best Case Series: Developmental Support and Prospective Research Projects (RFP). Dr. Jeffrey White, Office of Cancer Complementary and Alternative Medicine (OCCAM), reminded members that the NCI Best Case Series (BCS) Program was established in response to a request from Congress in the early 1990s to retrospectively identify patients who benefitted from treatment with an unconventional modality. Although interest in the BCS has increased steadily, the number of completed series has remained low, and few have resulted in funded research projects. Barriers to progress include difficulties in preparing the required BCS documentation, lack of funding support, and lack of practitioner research experience. The proposed Broad Agency Announcement (BAA) is designed to overcome those obstacles and support the development of BCS submissions and additional prospective research activities when warranted through the award

of Phase I/II Fast Track and Phase II only contracts. Phase I/II Fast Track contracts would be awarded for collaborative projects that pair a clinical cancer investigator with a CAM practitioner. Phase I products would include documentation of a series of patients that fully meets the NCI BCS Program criteria and a proposed budget for an appropriate prospective research project that would be submitted for review before Phase II funding.

Estimated funding would be $50 K for one competitive Phase I proposal for approximately 9 months, and up to $350 K for an appropriate followup prospective research proposal over 2 to 3 years.

In discussion, the following points were raised:

- Lowering the funding rate and funding more Phase I partnerships should be considered.
- The entire context of the science appears to be lost in the proposal; applicants should be responsible for proposing testable hypotheses to be addressed in the trials.
- Strategies should be developed for moving toward better communication about negative results from CAM cancer treatment. Providing a higher level of evidence that certain commonly used approaches are not beneficial is a worthwhile goal, all submitted cases that fail to make the cut, as well as results of the Phase II trials, should be publicized.
- Areas of CAM expertise that are developing in the academic centers should be embraced and their experience evaluated rather than developing an alternative path.

Motion: The concept entitled “NCI Best Case Series: Developmental Support and Prospective Research Projects (RFP),” was approved with the modification that three proposals would be funded at $15-20 K per partnership in the Phase I process, with 11 members in favor and 9 opposed.

Division of Cancer Treatment and Diagnosis

Early Therapeutics Development With Phase II Emphasis

(RFP Recompetition). Dr. James Zwiebel, Associate Chief for Biologics Evaluation, Investigational Drug Branch, Cancer Therapy Evaluation Program (CTEP), DCTD, stated that this proposal had been reviewed by a BSA subcommittee, which requested clarification on several issues. Members were reminded that CTEP's role in drug development is to accelerate development of promising new agents; broaden development in relevant tumor types; explore combinations of targeted agents as a high priority; and explore alternative methods of drug administration, mechanisms of action, and proof of principle of the targeted therapies. Candidate agents are obtained from industry, academia, and NCI's Developmental Therapeutics Program (DTP). CTEP has agreements with approximately 80 industry partners for 143 investigational agents and files 15-20 new investigational new drugs each year. DCTD's Drug Development Group decides, approves, and prioritizes the commitment of NCI preclinical or clinical resources for development of a particular agent with the help of extramural reviewers. In the current Phase II program, eight 3-year contracts were awarded in FY 2001 and extended for 2 additional years. The current program will end in FY 2005. Most contracts involve multi-institutional consortia, all with the capability to carry out correlative studies. At initiation of the program, the goal was to increase accrual from the 375 enrolled at the end of the previous program to 1,600 at the end of the 5-year project period.

Dr. Zwiebel summarized performance in the current Phase II program in terms of program objectives: (1) activated protocols increased from 76 in year 1 to 121 as of FY 2003; (2) completed protocols more than doubled in the first 3 years of the contract over the number completed in the previous program; (3) patient enrollment increased 20-30 percent in each year and the 1,600 target is expected to be reached by FY 2005; and (4) a wide variety of agents is being explored, including small molecules, biologic agents with specific molecular targets, alkylating agents, monoclonal antibodies, and event vaccines.

Members were told that in the Phase II recompetition, eight multi-institutional consortia are proposed. Offerors will be rated on their ability to initiate 4-8 trials per year per contract, enroll 150-250 patients per contract year, implement and complete trials rapidly, and have the capability to carry out correlative studies. Costs are estimated to total $1.5 M per consortium per year, with an estimate

of $12 M total per year for 8 consortia, with $6 K per patient.

