

Board of Scientific Advisors

Meeting Minutes

June 26-27, 2003

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

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The Board of Scientific Advisors (BSA or Board), National Cancer Institute (NCI), convened for its 24th regular meeting on Thursday, June 26, 2003, 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 was open to the public from 8:00 a.m. until 6:13 p.m. on 26 June for opening remarks from the Chair; the Director's report; a mini-symposium on Future Directions for NCI Imaging; an Institute of Medicine/National Cancer Policy Board (IOM/NCPB): Fulfilling the Potential of Cancer Prevention and Early Detection; an update on NCI/Congressional relations; ongoing and new business; an overview of the Biotechnology Program; and new and reissued Request for Applications (RFA) and Cooperative Agreement (Coop. Agr.) concepts. On 27 June, from 8:30 a.m. until adjournment at 12:00 noon, presentations included a special recognition; a report from the Director, NIH; the Cancer Genetics Network Progress report, a status report on the Bypass Budget; and Prostate Cancer Prevention Trial (PCPT) results.

Board Members present:

Dr. Frederick R. Appelbaum
(Chair)
Dr. David S. Alberts
Dr. Hoda Anton-Culver
Dr. Neil J. Clendeninn
Dr. Thomas Curran
Dr. Mary Beryl Daly
Dr. Raymond N. DuBois, Jr.
Dr. H. Shelton Earp III
Dr. Susan B. Horwitz
Dr. Hedvig Hricak
Dr. Eric Hunter
Ms. Paula Kim
Dr. Kenneth W. Kinzler
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. Mack Roach III
Dr. Richard L. Schilsky
Dr. Ellen V. Sigal
Dr. Margaret R. Spitz
Dr. William C. Wood
Dr. Robert C. Young

Board Members absent:

Dr. David B. Abrams
Dr. Esther H. Chang
Dr. Patricia A. Ganz
Dr. William G. Kaelin, Jr.
Dr. W. Gillies McKenna

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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Research; Dr. Deborah Bowen

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XV. Prostate Cancer Prevention Trial (PCPT) Results; Dr. Peter Greenwald and Dr. Howard Parnes

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

Dr. Appelbaum called to order the 24th 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 confirmed meeting dates through November 2005. Dr. Appelbaum 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.

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II. CONSIDERATION OF THE 14-15 NOVEMBER 2002 MEETING MINUTES - DR. FREDERICK APPELBAUM

Motion: The minutes of the 3-4 March 2003 meeting were unanimously approved.

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III. NCI DIRECTOR'S REPORT-DR. ANDREW von ESCHENBACH

Dr. von Eschenbach presented the budget and staffing update.

Budget Update. Dr. von Eschenbach reported that, in recent

legislation, the NCI received an appropriation for FY 2003 of \$4.6B, a 10 percent or \$415M increase over FY 2002. Most of the additional dollars was allocated to the Research Project Grant (RPG) pool, the source of funding for 4,813 RPGs in FY 2003, of which 1,379 were competing awards. This represents an increase over FY 2002 of 325 grants. Dr. von Eschenbach noted that the increases in numbers and size of grants have combined to reduce the percentage of grants funded from the 22nd to the 20th percentile. The constant increases in numbers of R01 applications received by the NCI and the 4 percent increase in their individual costs will continue to present a challenge to the NCI budget process, but the intent is to maintain the 20th percentile level of funding. The training budget increased by 14 percent. An increase of 3.5 percent for NIH overall has been requested in the FY 2004 President's Budget. The request for NCI is \$4.7B, an increase of \$161M.

Dr. von Eschenbach stated that, in an effort to carry out its comprehensive responsibilities, the NCI is actively collaborating with other Institutes and also is working to see how the NCI mission might integrate into the larger NIH road map. Mechanisms for collaborations and partnerships are being sought to leverage NCI resources for expanded impact. Over the past year, senior NCI leadership have been working to develop a strategic plan coupled with a business plan to ensure a balanced portfolio in terms of opportunities and needs. The challenge goal that evolved from the strategic planning, which has been adopted by the NCI, is to eliminate the suffering and death due to cancer by 2015. Dr. von Eschenbach informed members that the NCI strategy will be to address cancer as a systems problem that requires a systems solution and significant collaborations and cooperation. Long-range strategic initiatives include focuses in molecular epidemiology and integrative cancer biology; strategic development of cancer interventions; programs in early detection, prevention, and prediction; an integrated clinical trials system; a focus on overcoming health disparities; and the development of a bioinformatics infrastructure.

Dr. von Eschenbach stated that a task force will be assembled to conduct a comprehensive, systematic review and assessment of NCI's clinical trials system and infrastructure. That program will be integrated with the larger NIH agenda to re-engineer the clinical research infrastructure nationwide.

NCI Staffing Update. Dr. von Eschenbach announced that Dr. Robert Croyle had accepted the position of Director, Division of Cancer Control and Population Sciences (DCCPS), and Dr. Frank Balis had been named Clinical Director, Center for Cancer Research.

In discussion, the following points were made:

- The NCI is exploring a variety of partnership opportunities in addition to those with other U.S. agencies. Examples are the NIH Foundation mechanism for partnering with five pharmaceutical companies to create a pool of resources to enhance clinical trials accrual and value-added strategic partnering with the American Cancer Society (ACS) to enhance accrual to the Spiral CT Trial. In discussions with private foundations, interest has been expressed in enhancing the NCI training program to create more physician scientists and in addressing the problem of health disparities in minority and underserved communities through a patient navigator program.
- Concept review presentations and/or reporting should include a mechanism to indicate RFAs that are ending through termination or conclusion of funding cycles and information on how each RFA concept fits into the Institute's strategic planning goals.

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IV. FUTURE DIRECTIONS FOR NCI IMAGING-DR. DANIEL SULLIVAN

Dr. Daniel Sullivan, Director, Cancer Imaging Program (formerly known as Biomedical Imaging Program), Division of Cancer Treatment and Diagnosis (DCTD), explained that the name change reflects an organizational change created by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) within the NIH. Dr. Sullivan noted that the Cancer Imaging Program (CIP) mission and functional statements have been reassessed to align them with changes in scientific opportunities and budget realities,

as well as the NIH organizational change. Molecular imaging, clinical trials, and image-guided interventions were deemed investment priorities because of their potential to help achieve the 2015 challenge goal. He explained that the mini-symposium would explore: (1) the potential advantages of biomedical imaging in providing spatial information and molecular information that reflects the true biologic state of the tumor; (2) methodologies necessary to test and validate biomedical imaging advances for clinical use; and (3) interrelationships of imaging and NCI-funded imaging research on the commercial development of drugs and imaging devices.

