DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
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NATIONAL CANCER INSTITUTE
14th CLINICAL TRIALS AND TRANSLATIONAL RESEARCH
ADVISORY COMMITTEE MEETING

Summary of Meeting

July 13, 2011

Building 31 C, Conference Room 10
National Institutes of Health
Bethesda, Maryland

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
BETHESDA, MARYLAND
Summary of Meeting
July 13, 2011

The 14th meeting of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was convened on Wednesday, July 13, 2011, at 9:00 a.m. in Conference Room 10, C-Wing, 6th floor, Building 31 on the National Institutes of Health (NIH) main campus in Bethesda, MD. The CTAC Chair, Dr. James L. Abbruzzese, Chairman, Department of Gastrointestinal Medical Oncology, The University of Texas M.D. Anderson Cancer Center, presided. The meeting was adjourned at 2:20 p.m.

Chair
James L. Abbruzzese

CTAC Members
Peter C. Adamson
Susan G. Arbuck (absent)
Monica M. Bertagnolli
Deborah W. Bruner
Curt I. Civin
Kenneth H. Cowan
Everett Dodson
Olivera Finn (absent)
Stephen S. Grubbs
Sandra J. Horning
Scott M. Lippman
Nancy P. Mendenhall (absent)
Lisa A. Newman
David R. Parkinson (absent)
Edith A. Perez (absent)
Nancy Roach
Daniel J. Sargent
Richard L. Schilsky
Mitchell Schnall
Peter G. Shields
Joel E. Tepper
James L. Wade, III (absent)

***Ex Officio* Members**
James H. Doroshow, NCI
Paulette S. Gray, NCI
Rosemarie Hakim, CMS
Lee Helman, NCI
Michael J. Kelley, VA
Richard Pazdur, FDA (absent)
John F. Potter, DOD
Alan Rabson, NCI (absent)

Executive Secretary
Sheila A. Prindiville, NCI

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WEDNESDAY, JULY 13, 2011

I. CALL TO ORDER, OPENING REMARKS, AND NCI UPDATE—DRS. JAMES ABBRUZZESE AND JAMES DOROSHOW

Dr. James Abbruzzese called the 14th CTAC meeting to order. Dr. Abbruzzese then reviewed the confidentiality and conflict-of-interest practices required of Committee members during their deliberations. Members of the public were invited to submit written comments related to items discussed during the meeting to Dr. Sheila A. Prindiville, Director, Coordinating Center for Clinical Trials (CCCT), NCI, within 10 days of the meeting. Any written statements by members of the public will be given careful consideration and attention.

Motion. A motion was made to approve the minutes of the March 3, 2011, CTAC meeting. The motion was seconded, and the minutes were approved unanimously.

NCI Update. Dr. Doroshow reminded CTAC members of the upcoming NCI Translational Science Meeting on July 28-29, 2011, in Washington, DC. The focus of this meeting is on the interaction of genomics with clinical and translational research.

II. TRANSFORMING NCI'S CLINICAL TRIALS SYSTEM—DRS. JAMES DOROSHOW AND JEFFREY ABRAMS

Jeffrey Abrams, M.D., Associate Director, Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), NCI, presented an update on NCI's efforts to transform its clinical trials system.

There have been a number of reviews of NCI's clinical trials system, all of which have emphasized the need for a public clinical trials system and improved speed and efficiency in the development and conduct of clinical trials. Innovative science needs better trial design, but trials also must be prioritized to ensure proper support and timely completion. Incentives should be put in place to encourage physician and patient participation in the system and to take advantage of the advances in cancer biology. A more highly integrated network should be instituted. These reports have been presented to the National Cancer Advisory Board (NCAB), the Board of Scientific Advisors (BSA), and the CTAC.

The American Society of Clinical Oncology (ASCO) recently released its own recommendations for a National Clinical Trials Network (NCTN). Its first recommendation is to enhance inclusion of innovative and clinically meaningful science and decrease duplication across all NCI-supported clinical trials. The Network must improve connections between NCI translational and early-phase clinical trial mechanisms. The NCTN should be open to scientific concepts from outside of the Cooperative Groups and other NCI-supported mechanisms. The system should prioritize trials that are practice changing and have meaningful clinical benefit; these are often multimodality treatments, adjuvant therapy, combinations of novel agents, and screening and prevention strategies and therapies for rare diseases.

