Board of Scientific Advisors

Meeting Minutes

March 15-16, 2004

Conference Room 10, C Wing, Building 31
Bethesda, Maryland 20892

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The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 26th meeting on Monday, 15 March 2004, in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Frederick Appelbaum, Director, Clinical Research Division, Fred Hutchinson Cancer Research Center, presided as Chair. The meeting followed the 9th Joint meeting of the BSA and the Board of Scientific Counselors (BSC), NCI.

The meeting was open to the public from 11:10 a.m. until 5:12 p.m. on 15 March for the annual ethics overview and NIH Conflict-of-Interest issues; P30/P50 Working Group report: P30 Implementation Plan; re-evaluation of paylist report; ongoing and new business; and new and re-issued Requests for Applications (RFAs) and Cooperative Agreements. On 16 March, from 8:30 a. m. until adjournment at 12:00 noon, a minisymposium was presented on the NCI initiative entitled Improving the Quality of Cancer Care; and updates on the Cancer Bioinformatics Grid (caBIG) and Clinical Trials for Cancer Prevention.

Board Members present:
Dr. Frederick R. Appelbaum (Chair)
Dr. David B. Abrams
Dr. David S. Alberts
Dr. Hoda Anton-Culver
Dr. Neil J. Clendeninn
Dr. Thomas Curran
Dr. Mary Beryl Daly
Dr. H. Shelton Earp III
Dr. Patricia A. Ganz
Dr. William N. Hait
Dr. Susan B. Horwitz
Dr. Hedvig Hricak
Dr. Eric Hunter
Ms. Paula Kim
Dr. Herbert Y. Kressel
Dr. Michael P. Link
Dr. Lynn M. Matrisian
Dr. Christine A. Miaskowski
Dr. Enrico Mihich
Dr. John D. Minna
Dr. Nancy E. Mueller
Dr. Richard L. Schilsky
Dr. Ellen V. Sigal
Dr. Margaret R. Spitz
Dr. William C. Wood
Dr. Robert C. Young

Board Members absent:
Dr. Esther G. Chang
Dr. Raymond N. DuBois, Jr.
Dr. William G. Kaelin, Jr.
Dr. Kenneth W. Kinzler
Dr. W. Gillies McKenna
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.

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I. CALL TO ORDER AND OPENING REMARKS - DR. FREDERICK APPELBAUM

Dr. Appelbaum called to order the 26th regular meeting of the BSA and welcomed members of the Board, NIH and NCI staff, guests, and members of the public. He reminded Board members of the conflict-of-interest guidelines and called attention to the 2005 meeting dates and confirmed the 2006 dates. Dr. Appelbaum then invited the public to submit to Dr. Paulette Gray, Acting Director, Division of Extramural Activities, in writing and within 10 days, comments regarding items discussed during the meeting.

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II. CONSIDERATION OF THE 13-14 NOVEMBER 2003 MEETING MINUTES- DR. FREDERICK APPELBAUM

Motion: The minutes of the 13-14 November 2003 meeting were approved unanimously.

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III. ANNUAL ETHICS OVERVIEW AND NIH CONFLICT-OF-INTEREST ISSUES- DR. MAUREEN WILSON

Dr. Maureen Wilson, Assistant Director, Ethics Office, NCI, provided an overview on changes in policies and outlook for review of outside activities and awards, which apply to NIH employees and to Board members by virtue of their being special government employees. As background, Dr. Wilson reminded members of the distinctions between the two categories within the conflict-of-interest listings: statutory (legal) conflict of interest, and regulatory (appearance of) conflict of interest. She reviewed provisions in the 1985 Policy Manual, noting that teaching, lecturing, and writing had always been permitted if activity did not create actual or apparent conflict of interest. Consulting for industry, which previously had been prohibited, was allowed in the 1985 Policy Manual if it utilized the general knowledge and expertise of the employee. Consulting with a company in which the employee owned stock also was prohibited. This change in policy recognized the increasing importance of industry in biomedical research and encouragement by the Executive Branch of closer cooperation between the governmental and private sectors. Dr. Wilson noted that the 1988 Policy Manual continued to allow consulting and lecturing for industry, with the same compensation limits. The policy did acknowledge that there could be, more or less, a conflict of interest depending on the size of the institute or center (IC) and the level of an employee's responsibilities.

In 1991, an honorarium ban was enacted, which prohibited an employee from receiving payment for an appearance, speech, or article, regardless of whether the topic related to official duties. Exceptions existed for a series of three or more different but related appearances, speeches, or articles; the writing and editing of a book

or chapter of a book, editing for a scientific journal, or teaching a course as part of a regularly scheduled curriculum of an accredited institution of higher learning. In 1993, the Office of Government Ethics (OGE) issued a new set of standards of conduct (SoC) regulations, which permitted agencies to promulgate supplemental agency-specific regulations. The 1993 SoC regulations prohibited outside activities: 1) if they violated another regulation or statute; or 2) if, because of statutory or apparent conflict of interest, they would cause an employee to be restricted from his or her government duties. In the1993 NIH Policy Manual, high-level officials were still limited to the same activities: writing and editing, outside professional practice, and membership on committees that selected recipients of awards or prizes or prepared examinations for professional associations.

An OGE audit of the NIH in 1995 found that the 1993 NIH policy was not in compliance with the OGE-promulgated SoC regulations, in that the NIH was more restrictive than the regulations allowed. The restriction on entities with which an employee could consult was too broad, and OGE regulations looked to an employee's specific assignments, not that of the laboratory, branch, or IC. Additional areas of noncompliance were in setting compensation and service limits, and in prohibiting the receipt of stock, stock options, or any other type of compensation. Dr. Wilson noted that the NIH was given an option of asking for permission to issue its own set of regulations or adhering to the OGE regulations. The NIH decided not to issue supplemental regulations, but to make its policy consistent with government-wide regulations.