New Approaches to Imaging Agent Development. Dr. Ralph Weissleder, Professor, Harvard Medical School, and Director, Center for Molecular Imaging Research, proposed that imaging agents are essential to imaging at the molecular level. Dr. Weissleder cited results of a study of the noninvasive detection of clinically occult lymph-node metastases in prostate cancer published recently in the New England Journal of Medicine (NEJM). The study in 80 patients showed that the addition of an imaging agent to imaging technologies increases the sensitivity or specificity for lymph-node metastasis from an overall 50 percent to above 95 percent, a result similar to that of sentinel lymph-node biopsies, but without the morbidity and at greatly reduced cost. He noted that this small study also is an example of the long time it takes a new agent to translate from the laboratory to the clinic and larger prospective clinical trials.

Dr. Weissleder stated that the overall development time for an imaging agent must be slashed if the challenge goal is to be met. He suggested that 100 new imaging agents should be brought to clinical trial stage this year and that development by the pharmaceutical industry is unlikely. He proposed that three scientific opportunities exist to: (1) develop different imaging agents for relevant molecular targets; (2) align developments of diagnostic and therapeutic agents; and (3) develop specific molecular imaging agents for early diagnosis, characterization, treatment assessment, and relapse.

Dr. Weissleder reviewed the classes of molecular imaging agents in use today, i.e., nonspecific agents; targeted probes; and smart, activatable sensing probes. He noted that smart, activatable sensing probes require high-throughput screening, arrays, combinatorial

chemistry, and other technologies that are well introduced in pharmaceutical companies but essentially unheard of in the traditional imaging community. Dr. Weissleder proposed that extraordinary opportunities exist for developing magnetic nanoparticles; near-infrared (NIR) fluorochromes and activatable reporters; and PET/SPECT tracers and modified scaffolds.

In summation, Dr. Weissleder listed the issues to be resolved: (1) how to accelerate development of needed target agents; (2) how to facilitate translation into the clinic; and (3) how to combine experimental diagnostic and therapeutic agents in clinical trials. He proposed that one option would be to develop dedicated centers for imaging agent development using high throughput screening, with a focus on different platforms of agents. The centers should have a clinical track record so that some of the agents can be taken directly into the clinic. The mechanism also should involve direct Food and Drug Administration (FDA) review and speed should be a driving factor.

Clinical Trials of Imaging Methods for Oncology. Dr. Bruce Hillman, Theodore Keats Professor of Radiology, University of Virginia, and Principal Investigator (PI), American College of Radiology Imaging Network (ACRIN), presented an overview of imaging clinical trials in general and the ACRIN experience in addressing some of the challenges posed in developing and implementing this type of trial. Dr. Hillman noted that the rationale for conducting clinical trials of imaging is to provide scientific evidence as a basis for medical practice and to identify and promote appropriate use of the technology. He stated that imaging events tend to be remote from health outcomes, so a major challenge has been to relate findings in imaging examinations to how they impact the patient's health, as well as society's health in terms of the cost of using that technology. The logistical problems inherent in the need to accrue subjects "upstream" from imaging, on the basis of a set of signs and symptoms were summarized.

Dr. Hillman stated that the decision to address the issues through a clinical trials network dedicated to imaging culminated in an RFA in 1997, an award that created ACRIN in 1998, and funding for the 5-year project period which began in March 1999 and totals \$23M. ACRIN was designed to provide the resources and infrastructure to address the barriers and special issues noted above. It conducts multicenter, multidisciplinary trials of both diagnostic imaging and

image-guided treatments. It is a nonmember organization to provide easy entry and easy exit to individuals and institutions who wish to participate in ACRIN trials. The overarching goal in the trials is to provide information that results in earlier cancer diagnosis, allays concerns of those who do not have cancer, and improves the length and quality of life of cancer patients.

Dr. Hillman stated that ACRIN has addressed the goal by balancing its portfolio to evaluate emerging technologies, establishing technologies that may be appropriately used, assessing the value of screening in high-risk subjects, evaluating the role of imaging in reducing anxiety and improving quality of life, and addressing the dearth of well-trained clinical researchers in medical imaging. In 4 years, ACRIN has succeeded in creating a functioning clinical trials network that has undertaken 18 trials so far (4 closed, 8 open, 6 in development) and one is under consideration. These studies are balanced among screening, diagnosis and staging, treatment, and treatment response. Fully 13 of 18 trials involve major collaborations with other NCI initiatives, industries, and foundations. A unique informatics infrastructure, entirely Web-based, has been established. Semi-annual meetings are held to address strategy and trials development, and dissemination. The charge to train new researchers is being implemented with the help of an NCI R25T grant and funding from Avon.

Dr. Hillman noted that a renewal application for ACRIN is under review. Future directions would include developing into more of a grassroots organization, transitioning from a target-of-opportunity approach for selecting clinical trials to a more strategic approach. Exceptional opportunities are seen in four areas: (1) image-guided intervention techniques that can provide local palliation and reduce morbidity and mortality of cancer; (2) imaging screening that can reduce the morbidity and mortality of cancer; (3) molecular imaging methods that can improve detection, diagnosis, staging, and treatment of cancer, as well as elucidate the pathophysiology of cancer; and (4) metabolic and functional imaging that can evaluate the effectiveness of treatment earlier and better than current gross anatomic imaging or clinical followup.

Role of *In Vivo* Imaging in Pharmaceutical Development. Dr. Wayne Carter, Senior Director, Clinical Technology, Pfizer Global Research and Development, presented the perspective of the pharmaceutical industry in relation to molecular imaging and

clinical trials. Dr. Carter noted that Pfizer is investing in technology development because the current business model is under threat from rising research and development (R&D) costs and expiring patents. Moreover, former R&D bottlenecks have shifted, and the problem now is finding out what does or does not work, cheaply and efficiently. Questions to address in preclinical and clinical drug development are whether the candidate hits the target and whether it has an effect on mechanism of action and disease progression. Quantitative imaging tools are needed for accurately assessing various endpoints other than survival times. Issues related to developing quantitative imaging tools include reaching a consensus regarding validation criteria, ensuring reproducibility, establishing quality standards, and creating a paradigm with appropriate preclinical to clinical translation. In addition, public forums are needed to discuss, debate, and build consensus toward gaining acceptance of the new technologies through education.

Work being done to enable Positron Emission Tomography (PET) imaging, which is widely available as a diagnostic technology, to be used in monitoring therapeutic interventions relevant to various tumor types or cancer agents, specifically growth inhibitors, was discussed. Dr. Carter showed how methodology is being standardized in some studies for using PET imaging to measure metabolic activity in tumors. In other studies, PET imaging is being used to measure the proliferative activity of tumors. The types of information needed for making decisions and building consensus among industry and academic investigators were presented. Dr. Carter expressed the view that mathematics will be one of the most important technologies for imaging agent development. Mathematics is needed to accurately assess images that are generated and to solve the math problems inherent in proteomics, metabonomics, genomics, and laboratory biomarkers. He noted that the challenge of identifying multivariate signatures from these multiple sources of information will outperform the human brain and require the use of mathematics to help with decision making.