Additionally, ASCO emphasized that review and activation of clinical trials needs to occur in a timely manner. Review of concepts and protocols should be for value added, rather than focusing on minor changes. ASCO asked that NCI clarify the role of the Scientific Steering Committees (SSCs) and Task Forces in the review process. NCI should also promote efficiency through standardization of protocols, including common case report forms, consents, and auditing rules. ASCO suggested using the Central Institutional Review Board (CIRB) as the IRB of record for the NCTN—something that other NCI advisory boards have suggested as well.

The ASCO recommendations also suggested that the Network should be the chief vehicle for Phase II and III trials; all NCI-funded mechanisms should be held accountable for their participation in the Network. NCI should increase funding for its supported clinical trials. For trials prioritized by NCTN, funding should be sufficient to reimburse research costs. Also, the Biomarker, Imaging, Quality of Life, and Cost Effectiveness Analyses Funding Program (BISQFP) should be expanded. The review criteria should recognize the role of Cooperative Groups in training and career development, and review criteria for other NCI-supported mechanisms (i.e., Specialized Programs of Research Excellence [SPOREs] and Cancer Centers) should offer credit for scientific leadership provided by faculty.

The scientific rationale for transforming the current clinical trials system begins with the need to consolidate the system. Consolidating the Cooperative Groups will increase NCI's ability to prioritize molecular characterization resources and develop molecularly driven trial designs, which is critical to the success of multisite clinical trials that often require screening of large patient populations. NCI will likely support fewer trials—particularly Phase III trials—than in the past, but having fewer groups will facilitate prioritization. It will also be necessary to remove disincentives to studying rare diseases. This can be aided by harmonizing procedures and instituting a common front-end information technology (IT) infrastructure for clinical management and time resource management. Additionally, scientific interactions around imaging can be facilitated by integrating the American College of Radiology Imaging Network (ACRIN). An integrated national biobanking resource can ensure optimal use of tissue specimens in trials. Open access to the NCTN for clinical and translational investigators not currently involved in the Cooperative Group system will ensure the best competition of ideas and movement of high-priority science into trials.

The NCTN would consolidate the current Cooperative Groups into no more than four adult groups and one pediatric group, all with multimodality capacity in a broad range of diseases and full commitment to the Network. Dr. Abrams noted that NCI has developed strategies to facilitate this integration. NIH grants permit multiple principal investigators (PIs), which should help with leadership transitions and, hopefully, encourage collaboration and continued investment in the system. NCI will also incentivize the transition with resources and support in order to make the potentially disruptive process of combining cultures, staff, and resources a bit smoother. In the beginning, some distributed data management and operations will be allowed. NCI also proposes combining rather than disbanding disease committees, which will require reconfiguration of the review system.

The new NCTN would include a national biospecimen banking system, which would serve the Cooperative Groups, Phase III trials, and other NCI trial mechanisms. This open system would help ensure the best competition of ideas.

The proposed groups in the NCTN would be much more networked; trials prioritized by a steering committee would be open to all of the groups, with no endorsement system. Every trial would be a Network trial. Disease committees would continue to develop ideas for submission to steering committees. Statistical coordination would be critical; to support communication and cooperation between the researchers and statistics specialists, statistical centers would not be separate from the groups. A strategically oriented oversight panel would facilitate balance of ideas across all levels of the Network, without functioning as another level of review. The Cancer Centers program may also be modified, with a new funding model based on increased per-case reimbursement for high-accruing sites. Finally, as recommended by the Institute of Medicine (IOM), NCI hopes to institute external peer review of all groups in the same review cycle, with new review criteria based on collaboration and evaluation as partners in the Network.

NCI has begun working toward the new system in several ways. Discussions regarding potential consolidation activities have been in progress with Cooperative Group chairs, and some consolidation has already begun. The Radiation Therapy Oncology Group and the National Surgical Adjuvant Breast and Bowel Project have announced a partnership, which the Gynecologic Oncology Group may join; the North Central Cancer Treatment Group Cancer and Leukemia Group B (CALGB) and the American College of Surgeons Oncology Group (ACOSOG) have merged to form a new group, the Alliance. The Eastern Cooperative Oncology Group and ACRIN have also announced a partnership that brings imaging into the therapeutic world and is an example of consolidation that promotes tighter integration across the Network.

