

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE**

48th Meeting

BOARD OF SCIENTIFIC ADVISORS

Minutes of Meeting

**March 1, 2011
Building 31C, Conference Room 10
Bethesda, Maryland**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE**

BOARD OF SCIENTIFIC ADVISORS

MINUTES OF MEETING

March 1, 2011

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 48th meeting on Tuesday, 1 March 2011, at 9:00 a.m. in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Richard L. Schilsky, Professor of Medicine, Section of Hematology and Oncology, Biological Sciences Division, University of Chicago Pritzker School of Medicine, presided as Chair. The meeting was open to the public from 9:00 a.m. until 4:23 p.m. on 1 March for the NCI Director's report; a report on NCI Congressional relations; consideration of request for applications (RFA) and Cooperative Agreements (Coop. Agr.) new and reissuance concepts presented by NCI program staff; a report from the Cancer Bioinformatics Grid (caBIG[®]) Working Group; and a status report on the implementation of the Institute of Medicine (IOM) clinical trials report recommendations.

BSA Board Members Present:

Dr. Richard L. Schilsky (Chair)
Dr. Paul M. Allen
Dr. Andrea Califano
Dr. Michael A. Caligiuri
Dr. Arul M. Chinnaiyan
Dr. Curt I. Civin
Dr. Chi V. Dang
Dr. Robert B. Diasio
Dr. Betty R. Ferrell
Dr. Kathleen M. Foley
Dr. Sanjiv S. Gambhir
Dr. Joe W. Gray
Dr. Mary J. C. Hendrix
Dr. Timothy J. Kinsella
Dr. Joshua LaBaer
Mr. Don Listwin
Dr. Maria E. Martinez
Dr. James L. Omel

Dr. Edith A. Perez
Dr. Victor J. Strecher
Dr. Louise C. Strong
Dr. Jean Y. J. Wang
Dr. Irving L. Weissman
Dr. James K. Willson

Board Members Absent:

Dr. Christine Ambrosone
Dr. Ronald A. DePinho
Dr. Jeffrey A. Drebin
Dr. Todd R. Golub
Dr. Christopher J. Logothetis
Dr. Stuart L. Schreiber
Dr. Bruce W. Stillman
Dr. Frank M. Torti

Others present: Members of NCI's Scientific Program Leaders (SPL), NCI staff, members of the extramural community, and press representatives.

TABLE OF CONTENTS

I.	Call to Order and Opening Remarks—Dr. Richard L. Schilsky.....	1
II.	Consideration of the 1 November 2010 Meeting Minutes—Dr. Richard L. Schilsky.....	1
III.	Report of the Director, NCI—Dr. Harold Varmus	1
IV.	NCI/Congressional Relations—Ms. Susan Erickson.....	2
V.	Ongoing and New Business—Dr. Richard L. Schilsky.....	2
VI.	RFP/RFA/Cooperative Agreement Concepts—Presented by NCI Program Staff.....	3
	Division of Cancer Treatment and Diagnosis	
	National Specimen Banks To Support NCI Clinical Trials Network	
	(RFA/Coop. Agr. New).....	3
	Office of the Director	
	Cancer Target Discovery and Development Network Centers	
	(RFA/Coop. Agr. New).....	4
	Division of Cancer Prevention	
	Alliance of Glycobiologists for Detection of Cancer: A Trans-NIH Program	
	(RFA/Coop. Agr. Reissuance)	5
VII.	Cancer Bioinformatics Grid (caBIG®) Working Group Report—Dr. Andrea Califano	6
VIII.	Status Report: Implementation of the Institute of Medicine (IOM) Clinical Trials Report	
	Recommendations—Dr. James H. Doroshow.....	8
IX.	Adjournment—Dr. Richard L. Schilsky.....	9

I. CALL TO ORDER AND OPENING REMARKS - DR. RICHARD L. SCHILSKY

Dr. Richard L. Schilsky called to order the 48th regular meeting of the BSA and welcomed current and new 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 confidentiality requirements. Members of the public were invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), in writing and within 10 days, comments regarding items discussed during the meeting.