To move forward in this area, several questions need to be answered, such as: Should a "safe harbor" be developed for imaging data or should novel endpoints be explored in the clinical trials? What does validation require? Should we establish an interdisciplinary imaging review group? Do regulatory agencies have appropriate expertise?

Oncologic Image-Guided Interventions. Dr. Clare Tempany-Afdahl, Associate Professor of Radiology, Brigham and Women's Hospital, Harvard Medical School, explored the use of image-guided ablative therapy as a viable alternative to molecularly targeted therapies. Dr. Tempany-Afdahl stated that image-guided therapy (IGT) integrates the many advances in imaging into the operating room to create a therapy delivery system. The role of image guidance is to maximize therapy to a given target with no loco-regional effects. Image guidance defines the target, directs therapy, and delivers and controls therapy. Ultimately, disease is eradicated, controlled, relieved, or palliated. She noted that molecular imaging has great potential for characterizing tumors, and imaging and surgical approaches can be used to deliver therapy to the site. Surgical planning tools include diagnostic imaging for tumor localization, interactive imaging for navigation, dynamic imaging for monitoring, and quantitative imaging for followup and control.

Advances being made in the field were described. Specifically magnetic resonance imaging (MRI) is used to plan treatment delivery that spares normal structures, and interactive imaging is used during the procedure to guide the delivery of I-125 radiation sources into the prostate. MRI is used to detect, stage, and determine the extent of disease. In conjunction with other laboratories, image analysis and segmentation algorithms are being customized for the development of interactive imaging processes. A 3-D slicer has been adapted for target definition, trajectory planning, and guidance.

Dr. Tempany-Afdahl also described progress in utilizing focused ultrasound (FUS) as a completely noninvasive method for performing ablative surgery. FUS was first proposed in 1962 and is now reaching the clinical trial stage. Implementation of the surgery was delayed due to lack of methods for targeting, guidance, and temperature monitoring. FUS is being studied at Brigham's for treating uterine leiomyomas.

Target definition, navigation, monitoring, and control as directions for future IGT research were described. Examples of how they are currently being addressed were presented. Members were told that MR image-guided systems and other image-guidance tools are being developed in many different shapes and sizes. She noted that

this presents a challenge to physicians of ensuring that images function in all of the different systems. One potential approach is to use robotic assist devices. But that validation methodology must be organ- and disease-specific; procedures must be developed, tested for safety and efficacy, and then subjected to clinical trial to demonstrate patient safety, toxicity profiles, and long- and short-term outcomes. Another important IGT research area is the development of dynamic imaging tools that can monitor delivery of the therapy. In summary, members were told that future research areas for IGT in prostate and other cancers are improved image navigation, monitoring, and control to develop targeted treatment and delivery systems.

Relationship Between Industry and Federally Funded Imaging Research. Mr. Scott Donnelly, Senior Vice President, GE Global Research, explored the role of industry in collaborations with the NCI to bring imaging technologies to market. As a recent precedent, Mr. Donnelly cited the GE and NCI partnership during the development of an all-digital system for mammography. In a current program where the industry-government collaboration is critical to success, tomographic mammography combined with ultrasound is being clinically tested to see whether the fusion of those two modalities can dramatically change the efficacy of both the screening and the diagnostic followup associated with breast cancer.

From an industry perspective, the biomedical imaging strategy of the future is to move from industry's historical anatomically based imaging modalities to a focus on function and on specific disease-based modalities, where a targeted contrast agent can be important. Major platforms in which industry will invest are MRI and PET imaging agents, optical imaging, and bioinformatics. Another very focused area continues to be disease-specific research on a number of different diseases that require specific solutions. In addition to establishing platforms, industry will need to work with clinical investigators to translate these technologies into the clinic. Examples of the types of imaging agent research being done in both areas were given. In platform technology development, a challenge for industry will be to develop imaging agents that are conducive for application to nanomolar types of concentrations and can be targeted to very specific diseases. In disease specific-research, polylysine is being used as a cancer-specific agent to find and image angiogenesis.

Mr. Donnelly listed considerations for future imaging research. He noted that (1) there is a need for both platform and disease-specific research; (2) future imaging is tied clinically to therapeutics, in vitro diagnostics, and genomics; (3) industry roles are increasing in drug discovery and clinical trials; (4) the NIH and the NCI will have an increased role in partnering with industry; and (5) industry and government collaboration will be critical to success not only in developing and validating the technologies, but also in expediting transfer to the market. Mr. Donnelly concluded that new models are needed not only for technical development, but also for working through the regulatory processes up to and including reimbursement to bring these new technologies to the marketplace if the 2015 challenge goal is to be met.

In discussion, the following points were made:

- The greatest barrier to introducing imaging technology into the clinic is having enough well-trained personnel. The NCI can play a role in expanding training opportunities for diagnostic radiologists and setting minimum standards for their involvement in clinical studies. ASCO and American Association for Cancer Research (AACR) training programs for oncologists might be good models.
- A training initiative in which there are opportunities for focused clinical research should be considered.
- ACRIN is not the appropriate place for all imaging trials; some provision should be made for correlative imaging studies, imaging committees, and involvement in the other cooperative groups.
- Public awareness of ACRIN is accomplished through collaborations that have been developed, appearances
- Regulatory issues, training issues, and policy issues in terms of reimbursement will have to be addressed to successfully advance this field.

V. IOM/NCPB REPORT: FULFILLING THE POTENTIAL OF CANCER PREVENTION AND EARLY DETECTION- DR. NANCY MUELLER

Dr. Nancy Mueller, Associate Director for Population Sciences, Dana-Farber/Harvard Cancer Center, Harvard School of Public Health, gave an overview of the report produced by the National Cancer Policy Board (NCPB). The report deals with four basic questions: (1) What lifestyle and health care behaviors contribute to the burden of cancer? (2) What share of new cases of cancer and cancer deaths could be prevented with changes in lifestyle and health care behaviors? (3) What interventions work to bring about health-enhancing behavioral change? and (4) What steps can be taken to overcome barriers to using effective interventions and improving what is known about cancer prevention and early detection? Dr. Mueller stated that these questions were addressed in relation to modifiable lifestyle factors that influence the risk of cancer, namely tobacco use, physical inactivity, overweight and obesity, and unhealthy diet. The role of early detection was considered, and the effectiveness of interventions on major risk factors was evaluated, together with the intervention roles of the health care system and governmental agencies.