Dr. Wilson reminded members of the concerns raised by the media recently about how the NIH relates to the extramural community; the kinds and nature of compensation that can be received and how it impacts the ability of the NIH to carry out its public health mission. She briefly reviewed: 1) the letters of inquiry received from Congressmen Greenwood and Tauzin regarding lecture awards and the letter in response from Dr. Elias Zerhouni, Director, NIH, outlining NIH policy in those areas; and 2) the Los Angeles Times article raising concerns about consulting relationships between NIH employees and industry and Dr. Zerhouni's response to Congressmen Greenwood and Tauzin outlining NIH positions, rules, and regulations, as well as a review of ongoing activities. To date, the NIH has acted as follows: 1) centralized ethics reviews for all senior NIH officials; 2) reviewed all biotechnology and

pharmaceutical outside activities since 1999; 3) reviewed all ongoing outside activities; 4) established the NIH Ethics Advisory Committee (NEAC); 5) established a Blue Ribbon Panel to provide advice through the Advisory Committee to the Director (ACD); and 6) expanded the financial disclosure policy.

In regard to the expanded financial disclosure policy, Dr. Wilson noted that at the time of the 1995 audit, the NIH had approximately 77 individuals who filed public financial disclosures. On the advice of the auditors, the number was reduced to 22 in compliance with the OGE regulations and over time has reached a low of 14 NIH personnel who file publicly. The NIH has since applied to the OGE and received approval to add to that number. Certain other positions have now been designated for filing. Dr. Wilson then described the NEAC review process that applies to any outside activity for senior NIH staff. She noted that the amount and type of income for both existing activities and future proposed activities will be reviewed for the appearance (regulatory not statutory) of conflict, and high-level officials will be reviewed by Dr. Raynard Kington, Deputy Director and Deputy Ethics Counselor (DEC), NIH.

Dr. Wilson reviewed the NIH current policy on outside activities, which permits compensated outside activity that involves the results of government research that have been publicly available for more than a year with provisions. She noted that, in addition to actions being taken by the NIH, other reviews of NIH conflict-of-interest policies include those being conducted by the Blue Ribbon Panel, the OGE audit, Inspector General and Government Accounting Office reviews, and Congressional interest. The external reviews will result in recommendations for improvement in those areas as appropriate, and the recommendations will be conveyed to the NIH Director for action. BSA will not be covered by any of the outside audits, but the audits will affect how the NIH relates to the extramural community. In that regard, the Blue Ribbon Panel now is in the process of soliciting testimony from the public.

In discussion, the following points were made:

- Specific situations for Board members, such as invitations to be an advisor or to give lectures at a university abroad or invitations to speak at an NCI-cosponsored international

scientific meeting, should be referred to Drs. Gray or Wilson for assistance.

- The regulations could restrict access to the expertise that exists within the NIH by putting up roadblocks to having NCI investigators speak at institutions around the United States. A balance should be found to permit the dissemination of this information into the community in accordance with the public health mission of the NIH.

- The NCI is committed to ensuring that its employees have the full opportunity to work collaboratively throughout the community and to finding mechanisms to bring the community into the process.

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IV. P30/P50 WORKING GROUP REPORT: P30 IMPLEMENTATION PLAN- DR. KAREN ANTMAN

Dr. Karen Antman, Consultant to the Director, OD, NCI, presented the NCI's draft implementation plan in response to the P30/P50 Working Group report, specifically as it relates to the NCI-designated Cancer Center (CC) program and the revision of the Cancer Center Support Grant ([CCSG] or P30) guidelines. Review of the Special Programs for Research Excellence (SPOREs) recommendations and the supporting P50 grant mechanism currently is underway and will be reported at a later date. Dr. Antman informed members that the goals of the CCSG revisions are to implement the P30/P50 Working Group recommendations, simplify guidelines, and make the guidelines user-friendly for intended audiences, in particular the CC Directors, program and core directors, university and hospital administrators, NCI staff and review committees, the public, the NIH, and Congress.

Dr. Antman presented an overview of the working group recommendations and NCI's response to each of those recommendations. She noted that the Cancer Centers Program is developing a plan for equalizing both the size and number of CC applications coming in throughout the year. She described future CCs envisioned by the P30/P50 working group as: 1) incubators for

high-risk, high-reward initiatives; 2) preferred testing or launching sites for NCI programs; 3) users of electronic review and data submission; and 4) hubs with collaborating regional organizations. The importance of building a better infrastructure for CCs so that research can proceed at whatever speed the science drives the process was emphasized.

In the discussion, the following points were made:

- Guidelines for the review process and site visitors should correspond to the CCSG guidelines; the goals of program and review should be harmonized.

- In an analysis of requested and recommended clinical budgets in the CCSGs over the past five years, the funding received was found to be close to the funding requested on average.

- CC utilization of the central IRB is increasing.

- Language should be incorporated in the guidelines to provide incentives or recognize the opportunity for CCs to provide core resources to support clinical trials conducted by the Cooperative Groups.

- Dissemination should be articulated more explicitly in the CCSG guidelines as a trans-disciplinary team criterion for the CCs. Supplemental grants for dissemination cores at existing CCs should be considered.

- The clinical and population sciences were recognized as two research areas that traditionally have been underfunded and should be emphasized in future funding decisions.

- Review teams should receive orientation and be reminded to review carefully the CCSG guidelines before the site visit.

- An outreach infrastructure and synergizing with state cancer plans are critical issues.

V. WORKING LUNCH

Re-evaluation of the Paylist Report: Keep, Change, or Discard.

Mr. Stephen Hazen, Chief, Extramural Financial Data Branch, OD, NCI, reminded members that the BSA Current Payline Report was created in 1996 for the inaugural BSA, and has been modified slightly during the intervening years. Mr. Hazen asked that the Board review the report in its present form to determine whether it continues to fill a need. He explained that the 1996 report showed the percentile ranking or priority score ranking for Traditional (R01s), Program Projects (P01s), First Independent Research Support & Transition (FIRST) Awards (R29s), Core Centers (P30), Clinical Groups (U10), National Research Service Award, Individual (F32/33), Institutional (T32), and Cancer Control (Community Clinical Oncology Programs [CCOPS]-U10s) from 2 years ago, 1 year ago, the previous Board meeting, and the current Board meeting. Differences in the report since then are that R29s were discontinued in 2002, First-Time (R01s) became somewhat equivalent to the FIRSTs, and a separate payline is now being set for these. In addition, a payline is no longer being set for Program Projects (P01s). Mr. Hazen suggested two changes in format for the Board to consider: 1) Because there is no longer a P01 payline, that line could be eliminated; and 2) the differential payline for First-Time R01 investigators could be added. He asked the Board to provide advice as to whether the information contained in the report continues to be useful, whether any recommendations are based on data provided in the report, and whether the information provided in the report is available in other places in a more timely manner.