II. CONSIDERATION OF THE 1 NOVEMBER 2010 MEETING MINUTES - DR. RICHARD L. SCHILSKY

Motion: The minutes of the 1 November 2010 meeting were approved unanimously.

III. REPORT OF THE DIRECTOR, NCI - DR. HAROLD VARMUS

Dr. Harold Varmus, Director, NCI, welcomed members and provided information about the NCI's budget for fiscal years (FY) 2011 and 2012, as well as NCI and NIH activities of interest.

Budget: Dr. Varmus informed members that the President's Budget (PB) for FY 2012 includes a 2.4 percent increase over FY 2010 levels for the NIH. He reminded members that the NCI is currently operating under a Continuing Resolution (CR) at the FY 2010 budget level. In expectation of continued uncertainty about the budget, the NCI is conducting more intense reviews of applications, with awards to early-stage and new investigators considered a priority. Discussions among the NCI leadership have included: the reduction of payments for noncompeting grants; careful examination of NCI contracts; and small funding decreases to existing programs, including to the NCI-supported Cancer Centers.

NCI Activities: Members were told that the new members of the National Cancer Advisory Board (NCAB) had been appointed, and appointments to the President's Cancer Panel (PCP) are expected. Other recent NCI events included: the second NCI Town Hall meeting, a meeting of the Cancer Center directors, three additional Provocative Questions Initiative workshops to address provocative questions

about cancer, and several retreats, including the NCI's Intramural Research Program, and the Scientific Program Leaders (SPLs) with staff from the Office of the Director (OD), and a joint workshop with the National Institute of Allergy and Infectious Diseases (NIAID) on the development of Epstein-Barr virus vaccines. Dr. Varmus stated that the NCI is preparing its annual bypass budget with a narrative report, which includes a request for a 15 percent budget increase. The report highlights six types of cancers that illustrate how recent advances in basic science, prevention, and therapeutic research apply to cancer patients.

Dr. Varmus reminded the Board that recruitment continues for several positions: Deputy Director for Clinical and Translational Research; and Directors of the Division of Cancer Prevention, Center for Global Health, and Center for Cancer Genomics. He encouraged members to submit recommendations for candidates for these positions. Members were told that the NIH-wide reorganization activities of interest include the proposed: 1) creation of a new Institute for Substance Use, Abuse, and Addiction that would integrate the relevant research portfolios from the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and other NIH Institutes and Centers; and, 2) the National Center for Advancing Translational Sciences (NCATS), which is expected to have a beneficial, catalytic effect for the NCI. Dr. Varmus next reviewed the agenda for today's meeting.

In the discussion, the following points were made:

- < The Provocative Questions Initiative has stimulated discussions at other organizations that have the potential to change the way diseases and important biological questions are considered. Future activities may include encouraging discussion and collaborative groups at research institutions and an NCI study section to review provocative questions applications.
- < The Director of NCI's new Center for Global Health will consider ways to apply relatively low-cost prevention and treatment strategies to reduce the cancer burden in poor countries, including through screening, vaccination, and palliation.
- < The NCATS will serve as a catalyst for translational research across the NIH and will provide resources and cores, including the Clinical and Translational Science Awards (CTSAs), Chemical Genetics Core Facility, and the Cures Acceleration Network (CAN), as well as support for therapies of rare and neglected diseases.

IV. NCI/CONGRESSIONAL RELATIONS - MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Government and Congressional Relations (OGCR), informed members that the PB for FY 2012 was announced on 14 February, with \$31.0 B for the NIH and \$5.1 B for the NCI. Ms. Erickson described House and Senate Committee assignments in the 112th Congress and provided updates about legislation of interest to the NIH and NCI. Members were told that future legislative updates to the BSA would be provided on an as-needed basis.

V. ONGOING AND NEW BUSINESS - DR. RICHARD L. SCHILSKY

Dr. Schilsky encouraged members to submit potential agenda items for future Board meetings.

In the discussion, the following points were made:

- < The size of the NCI intramural program has been decreased over the past five years. Collaborations between NCI intramural investigators and extramural researchers should be encouraged. The Institute is considering ways to facilitate the process for developing Cooperative Research and Development Agreements (CRADAs) and improve the likelihood that industry will seek consultation with intramural investigators.