From deliberations on these questions, the NCPB formulated the following recommendations: 1) legislative support for tobacco control and a national strategy for obesity, unhealthy diet, and physical activity to be developed by the Department of Health and Human Services; 2) continuing and adequately funding the Centers for Disease Control and Prevention's (CDC) state and local cancer control programs, and integration of those programs, insurance coverage of evidence-based cancer prevention and early detection, and support for these same services among medically underserved populations; 3) continuing evaluation of prevention services in federal health programs, and support for education and training for health care providers; 4) continuing assessment of the effectiveness of interventions in screening to add to the evidence base as well as focusing on how to improve public understanding of healthy lifestyles and the effectiveness of cancer screening; 5) focusing on how to target lifestyle interventions to particular subgroups within the U.S. population, taking into account cultural, ethical, and ethnic differences; and 6) support for applied behavioral and dissemination research.

The NCPB concluded that the combined effect of tobacco use, obesity and overweight, unhealthy diet, and inactivity is associated with up to 60 percent of U.S. cancer deaths. The NCPB also concluded that the prevalence of screening is unacceptably low, and that the prevalence of screening varies by ethnicity and by economic resources. It was estimated that cancer incidence could be reduced by 19 percent and cancer mortality by 29 percent by 2015 if efforts to act on current knowledge were redoubled

In the discussion, the following points were made:

- The NCI plays a leadership role in the larger cancer health agenda through partnerships. Five trans-HHS strategic initiatives have been established. The NCI is supporting and directly leading the two initiatives, one related to eliminating health care disparities and the other a trans-NIH obesity working group. In addition, DCCPS and the Division of Cancer Prevention (DCP) are collaborating in a trans-NIH approach to energy balance that integrates diet and physical activity and their interactions, with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung, and Blood Institute (NHLBI) as the lead institutes.
- The NCI also has a role as an evidence generator to inform the programmatic activities of CDC, ACS, state health departments, and many others. A discussion at the NCPB was the stimulus for creating the diffusion and dissemination program called Cancer Control Portal. The NCI is represented on the new HHS Research Coordinating Committee for public health-related research.

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VI. NCI/CONGRESSIONAL RELATIONS-MS. SUSAN ERICKSON

Ms. Susan Erickson, Acting Director, Office of Policy Analysis and Response, NCI, reported on activities in the House and Senate committees to mark up the 2004 appropriations legislation for Labor, HHS and Education. Ms. Erickson briefly reviewed recent

hearings at which NCI staff were witnesses. She also reviewed provisions in the National Cancer Act of 2003.

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VII. ONGOING AND NEW BUSINESS-DR. FREDERICK APPELBAUM

ONS "NCI Listens" 2003 Reports. Dr. Christine Miaskowski, Professor and Chair, Department of Physiological Nursing, University of California at San Francisco, reported that Dr. Paulette Gray and Ms. Mary McCabe participated at the bi-annual Oncology Nursing Society (ONS)/American Cancer Society Seventh National Conference on Cancer Nursing Research in January. Because many of the participants were pre- and post-doctoral candidates, much of the "NCI Listens" discussion focused on training resources within the NCI. Another discussion explored the potential impact of the Health Insurance Portability and Accountability Act (HIPAA) legislation on recruitment to clinical trials.

Dr. Miaskowski reported that Drs. Robert Croyle, Gray, and Ms. Paula Kim participated at an "NCI Listens" session of the annual ONS meeting held in April. Dr. Croyle presented an overview of current NCI activities and strategic plans related to the 2015 challenge goal. In the discussion, a recommendation was made to include nurse scientists on Progress Review Groups. The final report of an NCI-funded study to determine ONS Research Priorities will be sent to the BSA. Another discussion focused on early implications of the HIPAA ruling on recruitment to clinical trials as perceived by nurse scientists.

In the discussion, the following points were made:

- Dr. Miaskowski agreed to identify a mechanism whereby representatives from the cooperative group nursing committees could make presentations at ONS meetings to stimulate interactions between nurses and the cooperative groups.
- Oncology nursing with a focus on issues such as outcome

and survivorship should be a future BSA agenda item.

BSA at National Meetings-2003 Sessions: AACR, ASPO.

Members and staff representing the BSA during "NCI Listen" sessions at upcoming annual national meetings are:

- **American Association for Cancer Research (AACR):**
July 11-14, 2003, Washington, DC; Drs. Enrico Mihich (Chair), Anna Barker, Thomas Curran, H. Shelton Earp III, Ellen Feigal, Paulette Gray, Carolyn Strete, Edward Sausville, and John Sogn.
- **American Society of Preventive Oncology (ASPO):**
March 2004, Washington DC; Drs. Mary Beryl Daly (Chair), Hoda Anton-Culver, Paulette Gray, Hedvig Hricak, Nancy Mueller, and Margaret Spitz.

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VIII. WORKING LUNCH

NCI's 2015 Challenge Goal: Enabling Technologies. Dr. Anna Barker, Deputy Director for Strategic Scientific Initiatives, reported that many interfaces in the discovery to delivery continuum are needed to accelerate the delivery of the new preventive, diagnostic, and treatment interventions into patients. Dr. Barker noted that the pace of change has created unprecedented data management needs. Genomics and proteomics discoveries have created the need for resources and technology to validate the hundreds of targets already identified and thousands to come. NCI strategic planning is focusing on the technology and new approaches needed to capitalize on current opportunities. The challenges are to enable, accelerate, and optimize efforts in the areas of: 1) integrative science (systems/integrative biology); 2) enabling technologies that will move discoveries in proteomics, nanotechnology, and imaging into agents and interventions for the public; 3) common bioinformatics platforms; 4) development and validation of targeted agents; and 5) responsive partnerships. Strategic planning goals are focused on: 1) supporting innovative drug discovery research and technology development; 2) identifying creative technology development programs; 3) taking a bigger role as

integrator to promote seamless technology transfer; 4) considering precompetitive initiatives where there is little interest in the private sector and demonstration projects to reduce risk to biotechnology companies; and 5) designing and implementing mutually beneficial public-private partnerships and intra-government partnerships.

Examples of several areas where the NCI is assuming a leadership position were given. Tissue access was identified as one major area that is being addressed by an NCI initiative to create a national resource that would be precompetitive and accessible to all investigators. Tissue specimens will be compatible with the development of proteomics- and genomics-based interventions, and HIPAA-related privacy concerns will be addressed. The NCI also is pioneering new biomedical research technologies in the areas of proteomics, nanotechnology, biomarkers, imaging capabilities, and biocomputing.

Dr. Barker noted that the paradigm shift in cancer control from "find it and remove" to "target and control" has created new challenges calling for new strategies. Complex issues to be dealt with include the costs and uncertainty related to developing the large numbers of targets; how to use biomarkers in both discovery and development; an adequate source of annotated and quality-assured tissues; partnerships; new models for clinical trials; and issues related to delivery of targeted interventions to tumors.

In summary, Dr. Barker informed Board members that NCI initiatives to accelerate progress are in the areas of capturing results of discovery, optimizing technology transfer, platform development, technology development planning, specialty preclinical development, scalable synthesis, and encouraging entrepreneurs through various mechanisms. These initiatives will be coming forward as mechanisms offered to the extramural community.