In response to the BSA subcommittee's questions about the other component of the clinical trials program, Dr. Zwiebel explained that the Translational Research Initiative (TRI) was 1) established to address the need to better understand target effects and develop therapeutics in a timely manner; 2) leverages existing resources, for example, assays already developed via other NCI funding mechanisms; 3) supports correlative studies across multiple components of the CTEP clinical trials program; and 4) provides the flexibility to direct funding to laboratories with unique expertise. Requests for TRI funding are reviewed with a Letter of Intent, including a 1-page budget plus justification, by NCI staff according to extensive criteria. TRI awards have numbered 111 over 3 years, with about $2 M committed per year. Funds are not disbursed until the work is completed. Total funding to date is $1,153,170 for a total of 907 enrolled patients.

Dr. Richard Schilsky, BSA Subcommittee Chair, confirmed that the questions raised by the Subcommittee had been answered. Specifically, questions related to how the Phase II program fits into NCI's overall clinical trials program, how candidate agents were chosen for clinical development, and the TRI and its funding source.

Motion: A motion to concur in the recompetition of the RFP for Early Therapeutics Development With Phase II Emphasis was seconded and approved unanimously.

AIDS Malignancies Clinical Trials Consortium (RFA/ Cooperative Agreement Re-Issuance).

Dr. Jodi Black, Program Officer, AIDS Malignancy Program, DCTD, reminded members that the AIDS Malignancies Clinical Trials Consortium, or AIDS Malignancy Consortium (AMC), is a multisite cooperative group network focused on studying cancer in the context of HIV infection. Evidence of the continuing scientific need for this research has been amply documented. Reissuance of the RFA/ Cooperative Agreement is proposed with structural changes to make the AMC more efficient. In addition, a

collaboration with NIAID's Division of AIDS (DAIDS) will integrate the AMC and its cancer agenda into the clinical trials networks that the DAIDS is building. The AMC mission is to evaluate clinical interventions for treatment and prevention of cancer in HIV-positive patients, investigate the biology of these malignancies in the context of clinical trials, and donate specimens and clinical data to the AIDS and cancer specimen resources for use by all requesting investigators. In the current AMC, 14 individually funded cooperative agreements (U01s) were awarded with about 20 subcontracting affiliated sites and an operations center. This configuration left little ability to shift funds to better performing sites or delete poorly performing sites. In the proposed new structure, one U01 will be issued to fund one Leadership Group, which will consist of the Group Chair; Operations, Data Management, and Statistics Center Principal Investigators (PIs); the PIs of 6-10 main member core sites; NCI intra- and extramural staff; and DAIDS staff. The Leadership Group will be responsible for the scientific agenda, governance, and fiscal accountability of the AMC. The Operations Center, funded through a subcontract with a contract research organization, will be responsible for fund disbursement to the core sites, statistics and data management, managing patient recruitment and retention funds, and managing the reserve funds. The reserve funds are to be used for correlative, translational, and international studies; training; and community representatives. Non-core sites will be able to accrue patients and be paid on a capitation basis. A new performance evaluation proposal will be embedded in the text of the RFA to deal with poorly performing sites. Improvements are anticipated in the areas of funding control, accountability, recruitment incentives, ability to recruit from non-core sites and to include provisional sites, faster accrual and cost effectiveness through the interface with DAIDS, enhanced intramural program interaction, and international expansion.

In response to BSA Subcommittee requests, Dr. Black highlighted accomplishments of the current AMC and barriers to accrual. In the area of accomplishments, 22 trials were initiated, enrolling 836 patients; 13 were completed; three currently are open; and 6 closed due to slow accrual or sponsor withdrawal. Two new protocols are undergoing IRB or amendment review, and seven are in development using agents that span the diseases for AIDS malignancies. Barriers to accrual include changed demographics of the patient population, the shift to community patient care centers

versus academic centers, patient compliance issues, intensive protocol requirements, patient expectations for reimbursement and total care, tightening institution admission policies, lack of outreach mechanisms, and lack of industry support. In closing, Dr. Black noted that with the changing demographics of the HIV/AIDS population, the consequences of HIV disease have become a problem for minority populations. Forty percent of the patients enrolled onto AMC trials fall into the minority category. Thus, the AMC is contributing to bridging the gap between discovery and health care delivery in underserved populations.

