

# Board of Scientific Advisors

## Meeting Minutes

June 24-25, 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 their 27th meeting on Monday, June 24, 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 was open to the public from 8:30 a.m. until 6:30 p.m. on 24 June for the NCI Director's Report; updates on NCI/Congressional relations and grant paylines and trends in applications; special recognition of retiring members; an update on the NCI Alliance for Nanotechnology in Cancer; ongoing and new business; a discussion of current ethics issues; an update on NIH Roadmap Initiatives; and new and reissued Requests for Applications (RFAs), Requests for Proposals (RFPs), and Cooperative Agreements. On 25 June, the meeting was open to the public and lasted from 8:30 a.m. until adjournment at 12:00 noon; presentations included the *Annual Report to the Nation on the Status of Cancer*, the Clinical Trials Working Group Report, an update on the management of Bio-Specimen Resources and the Food and Drug Administration (FDA)/NCI Task Force, and a status report on NCI/Centers for Medicare and Medicaid Services (CMS) collaborative activities.

<b>Board Members present:</b>	Dr. William C. Wood
Dr. Frederick R. Appelbaum	Dr. Robert C. Young
(Chair)	
Dr. David B. Abrams	<b>Board Members absent:</b>
Dr. David S. Alberts	Dr. Esther Chang
Dr. Hoda Anton-Culver	Dr. Neil J. Clendeninn
Dr. Thomas Curran	Dr. Mary Beryl Daly
Dr. Raymond N. DuBois, Jr.	Dr. Hedvig Hricak
Dr. H. Shelton Earp III	Dr. Eric Hunter
Dr. Patricia A. Ganz	Dr. William G. Kaelin, Jr.
Dr. William N. Hait	Dr. Kenneth W. Kinzler
Dr. Susan B. Horwitz	Dr. Herbert Y. Kressel
Ms. Paula Kim	Dr. Lynn M. Matrisian
Dr. Michael P. Link	Dr. W. Gillies McKenna
Dr. Enrico Mihich	Dr. Christine A. Miaskowski
Dr. Nancy E. Mueller	Dr. John D. Minna
Dr. Mack Roach III	
Dr. Richard L. Schilsky	<b>NCAB Liaison:</b>
Dr. Ellen V. Sigal	TBN
Dr. Margaret R. Spitz	

**Others present:** Members of NCI's Executive Committee (EC), NCI Staff, Members of the Extramural Community, and Press Representatives.

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*Division of Cancer Control and Population Sciences  
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- Laboratory Assessment of Tobacco Use Behavior and Exposure to Toxins Among Users of New tobacco Products Promoted to Reduce Harm (RFP)
- Cancer Genetics Network (RFP)

*Office of the Director (OD)*

- Cancer Nanotechnology Concepts: Centers of Nanotechnology Excellence (RFA/Coop. Agr.); CCNE Coordinating Center (RFA); Multidisciplinary Career Development Cancer Nanotechnology; Education (RFA); Cancer Nanotechnology Education (RFA)

XI. **Re-Issued RFA Concepts**; Presented by NCI Program Staff  
*Office of the Deputy Director for Extramural Sciences*

- Minority Institution/Cancer Center Partnership (MI/CCP) (RFA Re-issuances) : Planning Grant for MI/CCP Partnership (RFA); Cooperative Planning Grant for Comprehensive MI/CCP (RFA); Comprehensive MI/CCP Partnership (RFA)

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XIII. *Clinical Trials Working Group Report*; Dr. James Doroshow

XIV. *Updates: Management of Bio-Specimen Resources and the FDA/NCI Task Force*; Dr. Anna Barker

XV. *Status Report: NCI/CMS Collaborative Activities*; Dr. Mark Clanton

XVI. *Adjournment*; Dr. Frederick Applebaum

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

Dr. Appelbaum called to order the 27th 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 future meeting dates. Comments

from the public regarding items discussed during the meeting may be submitted to Dr. Paulette Gray, BSA Executive Secretary, in writing within 10 days of the meeting.

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## **II. CONSIDERATION OF THE 15-16 MARCH 2004 MEETING MINUTES- DR. FREDERICK APPELBAUM**

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

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## **III. REPORT OF THE DIRECTOR, NCI - DR. ANDREW VON ESCHENBACH**

Dr. von Eschenbach recognized and acknowledged members who were rotating off the Board. He thanked them for their years of outstanding and dedicated service to the NCI and the Board of Scientific Advisors. NCI Director Service Awards were presented to Drs. Mary Daly, Herbert Kressel, Gillies McKenna, Henry Mihich, John Minna, Nancy Mueller, and William Wood. A Director's Service Certificate was presented to Dr. Appelbaum in recognition of exemplary leadership as a member, the second Chair of the BSA and for overall contributions to the restructuring of the NCI and the National Cancer Program.

**Staff Appointments.** Dr. von Eschenbach informed the Board of recent personnel appointments: Drs. James Doroshow, Director, Division of Cancer Treatment and Diagnosis (DCTD); Joseph Tomaszewski, Acting Director, Developmental Therapeutics Program (DTP), DCTD; Jeffrey Abrams, Acting Chief, Clinical Investigations Branch, Cancer Therapy Evaluation Program (CTEP), DCTD; and Peggy Rhodes as Special Assistant to the Director for Media Activities.

**NIH Conflict of Interest Issues.** Issues that have been raised related to conflict of interest and relationships with organizations outside of the NIH were presented. Members were told that a

hearing was held before the House Committee on Energy and Commerce's Subcommittee on Oversight and Investigations entitled "NIH Ethics Concerns, Consulting Agreements, and Outside Awards." Dr. Elias Zerhouni, Director, NIH, testified along with a panel that included Drs. Anna Barker, Maureen Wilson, and Carl Barrett from the NCI. Dr. Zerhouni testified with regard to the steps that have been underway at the NIH for strengthening the policies and practices related to the review and approval of outside relationships, as well as the processes and mechanisms of reporting and disclosure. He noted that the intent has been to continue to provide an environment in which the best scientific and clinical minds can be recruited to the NIH and the NCI, at the same time recognizing that relationships with extramural entities will continue to be important and that those relationships must be managed in a way to protect the public trust. Members were informed that changes in policies and process are underway that will affect the number of people to whom disclosure and reporting policies apply. In addition, the processes and mechanisms with regard to oversight and review will be centralized at the NIH under the direction of Dr. Raynard Kington and an advisory committee of peers. Dr. Joseph Fraumeni, Director, Division of Cancer Epidemiology and Genetics (DCEG) will represent the NCI.