In the discussion, the following points were made:

- The concept of a national tissue resource is a collaborative effort between the NCI and the National Dialogue on Cancer. It will be a new resource for genomics and proteomics research.

- Budgeting for the new technologic initiatives will be challenging, but will present opportunities for new partnerships.

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IX. RFA/COOPERATIVE AGREEMENTS NEW CONCEPTS - PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Treatment and Diagnosis

Strategic Partnering To Evaluate Cancer Signatures (Coop. Agr.). Dr. Sheila Taube, Associate Director, Cancer Diagnosis Program (CDP), DCTD, reminded BSA members that this concept had been submitted in March under the title "Consortia for Clinical Development of Molecular Profiles in Cancer." Questions raised at that time were: whether the concept was timely scientifically; whether it would fragment existing patient resources; and whether an RFA was necessary. Dr. Taube noted that the proposed initiative was developed within the context of CDP's Program for the Assessment of Clinical Cancer Tests (PACCT), which was launched in September 2000. PACCT goals are to link development of new diagnostics to clinical needs, thereby ensuring efficient and effective translation to the clinic. Barriers have been identified, and a pathway for bringing markers and technologies to the clinic has been defined and set forth in a guidelines document.

Dr. James Jacobson, Technology Development Branch, CDP, informed members that scientific efforts in genomics and proteomics to date have been on discovery. The proposed initiative would move promising molecular profiles to the development and delivery aspects of the cancer continuum through a focused, collaborative effort. Dr. Jacobson stated that the intent of the initiative is to provide the resources to: 1) evaluate the molecular profiles to decide which can impact patient management and patient outcomes; and 2) facilitate their translation towards clinical application through the development of robust assay methodologies. He noted that this actually would build on existing resources and programs such as the SPOREs and the Early

Diagnosis Research Network (EDRN). Applicants must demonstrate analytical proficiency, statistical expertise, and specimen resources. Public release of data is required, and intellectual property issues must be addressed. Clinical trials would be initiated. A Steering Committee will be formed to address problems and issues common to the projects.

A budget of \$10M per year is requested to fund 4 to 5 U01 projects. The estimated cost for the 5-year project period is \$50M.

In the discussion, the following points were made:

- Procedures for communicating molecular risks to patients should be developed.
- A list should be compiled of promising "molecular profiles for tumor classification" that have already been identified and would be exploited through this program.

Motion. A motion to approve the DCTD Cooperative Agreement RFA concept entitled "Strategic Partnering to Evaluate Cancer Signatures" passed with 24 votes in favor and 1 abstention. More concrete examples should be incorporated in the written RFA for greater clarity.

Office of the Director

Innovative Molecular Analysis Technologies (IMAT) Program (RFAs). Dr. Greg Downing, Director, Office of Technology and Industrial Relations (OTIR), OD, NCI, reviewed the original goals, history, and achievements of IMAT. Dr. Downing stated that IMAT was issued as a Program Announcement (PA) in 1998 with the objectives of supporting technology development in cancer research. The Phased Innovation Award for technology development was established-R21 for the evaluation phase; R33 for the application phase with the companion SBIR/STTR mechanisms for small business applications. In 2000, the PA was reissued. The impact of IMAT in its first 5 years has resulted in the assemblage of a diverse community of researchers, development of innovative technologies, numbers of patents and licenses secured, formation of

corporate partnerships, as well as new startup companies.

Dr. Downing stated that the program is being presented for continuation in a modified format. Recommended revisions are: (1) announcements developed with more focused areas of programmatic interest to address technology gaps; (2) uncoupling the R21/R33 mechanisms to encourage applications with more innovative, high-risk strategies; and (3) convert the mechanism from PA to RFA. Three RFA concepts form the basis of the upgraded and refocused IMAT program: 1) the "Innovative Technologies for the Molecular Analysis of Cancer" proposes to fund technologies suitable for in vitro, in situ, or in vivo analysis of alterations and instabilities in genomic DNA; expression of genes and gene product; cellular localization; post-translational modification and functioning of proteins; and monitoring signal transduction networks involved in cancer, 2) "Innovations in Cancer Sample Preparation," goal is to develop products and methods that maximize quality and utility of samples for research, and 3) "Applications of Emerging Technologies for Cancer Research" goal is to develop robust technologies that reproducibly demonstrate responses as applied to biological and clinical research questions.

Dr. Downing stated that the proposed RFAs and the SBIRs integrate into NCI's technology pipeline and are consistent with strategic planning efforts. Ultimately, these technologies are expected to have impact and apply across both intra- and extramural programs. The program will be managed in OTIR.

An estimated \$7M is requested per year for the RFAs. A total of \$24M is estimated for the 3-year project period.

In the discussion, the following points were made:

- The dissemination of Cancer Sample Preparation project information should be addressed.
- A more focused approach should be considered in the solicitation for "Innovative Technologies for the Molecular Analysis of Cancer."
- Consideration should be given to balancing the allocation of

resources between R21s and R33s.

Motion. A motion to approve the three RFA concepts that comprise the proposed Innovative Molecular Analysis Technologies (IMAT) Program. SBIR passed with 22 in favor, 1 opposed, and 2 abstentions. It was recommended that the "Innovative Technologies for the Molecular Analysis of Cancer" be more focused and written with a better definition of areas of molecular analysis that are being sought.

Division of Cancer Biology

Integrative Cancer Biology Programs (RFA). Dr. Dinah Singer, Director, Division of Cancer Biology (DCB), DCTD, stated that this program is proposed in response to the need for a systematic approach to integrate the greatly expanded knowledge about cancer into a comprehensive model for analyzing the complex biological systems that are cancers. Dr. Dan Gallahan, Chief, Structural Biology and Molecular Applications Branch, DCB, stated that the proposal for Integrative Cancer Biology Programs (ICBPs) is to establish transdisciplinary programs with the expertise, knowledge, and infrastructure necessary to undertake a systems approach to cancer. The programs will be structured to enhance the understanding of cancer biology. Potential areas of focus include: mechanisms of gene expression, metabolic networks and components in cell physiology, cancer-related pathology, signaling networks and the control of cellular processes, and cell-cell and cell-matrix interactions. Critical areas needed in an ICBP include but are not limited to: basic cancer biology research, mathematical modeling, technology/nanotechnology development, large-scale data handling, bioinformatics, and training. Coordination of the proposed ICBP would be through a committee composed of ICBP PIs and NCI staff, bi-annual meetings, and NCI staff oversight and interaction.