In discussing the following point was made:

- The report provides information on the overall extramural funding climate as it relates to the NCI and is, therefore, critical to the Board's advisory role as a measure against which to review and prioritize RFA concepts.

- The P01 funding priority score continue to be included, even without a designated payline.

- Add information on the number of applications received and provide as much additional information and graphic displays as possible.

Ongoing and New Business

BSA at National Meetings: Members representing the BSA during "NCI Listens" sessions at upcoming meetings are: **Society of Behavioral Medicine**, 27-31 March, Baltimore, MD; Drs. David Abrams (chair), Robert Croyle (presenter), Paulette S. Gray, and Scott Leischow; **American Association for Cancer Research**, 30 March, Orlando, FL; Drs. Hoda Anton-Culver (chair), Dinah Singer, (presenter), Mark Clanton (presenter), H. Shelton Earp III, Ellen G. Feigal, Paulette S. Gray, William N. Hait, Enrico Mihich, and Carolyn Strete; Oncology Nursing Society, 29 April-2 May, Anaheim CA; Ms. Christine Miaskowski, (chair), Drs. Michael Stephanek (presenter) and Paulette S. Gray, and Ms. Paula Kim.

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VI. RFA/COOPERATIVE AGREEMENT CONCEPT REVIEWS-PRESENTED BY NCI PROGRAM STAFF

Office of the Director (OD)

Patient Navigator Research Program (RFA/Coop. Agr.). Dr. Roland Garcia, Program Director, Center to Reduce Cancer Health Disparities (CRCHD), stated that the goal of the proposed project is to reduce cancer health disparities by eliminating access barriers and facilitating timely access to quality cancer care in a culturally sensitive and appropriate manner, thereby preventing unnecessary suffering and premature death among underserved populations. Patient navigation refers to the support and guidance offered to persons with abnormal findings in accessing the cancer care system and overcoming barriers to quality standard care. It spans the cancer care continuum from the abnormal finding through completion of treatment, and it links providers and families with appropriate followup services. The objective of the proposed RFA is to challenge investigators to develop and implement structured patient navigation in communities that serve racial and ethnic minorities, people of lower socioeconomic status, residents of rural areas, and other underserved populations. The research design will include both intervention and comparison groups. Applicants must

define models for patient navigation, define settings and underserved population groups, and arrange necessary collaborations between community outpatient settings and treatment sites. They will collaborate with the CRCHD staff to develop evaluation metrics. Evaluation of individual projects will be based on differences between intervention and control groups in diagnosis, treatment, and resolution timeliness, and on the required evaluation plan and success measurement criteria. Evaluation of the overall program will be based on its effectiveness in different settings and the characteristics and best practices that contribute to project success.

The concept proposes an annual amount of $4.8M to fund an estimated six 5 year awards. Total estimated cost is $24M.

In discussion, the following points were made:

- The RFA should be written with a more targeted focus with regard to research questions, navigation model types, cancer settings, and the nature of the proposed comparison groups to provide the responder with guidance and facilitate the grant application review.

- Information acquired from the CDC's Women Well Check program to enhance cervical and breast cancer screening in underserved populations, and from the Indian Health Service's interagency study, should be used in the planning for the proposed patient navigation project. The CDC study has amassed considerable information on how to establish networks for diagnosis and treatment, as well as screening.

- A better definition of the concept is needed for the RFA; the hypotheses that are going to be preeminent in answering barriers to cancer care questions should be laid out.

- Applicants should be allowed to respond to a single area, as well as the whole.

- Process evaluation measures should be defined more clearly and should include questions of cost-effectiveness and scaleability.

- The scope of the RFA should be narrowed to ensure some homogeneity in the pool of applicants; a few more defined question and populations should be considered; the possibility of linkage to existing networks should be included; the primary outcome measures also should be more narrowly focused.

- Program staff should consider the possibility of initiating a broad inquiry among a population of interested investigators by convening a series of workshops to define what is a reasonable target for the initial RFA.

Motion. The Office of the Director RFA/Cooperative Agreement concept entitled "Patient Navigation Research Program" was approved pending that the RFA concept be rewritten to address the following BSA concerns: enhanced focus of the initiative; establishing linkages to existing networks; addressing comparability; scalability; cost-effectiveness; phased launching of the initiative; focusing on assessment of outcomes; establishing interim evaluative processes; and statistical modeling. Drs. Hoda Anton-Culver (Chair), Patricia Ganz, William Kaelin, Neil Clendeninn, and Ms. Paula Kim will serve on the BSA subcommittee to work with staff to refocus the concept.

Division of Cancer Prevention (DCP)

Circulating Cells in Cancer Detection (RFA).). Dr. Peter Greenwald, Director, DCP, explained that the concept to be presented is related to a Small Business Innovation Research (SBIR)/Small Business Technology Transfer Research (STTR) set aside, in accord with the mandate from Congress, to designate funding specifically for small business research. Dr. Mukesh Verma, Cancer Biomarkers Research Program, DCP, stated that the goal of the proposed project is to develop high-throughput methodologies for isolation and enrichment of exfoliated cells and circulating cells in the body fluid, which can be used for cancer detection, diagnosis, and risk assessment. The potential for using exfoliated cells in circulating DNA as a cancer detection and diagnostic tool has been demonstrated in studies of plasma DNA to detect lung cancer, pancreatic fluid to detect pancreatic cancer,

exfoliated cells from urine to detect bladder cancer, and Epstein Barre Virus DNA in blood to detect nasopharyngeal carcinoma. Barriers to the use of exfoliated cells for cancer detection are associated with low yield, low throughput, DNA purity and integrity, and cost. Specific aims for this project are to encourage development of new technologies for the isolation, preservation, and enrichment of exfoliated and circulating cells, and to develop high-throughput methodologies to isolate circulating DNA. Dr. Verma noted that there is a continued need for early detection and risk assessment, and noninvasive techniques likely are to be accepted in clinical practice. The project also will promote innovation in isolating exfoliated and circulating cells. Only 11 applications were received in three cycles in response to a previous program announcement for research to develop this enabling technology. This project proposes to address the problem by expanding the scope to include circulating DNA, using the SBIR/ STTR mechanism with set-aside funding, and promoting the project in conferences, workshops, and meetings.

Anticipated cost for the 2-year project period is $1M to fund 5-6 awards per year. Funding is to come from the congressionally mandated SBIR pool.