**Selected NCI Activities.** Dr. von Eschenbach reported briefly on several NCI activities. He noted that many would be presented in greater detail in the first edition of the NCI *Annual Report of Scientific Progress*. He informed members that 1) the Children's Oncology Group had committed to working with the NCI to establish a Pediatric Central Institutional Review Board (IRB), with important implications for streamlining the conduct of pediatric clinical trials and improving the regulatory processes associated with them; 2) he had accompanied Department of Health and Human Services (DHHS) Secretary Tommy Thompson and the Surgeon General of the United States Army on a visit to the Frederick Cancer Research and Development Center (FCRDC) and the Army facility at Fort Detrick. Included in the presentations on initiatives that are operative at the FCRDC was a tour of the Computational Biology Center and the Drug Development Program; 3) the NCI's international program under the leadership of Dr. Joseph Harford, Director, Office of International Affairs, continues to receive the Secretary, DHHS's encouragement and support, notably for the All Ireland Consortium and the emerging

relationship with Italy. Other activities include a visit with Secretary Thompson to Baghdad and to the King Hussein Cancer Center in Jordan. Also, he noted and Secretary Thompson will meet with the Russian Minister of Health in an upcoming trip to Moscow; and 4) a press release issued jointly by him and Dr. Mark McClellan, Director, CMS, announced the creation of the NCI-CMS Task Force, which will mirror and parallel the activity of the NCI-FDA Task Force. These collaborative relationships will enable the NCI to streamline and accelerate the discovery, delivery, and development process to ensure that the cancer agenda is moving forward to touch patients' lives and contribute to the elimination of suffering and death due to cancer.

**NCI Communications.** Members were told that 1) the *2004 Annual Report to the Nation* shows that consistent gains are being made with regard to reducing the burden of cancer in the United States, especially the mortality of cancer; 2) the *Cancer Bulletin* continues to enjoy success and appreciation as an important source of and opportunity for communication with the entire cancer community; 3) subscriptions to the Web site continue to increase; and 4) *De-brief*, an internal electronic communication vehicle, has been created to keep NCI members abreast of emerging issues. Dr. von Eschenbach stated that the NCI continues to seek other opportunities for communicating extensively with the community. As such, in addition to the above electronic publications, the new *Annual Report of Scientific Progress* and the Bypass Budget, an exposition of NCI's strategic priorities, will further educate the community.

**Budget.** Dr. von Eschenbach reported because preliminary discussions suggest further significant budgetary restrictions in Fiscal Year (FY) 2005, NCI leadership is working with the Divisions to review the entire portfolio of investments to identify resources that can be redeployed to emerging strategic and significant opportunities, as well as areas where greater efficiencies will free up resources for their application to other programs. In a recapitulation of the FY 2004 budget, Dr. von Eschenbach noted that the NCI received a 3.2 percent (about \$147M) increase and was able to maintain the R01 payline at the 20th percentile. A total of 5,400 research project grants (RPGs) were awarded, of which 1,439 were competing awards. He noted that this is the largest number of RPGs ever awarded, approximately 300 more than the previous year. He also stated that the Cancer Centers Program

received a 6 percent increase, the number of competing Type 5s was maintained, and 12 competing Special Programs of Research Excellence (SPOREs) grant applications were awarded.

**In discussion, the following points were made:**

- Consistent communication of accomplishments and progress throughout the NIH is increasingly important in the current legislative climate. For example, the decreases in incidence of lung cancer in both men and women due to smoking cessation rates, and increases in years of disease-free survival among prostate cancer patients, as shown in the 2004 Annual Report to the Nation, should be communicated as major changes in the most powerful ways.

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**IV. NCI/CONGRESSIONAL RELATIONS—MS. SUSAN ERICKSON**

Ms. Susan Erickson, Director, Office of Policy, Analysis, and Response, OD, presented an overview of congressional hearings held during May and June. In May, the House Government Reform Committee heard testimony from two panels on cancer clinical trials participation. The second in a series of conflict-of-interest hearings was held by the House Energy and Commerce Subcommittee on Oversight and Investigations. The hearing addressed “NIH Ethics Concerns: Consulting Arrangements and Outside Awards.” On June 2, the House Energy and Commerce Subcommittee on Health held a hearing to address “Scientific Opportunities and Public Needs: Balancing NIH’s Priority Setting Process” as a preliminary step to drafting legislation to reauthorize the NIH.

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**V. GRANT PAYLINES AND TRENDS IN APPLICATIONS - MR. STEPHEN HAZEN**

Mr. Stephen Hazen, Chief, Extramural Financial Data Branch, OD,

NCI, presented a report on grants and paylines modified to reflect requests and suggestions made at the March 2004 meeting. Members were reminded that the requested elements were: the R01 payline, number of applications submitted, and overall rate of success as well as an indication of how well the NCI is supporting R01s and other grants. Mr. Hazen reviewed the data elements included in the R01, P01, R21, and all RPG competing award categories, and noted that the figures change as estimates are reviewed and revised during the fiscal year to take into account the number of applications coming in and how the peer review has assessed the merit of given applications. The actual June 2004 R01 and P01 report was presented to provide further clarification for a few of the elements. In response to the Board's request, two potential graphs that showed the trend of: 1) success rate base (number of applications received by the NCI adjusted to exclude duplicates and revisions) and 2) competing award numbers. Members were told that any of the data elements of the grant report can be compared in a graph showing the trend over several years. Members were asked for input as to which would be most useful. Members were also asked whether: 1) the report satisfies BSA advisory needs, 2) the report should be presented annually or at each meeting, 3) the comparison with estimates from the prior report is useful, 4) other data items would be more useful or relevant, and 5) R21s, R03s and other grant types should be included.

**In discussion, the following points were made:**

- Suggestions of additional information to include were: 1) the best estimates of what is likely to happen in the coming fiscal year in the trend graphs, 2) the actual dollar amounts in the trend graphs, 3) the impact of BSA decisions regarding RFAs on the R01 payline, 4) R21 and R03 data, 5) an analysis showing the continuum of K awards to R01s, 6) trends of mechanisms in relation to the NCI scientific priorities, 7) information to show the effectiveness of funding by exception mechanisms, 8) number of SPORE applications and the success rate, and 9) a breakdown of the number of awards above and below \$500K.



## **VI. NCI ALLIANCE FOR NANOTECHNOLOGY IN CANCER - DRS. MAURO FERRARI AND GREGORY DOWNING**

Drs. Mauro Ferrari, Edgar Hendrickson Professor of Biomedical Engineering and Professor of Internal Medicine at The Ohio State University, and Gregory Downing, Program Director, Office of Advanced Technologies and Strategic Partnerships, NCI, presented the NCI Alliance for Nanotechnology in Cancer. Dr. Ferrari reported that the *Cancer Nanotechnology Strategic Plan* has progressed remarkably during the past year because of the input and wisdom acquired from broad sections of the cancer community both within and outside of the NCI. He briefly described the activities that led to the formulation of the draft strategic plan, noting that some of these activities are ongoing and future activities are scheduled so that the plan will continue to be refined.