One unique aspect of the proposed program would be to have a well-integrated and publically accessible bioinformatics platform that would be coordinated with the NCI Center for Bioinformatics. Centrally designed and administered bioinformatics standards and a repository would be developed. Data sharing through the common

platform would be required. The bioinformatics platform would interface with the NCI Cancer Biomedical Informatics Grid (CaBIG). A pre-application bioinformatics platform meeting would be co-sponsored with the Center for Bioinformatics far enough in advance for applicants to incorporate consensus bioinformatics approaches into their applications.

Proposed funding mechanisms are P50s (full program) and P20s (planning) awards. Estimated total costs per year for 2-3 P50s and 2-3 P20s is \$10M and for the 5-year project period is \$50M.

In the discussion, the following points were made:

- Partnering across institutes and with biotechnology and pharmaceutical entities could be sources for additional funding.
- A larger number of smaller initiatives should be considered to validate the underlying assumption that the complex process can be modeled.
- Evaluation metrics should be developed at the outset of the initiative.

Motion. A motion to approve the RFA concept entitled "Integrative Cancer Biology Programs," with more flexibility built into the funding mechanism so that there is the potential to fund, if appropriate, smaller centers, was unanimously approved. It was recommended that the planning meeting be scheduled earlier than proposed in the tentative timeline.

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**X. RFA/COOPERATIVE AGREEMENTS REISSUED
CONCEPTS- PRESENTED BY NCI PROGRAM STAFF**

Division of Cancer Treatment and Diagnosis

Small Animal Imaging Research Program (SAIRP) (RFA).

The BSA subcommittee reminded the Board that the original RFA resulted from a recommendation of the NCI Director's Imaging Sciences Working Group (ISWG). On the basis of its review, the Subcommittee concluded that the program has an excellent track record in the five Centers that were established, a good record of collaboration, and an outstanding publication record. BSA concurrence with the NCI reissuance was recommended. It was noted that the Mouse Models Consortium is growing and has great need of imaging, and that animal models provide important guidance for image-guided radiotherapy in humans.

Motion. A motion to concur with the NCI decision to reissue the DCTD RFA entitled "Small Animal Imaging Research Program (SAIRP)" was unanimously approved.

Division of Cancer Control and Population Sciences

Transdisciplinary Tobacco Use Research Centers (TTURCs) (RFA).. The BSA subcommittee informed members that they supported the reissuance unanimously and recommended BSA concurrence. The Subcommittee also recommended that the Centers increase their focus on epidemiology by identifying epidemiologists and statisticians in the vicinities of the TTURCS.

Motion. . A motion to concur with the NCI decision to reissue the DCCPS RFA entitled "Transdisciplinary Tobacco Use Research Centers (TTURCs)" along with the Subcommittee recommendation was unanimous.

Cancer Intervention and Surveillance Modeling Network (CISNET) (RFA/Coop. Agr.).. The BSA Subcommittee established to review the proposed reissuance requested additional information. Dr. Eric Feuer, Chief, Statistical Research and Applications Branch, DCCPS, reminded the Board that CISNET is an NCI-sponsored consortium focused on: (1) statistical modeling of the impact of cancer control interventions on current and future trends; and (2) optimal cancer control planning. In the original issuance, 17 four-year grants (U01s) were awarded in breast, prostate, colorectal, and lung cancer. Approximately \$13.5M would have been awarded when the second-round of grants end in 2006. CISNET continues to be responsive to the Bypass Budget provisions, and the NIH Director's approach for communicating

with Congress and the public. CISNET brings the most sophisticated tools available for evidence-based planning to: (1) be responsive to challenges due to the increasing pace of technology; (2) address emerging questions while they are still being debated in the public forum; (3) translate randomized controlled trial (RCT) evidence to the population setting; and (4) provide estimates of quantities that will never be derived from RCTs. Dr. Feuer reviewed the eight goals for the original projects and discussed accomplishments made in 2.5 years by the first-round grantees and 0.5 year by the second-round grantees.

Dr. Feuer stated that, in the proposed reissuance, CISNET would use the models developed in the first rounds of funding to continue to develop data sources and realistic scenarios for evaluating past intervention impact in population settings. One new goal would be to provide tools for the evaluation of the delivery of interventions at the population level. Another proposed new component would be coordinating centers for each cancer site for: (1) formulating, prioritizing, and coordinating work on base case and other questions; (2) negotiating common requests for outside data sources; (3) building consensus and coordinating critical evaluation of disparate results; (4) preparing inputs, and collecting and processing common outputs for model comparisons; and (5) coordinating a synthesis paper and group responses to inform policymakers.

Finally, Dr. Feuer addressed specific questions posed by the Subcommittee, e.g., purpose of the reissuance, validation, access to models, variability in the quality of work, openness of the competition, source of questions, and value of models in responding to current research challenges.

Two rounds of funding are envisioned with estimated awards of 6-9 modeling grants and 4 coordinating center grants in the first round and 5-8 modeling grants in the second. The 01 year set-aside is \$2.75M, and the estimated cost for the project is \$21.25M over a 7-year period.

In the discussion, the following points were made:

- Emphasis in the reissuance should be on making sure the models are working, valid, and providing accurate data.

- Adding other cancer sites for CISNET modeling should be considered.

Motion. . A motion to concur with the NCI decision to reissue the DCCPS RFA/Coop. Agr. entitled "Cancer Intervention and Surveillance Modeling Network (CISNET)" was approved; 20 in favor and 5 abstentions.

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XI. SPECIAL RECOGNITION-DR. ANDREW von ESCHENBACH AND DR. FREDERICK APPELBAUM

A special award was presented to Dr. Elias Zerhouni for his outstanding contributions as a BSA member and to the NCI agenda from 1998-2002, when he was appointed Director, NIH. Dr. von Eschenbach also noted that as NIH Director, Dr. Zerhouni has recognized the need to bring all of the agencies within the DHHS together in a way that will have a positive impact on the health of American citizens. In recognition of his tenure on the BSA, Drs. von Eschenbach and Appelbaum presented Dr. Zerhouni with the National Cancer Institute's Director's Service Award.

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XII. NIH DIRECTOR'S REPORT-DR. ELIAS ZERHOUNI

Dr. Elias Zerhouni described the NIH Roadmap Initiative process. Dr. Zerhouni stated that the process was developed during the past year to strengthen the national scientific strategic plan. With the tremendous acceleration in the pace of discoveries in the life sciences, the NIH recognized the need to accelerate the pace of discovery and make significant advances to contain future health care costs. To do this, a prioritization process was needed. Thus, participants in developing the NIH Roadmap were asked to identify today's scientific challenges, roadblocks to progress, solutions for removing roadblocks, and areas common to all Institutes but are the responsibility of the NIH as a whole. Several approaches to addressing those questions were developed. Additionally, several

meetings held with NIH and extramural scientists, and representatives from the public, to identify priority areas, resulted in the emergence of three priority areas: (1) developing NIH competing strategy to follow in looking at new pathways to discovery; (2) developing a framework for adapting the new scientific teams to the changing model of how science is conducted; and (3) re-engineering the clinical research enterprise. Dr. Zerhouni demonstrated how the Roadmap Initiative has been applied to develop a priority matrix for research into biological pathways and networks. He noted that extra- and intramural participants in the NIH Roadmap Initiatives are asked to consider whether: 1) the initiative is truly transforming; 2) the outcomes would be useful to the Institutes and Centers (ICs); 3) NIH can afford not to do it; 4) it will be compelling to stakeholders; and 5) it will position the NIH in a unique way. A series of planning events have been held since August 2002. The period of adaptive implementation is about to begin.