In discussion, the following points were made:

- The concept does not expand on what exactly is meant by circulating cells and how the targeted cells will be used.

- Parameters are needed for indicating cell or DNA quality, defining sample volume, and defining what is to be considered high throughput screening.

Motion. The Division of Cancer Prevention RFA (SBIR/STTR) concept entitled "Circulating Cells in Cancer Detection" was approved with 23 votes in favor, 1 opposed, and 1 abstention.

Division of Cancer Control and Population Sciences (DCCPS)

Status of the Cancer Genetics Network Re-issuance. Dr. Robert Croyle, Director, DCCPS, began the update on the Cancer Genetics

Network re-issuance review and the EC decision not to reissue by recognizing the need to keep the Board informed of larger initiatives that will not be presented for re-issuance concurrence, particularly in the current budget climate.

Issues relevant to the decision not to reissue a large initiative are the need to capitalize on what has been built. In some cases this means retaining core resources, data, or infrastructure through a contract mechanism; in other cases, the initiative could be scaled down to a small letter RFA for the phase-out process. Another important issue to consider is that the initiative may have accomplished a number of goals but was not reissued because of a flat budget and the need to redeploy funding to accomplish other priorities.

As background, Dr. Croyle reminded members that the Cancer Genetics Network (CGN) was an infrastructure for collaborative research into the genetic basis of human cancer susceptibility, which evolved from recommendations of the Cancer Genetics Working Group. Other goals were to integrate cancer genetics into medical practice, address associated educational, ethical, and psycho-social issues, and perform innovative small projects and selected pilot studies. The first formal EC discussions of the potential re-issuance of the CGN resulted in the recommendation for an 18-month extension to provide investigators with more time to demonstrate scientific progress, focus on minority recruitment for the CGN registry, and continue to develop infrastructure to support outside investigators. It was decided that a BSA Subcommittee would be asked to advise the EC on a re-issuance, i. e., to evaluate CGN progress which was reported to the BSA at the June 2003 meeting. Following the progress update and several conference calls with Epidemiology and Genetics Research Program (EGRP) staff, the Subcommittee provided feedback to the NCI regarding CGN's progress in November 2003, and the EC considered re-issuance in December in the climate of a trans-NCI review and comparison of all initiatives in a time of a flattening budget. The decision was made not to reissue the RFA but to retain core elements of the Registry. CGN principal investigators were informed of the EC decision shortly thereafter. Program staff were charged with looking into how the CGN registry of enrollees can be retained as a core resource, but at a reduced funding level. EGRP staff are also working to define some of the core elements of the data infrastructure and registry created by the CGN, which

could be retained for future research purposes.

Dr. Edward Trapido, Associate Director, EGRP, DCCPS, reminded members that the CGN was created as an infrastructure, not a research project; therefore, it was not designed to produce publications or findings. Instead, CGN accomplishments include: 1) the 23,995 probands enrolled in the recruitment pool representing 16,144 families; 2) 10 pilot studies that are underway; 3) utilization of the CGN by one intramural NCI project; 4) increasing minority enrollment; 5) a large, diverse registry of potential research subjects with active followup; 6) innovative informatics tools for collaborative, multi-center research; 7) pilot studies addressing the genetic basis of human cancer and ethical, legal, and social issue concerns; and 8) clinical trials integrating genetic risk information. Dr. Trapido noted that concerns of the BSA Subcommittee were the insufficient evidence of synergism among the investigators; a small amount of evidence that the CGN infrastructure was essential for the research completed or underway; a modest level of productivity given the cost and complexity of the initiative; overall cost for the eight program and three informatics sites; inadequate use of the infrastructure by outside investigators; and unimpressive minority recruitment at the time of the review. Dr. Trapido then reviewed issues surrounding termination of the initiative and next steps being considered. The large number of accrued subjects represent a valuable resource that could be tapped for future research. In addition, there is a commitment that has been made to subjects and their families and issues to consider related to access to confidentially collected data and informed consent documents at each institution. Funding will be needed to transfer the data and documents to a central source, maintain a streamlined CGN registry as a resource, and fulfill the commitment to some of the ongoing studies.

In discussion, the following points were made:

- Clearly specified outcome goals and measures also are needed for tracking progress, and a mid-project review should be conducted to introduce course changes to incorporate evolving scientific emphases, such as adding biospecimen collection to the CGN mission.

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VII. UPDATE: SPECIMEN RESOURCES SUBCOMMITTEE- DRS. FREDERICK APPELBAUM, ANNA BARKER, AND ROGER AAMODT

As background, Dr. Frederick Appelbaum noted that, at its November 2003 meeting, the BSA discussed specimen usage and the cooperative groups. A subcommittee composed of Drs. Appelbaum, Hoda Anton-Culver, Richard Schilsky, Raymond DuBois, and Ms. Paula Kim was established. To avoid overlap with the NCI Specimen Resources Working Group, Dr. Appelbaum noted that he had asked Dr. Barker to clarify a role for the BSA in overseeing the valuable specimen resource that exists in the Cooperative Groups (CGs), CCs, and SPOREs, and in working collaboratively in the formation of an National Bio-specimen Network (NBN) Blueprint.

Dr. Barker reminded members that the problem with bio-specimens is not too little information, but so much that there is a need systematically to begin to integrate the molecular and clinical data to produce the statistically powerful data sets that will be needed to drive advanced technology development and the new interventions that will be needed to realize the 2015 challenge goal. At the November meeting, she presented one model that was being considered, the NBN Blueprint, which was developed under the auspices of the C-Change (former National Dialogue on Cancer) research team, co-chaired by Ms. Kim, and based on a RAND study on best practices for bio-specimens. The expectations were that this huge undertaking would evolve into a state-of-the-art system for collecting and annotating patient-derived bio-specimens and associated data. Dr. Barker noted that the need for a bio-specimen network has long been advocated by the NCI's Progress Review Groups (PRGs); and related efforts have been initiated by the Prostate Funders Group, National Cancer Policy Board, and the NIH Foundation. At the November meeting, Dr. Barker indicated that the BSA should be involved in the planning for such an initiative. Dr. Barker noted that the NCI Bio-specimen Resources Committee/Task Force had been established earlier to coordinate intramural and extramural work in this area, and she introduced Dr. Roger Aamodt, Chief, Resources Development Branch, Division of Cancer Treatment and Diagnosis, to present an update of Committee's efforts to date.