Dr. Ferrari stated that the timing is right to develop nanotechnology applications for cancer because of tremendous advances in the biological sciences (e.g., the genomic revolution), understanding of the fundamental nature of cancer, and information technology and computational sciences. A technology link between fundamental biology and the capability to interpret enormous amounts of data is missing, and nanotechnology is expected to fill this niche. Several examples of nanotechnologies that could help address this need, such as carbon nanotubes/nanowires, cantilevers, nanoparticles, and DNA chips were presented. Dr. Ferrari noted that the NCI has taken the lead for a number of years in supporting nanotechnology and other innovations for cancer therapeutics and diagnostics. One of the Institute's overall goals in its nanotechnology strategic plan is to incorporate multiple functionalities on a single nanotechnological platform. Another is developing the ability to generate a signal amplification property to allow researchers to see cells and molecules that otherwise cannot be seen using conventional imaging technologies. Other goals related to nanotechnology applications in the cancer field include the ability to monitor therapeutic interventions and determine when a cell is mortally wounded or activated.

Dr. Ferrari informed members that the multiple functionalities to be incorporated in the nanotechnology development plan, include the ability to: 1) explore and interrogate fundamental science at the cellular level, tumor microenvironment level, systems level, and at

the level of linkages between molecular pathways; 2) detect the signs of disease early from serum or by biological fluids analysis, through proteomics, or from imaging technology; 3) follow what happens to the tumor lesion as it evolves and as it gets modified and, hopefully, contained or eliminated by therapeutic intervention; and 4) identify the molecular differences *in vivo* between an identical pathology in two different patients, thereby personalizing the understanding of the disease and the therapy that follows.

Dr. Downing explained that development of NCI's Cancer Nanotechnology Strategic Plan has been a team effort involving many intramural and extramural program scientists as well as input from a large number of extramural biologists and technology developers. He noted that the draft plan includes clear goals for the next 5 years, and that the plan intends to bring together institutions and scientists in developing strategies for technology development and its integration into NCI's cancer clinical trials programs and, ultimately, into the clinic.

The plan calls for the formation of an alliance, a comprehensive, systemized initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnology to cancer. Strategic plan goals that have been applied to the alliance include developing: 1) research tools to identify new biological targets; 2) agents to monitor predictive molecular changes and prevent precancerous cells from becoming malignant; 3) imaging agents and diagnostics to detect cancer in earliest, most easily treatable, presymptomatic stages; 4) multifunctional targeted devices to deliver multiple therapeutic agents directly to cancer cells; 5) systems to provide real-time assessments of therapeutic and surgical efficacy; and 6) novel methods to manage symptoms that reduce quality of life.

The plan, starting with an active technology development program, involves integrating teams and concepts that already have been successfully brought together. The goal is to streamline and interface with NCI's existing cancer research infrastructure at its Comprehensive Cancer Centers and SPOREs. The approach includes creation of dedicated Centers of Cancer Nanotechnology Excellence, which will foster multidisciplinary physical, engineering, and chemical science research teams interfacing with cancer biology in clinical applications. Interagency collaborations will be important in developing training initiatives tied to the plan.

Existing contracts and grants programs that have been very successful in developing technologies and commercialization pathways will be utilized.

Dr. Downing briefly highlighted the focused areas for technology development described. He noted that there is not a central database or location where one can go to develop basic reference data on how nanotechnology interfaces with cells and in living systems. Therefore, plans are to develop a facility at NCI's Frederick campus to develop a cascade of biological assays that can be used to characterize nanoparticles and other nanomaterials in these biological systems. The Frederick laboratory also is intended to facilitate collaborations among the NCI, academia, and private sector primarily through the use and development of public databases and knowledge as well as assay development mechanisms, serving perhaps as a nexus for developing a multidisciplinary research team and focusing on potential new clinical applications.

In conclusion, Dr. Downing noted that the alliance offers the scientific opportunity for accomplishment in leadership and transforming the field of cancer biology to examine ways that technologies can be developed in the laboratory and translated into the clinic in a streamlined approach, and to understand how the physical world interacts with the biological world. Ultimately, it offers a new strategy for providing cost savings for health care programs and offering new approaches to personalized medicine, as well as the opportunities for expanding biomedical careers and new avenues for career development.

**In discussion, the following points were made:**

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- It was pointed out that it is difficult for Board members who are not already familiar with nanotechnology to participate in discussions on it, and noted that having more information on nanotechnology and its potential application in the field of cancer would help the Board in making its decisions. Staff commented that a significant effort has been put forth in communicating this work to the scientific community, and that a great deal of information is available on the National Nanotechnology Initiative Web Site (<http://www.nano.gov>). Additionally, various meetings and publications

have been used to inform the scientific community. Additional avenues for dissemination are being pursued, as well.

- In addition to the standard pharmaceutical and biotechnology companies, support for funding and training related to these efforts is emerging from the computer science and photolithography industries as well as other organizations (e.g., American Chemical Society).
- The area of molecular pathology and identifying probes for the study of gene expression and protein trafficking aspects is a promising new area.

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## **VII. GRONGOING AND NEW BUSINESS - DR. FREDERICK APPELBAUM**

### **BSA at National Meetings/NCI Listens Sessions**

**American Association for Cancer Research (AACR).** Dr. Hoda Anton-Culver presented the written report on discussions at the AACR meeting held on March 30, 2004. She highlighted the need for BSA discussion to address participant requests for clarification of various aspects of training grants dealing with multidisciplinary research.

**Society of Behavioral Medicine (SBM).** Dr. David Abrams presented the report from the SBM meeting held on 25 March 2004. Dr. Abrams stated that a highlight included suggestions about making maximal use of secondary data analysis by posting the data on the Web to avoid overlap and duplication and to facilitate collaborations; interest in new initiatives in the area of cancer aging; and concerns about maintaining funding for new investigators.

**Other 2004 NCI Listens Sessions:** Cold Spring Harbor Laboratories (CSHL) Symposium, 20 August, Cold Spring Harbor, NY, Drs. William Kaelin (Chair), Dinah Singer (Presenter), and Paulette Gray; and the American Society for Therapeutic

Radiology and Oncology (ASTRO), 3-7 October, Atlanta, GA, Drs. Mack Roach (Chair), Norman Coleman (Presenter), James Doroshow (Presenter), and Paulette Gray.