- < Activities in the Center for Global Health will include collaborations between intramural and extramural scientists. Surveys of the NCI's portfolio are underway to determine the level of support provided for projects abroad and for research on domestic health and delivery systems that may be applicable in other countries.
- < Members encouraged the NCI to consider the merits of both the R01 and R21 grant mechanisms supporting individual investigators, and whether NCI should participate in the R21 Parent Announcement. The NCI will bring the question of appropriate use of the R21 mechanism back to the BSA at a future meeting.
- < The NCI will remain a primary user of NCATS Chemical Genomics Core with no significant shifts in funding expected. The Institute anticipates using NCATS' facilities occasionally to assist with research about less common or "orphan" cancers.

VI. RFP/RFA/COOPERATIVE AGREEMENT CONCEPTS - PRESENTED BY NCI PROGRAM STAFF

**Division of Cancer Treatment and Diagnosis
National Specimen Banks To Support NCI Clinical Trial Networks (RFA/Coop. Agr. New)**

Dr. Barbara Conley, Associate Director, Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis (DCTD), introduced the concept for national specimen banks to support NCI clinical trials networks. Dr. Conley reminded members that specimen banks are used to identify patient subgroups, promote the development of robust molecular technologies for specimen preservation, develop more effective diagnostic assays, and evaluate and validate markers. The Institute of Medicine (IOM) reviewed the NCI Cooperative Group's specimen banks and recommended a restructuring and consolidation of the banking system. The current system includes nine banks that collect specimens from 16 tumor/organ sites, including paraffin embedded specimens, frozen tissue (seven sites), blood and other fluids. Dr. Conley stated that the concept proposes the establishment of three prospective, national specimen banks that would use standard operating procedures, common data elements for annotation, and Office of Biorepositories and Biospecimen Research (OBBR) Best Practices in support of collection, storage and distribution of specimens on NCI Cooperative Group trials. The banks would provide a central tracking system and inventory database, application process, and review process, involving cooperative group scientists, statisticians, and outside experts, to allow access by other researchers outside of the groups.

Subcommittee Review. Dr. Michael A. Caligiuri, CEO, James Cancer Hospital and Solove Research Institute and Director, Comprehensive Cancer Center, Ohio State University, expressed the Subcommittee's appreciation for the reorganization and harmonization efforts for the sample collection, the continued external peer review process of the banks, and the high-impact publications that have resulted from the Cooperative Group setting. Dr. Caligiuri said that concerns include: inefficient access to samples by external investigators; uncertainty as to whether best practices for the efficient distribution of materials will be adopted; and the lack of evidence that a centralized service will provide more effective and flexible access to specimens. In addition, the proposed increased involvement of NCI staff in the banking oversight and the rationale for the requirement of pathology board certification for the U24 principal investigators (PIs) were unclear. Other concerns included the disparate number of proposed banks compared with the number of consolidated Cooperative Groups, reorganization of specimen banks before Cooperative Group alliances are completed, the need for standards and other guidance for applications by external investigators to access specimens, and support for maintenance of existing tissue specimens.

The first year cost is estimated at \$12.5 M for 3 U24 awards, with a total cost of \$62.5 M for 5 years.

In the discussion, the following points were made:

- < The tissue specimens and data will continue to be accessible to investigators and protected under Health Insurance Portability and Accountability Act (HIPAA) regulations. The availability of specimens annotated with clinical outcomes makes the banks a valuable resource.
- < The Cooperative Group banks should develop appropriate procedures for collection of solid tumor cell suspensions that are viable and frozen into aliquots.
- < Members encouraged the development of a single transparent Web site to expedite external investigators' access to the Cooperative Groups' specimens. A harmonized set of processes and clear metrics should be established and published.
- < Limitations of the current banking system include a disconnection between the tissue banks and the data centers and the lack of a central portal to obtain samples or to determine the appropriateness of samples for the research.
- < Data sharing should be bi-directional. A link-back mechanism could provide a means for researchers who access the specimens to redeposit data from their studies.
- < A future BSA agenda item will be a report on the Institute's approach to tissue collection in general as well as for Cancer Genome Atlas (TCGA) related activities.