Dr. Eric Hunter, BSA Subcommittee Chair, commented that issues identified as needing clarification had been addressed. Those issues were related to how 1) the AMC would be integrated with the AIDS Clinical Trial Group's HIV Prevention Trials Network Program, 2) to address the problems of recruitment, and 3) the international sites would be identified.

Motion: A motion to concur in the re-issuance of the RFA/ Cooperative Agreement for the AIDS Malignancies Clinical Trials Consortium was seconded and approved unanimously.

Division of Cancer Prevention

Bioengineering Approaches to Energy Balance and Obesity (NHLBI/RFA). Dr. Sharon Ross, Nutritional Science Research Group, DCP, informed members that this RFA is being issued jointly by the National Heart, Lung, and Blood Institute (NHLBI), NCI/DCP/DCCPS, National Institute on Aging (NIA), National Institute of Biomedical Imaging and Bioengineering, and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), with the NHLBI as the lead Institute. This presentation was for informational purposes only; no BSA action was required. The purpose of this project is to support the development of new and innovative bioengineering technologies to address problems in energy balance, intake, and expenditure associated with obesity. Strategies include sensors, devices, imaging, and other approaches that will be developed and evaluated through collaborations between biomedical engineers and scientists with expertise in obesity and nutrition. Possible outcomes include: (1) the

development and validation of biosensors to measure calorie consumption and energy expenditure; and (2) the identification of accurate new biomarkers that correlate with energy expenditure, caloric intake, physical activity, or total energy balance. Members were told that the NIH obesity-focused research portfolio has very few initiatives in the area of physical activity or metabolism. In addition, this RFA is consistent with NCI's 2015 challenge goal, and although the initial impact will be in the discovery phase of the cancer research continuum, the ultimate goal is to use these tools and approaches in a community intervention or delivery arena. The project also is consistent with NIH's Obesity Task Force goals and strategies. Pending approval by the NCI EC, the proposed NCI allocation would be $1 M per year for 4 years, and total contributions by participating Institutes and Centers (ICs) are estimated at $4.7 M per year. This project complements the Bioengineering Approaches to Energy Balance and Obesity Program Announcement (PA) calling for Small Business Innovation Research/Small Business Technology Transfer Research applications, and the same ICs are involved. The merits of this bioengineering approach are that it will encourage multidisciplinary approaches, develop and validate tools and approaches, and foster collaborations across Institutes.

X. NCAB WORKING GROUP: NATIONAL ADVANCED BIOMEDICAL TECHNOLOGY INTERIM REPORT—DR. ERIC LANDER

Dr. Eric Lander, Director of the Whitehead Institute/Massachusetts Institute of Technology Center for Genome Research, noted that the NCAB Working Group on Biomedical Technology has been in existence for the past year. The Biomedical Technology Working Group (BTWG), co-chaired by Dr. Lander, will present its initial formal report to the NCAB in February 2005. The recommendations he presented to the BSA were not yet voted on formally by the BTWG, whose members represent a broad variety of experience and expertise.

The recent revolution in biomedical technology has had a widespread impact. The NCI asked the BTWG to investigate possible transforming changes (i.e., opportunities to undertake projects or initiatives that create structures to propel investigators to build common knowledge bases and tool sets for use in the cancer field). The BTWG began its work by reviewing the efforts

of groups such as the Cancer Genome Anatomy Project, Alliance for Nanotechnology in Cancer, Cancer Biomedical Informatics Grid (caBIG), Early Detection Research Network, and Mouse Models of Human Cancers Consortium (MMHCC). The Division of Cancer Biology (DCB) also updated the BTWG regarding current think tank initiatives, and the BTWG examined the work of the Clinical Trials Working Group as well.