Dr. Aamodt stated that the Committee was established in 1998 to help the NCI develop rational processes to reconcile the many requests for human specimen resources with existing resources and future needs for new resources. The rationale was that a standing committee was needed to work from an existing knowledge base and thereby be prepared to continue discussions at future meetings. In the previous ad hoc committee model, continuity was difficult to maintain because of changing membership and the lack of time to prepare adequately for thoughtful deliberations in the meeting time available. Dr. Aamodt informed members that the group was created as a task force of the BSA to work within the parameters of federal committee legislation and that nine meetings had been held so far, either in person or by teleconference.

To date, the Committee has addressed the following issues: 1) the creation of a compendium of existing and commercial resources, future needs, and prioritization; 2) informatics and the need for standards; 3) an NCI database of research results; 4) statistical considerations; 5) ethics; 6) PRG recommendations; 7) translating molecular technologies; 8) specimen preparation and best practices; 9) evaluation of resource performance; 10) tissue micro-arrays; 11) international sources; and 12) the C-Change. Accomplishments of the Committee have been in the areas of: addressing questions and gathering feedback on NCI metrics to evaluate resources; formulating and testing the idea for a Shared Pathology Informatics Network (SPIN); developing an RFA for Specimen Resources needed to fill gaps; investigating the need for a resource of last resort for tissue specimens being discarded by pathology groups, and exploring the issue with outside groups, which led to the decision not to create such a resource; and helping to develop a plan similar to the NBN Blueprint.

In summary, Dr. Aamodt noted that BSA members serve on the Bio-specimen Resource Committee and that this Committee provides feedback to the BSA when it is warranted. Information on tissue resources and other specimen issues usually is conveyed through Dr. Sheila Taube, Associate Director, Cancer Diagnosis Program.

Dr. Barker stated that Drs. Taube and Aamodt have begun working on an inventory of NCI resources, which will include those in 61 CCs, 50 SPOREs, 14 Cooperative Groups, Cancer Family Registries, and large intramural initiatives, including the Prostate,

Lung, Colorectal, and Ovarian Cancer Screening Trial, Cooperative Human Tissue Network, SPIN, Early Detection Research Network (EDRN), and other organ-specific resources. Dr. Barker noted that the inventory is needed to delineate the NCI's resource base and establish best practices internally. In addition, pilot projects should be considered for information gathering, such as that of the Prostate Inter-SPORE Group and its development of best practices for the Prostate Cancer Funders. Dr. Barker pointed out that the NCI is currently engaged in collaborations with the United Kingdom in their bio-informatics and bio-specimen initiatives; indications are that, increasingly, international collaborations will be driven by many disease groups and nonprofit foundations. The NCI, therefore, should be prepared to speak rationally about the cancer tissue resource base and know that the best practices are being used across the entire span. She suggested, therefore, that a task for the BSA Subcommittee would be to ensure that the inventory of the NCI resource base is completed and that criteria have been developed for looking at those resources. Another suggestion would be that the Subcommittee charge NCI leadership with developing a white paper of recommendations and ideas for moving toward the ca-BIG-like change that is coming in the area of bio-specimen resources.

In discussion, the following points were made:

- As provisions of the Health Insurance Portability and Accountability Act move forward, it will be necessary to access and account for every specimen.

- The NCI's Specimen Resource Locator Web Site is a public-use database, with provisions for accepting requests for specimens. Another part of the Web Site is a much larger database of all the known resources and information about contacts. Access to information in this database can be obtained through the NCI Tissue Expeditor, which does not provide samples and cannot accept requests, because of a lack of personnel and resources. The NCI helps establish collaborations to obtain that information.

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VIII. IMPROVING THE QUALITY OF CANCER CARE- DRS. ROBERT CROYLE, RACHEL BALLARD-BARBASH, JOSEPH LIPSCOMB, STEVEN CLAUSER, MOLLA DONALDSON, AND ROBERT HIATT

Dr. Croyle informed the Board that the update on quality of cancer care initiatives would include some that have been heard in previous years as concepts and some collaborations with other agencies. It would present both a conceptual and content overview of the many and complex areas of this growing area of research. Dr. Ballard-Barbash, Associate Director, Applied Research Program, DCCPS, reminded members that there is an increasing consensus, both in cancer research and policy communities, about the need for work to improve the quality of cancer care. The NCI's response in this area has been to designate this area within the past four Bypass Budgets, with the goal of improving the quality of cancer care by strengthening the scientific evidence basis for private and public decision-making on care delivery, coverage, purchasing, regulation, and standards setting. A summation of the various initiatives and their coverage across the cancer continuum indicates that the major focus is in the area of diagnosis and treatment. A few efforts look across the entire continuum, including prevention. Dr. Ballard-Barbash gave an idea of the large number of organizations, both public and private, that are engaged in initiatives that cover research and delivery across the continuum, with the ultimate goal of moving quality of care (QOC) into the standard for clinical practice in the United States, not an exception.

Dr. Lipscomb, Chief, Outcomes Research Branch, DCCPS, stated that the NCI uses the Institute of Medicine's (IOM) definition of quality of cancer care: the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge. In the NCI, this means provision of evidence-based care across the cancer continuum in a timely and technically competent manner, with good communication, shared decision-making, and cultural sensitivity. Dr. Lipscomb noted that the classic framework for assessing, which was developed by Avidus Donavidian a quarter of a century ago, is based on measuring structure (e.g., physician certification), process (e.g., evidence-based interventions), and outcome (e.g., longer, better life). Another framework for this area of research is the cancer care improvement cycle. At any point in time there will be studies at

each of four different areas. Activities in all of these areas improve what is known at any given point in time about how to do QOC studies, and activities in all of these areas benefit from an improved science base.

To evaluate the state of the science in measuring outcomes that matter, the NCI established the Cancer Outcomes Measurement Working Group (COMWG) which focused on the question of how to define, measure, and ultimately how to use outcomes that matter to decision-makers in studies. Their approach was to look at the subjective outcomes, health-related quality of life (HRQOL), satisfaction, economic burden, and how they vary across the cancer continuum to determine which measures were valid, reliable, and feasible. Written reports based on the COMWG recommendations to the NCI on how to move the state of the science forward are forthcoming in the fall in a book, Outcomes Assessment in Cancer, being published by Cambridge University Press. Dr. Lipscomb stated that the next step is to see whether areas of potential agreement have emerged about the role of patient-reported outcomes in decision-making, either through a state-of-the-science meeting, an NIH consensus development conference, or a public-private effort to define voluntary consensus standards. A second step is to explore the implications of these findings for a research agenda. Research questions are: 1) What is the value added of these patient-reported outcomes over and above biomedical outcomes? and 2) What is meant by the concept of a "clinically meaningful difference"?