Motion. A motion to defer concurrence on the Division of Cancer Treatment and Diagnosis' (DCTD) request for application (RFA)/Cooperative Agreement (Coop. Agr.) entitled "National Specimen Banks to Support NCI Clinical Trials Network" was approved unanimously. The concept should be rewritten in view of the broader discussion and brought back to the BSA following establishment of the cooperative group alliances.

**Office of the Director
Cancer Target Discovery and Development Network Centers (RFA/Coop. Agr. New)**

Dr. Daniela S. Gerhard, Director, Office of Cancer Genomics (OCG), introduced the concept for an RFA that builds on the progress of the Cancer Target Discovery and Development (CTD²) pilot network, which was established using ARRA funds. Dr. Gerhard stated that the NCI has made significant investments in a number of genomics projects that have generated large, publicly available datasets. The goal of the ARRA CTD² project was to determine if a network could be formed that could effectively fill the research gap between cancer genomics and cancer therapeutics research by facilitating the transition of genomics data to validated molecular targets and small molecule modulators.

During the pilot phase, the CTD² network includes five centers: Broad Institute, Cold Spring Harbor Laboratory, Columbia University, Dana-Farber Cancer Institute, and University of Texas Southwestern Medical Center. During the past 18 months, this innovative highly collaborative network has developed a process to translate genomic data into a series of experiments resulting in new and validated targets and small molecule modulators, as well as to identify context signatures. An example of the network's success is a number of significant discoveries in ovarian cancer, including the discovery of several candidate therapeutic targets and candidate small molecule modulators. The researchers also identified a genetic signature to stratify patients into two outcome groups, demonstrating that integration of several methods can yield exponential gains compared to improving any single method.

The proposed RFA is considered a new initiative with an open competition using the resource related cooperative agreement (U24) mechanism. Evaluation criteria include: the number and quality of publications, number of validated probes and/or targets identified, impact on the biomedical research community, and whether the results of projects transition to preclinical testing.

Subcommittee Review. Dr. Joe W. Gray, Director, Division of Life Sciences Associate Laboratory Director, Life Sciences Lawrence Berkeley National Laboratory, expressed the Subcommittee's support of the need to efficiently provide to the research community biological insights gained from the cancer genomics data that are becoming available. Dr. Gray noted that one concern was the use of the U24 RFA mechanism to accomplish this goal. Because the initiative aims to identify novel targets for cancer therapy, an area of research that is already well funded, the Subcommittee questioned whether the R01 or P01 mechanism would be more efficient at fostering disease-specific research. Can the U24 vehicle ensure the translation of genomics data? He stated that the subcommittee thought that perhaps the advantages of the U24 mechanism would include economies of scale and adequate resources for centers to ensure clinically translated results. Individual laboratories may not have the resources to span the translational continuum. The Subcommittee also voiced concerns about the inclusion of the whole clinical translational continuum and whether the initiative should be bounded at molecular target validation. Integration with TCGA should be clarified, and care should be taken to form teams with complementary and appropriate expertise, including the appropriate biological models needed.

The first year cost is estimated at \$10 M for 8-16 U24 awards, with a total cost of \$50 M for up to 5 years.

In the discussion, the following points were made:

- < The U24 mechanism will facilitate rapid translation and encourage collaborations that otherwise would be unlikely through investigator-initiated mechanisms.
- < Members queried whether the successes of CTD² were replicable beyond ovarian cancer. Program staff responded that ovarian cancer was presented as an example and many validated targets and molecular modulators have been discovered in other cancer types as well.
- < CTD² data will be made available to the genomics community in a homogenous, consumable form.

Motion. A motion to concur with the Office of the Director's RFA/Coop. Agr. entitled "Cancer Target Discovery and Development Network Centers" was approved with 20 yeas, 2 nays, and 2 abstentions.