The BTWG met in March 2004 to identify key opportunities for transforming projects. Five focus groups were established to gather input from the scientific community via in-person meetings, e-mail, and conferences. The groups were chaired by BTWG members and involved approximately 50 scientists from the community. The focus group topics and chairpersons were presented: 1) Characterization of Cancer in the Cell Focus Group (chaired by Dr. Lander); 2) Characterization of Cancer in the Organism Focus Group (chaired by Dr. Lee Hartwell); 3) Public Health Focus Group (chaired by Dr. Margaret Spitz) ; 4) Cancer Therapeutics and Clinical Trials Focus Group (chaired by Dr. Brian Drucker); and 5) The Technology Access, Development, and Dissemination Focus Group (chaired by Dr. Ben Shapiro). The major themes of each of the focus groups and the overall crosscutting themes that emerged from the five groups was presented.

Dr. Lander noted that the BTWG has not yet postulated its formal recommendations. Discussion continues to focus on a number of areas, including whether the NCI should establish a standing Cancer Technology Working Group (CTWG) comprised of appropriate experts who would seek community input. The CTWG would be charged with the tasks of identifying opportunities for technology-based programs and addressing key cancer challenges with the potential for broad impact on the understanding, prevention, diagnosis, and treatment of cancer. The CTWG also could establish project priorities based on importance and feasibility, develop recommendations, and estimate needed resources.

The BTWG explored the genomic basis of cancer and molecular detection topics more thoroughly and expects to develop formal recommendations in these areas. With regard to a potential Human Cancer Genomic Project, BTWG members agree that the basic technology exists to systematically identify the genomic alterations associated at a significant frequency with all major types of cancer.

The BTWG is considering the need for additional funding for such an effort.

In discussion, the following points were raised:

- This effort extends beyond the notion of identifying important questions and issues to developing a broader strategy that integrates science and developing technologies. The scientific questions will inform, drive, and accelerate technology development in a more focused manner. In turn, the technologies will accelerate the ability to answer the questions. This activity should result in a continuous acceleration of the pace of progress.
- A recommendation was made to facilitate crosstalk and crossreferencing between all of the NCI-sponsored initiatives developing recommendations in this area. The CTWG could play a key role in fostering such integration.
- This effort will provide a more thorough understanding of the etiology and more informed methods of prevention and treatment of very early cancer and predispositions.
- It is important to mobilize a coalition in support of this effort. This coalition should include representatives of the advocacy community, pharmaceutical industry, and basic and clinical science.

XI. CANCER GENOME ANATOMY PROJECT 2—DRS. ANNA BARKER AND DANIELA GERHARD

Dr. Anna Barker, NCI's Deputy Director for Strategic Initiatives, introduced Dr. Daniela Gerhard, Acting Director of NCI's Office of Cancer Genomics and Director of the Cancer Genome Anatomy Project 2 (CGAP). In providing an overview of CGAP and its current status, Dr. Gerhard informed members that the explosion of discovery in the biological sciences during the past 30 years has had a tremendous impact on the understanding of basic mechanisms of cellular growth regulation in cancer. Areas of study that have contributed to more personalized medicine include biochemistry, cell biology, proteomics, metabolomics, genetics, and genomics. CGAP has been involved in studies of expression profiling and survival prediction, for example, that have resulted in more targeted treatment plans for diffuse large B cell lymphoma patients with poor prognosis. Tumor genotype-directed treatment is another area of advancement in which CGAP2 has been involved.

She noted that the Office of Cancer Genomics (OCG) was established in 1996 to facilitate the interface of genomics and cancer research by establishing platform information and technology infrastructures. Data are sequence-based and available through caBIG and other public databases. CGAP's first project involved generation of expressed sequence tags to identify gene-transcribing cancer cells. Currently, CGAP is involved in the Serial Analysis of Gene Expression Project. CGAP also is conducting the SNP500Cancer Project, designed to generate resources for the identification and characterization of genomic variations in genes important to cancer. The data are integrated into HapMap, and the polymorphisms are used in population-based studies led by the Division of Cancer Epidemiology and Genetics (DCEG), including the Consortium for Breast and Prostate Cancer. The Initiative for Chemical Genetics is developing a systematic approach for harnessing synthetic chemistry to discover molecular mechanisms in basic cell biology. This project has been influential in informing the molecular libraries involved in NIH's Roadmap Initiative.

With regard to CGAP's efforts in the area of clinical genomics, a comprehensive approach is planned to identify the nucleotide changes within genes and other regions that increase the risk of cancer development. This approach will lead to clinically useful resources. CGAP's home page provides access to a variety of information, tools, downloadable data, and educational resources.