Members were told that further work is needed on how to negotiate a balance between finding measures that are adequately responsive for the outcome under study, while promoting comparability of findings across studies. One approach in this regard was emphasized by the COMWG and has been found to complement a trans-NIH Roadmap Initiative: Dynamic Assessment of Patient-reported Chronic Disease Outcomes. The NCI and its phycho-metricians have been playing a major role in shaping this initiative, which will create an Internet-based Patient-Reported Outcomes Measurement Information System (PROMIS). This initiative is intended to lay the groundwork for a public-private partnership to extend the PROMIS beyond the 5-year development stage.

In discussion, the following points were made:

- Measuring the satisfaction of those participating in Cooperative Group clinical trials would be a potentially useful tool for encouraging other patients to enter clinical trials.

Identifying Quality-Enhancing Interventions. Dr. Steven Clauser, Senior Scientist, Outcomes Research Branch, DCCPS, addressed initiatives in the next leg of the cancer care quality improvement cycle. After outcomes that matter are identified and measured, the next step is to build an evidence base for improving the quality of cancer care. The NCI's strategy for this task is to quantify the population-level problem of interest related to QOC; understand structure, process, and outcome relationships and track them over time in the health care delivery system; and establish an intervention impact on outcomes that matter in the system. Dr. Clauser described completed and ongoing initiatives from the NCI research program that illustrate the utility of this approach to building an evidence base to understand and improve the health care delivery system related to cancer. As examples of studies to improve the quality of diagnosis and treatment of prostate cancer, he used the SEER-Medicare studies, which quantified the population problem and correlated structure, process, and outcomes data; the NCI-sponsored Prostate Cancer Outcomes Study (PCOS) that began to unveil the determinant of some of the process and outcome relationships, especially for patient-centered outcomes of care important to prostate cancer patients; NCI-sponsored longitudinal studies, including the Breast Cancer Surveillance Consortium, that documented both opportunities to improve mammography screening in the health care system and the need to improve and detect breast cancer through better testing and interpretation of results through mammography. These studies led to the initiation of the study entitled Detecting Early Tumors Enables Cancer Therapy (DETECT), a large, multi-site cohort study of breast cancer care that was designed to understand the implications of practice variation of breast cancer screening, detection, and followup on health outcomes in medical practices and the Health Maintenance Organizations (HMOs).

Dr. Clauser then discussed the recent population-based perspective study of newly diagnosed lung and colorectal cancer patients; the Cancer Care Outcomes Research and Surveillance Consortium (CanCORS), established in 2001 as an RFA-supported cooperative agreement funded jointly by the NCI and the Veterans

Administration (VA) to improve the QOC for patients with lung and colorectal cancer. If successful, CanCors will create a comprehensive longitudinal data set to examine, in great detail and precision, the determinates of quality care in lung and colorectal cancer. Dr. Clauser noted that the CanCORS study naturally complements the American Society for Clinical Oncology's National Initiative for Cancer Care Quality.

In discussion, the following points were made:

- Plans for disseminating the findings from NCI's QOC research include linkages to the PDQ system for use by patients and physicians, and seminars and conferences that make this data available. The intent is that investigators can take the next steps to develop the science in this area, such as proving and targeting interventions that can be used to enhance the delivery system. Patient advocacy groups are included in developing the process.

- Reduction in variability of care should be an important emphasis of the research because of the potential for making a significant impact on quality care delivery to improve outcomes.

Impacting Cancer Care Delivery. Dr. Clauser reminded members that the NCI is a science-based organization and cannot directly improve the delivery of care on its own. Rather, it depends on developing partnerships with those organizations that can have a direct influence on the delivery system and ensuring that they use the best available science to try to improve care and outcomes that matter. Dr. Clauser cited cancer prevention rate trends from the National Committee on Quality Assurance Health Employer Data Information Set that demonstrate that quality measurement matters. These experiences have led the NCI to spearhead the creation of a public-private effort to create a core set of cancer quality measures. The Cancer Care Quality Measures Project (CanQual) was convened by the nonprofit National Quality Forum (NQF), whose 1,000+ membership represent the gamut of organizations that are dedicated both to the standardization of quality measurement and the improvement of health care throughout the delivery system. Measurements that derive from the CanQual project generally are considered voluntary consensus standards, which gives them some regulatory status with public agencies that use these measures for

quality improvement initiatives. Questions to be discussed are: 1) What are the most critical quality gaps? 2) How can the gaps be measured and closed? and 3) How can the measures be made suitable to support QOC improvement strategies?

Dr. Clauser noted that the CanQual Steering Committee was created in 2001 to guide the measurement-development process, completed Phase I of the project by identifying tumor-specific (breast, colorectal, prostate) and cross-cutting focus areas which were access to care, including clinical trials, communications and coordination of care, prevention and screening, and symptom management and end-of-life care. Phase II will assess the evidence and provide recommendations to the NQF on cancer core quality measures and research recommendations for further development. In Phase III, CanQual will continue to build the evidence base for cancer QOC measurement; work with partners to adopt QOC measures and evaluate their dissemination and use; and work with provider and quality improvement organizations to implement QOC-enhancing interventions, track improvements in QOC, and feed findings back to policymakers at all levels.

Dr. Molla Donaldson, Outcomes Research Branch, DCCPS, presented an update on the work of the Quality Cancer Care Committee (QCCC) and its projects to improve cancer care. The QCCC is a trans-agency committee, which includes all federal agencies that deliver, pay for, regulate, and conduct research on cancer care. The purpose of the QCCC is to understand the needs of various agencies for research related to cancer care and then ensure that decisions are informed by the best scientific evidence. The QCCC also identifies knowledge gaps and stimulates interagency projects. Finally, the QCCC provides a forum for the interaction of research and application arms of the federal government to explore complex issues of interest to multiple agencies. Several collaborative projects supported by the NCI are: 1) the Center for Medicare and Medicaid Services to improve colorectal cancer screening for the elderly; 2) a quality enhancement research initiative for colorectal cancer with the VA; and 3) a Health Resources and Service Administration (HRSA) project to improve screening and followup care for breast, colorectal, and cervical cancer in primary health care clinics.