**Division of Cancer Prevention
Alliance of Glycobiologists for Detection of Cancer:
A Trans-NIH Program (RFA/Coop. Agr. Reissuance)**

Dr. Karl Krueger, Program Director, Division of Cancer Prevention, presented the concept for an RFA reissuance to continue funding the Tumor Glycomics Laboratories, the core component of the Alliance of Glycobiologists for Detection of Cancer (the Alliance). Dr. Krueger stated that the Alliance's mission is to elucidate the structure and function of glycans that contribute to oncogenesis and to exploit aberrant glycosylation in cancer for the development of translational applications for cancer prevention, detection, and diagnosis. Glycoscience is an important area of research as glycans contribute to malignant cellular properties and glycoproteins are important cancer biomarkers. The Alliance leverages existing infrastructures of the following NIH programs: the Consortium for Functional Glycomics, funded by the National Institute of General Medical Sciences (NIGMS); the Glycotechnology Resource Centers, funded by the National Center for Research Resources (NCRR); and the NCI Early Detection Research Network (EDRN). The Alliance has made a number of tools available to the public including synthetic glycan/glycoprotein arrays, bioinformatics tools, human chromosomal "glycol-genome map", protocols to analyze n-glycan profiles, and various reagents.

Since the 2007 initiation of funding for seven Tumor Glycomics Laboratories, progress made by the Alliance includes the identification of nine novel glycan structures associated with cancer, 12 tumor-derived glycoproteins with altered glycan structures, and discrete glycan and antibody profiles from sera of cancer patients. Future directions include the validation of candidate glycan markers, integration of recent developments in cancer biology in the search for new glycan targets, and exploitation of immune system response to provide novel leads in cancer prevention.

The RFA reissuance would be an open competition. A network structure adds value by providing resources beyond the scope of individual laboratories, facilitating sharing of resources and technologies to develop translatable products, and making data publically available through the NIGMS-supported glycans database. A U01 cooperative agreement is necessary to coordinate collaborations and ensure access to resources, specimens, and epidemiological expertise from other participating NIH programs.

Subcommittee Review. Dr. James K. Willson, Director, Simmons Comprehensive Cancer Center, University of Texas, informed members that the Subcommittee expressed support for the trans-NIH approach of the Alliance, noting that promising discoveries have been made. Dr. Willson stated that progress during the current activity had been modest and uneven, as measured by the number of high-impact publications generated by the programs. Even so, the Subcommittee questioned the readiness of the field of glycomics for a translational focus and the use of a cooperative agreement for this work. Members were told that perhaps the field would be better served by a focus on basic biology and specific glycans funded through investigator-initiated mechanisms.

The first year cost is estimated at \$3.5 M for 6-7 U01 awards, with a total cost of \$17.5 M for 5 years.

In the discussion, the following points were made:

- < Program noted that the Alliance is a 3-year-old activity, in which the first year was used to establish the initiative. The Alliance's productivity is comparable to other programs for a modest investment.
- < An RFA will ensure the translation of glycomic discoveries and allow sharing of specimens and tools across Alliance laboratories and other NIH consortia.
- < The next phase should consider more emphasis on mechanistic studies in order to move toward translational research.
- < The initiative should focus on integrating chemists with biologists to ensure success.

Motion. A motion to concur with the reissuance of the Division of Cancer Prevention's (DCP) RFA/Coop. Agr. entitled "Alliance of Glycobiologists for Detection of Cancer: A Trans-NIH Program" was approved with 22 yeas, 2 nay, and no abstentions. The RFA should also focus on how the alliance will share, going forward, with chemist as well as enable biology.

VII. CANCER BIOINFORMATICS GRID (caBIG®) WORKING GROUP REPORT — DR. ANDREA CALIFANO

Dr. Andrea Califano, Director, Columbia Initiative in Systems Biology, Columbia University, and Chair of the *ad hoc* caBIG® Working Group, informed members that the mission is to create an information network enabling all constituencies in the cancer community to share data and knowledge. Dr. Califano stated that the working group was charged with advising the BSA regarding the goals, accomplishments, challenges, and community outreach of caBIG® and areas that require greater attention in the future development of the

program. Areas covered by the assessment included clinical infrastructure, analytical tools development, research infrastructure, and program administration, contracts management, and budget.