In April 2004, NCI and the National Human Genome Research Institute conducted a workshop titled "Exploring Cancer Through Genomic Sequence Comparisons." A "strawperson" approach has been developed to help define needed components and resources. The aim is to develop milestones and deliverables that will be useful in the clinic. To meet the challenge of sequencing important genomic regions, two to four precisely defined subtypes with at least 100 specimens each will be selected. Precancerous, metastatic, and stromal samples will be required.

Dr. Gerhard summarized that the OCG has made major contributions to cancer genomics by driving the development of information and resources and disseminating them directly to the research community. Genomics has reached a crossroads and is moving into the clinic. During its next phase, CGAP will provide clinical genomics data that ultimately will affect cancer patients

positively.

In discussion, the following points were raised:

- To accelerate translational research and the movement of any genome results to the clinic, efforts should be made to develop biology-driven technology for detection (both biomarkers and imaging). These efforts should be undertaken in parallel versus sequentially.
- In response to a question regarding CGAP usage, it was noted with regard to RNAi resources that more than 400,000 clones have been distributed in the 6 months that they have been available. The number of "hits" on the CGAP Web Site is hundreds of thousands per year.
- The SNP500 database is an excellent resource for molecular epidemiologists who are involved in gene-environment studies.
- There is a need to develop a large human cohort that focuses specifically on genome, the environment, and the possibility of early detection in the proteome; and then to follow through to treatment and outcome research and to link the biology of the tumors back to the biology of the individuals. This is a large enterprise, but it is key to the success of other efforts. On the other hand, various population-based molecular epidemiology studies have been instituted within the past year that could provide the 250-1,000 cases needed for CGAP efforts.

XII. AN ANALYSIS OF NCI-SUPPORTED BIOSPECIMEN RESOURCES—DRS. ANNA BARKER AND JULIE SCHNEIDER

Dr. Barker highlighted NCI efforts in the area of biospecimen resources in response to a query by the BSA. Over the past 2.5 years, the NCI has been investigating this area and has collaborated with scientists around the world. The Rand Corporation produced a report on the topic a few years ago and noted that there are more than 300 million tissue samples in this country, and that samples are accumulating at the rate of approximately 20 million per year. The NCI and the cancer community are responsible for many, and perhaps most, of these specimens. The NCI asked the Rand Corporation to re-examine the issue on the basis of cancer alone.

That report was made available to the BSA a few months ago.

Dr. Julie Schneider, of NCI's Office of Technology and Industrial Relations, presented findings from a recent review of NCI biospecimen resource activities. She noted that the analysis involved reviewing relevant literature, analyzing preliminary cost data from NCI's Financial Management Branch, and analyzing results of a questionnaire distributed to appropriate NCI program staff. Followup interviews also were conducted to clarify questionnaire responses. Limitations of the report include: (1) there is no comprehensive list of all NCI-supported programs that support biorepository-related activities (in particular, no collections that are supported by R01 grants were captured in this report; thus, the results represent an underestimate of NCI's total investment in this area); (2) the lack of common definitions for biorepository-related terms made it difficult to acquire comparable data across programs; (3) limited data were available about biorepository activities at the NCI; and (4) redundant data were submitted by overlapping programs in at least one instance.

Report findings indicated that 1) there is no coordinated management of the total portfolio of biorepositories that are supported by the NCI.; 2) ninety-five percent of reporting entities reported collecting fresh-frozen material; 3) ninety-seven percent of programs reported having some sort of database; fewer than 50 percent employed an automated specimen tracking system (e.g., barcoding); 4) the Cooperative Human Tissue Network (CHTN) distributed to a large number of nonaffiliated investigators, while other entities distributed largely to affiliated investigators. This raises a concern that investigators who do not have access to the Cooperative Groups, Cancer Centers, and SPOREs may have difficulty accessing specimens for epidemiology, translational, and clinical trial research because the CHTN focuses on supporting basic studies; 5) although most programs provided biospecimens for genomic and proteomic research, collection, storage, annotation, and quality control/quality assurance, methods varied substantially among programs; 6) NCI's investments in the repositories totaled approximately $53 M for FY 2003 (this figure does not include individual investigator collections); and 7) the 125 programs that provided data stored about 4 million specimens.