Dr. Donaldson noted that the HRSA-NCI-CDC collaboration that is promoting cancer screening and followup is in its third year. The

group chose goals related to cancer screening, adequate notification of results, and timely followup. The project began with 10 pilot sites in HRSA-supported community health centers and has grown to 21 teams involved in community health centers from California to Georgia. The interdisciplinary teams include front-line health practitioners and leadership as well as administrative and clerical staff involved in planning and implementing interventions and tracking change. Preliminary data on cancer screening indicate that in January 2004, 63 percent of women aged 21 or older had Pap tests in the past 3 years, compared with 40 percent at baseline in July 2003.

Dr. Donaldson noted that several QCCC projects are under development: 1) a collaboration with the Indian Health Service to improve palliative care and pain management among American Indian and Alaska Native populations with cancer; 2) a project to track health plan adherence to colorectal cancer screening; and 3) one that emphasizes the NCI's role in providing a forum for public-private discussions on fostering a national cancer data system to support improved care delivery, clinical research, and public health.

In closing, Dr. Donaldson described an initiative begun last year to translate and implement findings to impact the delivery of care. Redesigning Cancer Care (CaRe) evolved from observations by clinicians and patients and confirmation in reports of the IOM and the National Cancer Policy Board that QOC is uneven and does not reliably provide the care that patients, their families, and oncologists want. The conclusion was that a major effort was needed to substantially improve care at a threshold level. CaRe will: 1) articulate a framework and strategy for a larger initiative to improve the care of patients with cancer; 2) ensure dissemination and usage of best practices in diagnosing and delivering cancer care; 3) re-design cancer care across the continuum and in all practice settings; and 4) develop model systems to integrate clinical information, patient reports, and population-level surveillance. The CaRe initiative is at the point of framing the direction and scope of a larger, long-term project to get underway this year, with the hope of implementing what is learned. The NCI role will be as convener, providing a science base and partnership with foundations, other federal agencies, and private sector organizations.

In discussion, the following points were made:

- It should have been possible by now to develop a set of guidelines that everybody who takes care of cancer patients would agree makes sense to apply.

- Although cancer care is worse for a variety of populations that are underserved, it would be a mistake to imply to the public that the problem lies solely there. Many people with good access to care and adequate insurance options also are getting less than optimal medical care.

Monitoring Progress and Identifying Opportunities. Dr. Robert Hiatt stated that the NCI is working with public and private partners to foster the development of a national cancer data system as recommended by the IOM, but building on what already is known. The objectives are to track the impact of existing evidence-based guidelines and core measures, identify disparities in access to high-quality care, and reassess over time whether existing quality benchmarks actually lead to improved outcomes. Key steps toward building capacity is 1) to encourage innovative use of existing data sources such as registries, medical records, administrative files of Medicare, Medicaid, and private payers; and surveys of patients, providers, at-risk individuals, and cancer care decision-makers; and 2) to accelerate development and linkage of multiple data sources to enhance timeliness, scope, and level of detail in monitoring, and to capture the complexity of cancer care to facilitate advanced statistical modeling of structure-process-outcomes relationships. Dr. Hiatt noted that current research builds on the firm foundation of SEER Patterns of Care and QOC studies; the SEER-Medicare studies, which linked the two population-based sources; and QOC research networks, such as the Breast Cancer Surveillance Consortium, CanCors, Cancer Research Network, and the National Coordinating Council on Cancer Surveillance.

Turning next to a 10-year view down the cancer information highway, Dr. Hiatt outlined key themes of the Summit on Cancer Surveillance and Information Systems, a futures project sponsored in 2004 by C-Change. He noted that the cancer community must: 1) embrace an expanded scope and vision for surveillance; 2) establish uniform standards for data collection and reporting are needed; 3) initiate automated data capture which is pivotal to high-quality, affordable systems to monitor and improve cancer quality; 4) establish a uniform patient identifier that meets confidentiality

requirements should be advanced; 5) develop incentives so that key public and private partners (e.g., providers and private insurers) will participate in data system development; 6) link high-quality data sets to facilitate QOC analysis; and 7) design flexible data systems to adapt to health care system changes over time. Dr. Hiatt noted that the meeting report will be summarized in several publications.

In discussion, the following points were made:

- The proposed national cancer data system has the potential to provide the capacity to harvest the information on post-hospital care that is lacking in existing data registries, recognizing that the greatest percentage of cancer care, including radiation therapy, is given on an outpatient basis.

- The NCI should take advantage of the leadership opportunity in this research area, as it exercised in the area of tobacco cessation and control.

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IX. UPDATE: caBIG-DR. KENNETH BUETOW

Dr. Kenneth Buetow, Director, NCI Center for Bioinformatics (NCICB), reminded members that the goal was to create a virtual web of interconnected data, individuals, and organizations to redefine how research is conducted, care is provided, and patients and participants interact with the biomedical research enterprise. The first step was to create caBIG, a common, widely distributed infrastructure that not only shares vocabulary, data elements, and data models, but also shares and recycles applications, with the goal of making raw published cancer data available for mining and integration. Dr. Buetow noted that the caBIG infrastructure joins diverse data within an institution and will facilitate the sharing of infrastructure, applications, and data throughout the cancer community, including the CCs, CGs, and various Consortia. All data and data applications and infrastructure will be available to everyone. Underlying principles for caBIG are open source, open access, open development, and federation, in that the infrastructure will support everyone's activities in situ through the Worldwide

Web.

Dr. Buetow described progress in implementing the caBIG action plan. Specifically, that a pilot network of CCs that agree to embrace caBIG principles has been established. Dr. Buetow briefly reviewed the extent of community engagement in developing the caBIG program noting that the areas of overwhelming interest were clinical data management tools and databases, translational research data tools, and tissue and pathology tools. The domain workspaces to be launched during the pilot phase are for Clinical Trial Management Systems, Integrative Cancer Research, and Tissue Banks and Pathology Tools. Two cross-cutting workspaces also will be launched; one responsible for vocabularies and common data elements, and one to develop architectural standards and provide assistance as necessary to other workspaces. Three Strategic Planning Groups will address issues related to data sharing and intellectual property, develop strategies for providing training, and assist in identifying strategic priorities.