The working group met with caBIG[®] leadership and primary contractors and then conducted interviews. The interviewees represented caBIG[®] constituencies from industry, clinical trials groups, and leaders of TCGA laboratories and NCI-designated Cancer Centers listed as caBIG[®] users. Investigators expressed support for the original mission of caBIG[®], and there was broad agreement that support for clinical and bioinformatic tools is critical for achieving NCI's goals. Concerns expressed about the program included: 1) the long-term vision being driven by technology not progress in cancer treatment and prevention; 2) a lack of applications demonstrating value to investigators; 3) lack of external and independent scientific oversight; and 4) a disconnection between caBIG[®] leadership and the cancer research community resulting from the heavy use of contractors to manage the program.

Dr. Califano informed members that the primary contributions of caBIG[®] have been the development of community-driven standards for data exchange and interoperability; development, dissemination, and maintenance of tools developed by the academic community; and the provision of a community forum on the interoperability of software tools. However, only a few of the software tools developed have been widely adopted by the research community. Reasons cited for limited adoption of software tools were: 1) reengineered too often; 2) overdesigned and ambitious; 3) required significant technical knowledge and informatics resources; 4) commercial tools available and ready to use; and, 5) very few tools have interoperability with each other. caBIG[®] imaging tools and caTissue are examples of software whose development was facilitated by academic input from the community and are now widely used in cancer centers.

Tools for managing clinical data were considered a high priority for cancer centers. The overall development costs for caBIG[®] Clinical Trial Management System (CTMS) was approximately \$100M from FY2004 to 2010. However, few NCI cancer centers use the tools because of 1) the existence of critical legacy systems, 2) tools are incomplete and too generic, 3) high maintenance costs, and 4) interfaces vary across tools and don't link to Adverse Event Expedited Reporting System (AdeERS).

Members were told that interviewees expressed a strong consensus that the management structure is too complex and that internal funding decisions are neither transparent nor peer reviewed. Contractors were perceived as experts in technology but not science. Interviewees also voiced concerns that potential conflicts of interest existed if the same organization sets the standards and then uses the standards to promote their own software.

The *ad hoc* Working Group concluded that support for clinical informatics tools and algorithmic advances is critical for the NCI mission; however, the overall impact of caBIG[®] is not commensurate with the level of investment in the program. The impact of caBIG[®] has been compromised by poor implementation approaches and lack of external oversight. Recommendations for the short term include: 1) an immediate moratorium on contractor-based software development projects; 2) a 1-year moratorium on new projects and contracts; 3) a 1-year extension on current caBIG[®] supported academic efforts; 4) establishment of an independent oversight committee; and, 5) a thorough audit of caBIG[®] budgets and expenditures. For the long term, strategic recommendations include: 1) the creation of a Scientific Advisory Group (SAG) for NCI biomedical informatics initiatives, which could be a BSA subcommittee; 2) refocus of caBIG[®] to its original mission; 3) separation of the caBIG[®] clinical and bioinformatics components; 4) use of established mechanisms for concept clearance and peer review of informatics initiatives; and, 5) the promotion of interoperability and data sharing by making them key review criteria for most awards.

In the discussion, the following points were made:

< Members expressed support for the need to fund software development and algorithms research for

genomics research where the existing data have not been thoroughly analyzed. caBIG[®] may have sufficient influence to establish data output standards that would facilitate the development of software tools.

- < caBIG[®] should focus on setting the data standards supporting the development of commercial software, but should not necessarily engage in the development of its own brand of software.
- < Some commercial vendors have opted not to expand or support community developed software because of the expansive open source software licensing approach that caBIG[®] has adopted. Revision of this license could support software development by commercial vendors.
- < NCI should consider encouraging small businesses to apply for SBIR/STTR funds for the development of needed software tools.

Motion. A motion to accept the report of the BSA Cancer Bioinformatics Grid (caBIG[®]) Working Group was approved unanimously.