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## **VIII. CURRENT ETHICS ISSUES - DR. MAUREEN WILSON**

To provide a framework for the discussion on ethics issues that were the subject of House Subcommittee hearings, Dr. Maureen Wilson, Assistant Director, Ethics Office, NCI, reviewed the history of the Blue Ribbon Panel's report and the beginning of Dr. Zerhouni's look at conflict-of-interest issues at the NIH. Dr. Wilson noted that the Panel was charged with reviewing the existing laws and policies and the presence of real or apparent conflict-of-interest where NIH employees are receiving compensation from outside sources. The Panel raised concerns that the ethics rules had changed in interpretation and that the changes had potential for impacting NIH employees and their ability to abide by those rules. Dr. Wilson reviewed the series of recommendations made by the Panel. She told members that during this timeframe the NIH Ethics Advisory Committee (NIHEAC) was constituted to give consistency to ethics review across the Institutes and Centers (ICs) that comprise the NIH. The NIHEAC is conducting a central review on the outside activities of all senior staff. Members also were reminded that the Inspector General, Office of Government Ethics (OGE) and Congress also are reviewing NIH rules and procedures.

Dr. Wilson briefly reviewed procedural and process changes adopted or being considered by the NIH and other issues addressed in Dr. Zerhouni's report to Congress. She stated that the intent is to clearly establish what can and cannot be done or held by staff who file financial disclosure, and to extend this to other NIH employees in a way that limits their potential for running afoul of conflict-of-interest concerns. Dr. Wilson noted that rulemaking may be required in some cases to deal with existing regulations, which will involve working with the OGE because of the ethics focus and with the Office of General Counsel because the personal freedom of employees and institutional rights are being dealt with. The concern is to enhance the public trust by imparting knowledge of

what the interests are that may affect the research that is being carried out. Increased transparency will be required. An added concern, however, is how some of the changes will affect NIH's ability to recruit and retain some scientists.

**In discussion, the following points were raised:**

- In the current fiscal climate of restricted fiscal resources and FTEs, interactions with industry and other academic centers are going to be critical. There is a danger that the rules will be overly interpreted and pose limits on future research efforts.
- Conflict-of-interest policies should focus on four key areas: 1) education, 2) disclosure, 3) appropriate management plans, and 4) implementation monitoring.

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**IX. THE NIH ROADMAP INITIATIVES - DRS.  
DUSHANKA KLEINMAN AND J. CARL BARRETT**

Dr. Dushanka Kleinman, Assistant Director for Roadmap Coordination, Office of the Director, NIH, informed members that the Roadmap Initiative was instituted by Dr. Zerhouni after a review of the NIH when he became Director to address public health needs, emerging scientific opportunities, and changing demographics. The Initiative positions the NIH to conduct research differently and accounts for 1 percent of the budget at this time. Members also were reminded that suggestions concerning scientific opportunities, roadblocks to progress, and how to overcome them were generated in consultations and meetings with about 300 cancer stakeholders, then developed into an array of priority initiatives by working groups within the NIH. IC Directors participated in the selection of those that had the most promise to make an impact on public health and represented initiatives on which the NIH is uniquely positioned to act. Three theme areas that emerged were: 1) New Paths to Discovery, 2) Research Teams of the Future, and 3) Re-Engineering the Clinical Research Enterprise. Nine Roadmap Implementation Working Groups (RIWGs) were formed, and multiple project teams have been created in about 28

initiative areas to oversee about 60 ongoing projects.

Operating principles for the Roadmap are that management: 1) reflect the collaborative process used to develop the initiatives; 2) be informed by, but not bound to, current NIH practices; 3) maintain central administrative services; 4) provide routine updates and clear communication; and 5) include prospective evaluation. Responsibility for overall governance, coordination/facilitation, and evaluation rests with the Roadmap Implementation Coordination Committee (RICC), which is made up of RIWG Co-Chairs and Directors of various NIH OD offices. IC-designated Roadmap Liaisons speak on behalf of IC Directors and monitor the impact of the Roadmap and its integration with Institute-specific initiatives.

Dr. Kleinman presented Roadmap initiatives already or soon to be advertised for FY 2005 funding to illustrate that there are opportunities across all of the theme areas for both intramural and extramural participation. Implementation issues that cut across all the initiatives are communication beyond and within the NIH, evaluation of the overall Roadmap at the initiative level, and the new research authority granted by Congress. The new flexible research authority is being pilot tested on the nanomedicine initiative and will be considered for possible extension to other initiatives after evaluation. NIH Roadmap goals guiding these evaluations are to: 1) accelerate basic research discoveries and speed translation of those discoveries into clinical practice, and 2) explicitly address roadblocks that slow the pace of medical research in improving the health of the American people. Members were reminded that further information on Roadmap activity can be obtained on the Web site at <http://grants.nih.gov/grants>.

Dr. J. Carl Barrett, Director, Center for Cancer Research, NCI, further explained what the Roadmap Initiative is and is not, what implementation progress has been made, and how the NCI complements and synergizes with the ongoing Roadmap activities. Dr. Barrett stated that the NIH Roadmap is a framework of priorities the NIH as a whole must address to optimize its entire research portfolio; a vision for a more efficient, innovative, and productive system of biomedical and behavioral research; and a set of initiatives that are central to extending the quality of healthy life for people in this country and around the world.

He informed members that the initiatives within the theme area of 1) New Pathways to Discovery theme address technologies and approaches necessary to meet contemporary research challenges; 2) Research Teams of the Future provide mechanisms for interdisciplinary research, high-risk strategies, and public-private partnerships, at the same time preserving investigator-initiated strategies. Dr. Barrett noted that lessons learned about multidisciplinary and interdisciplinary research in the NIH Intramural Research Program from a survey conducted among all NIH ICs will be reported to the BSA at the fall meeting; and 3) Reengineering the Clinical Research Enterprise, address the need for creating better integrated networks of academic centers to encourage development of technologies for the assessment of clinical outcomes, harmonize the regulatory processes, and enhance training for clinical researchers. Dr. Barrett noted that the NCI Cancer Centers are models for this, as is NCI's Rapid Access to Intervention Development (RAID) Program. Expansion of the RAID Program is under consideration. Roadmap Initiatives with the NCI as lead are the Comprehensive Trans-NIH Imaging Probe Database, the National Electronic Clinical Trials and Research (NECTAR) Network, and the Translational Research Core Services RAID-like program.