In discussion, the following points were made:

- NIH Roadmap Initiatives are investigator-driven through competitive grants. This allows for a diversity of approaches that can incorporate serendipitous scientific discoveries.
- Specific mechanisms should be put in place to facilitate public-private partnerships.
- A Blue Ribbon Panel has been assembled to review the intramural clinical complex and to advise the Director on what strategic decisions need to be made.

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XIII. GENETICS NETWORK PROGRESS REPORT-DR. EDWARD TRAPIDO

Dr. Edward Trapido, Associate Director, Epidemiology and Genetics Research Program (EGRP), DCCPS, stated that the report would review CGN scientific accomplishments as a basis for assessing whether CGN is and will continue to be scientifically

relevant and useful. The concept for reissuing the RFA will be presented for BSA review and concurrence in November 2003. Dr. Trapido stated that the CGN is part of the NCI genetics research program and is consistent with the Discovery/Development/Delivery continuum and Bypass Budget goals. Questions of interest to clinical epidemiologists, are: What do high-risk families do with knowledge of their genetic predisposition to cancer? Should they change risk behaviors or screening practices? What should be communicated to the families at high risk? and How should their health be monitored?

CGN Overview. Dr. Carol Kasten-Sportes, Clinical and Genetic Epidemiology Research (CGER) Branch, EGRP, DCCPS, provided an overview of the CGN management structure, how it does research, and the Informatics Technology Groups (ITGs). Dr. Kasten-Sportes informed members that the CGN is a research infrastructure comprising a multisite registry of persons with cancer or at high risk of cancer and their families. The registry is used for investigations on the genetics of cancer and related issues. There are 11 CGN sites (8 Participating Centers and 3 Informatics Technology Groups (ITGs)). The CGN's Informatics Technology Groups are at the Massachusetts General Hospital (MGH), Yale University, and University of California (UCI). The ITGs are responsible for design, implementation, and maintenance of information management systems that support multi-center CGN-wide research protocols. The UCI site maintains the core database, the MGH site is the statistical coordinating center, and the Yale site is responsible for software development.

The CGN Steering Committee, composed of principal investigators from each of the eight CGN Centers, provides governance and sets future goals. Four patient advocates rotate among the three Informatics Centers. An Advisory Committee, composed of senior scientists with broad expertise in cancer genetics research, provides overall advice on scientific matters, and suggests future directions to the Steering Committee. Working groups, either temporary or permanent, are assembled to fill immediate deficits or ongoing needs.

Dr. Kasten-Sportes cited several CGN's major accomplishments. She noted that CGN had enrolled over 20,000 probands in the recruitment pool representing 15,163 families as of March 2000; thereby enriching the CGN as a genetic research tool. Other

established 10 pilot studies; 61 articles published or in press directly using CGN resources; 79 grant applications; and utilization in one intramural NCI project. In addition, CGN had established integral and important partnerships with the Early Detection Research Network (EDRN), the Cancer Family Registries (CFR), the Specialized Programs of Research Excellence (SPOREs), the NCI intramural studies, the Gynecologic Oncology Group (GOG), and the Surveillance, Epidemiology and End Results Program (SEER). Dr. Kasten-Sportes concluded that the CGN is a well-established resource with a cohesive infrastructure that has a large and growing recruitment.

Enrollee Characteristics and Minority Recruitment Research.

Dr. Deborah Bowen, CGN Principal Investigator, Fred Hutchinson Cancer Research Center, described enrollee characteristics and discussed minority recruitment. Dr. Bowen told members that new enrollee characteristics and recruiting includes individuals without a cancer history, but are mostly from high-risk families; individuals with one cancer; and individuals with two or more cancers. She described how genetic, background, and risk factor data from a diversity of cancer sites are pooled at the ITGs to make a resource that is attractive for NCI and extramural investigators.

Members were told that the CGN has four population-based sites that recruit primarily through the SEER program, and four clinic-based sites that recruit generally through high-risk clinics. Although the population-based centers contribute a larger number of cases, the clinic-based sites, which are based on high-risk clinic recruitment, contribute more high-risk families. Having both types of information contributes to the diversity of pilot studies that have been and can be undertaken. The CGN engages in followup with all participants, thereby ensuring that they are available to provide additional information needed for specific studies. Annual and cumulative recruitment to the pilot studies have shown that CGN can be accessed for targeted and specific hypothesis-driven studies.

Minority recruitment was an issue identified by the CGN Steering Committee when it was observed that within the CGN recruitment was only approximately 9 percent. The Steering Committee thought the number could be improved upon and established the Minority Recruitment Committee (MRC) which has a mandate to look at specific methods to improve minority recruitment, particularly among African-Americans, Hispanics, and Asians.

Following its formation, the MRC designed randomized trials to test different strategies for enhancing minority recruitment within four clusters of Centers and their collaborating sites. The protocol was completed within 1 year and analysis is ongoing, but valuable contributions have already been identified. For example, minority recruitment research has provided genetics researchers with ideas on how to accrue and keep more minorities in their studies, thereby improving gene-environment interaction studies that ultimately benefit the broader community. Dr. Bowen noted that the data from this research will be pooled into the CGN databases to guide future CGN recruitment efforts, support independent research projects, and serve as a resource for other investigators.

Ovarian Cancer Screening Study in High-Risk Women. Dr. Steven Skates, Massachusetts General Hospital, noted that pilot studies are an integral part of the CGN, and they enable investigators to answer urgent questions in cancer genetics. Dr. Skates described the Risk of Ovarian Cancer Algorithm (ROCA) study, a 2-year pilot study initiated by the CGN and conducted in collaboration with the Ovarian SPOREs, the GOG, the EDRN, and other centers. He noted that the ROCA targets more than 2,400 women, 1,600 from CGN sites, 800 through the GOG, and more through the other sites. The ROCA uses longitudinal CA125 measurements to monitor each individual woman over time to ascertain whether she is at risk for developing ovarian cancer and to ascertain that risk as early as possible for intervention.

Dr. Skates informed members that the ROCA study design requires each woman to have a regular CA125 test. The study calculates her risk of having an overt pattern or pattern that rises due to the presence of ovarian cancer versus a flat pattern with background fluctuations. He also noted that menopausal status and race were the two big factors that seemed to affect CA125 levels. At the 98th percentile, premenopausal women CA125 levels were significantly elevated and their cut point was 48 while their postmenopausal women counterparts had lower CA125 levels and a cut point of 35. However, in African-Americans, levels were low in both pre- and postmenopausal women.