Dr. Buetow noted that products to be delivered by caBIG in the next 2-3 years are a standards-based Clinical Trials Management System; a Tissue Management System; a "Plug and Play" analytic tool set; and a diverse library of raw, structured data. The Management System will enable electronic Investigational New Drug (IND) filing and regulatory reporting with the FDA, electronic management of trials, and integration of diverse trials. Near-term caBIG deliverables for use in cancer research today are the foundation on which caBIG is being built: clinical trials, molecular pathology, cancer genomics, and animal models. At the core of caBIG is the caCORE technology, which holds the portfolio of controlled vocabularies (NCI's enterprise vocabulary systems), common data elements, and biomedical objects. Structured and common data elements are available through publicly accessible resources for the systematic generation of clinical trials data.

Dr. Buetow described other caBIG products that are available immediately as open source software. He noted that the caBIG community will only enhance the richness and collection of tools and data associated with it in the form of ontologies, additional applications, and data from a variety of different sources. Additional information is available at http://cabig.nci.nih.gov/.

In discussion, the following points were made:

- The caBIG data sharing and intellectual capital working group is addressing the dual problem of building infrastructure to support the sharing of appropriately consented information linked to human specimens and then building a network with the capacity for sharing safe-harbor data.

- A simplified, tiered patient consent process standardized on a national basis could be one means of addressing the issues associated with using bio-specimen data. caBIG staff should continue to work with advocacy groups to enlist their help and tap into patients' willingness to participate in cancer research.

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X. UPDATE: CLINICAL TRIALS FOR CANCER PREVENTION- DR. PETER GREENWALD

Dr. Peter Greenwald, Director, DCP, reminded members that cancer prevention research has two broad directions: 1) lifestyle or public health, which involves tobacco control, eating behavior, and physical activity; and 2) medical, which involves identifying risk factors and applying chemo-preventive measures to reduce risk. Dr. Greenwald presented an update on clinical trials in the areas of lung cancer prevention in former smokers, breast cancer prevention, and prostate cancer prevention from the medical perspective. Members were reminded that public health approaches for lung cancer prevention include increasing the cost through taxation, creating a smoke-free environment, and focusing on youth and on smoking cessation in adults. In the area of chemo-prevention, Dr. Greenwald noted that the development of anti-nicotine vaccines is one of the most promising research areas today. He described Phase II trials being conducted on chemo-preventive agents: 1) a three-arm study of comparing alpha-tocopherol plus 13 cis-retinoic acid (13cRA) versus 9-cis-retinoic acid (9cRA) versus placebo; and 2) a Phase IIb study of anethole dithiolethione (ADT) versus placebo on bronchial dysplasia, with bronchoscopic examinations at initiation and 6 months.

In providing an update on breast cancer prevention trials, Dr. Greenwald informed members that noted that weight gain as an adult and obesity, estrogen and progestin use, and alcohol use are lifestyle risk factors for breast cancer. He reviewed findings in several completed chemo-prevention trials, such as: 1) The Breast Cancer Prevention Trial, conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP) through the CCOP; and 2) the Multiple Outcomes of Raloxifene Evaluation Trial; and 3) studied a second-generation selective ER modulator (SERM) aimed at preventing osteoporosis. Dr. Greenwald noted that although women with osteoporosis are not at particularly high risk for breast cancer, the findings were striking enough to provide the rationale for a head-to-head comparison of tamoxifen and raloxifene, which is ongoing in the Study of Tamoxifen and Raloxifene (STAR) trial. More than 18,000 women have been accrued to STAR, somewhat ahead of schedule.

Dr. Greenwald also discussed aromatase inhibitors and inactivators, noting that there have been 3 generations of these compounds that block the conversion of androgens to estrone or estradiol. Anastrozole, an aromatase inhibitor, was used in an adjuvant setting in the Arimidex [anastrozole], Tamoxifen, Alone or in Combination trial. In other aromatase research, the International Breast Intervention Study II is comparing anastrozole to placebo in high-risk women as one-half of the study, and anastrozole to tamoxifen in women with locally excised ductal carcinoma in situ in the other one-half.

Turning to biomarker endpoints and the ER-negative priority, Dr. Greenwald stated that the NCI is attempting to find ways to study agents that will reduce the occurrence of breast cancer that is either ER-positive and not responsive to SERMs, or ER-negative. The search, therefore, is for agents that do not work through the hormonally driven pathways. One example is the Breast Biomarker Modulation Trial conducted by the Texas Cancer Genetics Consortium, which is studying the compound bexarotene in women with genetically defined high-risk BRCA genes. Another set of studies uses a breast aspiration procedure around the areola before and after a chemo-preventive intervention to characterize the breast tissue. Dr. Greenwald noted that several compounds are under development that may be useful in reducing ER-negative tumors.

Members were told that the Rapid Access to Prevention Intervention Development (RAPID) program was established to help academic scientists in the development of preclinical and early clinical chemo-preventive drugs through the use of NCI contracts. Indole-3-carbinol (I-3-C), a phytochemical found in cruciferous vegetables and associated in epidemiological studies with lower rates of cancers, was studied under the RAPID program. These studies led to an NCI-sponsored Phase I pharmacokinetics and safety evaluation under an IND with the FDA. The IND was filed in January 2004. Under the RAPID program, the NCI is supporting this compound for clinical trial development.

Dr. Greenwald presented an update on the Prostate Cancer Prevention Trial, which used the drug finasteride to interfere in the prostate with the conversion of testosterone to the androgen, dihydrotestosterone (DHT). He also discussed the Alpha Tocopherol [Vitamin E] Beta Carotene (ATBC) study which had its beginnings in the United States-Finland Lung Cancer Intervention Trial in the 1980s. Data from a small trial in Arizona of selenized yeast or yeast alone to test the occurrence of skin cancers, the Harvard Health Professional Follow-up study of nearly 34,000 men in which the level of selenium in toe nails was measured, and the Baltimore Longitudinal Follow-up Study where Johns Hopkins investigators found that the group with the highest selenium level had a lower rate of prostate cancer were presented. He noted that these cumulative epidemiological data led to the decision to launch the Selenium and Vitamin E Cancer Prevention Trial.

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XI. ADJOURNMENT-DR. FREDERICK APPELBAUM

There being no further business, the 26th meeting of the BSA was adjourned at 12:00 noon on Tuesday, March 16, 2004.

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