Dr. Barrett informed members that the NIH Roadmap should be viewed both as a product in the form of RFAs and other infrastructures and a process that has brought together IC experts to consider best practices and approaches that might work collectively. Funding for FY 2004 is \$128.3 M, to be derived from a tap across the ICs on a proportionate basis to their constant percentage bases. He briefly discussed how the NIH Roadmap benefits the cancer research enterprise, by speeding removal of major and fundamental roadblocks common to all diseases; providing an opportunity for all ICs to communicate and compare best practices, working together to solve issues; providing a common trans-NIH pool of transforming investments open to all disease areas for competition. He showed how current NCI initiatives in the seven strategic priority areas of NCI's 2015 Challenge Goal are consistent with and complement Roadmap initiatives in the three theme areas. He noted in summary that the NIH Roadmap pools resources for specific enabling investments that individual Institutes could not undertake and will facilitate pioneering research, enable rapid development of promising breakthroughs, and accelerate understanding of the complexity of



molecular interactions that lead to disease.

**In discussion, the following points were raised:**

- Overall Roadmap overview and solicitation information is available on the Web at <http://nihroadmap.nih.gov>. Board members can join a listserv at that site to receive periodic notices on new items. The Roadmap also is being publicized through professional society meetings and through NCI communication vehicles such as the Cancer Bulletin.

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**X. RFA/COOPERATIVE AGREEMENT AND RFP  
CONCEPTS - PRESENTED BY NCI PROGRAM STAFF**

**Division of Cancer Control and Population Sciences (DCCPS)**

**Laboratory Assessment of Tobacco Use Behavior and Exposure to Toxins Among Users of New Tobacco Products Promoted To Reduce Harm (RFP)**. Drs. Mirjana Djordjevic, Tobacco Control Research Branch, informed members that the proposed RFP evolved from the NCI Executive Committee's (EC) recommendation to issue a proposed concept to foster research on new potential reduced-exposure products as a Program Announcement (PA) rather than as an RFA, and develop a research and development (R&D) contract to fund the product-testing component of the Tobacco concept. The PA was published in the *NIH Guide* on 20 May 2004. The purpose of the proposed concept is to advance knowledge on toxicological and addictive properties of new tobacco products and their relationship to behavior. Plans are to: 1) assess individual behaviors among users of new products; 2) develop and validate methods and biomarkers to measure delivered dosages and uptake of nicotine and select toxic and carcinogenic agents under actual conditions of product use; 3) establish and maintain a shared database of laboratory methods, product characteristics, and emissions and uptake of tobacco and smoke constituents; and 4) provide advice and expertise on the evaluation of these products to federal regulatory agencies such as

the Federal Trade Commission (FTC) and FDA, policymakers, and consumers. Dr. Djordjevic explained that the R&D contract will complement the PA by permitting rapid response to immediate research, public health, and regulatory needs; whereas, the PA will act in the long run to stimulate investigator-initiated research in bio-behavioral science and develop a cadre of independent experts, new laboratory methods, and candidate biomarkers. A 10-15 member Expert Consulting Committee will be established with membership drawn from appropriate NCI Divisions, other Institutes, other government agencies, and external scientific experts. The Committee will meet at least twice a year to establish research priorities and make recommendations regarding methods and approaches.

Estimated costs for the 5-year project period is \$3 M per year for a \$15 M total investment.

**In discussion, the following points were raised:**

- New tobacco products have the potential to reverse smoking cessation trends that have been on a downward curve for 50 years.
- Interaction between smokers and products is a key issue, one that has resulted in previous underestimations of risk, for example, of the low tar/low nicotine products that appear to have contributed to the rise in peripheral adenocarcinoma incidence 20-30 years later, because of deeper inhalation by smokers.
- The NCI has adopted a network-centric approach to tobacco control and is bringing investigators from all tobacco-related funded initiatives together to create linkages proactively.
- Additional funding for the proposed project will be sought through collaborations with other interested Institutes and agencies.

**Motion.** The motion to approve the DCCPS RFP concept entitled “Laboratory Assessment of Tobacco Use Behavior and Exposure to Toxins Among Users of New Tobacco Products Promoted To Reduce Harm” was approved unanimously.

**Cancer Genetics Network (RFP)**. Dr. Carol Kasten, Cancer Genetics Network (CGN) Program Director, Clinical and Genetic Epidemiology Research Branch, stated that the proposed RFP was developed in response to the NCI EC's decision not to reissue the CGN RFA, but to retain core elements of the registry as a valuable research resource for future studies. EC deliberations on the reissuance were informed by a 2003 evaluation of CGN progress by a BSA Subcommittee established at the request of the Director, DCCPS. At its March 2004 meeting, the BSA concurred with the EC decision and supported continuation of the CGN in a streamlined form. As proposed, key CGN functions to be maintained are: 1) the core database of more than 24,000 enrollees, 2) biospecimens accumulated over CGN's 6 years, 3) curation of resources to ensure their value to investigators in future research, 4) annual enrollee followup, and 5) Principal Investigator (PI) support for tasks such as ensuring annual followup and writing IRB applications for collaborations. Current CGN functions to be dropped include: 1) new enrollments not funded by peer-reviewed grants, 2) infrastructure resources utilized for multiple studies and core enrollment, and 3) the pilot study research mechanism. The proposed contract structure will include a new Statistical Coordinating Center (SCC) to be the hub of all streamlined CGN functions and to subcontract to all current CGN Centers and affiliated sites. New CGN SCC responsibilities will be to unify and maintain CGN Core and special studies databases, centrally track the biospecimen repository, maintain a centralized Web-based document repository for all CGN and outside investigator forms, develop and implement the CGN marketing plan, respond to queries from outside investigators, and aid outside investigators' research. Future goals of the streamlined CGN as proposed are to support studies on the genetic basis of cancer; support studies integrating cancer genetics into medical practice; and address behavioral science, educational, and ethical issues that are the consequence of genetic research. The RFP to support the registry (minus the CGN) would be a support contract, not an R&D contract.

A project period of 5 years with 2 additional option years to accommodate R01 timeframes is proposed. Estimated costs are \$2.2 M for the first year and \$11.7 M total for 1 contract and 17 subcontracts .

**In discussion, the following points were raised:**

- Lessons learned from the CGN experience should be applied to developing a good model for these kinds of large projects that will likely be undertaken in the future.
- An evaluation of the productivity of the streamlined CGN and its use 5 years from now should be built into the contract.
- Utilization of these resources requires that they be user-friendly for investigators. Transparency and clear communication to the extramural community who may want to use these resources also is important.
- Access to specimens and the need for re consent are some of the complexities of doing human subjects research at the present time. Best practices identified through the streamlined CGN should be transferred to other clinical research networks and to inform some of the new processes and programs being initiated.