The findings of the report led to the identification of key barriers, including: (1) the lack of common management principles hinders

the development of best practices and standard operating procedures (SOPs), (2) the lack of common definitions of terms also hinders efforts toward more coordinated management, and (3) common access to information about the range of biorepository efforts supported by the NCI is lacking. Dr. Schneider concluded by noting that several NCI programs are working to address these issues.

Dr. Barker summarized the recommendations that were developed based on the report's findings. She noted that additional data will be collected, and additional recommendations may be formulated based on the additional findings. The recommendations made thus far include: 1) Establish a group within the NCI to explore this topic intramurally and internally, and promote continuity across the Divisions with regard to programs being funded; 2) Convene a workshop (probably early next year) to solicit broad input from the community to identify best practices and to support the development of SOPs and policies; 3) Consider developing a pilot program based on the identified best practices to ensure that they produce the desired outcomes in terms of continuity, uniformity, and quality assurance of results; 4) Develop a research program in biospecimen banking research to inform the development and refinement of SOPs; 5) Facilitate tracking and budget information for these activities (Health Insurance Portability and Accountability Act, patient protection of biospecimens, and access are key issues in this area); 6) Institute a National Biospecimen Network that is open to all diseases; and 7) Have the NCI assume an international leadership role in this area.

In discussion, the following points were raised:

- The legal, HIPAA, and intellectual property considerations are substantial.
- The cost and mechanisms of support for such a network are very challenging.
- Areas in which the NCI is seeking BSA input include overcoming barriers, ensuring fair representation in discussion of issues, and HIPAA concerns.
- It would be better to disseminate the findings regarding NCI-supported resources sooner rather than later, even if this is carried out in a very informal manner.
- Access issues include uniformity, prioritization, and SOPs.
- The collection of samples should be linked to clinical

annotation and to an understanding of the underlying study design that produced the samples. A working group should be established to develop recommendations regarding study designs for optimal ways of collecting specimens.

XIII. P30/P50 IMPLEMENTATION: SPOREs—DR. KAREN ANTMAN

Dr. Karen Antman, Deputy Director of NCI for Translational and Clinical Sciences, presented an overview of the SPOREs. In 1991, Congress appropriated $20 million to create the program. With BSA reviews in 1998, the SPORE Program was extended to include ovarian SPOREs. In 1999, NCI's EC changed the mechanism from an RFA to a PA, and 10 additional diseases were added. The EC also approved the Clinical Trials Supplemental Program in 1999. The program was expanded further in 2000, and the P30/P50 Working Group reported back in 2003.

SPOREs support interdisciplinary teams dedicated to translational research focused on a specific human cancer or group of cancers (e. g., gastrointestinal [GI] cancer). The addition of multiple tumors increased the budget, and the number of SPOREs expanded to about 60 in 2004. The program increased in complexity as more tumors were added. Comparing U.S. cancer deaths with the incidence of various tumors in the SPORE Program shows that GI and lung cancer are underrepresented.

An assessment of the SPORE pipeline begins with the mandate to move scientific projects into clinical applications. Two bottlenecks have been identified in translational research: preclinical development and early phase clinical trials. This topic was discussed at the 11th Annual SPORE Workshop in July 2003. Eight preclinical drug development projects and 12 biomarkers were identified and prioritized. There are three planned SPORE phases: (1) 1993-1999 for preclinical development, (2) 2000-2004 for a focus on organ disease, and (3) 2004-2010 for human molecular targets. There are 297 SPORE translational projects, 230 developmental projects, and 115 career development projects, for a total of 642 projects across the program in 21 thematic categories. In terms of clinical orientation, 347 projects involve therapy or treatment, 65 involve prevention, and 527 involve biomarkers.

The SPOREs Program has been moderately integrated with other cancer projects, and further integration is desired. In clinical trials, ongoing collaborations are taking place with the Cancer and Leukemia Group B (CALGB), Gynecologic Oncology Group, American College of Radiology Imaging Network (ACRIN), Cancer Genetics Network, Rapid Access to Intervention Development Program, EDRN, the Director's Challenge, and the intramural program. Meetings have taken place with the DCB, NCI's intramural program, DCCPS, and DCP. Special initiatives include the NCI-Avon project, National Biospecimen Network, and Lung Cancer Biomarker and Chemoprevention Consortium.