The next steps in the definitive ovarian cancer screening trial in high-risk women are to: (1) compare sensitivities between technologies at fixed specificity; (2) have enough subjects with a similar outcome between different technologies; and (3) compare

the sensitivity and number of surgeries per ovarian cancer. The intent of the ROCA study is to develop algorithms based on multiple biomarker longitudinal data that will increase the sensitivity and specificity of this approach, and eventually to move forward with a definitive ovarian cancer screening trial in high-risk women with blood markers as a first line test.

Scientific Accomplishments and Future Directions for the CGN. Dr. Barbara Weber restated the aims of the CGN as described in the RFA, highlighted one tool developed through the CGN, and discussed future directions for the CGN. Dr. Weber informed members that the CGN aims to create an infrastructure for collaborative research into the genetic basis of human cancer susceptibility, integrate cancer genetics into the medical practice, and address associated education, ethical, and psychosocial issues. More specifically, the CGN aims to develop a registry of potential research subjects, collect core data and followup information of all registry participants, collect biospecimens for specific projects, develop pilot studies, and develop innovative informatics tools for collaborative research.

The Trial Database (TrialDB), Dr. Weber noted, is an informatics tool developed for the CGN by Prakash Nadkarni. One can now customize reports, receive interpretation of those reports, evaluate an entire study at once and find out, for example, when the CA125 was generated, what it was, and use the algorithm to identify the risk, and because of that risk and the study schema, what that person should be doing next.

Assuming the Board agrees that the CGN is useful and should be renewed, Dr. Weber recommended that the reissuance be competitive. This would allow for each site to be individually reviewed. In addition, the opportunity would exist for additional sites to come in and current sites to be dropped.

In discussion, the following points were made:

- There are extensive electronic methods in place to check CGN data. Data gets checked first at the collaborating sites, and the data gets checked again when the primary center submits their data to the UCI. Each quarter, the CGN gets reports on data discrepancies, and there is a system in place

to fix problems that occur when a center or a site has more than a certain number of errors in their data transmission.

- All CGN pilot study participants are supported by internal CGN funds. The SPOREs and the GOG contribute their own funds. The CDC provided some targeted funds for ovarian cancer research in the second year of the ROCA study.

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XIV. STATUS REPORT: BYPASS BUDGET-MS. CHERIE NICHOLS

Ms. Cherie Nichols, Director of the Office of Science, Planning, and Assessment, NCI, discussed strategies to improve the Bypass Budget feedback process, especially from external reviewers. After the 2004 Bypass Budget was distributed, the Office of Science, Planning, and Assessment solicited comments from reviewers on the NCI goal statements, objectives, critical activities, and persons or entities the NCI should partner with in view of the upcoming 2005 Bypass Budget. Of the 400 letters distributed, comments were received from 38 individuals and organizations. Ms. Nichols suggested that this disappointing response rate reveals the need to broaden the audience by identifying additional individuals as interested parties.

Ms. Nichols also suggested combining comment solicitation with other activities such as meetings with NCI leaders, professional organizations, and advocacy groups. Current plans are to get the 2005 Bypass Budget out by November 2003. Comments from institutions, organizations, and individuals would be due in January 2004.

In discussion, the following points were made:

- Individuals do not comment on the Bypass Budget because they feel it is too late in the process to influence change. To increase community involvement in the planning process, several themes emerged including leveraging partnerships;

enhancing innovation; integration across the discovery, development, and delivery continuum; and information and resource sharing.

- Consideration should be given to distributing the Bypass Budget earlier and assigning individuals with specific expertise to review specific sections.
- It may be useful to discuss the Bypass Budget with advisory boards, such as the BSA, the Board of Scientific Counselors, or the National Cancer Advisory Board. Professional societies, such as AACR and ASCO, etc. also can play a meaningful role.
- To stimulate response from the extramural community, scientists, members from the advisory boards, advocates, and others from the community at large, with specific topical expertise should review various sections of the Bypass Budget.
- The Office of Science Planning and Assessment should consider a series of documents tailored to different audiences, rather than one document to cover all topics and to address all audiences.

Consideration should be given to convening a group of BSA members to examine ways to get broader input from the extramural community and to consider strategies for increased public participation in the Bypass Budget process.

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XV. PROSTATE CANCER PREVENTION TRIAL (PCPT) RESULTS-DR. PETER GREENWALD AND DR. HOWARD PARNES

Dr. Peter Greenwald, Director, DCP, introduced the progress report on the NCI-sponsored Prostate Cancer Prevention Trial (PCPT) and Dr. Howard Parnes, Chief, Prostate and Urologic Cancer Research Group, DCP, discussed the PCPT specifics and findings.

Dr. Parnes stated prostate cancer is linked to male hormones, particularly the potent male hormone (DHT), in the prostate gland. Finasteride is a drug that inhibits the enzyme responsible for the formation of DHT in the prostate gland. In 1992, two clinical trials showed the efficacy and safety of finasteride for the treatment of benign prostatic hyperplasia. The results of these two trials led the FDA to approve the drug for benign enlargement of the prostate and associated symptoms of difficulty in urination. Dr. Parnes stated that the primary objective of the PCPT was to determine whether finasteride administered for a period of 7 years could reduce the period prevalence of prostate cancer, during the course of routine management with PSA and DRA. More than 18,000 men were recruited for this trial. The study was conducted throughout the United States in more than 200 study sites coordinated by the Southwest Oncology Group.

Approximately 9,500 men were randomized to either the finasteride arm or the placebo arm of the study. Among men randomized to finasteride, there were 803 cases of prostate cancer, 18.4 percent. Among men randomized to placebo, there were 1,147 cases of prostate cancer, or 24.4 percent. Thus, there was an absolute reduction of 6 percent and a relative risk reduction of 24.8 percent for men randomized to finasteride. However, the percent of men with high-grade disease increased for men randomized to finasteride. Similar results were found for end-of-study biopsies. Dr. Parnes noted that comparable risk reduction was observed when looking across subgroups by age and race.

PCPT is the first clinical trial in which an intervention in healthy men has been shown to reduce the risk of prostate cancer. The PCPT will continue to do extensive studies on the genetic tissue that has been collected in the biorepository. Dr. Parnes asserted that cancer prevention is complex and involves weighing risks and benefits.

In discussion, the following points were made:

- A study recently initiated to examine dutasteride isoenzymes, a dual inhibitor includes 8,000 men who have an elevated PSA and a negative biopsy. The study is being conducted in Europe and the United States. (NCI is not involved.)

Adjournment: The meeting was adjourned at 12:15 p.m. on Friday, 27 June 2003.

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