VIII. STATUS REPORT: IMPLEMENTATION OF THE INSTITUTE OF MEDICINE (IOM) CLINICAL TRIALS REPORT RECOMMENDATIONS—DR. JAMES H. DOROSHOW

Dr. James H. Doroshow, Director, DCTD, provided an update on the implementation of recommendations presented in the IOM Clinical Trials Report. Dr. Doroshow reminded members that NCI's Clinical Trials Program aims to provide a national network comprised of Cooperative Groups interacting to co-develop, co-implement, and co-conduct innovative and practice-changing trials to improve the Nation's cancer care. Changes underway will support a comprehensive approach to rapidly initiate and complete large randomized, multisite Phase II and Phase III clinical trials, as well as refine the peer review system and institute substantial operation, management, and cultural changes.

The Program's transformation includes consolidating groups to better support molecular assays, prioritizing Phase III trials, promoting the study of less common diseases, and sharing information technology (IT) infrastructure. Other changes include: 1) the integration of American College of Radiology Imaging Network (ACRIN); 2) harmonization of scientific and administrative procedures; 3) a unified tissue banking and distribution system; and, 4) improved access for clinical and translational investigators not currently involved in the Cooperative Group platform. Additional changes include the unification of system processes, revised incentives to promote collaboration and efficiency, such as new peer review criteria and a single operations committee to resolve issues quickly, and integration into four adult groups and continuation of one pediatric group.

Dr. Doroshow told members that, in the new system, groups will be fully integrated infrastructures that can move from idea generation to trial implementation, accrual, and analysis. Moreover, NCI-supported Cancer Centers will help set the direction of the network as critical members of an across-disease, strategic oversight committee. Modification of reimbursement models to recognize the critical contribution of Cancer Centers is under consideration. Consolidation of the adult groups presents several challenges and risks due to infrastructure change, increased costs, potential leadership issues, and the engagement of multiple stakeholders into the process.

Governance principles that will guide improvements to the clinical trials system include: 1) the NCI and Group leadership managing the Program as a collaborative national program to reach shared goals; 2) support for the public-private nature of the Program requires collaborative decision making; and, 3) review of the system as both a scientific and operational enterprise. Review will no longer focus solely on trials developed by specific disease committees, but will also assess the role of the Group as part of an integrated clinical trial system. The proposed new organizational structure for NCI's Clinical Trials Program will foster interactions among the adult and pediatric Groups as well as other groups (e.g., Cancer Centers,

other academic centers, Community Clinical Oncology Program (CCOPs), community practices, and international stakeholders), and encourage all who participate in NCI's clinical trials activities to work better together. Dr. Doroshow reviewed the proposed timeline and next steps and told members that a new concept for a national clinical trials network will be presented at the November 2011 BSA meeting. **In the discussion, the following points were made:**

- < Cooperative Groups have benefited from the active participation of Specialized Programs of Research Excellence (SPORE) principal investigators on the scientific steering committees.
- < Members noted that Cooperative Groups would benefit from more information on plans for tumor bank reorganization.
- < A challenge in the consolidation of the Cooperative Groups is the potential effect on mentorship and loss of young investigators.
- < The NCI should consider establishing a mentoring program that improves interactions between the Cooperative Groups and TCGA. In addition, Cancer Center Directors should be encouraged to help genome scientists become familiar with the Cooperative Group organization and resources.
- < Outcomes of the streamlining process are expected to be completion of a smaller number of trials more rapidly with greater efficiency.
- < The NCI should consider participation of basic and preclinical scientists in the transformation of its clinical trials system. The Institute also should share with the broader cancer community the advantages and disadvantages of various group structures.
- < A subcommittee of the Clinical Trials and Translational Research Advisory Committee (CTAC) is harmonizing the guidelines for the Cooperative Groups, Cancer Centers, and SPOREs, as well as considering ways to identify and create incentives for collaboration.

IX. ADJOURNMENT - DR. RICHARD L. SCHILSKY

There being no further business, the 48th regular meeting of the Board of Scientific Advisors was adjourned at 4:23 p.m. on Tuesday, 1 March 2011.

Date

Richard L. Schilsky, M.D.
Chair, Board of Scientific Advisors

Date

Paulette S. Gray, Ph.D.
Executive Secretary, Board of Scientific Advisors