**Motion.** A motion for the BSA to concur in the proposed DCCPS RFP entitled “Cancer Genetics Network” was seconded and approved, with no votes against and three abstentions.

**Office of the Director (OD)**

**Cancer Nanotechnology Concepts: Centers of Nanotechnology Excellence (Coop. Agr.); CCNE Coordinating Center (RFA); Multidisciplinary Career Development Cancer Nanotechnology Education (RFA); Cancer Nanotechnology Education (RFA).**

Dr. Gregory Downing, Director, Office of Technology and Industrial Relations, informed members that the four proposed Cancer Nanotechnology Concepts are to address the objectives of the NCI Cancer Nanotechnology Plan (CNPlan). Dr. Downing noted that the were 1) cooperative agreements (U54s) to create 3-5 Centers of Cancer Nanotechnology Excellence (CCNEs) with the goal of integrating nanotechnology platforms into basic and applied cancer research to rapidly facilitate clinical applications; 2) an RFA

(U01 mechanism) to establish a CCNE Coordinating Center to integrate the CCNE network; 3) creation of multidisciplinary nanotechnology research teams and support for the career development of individual investigators who will become future team leaders (individual investigator awards are F33s, K08, K25, F32s, T32s, and Bioengineering Research Partnerships); and 4) Cancer Nanotechnology Education, the use of the R25 mechanism for a 3-year initiative to develop continuing education programs, especially in conjunction with the Cancer Centers. Members were told that a Request for Information is currently being advertised in conjunction with the CNPlan to facilitate grants and contracts program development in six key technology areas.

Program Evaluation will occur in the six high-impact programmatic areas identified in the CNPlan: molecular imaging and early detection, in vivo imaging, reporters of efficacy, multifunctional therapeutics, prevention and control, and research enablers. Performance milestones have been established at both the project and program level, and interfaces have been established with the NIH Roadmap Initiative.

Estimated costs for the 5-year project period is \$186.5 M and a first year set-aside of approximately \$20.9 M for 1 (U01), 3-5 (U54), 6 (F32), 8 (F33), 8-10 (K08/K25), 50-75 (T32), and 5 (R25).

**In discussion, the following points were raised:**

- The mechanism for phase-out of large-scale science projects should be considered along with planning for initiation of those projects.
- Areas of concern with regard to the proposed initiatives were: integration with the NIH Roadmap Initiative in nanomedicine; interface with industry and possible intellectual property and conflict-of-interest issues; the need for clarity on how the relationships with the FDA will work as new materials would be brought into the medical environment; the possibility that 5 years may be too short a timeframe to achieve clinical applications; possible duplication with ongoing industrial activities; the potentially large set-aside for this new area that will not be viewed as traditional investigator-mediated, grant-funded research; the

availability of teachers with the appropriate expertise to implement the training initiatives; the role of the Coordinating Center; the extent of evaluation at the end of the planning process that would determine how much growth with respect to establishing CCNEs is feasible and how rapidly; the system's ability to absorb and fund the cohort of new investigators that is envisioned to come out of the training program at the end of 3 years; the need for a more gradual step up of the training component; and the need for additional information about underlying science of the program as well as details on the mechanisms and processes envisioned in the implementation.

**Motion.** A motion to approve the OD Cancer Nanotechnology Concepts with provision for yearly reviews to allow for modification and scalability as the initiative progresses was moved, seconded and amended to specify that the training component would be started at year 3. The motion and amendment were withdrawn.

**Motion.** A motion to approve in principle the OD Cancer Nanotechnology Concepts subject to input from two BSA subgroups (one to examine the science, the other to look at structure) was not approved.

**Motion.** A motion to appointed a BSA subcommittee to address scientific and administrative concerns relative to the OD Cancer Nanotechnology Concepts that were raised in the discussion and make a recommendation to the whole Board by conference call in preparation for a vote on the RFA concepts, also by conference call was unanimously approved. Members of the Cancer Nanotechnology Concepts Subcommittees are Drs. Thomas Curran, Shelton Earp, William Hait, Susan Horwitz, Michael Link, Enrico Mihich, Mack Roach, Richard Schilsky, and Ms. Paula Kim.

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**Office of the Deputy Director for Extramural Sciences  
(ODDES)**

**Minority Institution/Cancer Center Partnership (MI/CCP) Concepts (RFA Re-issuances): Planning Grant for MI/CCP Partnership (RFA); Cooperative Planning Grant for Comprehensive MI/CCP (RFA); Comprehensive MI/CCP Partnership (RFA).** Dr. Sanya Springfield, Chief, Comprehensive Minority Biomedical Branch (CMBB), reminded that the MI/CCP Program was approved by the BSA in 2001 to support collaborations and partnerships between Minority-Serving Institutions (MSIs) and NCI-designated Cancer Centers. General objectives were to increase the competitive research capacity at the MSIs, promote more research in areas disproportionately affecting minority populations, increase the effectiveness of Cancer Center outreach to surrounding minority communities, and provide models and new approaches to addressing the disproportionate cancer incidence and mortality rates in ethnic minority populations. The four areas targeted in the program are Cancer Research, Cancer Outreach, Cancer Training, and Cancer Education. Three broad funding mechanisms are utilized by the Program: 1) a P20 planning grant to provide support for up to 4 years, 2) a U56 cooperative planning grant that was created specifically for the Comprehensive Partnership Program, and 3) the renewable U54 cooperative agreement. The MI/CCP interacts and is involved with the CMBB program known as Continuing Umbrella of Research Experiences, which supports individual minority investigators from high school to their first academic appointment.

The estimated cost per year is \$2.5 M for an estimated 12 awards and a total cost of \$12.5 M over 4-years.

**Motion.** The motion to concur with the re-issuance of the MI/CCP RFAs was approved with no votes against and three abstentions.

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## **BRENDA EDWARDS**

Dr. Robert Croyle, Director, DCCPS, noted that the *Annual Report to the Nation* is a collaborative effort between the NCI and other organizations. This year, the American Cancer Society (ACS) took the lead in promoting collaboration and communication for the *Report*. Dr. Croyle credited involved NCI staff for their roles in this collaborative effort between the Centers for Disease Control and Prevention (CDC), ACS, and the North American Association of Central Cancer Registries. The NCI contributes analytical and statistical expertise toward the *Report's* interpretation of complex trends and patterns.