One recommendation is to slow SPORE growth to the rate of increase of R01s. In 2004, there were no cost-of-living adjustments. The PAs were already published, and a large number of grants received exceptional priority scores. Eight new SPOREs were funded at a cost of about $5 M. There currently are 59 SPOREs, or slots, with no planned new slots. PAs will be released only when renewals are competing, and the funding will be based on payline and programmatic needs. The SPORE Program cap was decreased from $2.75 M to $2.5 M in total costs, with the same number (four) of research projects. The prevention and population science project will be changed to "highly encourage" less common tumors.

A second recommendation is to allow SPOREs that focus on pathways, mechanisms, or population research. The program believes that its organ disease orientation should continue, with programmatic coordination of researchers working on the same pathway or disease mechanism. Another facet of this recommendation is to fuse cores with the Cancer Centers' cores. The program will check for overlap with the Cancer Center cores, highly specialized resources will be encouraged, and Cancer Centers will have to justify any similar cores. Matching funds will be required. This requirement, however, might be difficult to implement. Institutions caring for the underserved might be at a disadvantage; therefore, this recommendation might not be emphasized.

A third recommendation involves the development of a SPORE Parent Committee to review applications across sites. A standing Special Emphasis Panel is planned, with a two-tier review process, three meetings per year, and 4 years of service. Committee

membership will involve two members, with a broad range of scientific expertise, from each organ site. At least 50 percent of the members will be SPORE PIs. Senior investigators with multidisciplinary expertise, including translational science, would come into the program, and the initial members would be appointed to 1- to 3-year terms to balance the rotation. The metrics for funding would include a priority score for science. The burden of disease, including mortality, incidence, and years of life lost, involves programmatic aspects and other NCI funding mechanisms already in place.

A fourth recommendation involves the creation of a national clinical research and informatics system to be appropriately integrated with the Cancer Centers, Association of American Cancer Institutes, industry, and other interested parties. This recommendation already is underway with caBIG. Data sharing must be reported in the NCI database. The NCI will designate the appropriate database format and define the frequency of reporting and/or data sharing. It also would be helpful to have technical transfer plans that address intellectual property issues during the course of the award period.

A fifth recommendation involves describing and quantitating the contributions of the P30/P50 Programs on an annual basis. This recommendation is underway based on data in competing and noncompeting renewals.

In discussion, the following points were raised:

- During the peer review process, SPOREs that engage in collaborations with other NCI programs and other NCI networks will be rewarded.
- With one exception, the 59 SPOREs are in place at major Cancer Centers and at some smaller Cancer Centers. Seven are at M.D. Anderson, and others are at Hopkins, Fox Chase, Fred Hutchinson, Baylor, Case Western, Dana-Farber, Iowa, the Mayo Clinic, and Northwestern.
- Large numbers of SPOREs exist in common diseases; however, a mechanism is needed for research in less common diseases. Highly uncommon tumors probably require a consortium, not a SPORE.
- The standing committee for SPORE reviews will be rolled out in June.

- Efficient use of resources is the aim of “fusing” cores with the Cancer Centers.
- The technology transfer plan addresses intellectual property issues.
- An evaluation of the success of the career development component of SPORE rests on the mission of the program, which is to bring basic discoveries into the clinic by funding Phase I and Phase II clinical trials and early phase clinical interventions. More than 130 Phase I and Phase II clinical trials are now underway. The SPOREs are participating with CALGB, ACRIN, the Southwest Oncology Group, and Eastern Cooperative Oncology Group in 85 additional interventions. A total of 208 interventions include Phase I and Phase II clinical trials.
- A number of P30 Committee members thought that in time, some SPOREs would become translational program project grants. However, it was found that the science often was not mature enough to result in meaningful therapeutic translation.

XIV. ADJOURNMENT—DR. ROBERT YOUNG

There being no further business, the 29th meeting of the BSA was adjourned at 12:20 p.m. on Tuesday, November 9, 2004.

top