Dr. Brenda Edwards, Associate Director, Surveillance Research Program (SRP) informed members that the SRP includes the Surveillance, Epidemiology, and End Results (SEER) Program registries and other analytic projects that involve the collection, synthesis, and interpretation of data and trends. Dr. Edwards stated that the *2004 Annual Report to the Nation* focuses on the number of cancer sites reported on was expanded to the top 15 sites, that there are special features on survival data (from the SEER Program) and state-specific information. Extensive information by racial/ethnic groups also is included. Long-term data and incidence rates and trends for several cancers were presented.

Members were told that the *Report* shows a 21.3 percent improvement in 5-year survival rates for men diagnosed more recently than for those diagnosed earlier. Survival increased by more than 10 percentage points for all sites, prostate, colon/rectum, NHL, melanoma, leukemia, and kidney cancers. The major reason for this improvement is the heavy preponderance of prostate cancer cases and the notable improvement in overall survival. The overall increase for women was smaller overall, at 7.7 percent, but survival rates for women did increase by more than 10 percentage points for colon/rectum, NHL, and breast cancers.

The Report also focuses on cancer prevalence (the number of people or the proportion of people alive who have been previously diagnosed with cancer). This measure was calculated using both incidence and survival data. Estimates were mapped to the total U. S. population. The new 2001 cancer prevalence estimate is 9.8 million individuals, which Dr. Edwards indicated may be a conservative number.



Dr. Edwards indicated that there is no single, simple way to characterize the cancer burden among racial and ethnic groups. To generalize, however, it can be said that cancer incidence and mortality rates vary by race/ethnicity, and interpreting new cancer rates will take time. Data are available at [www.surveillance.cancer.gov](http://www.surveillance.cancer.gov) under "Finding Statistics." Dr. Edwards presented a series of slides that showed incidence rates by race/ethnicity for various cancer sites based on SEER 1992 to 2001 data.

Although actual numbers of deaths from cancer have increased by 6 percent, when population growth and aging are accounted for, accrued cancer death rates actually have decreased by 4 percent and 8 percent, respectively. Measures of trends, age-adjusted rates, survival, and relative risk provide a clearer picture of progress being made against cancer. In closing, Dr. Edwards recognized Dr. Constance Lehair Percy, a colleague and pioneer in identifying smoking as a risk factor in cancer, who passed away earlier this year at the age of 89.

**In discussion, the following points were raised:**

- It would be helpful to have all of the data before they are fractionated so that data for the population as a whole, as opposed to just the subgroups, can be examined.
- It may be misleading to separate the racial/ethnic groups as if they are different species instead of accounting for socioeconomic factors. Some differences may disappear when socioeconomic factors are taken into account. It is important to try to understand and clarify the reasons for discrepancies in incidence and mortality rates between various racial/ethnic groups. Last year, a monograph was published that examined mortality incidence and survival rates using socioeconomic status (SES) and Census data. The ACS used this information in its Facts and Figures publication as well. The National Longitudinal Mortality Study also is incorporating SES factors along with racial/ethnicity data.
- Explanations for the decline in female breast cancer incidence among black women in 2001 may include substantial underreporting across all cancer sites and

changes in screening. This area will be studied further.

- Consideration should be given to strategically tailoring and targeting a consistent, focused message to specific subgroups and audiences (including Congress).
- Tobacco-related concerns may be overshadowed in the public consciousness by the current emphasis on obesity and fat. The campaign against tobacco use must be maintained. Specific messages should be targeted to young girls, who may think they need to smoke to control their weight.
- It was suggested that a small booklet be produced that contains information highlights from the Report. Such a booklet could be useful to staff, Congressional aides, and others. The information contained in the Bypass Budget could be used as a model for the types of information to be included.
- Information from the Report should be released to the public in a meaningful way that can be readily understood. This involves translation of scientific jargon and qualifications into clear messages with clear cues to action.
- A future discussion at a BSA meeting will include an update of plans to communicate the Report's data to the community. Another possible subject for discussion at a future BSA meeting is how to create a deeper and more effective resource and infrastructure that is more long term and strategic, perhaps over a 5-year period of sustained, focused, persistent, novel, and creative messages.

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### **XIII. CLINICAL TRIALS WORKING GROUP REPORT - DR. JAMES DOROSHOW**

Dr. James Doroshow, Co-chair, Clinical Trials Working Group (CTWG), and Director, DCTD, stated that the charge of the CTWG is to advise the National Cancer Advisory Board (NCAB) and its Subcommittee on Clinical Investigations on the development,

conduct, infrastructure, support, and coordination of clinical trials conducted across the NCI. The CTWG was directed by Dr. von Eschenbach to consider a revised clinical trials system for the future. Members were told that CTWG's efforts are based on work performed by the Armitage Committee, the subsequent Implementation Committee, and the P30/P50 Working Group to demonstrate and outline issues that were as relevant to the Committee in 1998 as they are today. For example, the major issues outlined by the Armitage Committee with respect to clinical trials included the need 1) to improve trial coordination, prioritization, design, methodologies, access, and accrual; 2) evaluate the framework within which trials are performed at the NCI; and 3) evaluate the declining availability of clinical investigators and support for clinical investigators. The P30/P50 Working Group also emphasized the need to examine how clinical research conducted in Cancer Centers and SPOREs is integrated nationally to better coordinate among the various venues in which clinical research is performed. A considerable amount of research is being conducted by groups outside of the cooperative groups, and efforts must be made to organize this information for the future.

Dr. Doroshow indicated that CTWG's membership includes broad representation from the oncology community involved in clinical trials. Members include representatives of Cancer Centers, SPOREs, Cooperative Groups, pharmaceutical firms, the FDA, the CMS, the Office for Human Research Protections (OHRP), multiple oncologic disciplines, the NCAB, BSA and all relevant NCI intramural and extramural programs, as well as patient advocates.

The CTWG's three objectives are to: 1) implement solutions for critical issues currently impairing the efficiency of the NCI-supported clinical trials system, 2) develop a blueprint for the conduct of future cancer clinical trials, and 3) guide the construction of the informatics infrastructure for managing and organizing clinical trials information at both the local and national levels. Two subcommittees to address the first two goals have been established. CTWG conducts monthly teleconferences and quarterly in-person meetings, and its subcommittees also will conduct numerous tele- and videoconferences.

The group has agreed that the most short-term issues are finding

better ways to 1) prioritize, coordinate, and integrate trials are priority areas; 2) defining exactly who is enrolled in a clinical trial and listing trial outcome, efficacy, and adverse event data for all NCI-supported trials; and 3) addressing the regulatory issues that slow the completion of clinical trials.

Dr. Doroshow indicated that there was also agreement among group members at the initial CTWG meeting that a new national trials system must involve a system of prioritization that is science based. This will involve coordinating both clinical and scientific multimodality expertise to perform an optimal peer review of the studies to be conducted. Without such a system, it will be impossible to eliminate redundant trials. However, before this system can be devised, an open-source, dynamic, interoperable bioinformatics infrastructure to support clinical trials must be developed. This will require institution of standardized procedures (e.g., standardized case report forms and data elements) and the development of a system that will provide automated reports and serve as a national repository for efficacy data to allow for easy patient entry, uniform consent documents, and data collection in any venue at which clinical trials are conducted. He indicated that key users must be taken into account in developing the system and input extends beyond government-funded investigators and university-Cancer Center-based investigators. Any system that is developed also will need to be interfaced with the appropriate regulatory agencies. Input from the FDA, CMS, and OHRP will be critical to this process.

Dr. Doroshow indicated that the CTWG would like to receive input from a wide variety of communities and potential constituencies. Members were urged to visit the CTWG's Web site (<http://integratedtrials.nci.nih.gov>) to give input and to receive CTWG progress updates.

**In discussion, the following points were raised:**

- Information regarding the name and location of NCI studies is readily available. The results of such studies are not currently available, however. Making that information accessible will be useful to academic investigators, practitioners, and patients.

- It is critical to assess the effects of changes that may be implemented by the CTWG in terms of their effects on clinical trial accrual rates. The further removed peer review is from the actual conduct of trials, the greater the probability that trials may be designed that are not completed for a variety of practical reasons.
- The possibility of applying the Heart Institute model to certain situations in the cancer field should be considered. In this model, a cooperative group is assembled around a question, as opposed to trying to identify a question that fits into a preconceived, precreated cooperative group.

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#### **XIV. UPDATES: MANAGEMENT OF BIOSPECIMEN RESOURCES AND THE FDA/NCI TASK FORCE - DR. ANNA BARKER**

Dr. Anna Barker, Deputy Director for Advanced Technologies and Strategic Partnerships, informed members that the FDA/NCI Interagency Oncology Task Force (IOTF), that the initial meetings of the IOTF focused on determining how the different cultures involved viewed the current state of affairs. Depending on the amount of science that is available for what they are attempting to regulate, the FDA functions largely by writing guidance for the community. Its work is driven by the quality and amount of available science and how it is pulled together. In analyzing the drug development process, the IOTF began by identifying and analyzing barriers and potential solutions. Dr. Barker stated that the FDA participants share NCI's goal of changing the paradigm to get new drugs to patients. FDA's primary goal, however, is to ensure the safety of drugs used by the public.

Members were told that the IOTF is divided into a series of subcommittees. Areas being addressed by the subcommittees include training, process, efficient management of oncology drugs and devices, clinically meaningful endpoints, bioinformatics, and various special issues, such as nanotechnology. An outcome of IOTF's work has been the critical path document recently developed by the FDA. Much of the Task Force's work is being

converted into guidance documents, which is part of FDA's regulatory process. The IOTF plans to circulate a report to the Board in the near future.

Dr. Barker reported a fellows training program has been planned and funded. The program should be underway by September and will involve NCI fellows going to the FDA. This program will be advertised broadly and is being funded by the NCI. At the end of 5 years, a significant workforce will have been developed that is expert in both regulatory science and oncology. A group has been established with FDA and NCI leadership personnel serving an ombudsman-like function to help NCI-supported investigators navigate the FDA system.

Other areas being investigated or where progress has been made are 1) pilot screening trials in terminal patients, 2) chemoprevention, 3) projects directed toward changing guidance documents, 4) piloting e-submissions of investigational new drugs (INDs), 5) HL7 standards, specifically for submission of clinical trials data, 6) simplifying terminologies, and 7) developing a single reporting infrastructure to be used by all involved groups.

In discussion, the following points were made:

- When queried as to the degree to which the FDA continues to be constrained by prevailing regulations and what needs to be done with respect to modifying the regulations to allow the FDA to implement some of the new strategies being advocated by others, staff responded that the FDA actually has the power to change the regulations, and there is a need to identify the issues and suggest changes to the regulations.
- A suggestion was that the Task Force focus on several of the divisions involved in drug development, especially in the preventive area.
- When asked if the IOTF had been involved in the prostate cancer surrogate effort, staff noted that the IOTF had, and it is attempting to determine which efforts have the best case scientifically. The Task Force also is trying to ascertain what the next steps in the process will be and how those

steps will translate into change.

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## **XV. STATUS REPORT: NCI/CMS COLLABORATIVE ACTIVITIES - DR. MARK CLANTON**

Dr. Mark Clanton, Deputy Director for Cancer Care and Delivery Systems, informed members that this effort involves opening doors and lines of communication, not necessarily driving decisions or policy in an agency. Dr. Clanton stated that the purpose of the collaboration is to combine scientific and clinical resources to help the CMS answer questions related to oncology therapy and, in particular, off-label oncology therapy. He noted that the collaborative group will focus on two issues. First, the ultimate goal is to develop a process that meets regulations and allows the NCI, FDA, and CMS to work together. Rather than have the CMS involved in drug approval, the aim is to have the CMS look back through discovery and translational science to determine what the FDA is considering and perhaps to anticipate new and combined drug therapies such that the CMS can make coverage decisions close to the time that the FDA approves the drugs. This will enable development of a formal process of anticipating the approval of drugs and drug combinations and providing earlier coverage for such therapies.

Second, the collaborative group will focus on technology assessment and consideration of molecular diagnostics, including bioinformatics, medical informatics, and molecular imaging. The CMS already is interested in these issues, and the collaborative group will be able to contribute additional expertise. Currently, it is difficult for the insurance process to review and approve off-label drug use and combined therapy. In particular, however, the commercial insurance process is not ready to consider devices that can perform multifunctional therapeutic or diagnostic functions, such as a nanodevice. The collaborative group aim is to make the insurance and technology assessment processes more anticipatory so that such devices can be examined in a more rational way when they become available and the issue of coverage emerges so that they are more immediately and more widely available to patients who need them.

## **In discussion, the following points were raised:**

- Because all Medicare coverage decisions are local, it is critical that the results of the NCI/CMS collaborative effort be received at the local, state, and intermediary levels. In fact, national coverage decisions can and do impact claim payment at the local level.
- The model that the CMS uses in determining coverage is similar to that used by most insurance companies in terms of connecting indication to approved therapy. It is expected that, as medicine moves more toward molecular medicine, more comprehensive decisions will be produced regarding what is covered.

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## **XVI. ADJOURNMENT-DR. FREDERICK APPELBAUM**

The 27th meeting of the BSA was adjourned at 12:00 noon on Friday, 25 June 2004.

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