NCI has instituted a comprehensive, around-the-clock patient registration system through the Cancer Trials Support Unit (CTSU) for all adult Cooperative Groups, with regulatory and site verification; the Children's Oncology Group (COG) will be included in the near future. NCI has also begun to implement timelines for concept evaluation, protocol development, and trial activation recommended by the Operational Efficiency Working Group (OEWG), with positive early results. The Groups are working with NCI on a single, harmonized approach to clinical trials management using Medidata Rave as the new platform for case report data management and analysis; they are also assessing their needs for protocol authoring. The Group chairs have also agreed to establish, with NCI, an ongoing collaborative management team to manage the operations of the Network via the Cooperative Agreement funding mechanism.

NCI would reconfigure the peer-review system to emphasize incentives for a national system; all trials would be open to all sites, and sites could credit any group to which they belong. Concepts would be evaluated and prioritized at the steering committee level; peer review of the groups, which would occur approximately every five years, would be more strategically focused on the overall direction and scientific quality of the trials being conducted by each group. Each group would be evaluated in terms of efficiency, coordination, timelines, accrual, and national collaboration. For the Network to work optimally, NCI would need to coordinate the groups with other NCI-funded programs, including the Community Clinical Oncology Programs (CCOPs), tumor banks, Cancer Centers, and SPOREs. The SSCs would be critical to the new system by providing prioritization of practice-changing, impactful ideas. Dr. Abrams asked for feedback from CTAC on two particular topics: whether the changes in review criteria will foster a collaborative network; and whether there are other measures/resources NCI should consider to make the Network available to investigators who are not affiliated with a Cooperative Group.

CTEP has spent the last six months soliciting input on the proposed NCTN from various stakeholders. The concept will be presented to the NCI Scientific Program Leaders in September and, if approved, to the BSA in November. If approved by the BSA in November 2011, the NCI Division of Extramural Activities and NIH review of the funding opportunity announcement (FOA) and guidelines should be complete in July 2012. The goal is to release the FOA in July 2012. Applications will be due in November 2012 and reviewed in February 2013. The target date for review by NCAB is May 2013, with funding beginning in early 2014.

CTAC, the first new federally chartered NCI advisory group in a decade, has been given responsibility for helping NCI to model the new clinical trials program. SSCs are critical to prioritization in the clinical trials system in making sure that the most important large Phase II and III treatment trials are given priority. Dr. Abrams pointed out the important role of co-chairs of SSCs and the record of consensus on concept reviews across SSCs. Over 180 concepts have been evaluated by the individual disease-specific steering committees; 46 percent have been approved and 53 of these concepts are now trials open to accrual. Additionally, the SSCs have been hosting Clinical Trials Planning Meetings

(CTPMs) to discuss what needs to be done to move a Phase III trial forward or what Phase II preparation might be needed.

The function of the SSCs is to evaluate and prioritize trial concepts received from Group and non-Group investigators for large Phase II and Phase III trials; some SSCs have created task forces to help with this evaluation. The second function is to strategize about meeting the needs of clinical research in their domains via task forces, working groups, and/or CTPMs. These strategies extend beyond the NCI system and would be utilized to keep the NCTN on track. An additional group, an across-disease/across-modality strategic group, would be formed under CTAC to strategize across disease and modality. This group would not function as another level of protocol-specific review but, rather, as a separate entity considering the NCTN's long-term plans and objectives. This group would monitor and assess the scientific effectiveness of the individual SSCs by addressing the following questions and recommending improvements, as needed: Is the steering committee making decisions that result, over time, in a portfolio that represents the most important, best-designed trials for its domain? Are approval decisions justified with clear and compelling rationale? Have changes required by the steering committee resulted in improved clinical trial designs? Are the standards used by each committee to judge scientific merit and clinical importance consistent? If there is variation, is it justified? Does each steering committee conduct task forces, working groups, or CTPMs to effectively meet the needs of clinical research in its domain? If so, how effective are these complimentary activities?

The strategic group would also monitor and assess the balance, coherence, and appropriateness of NCI's overall late-stage clinical trials portfolio by addressing additional questions: Is the portfolio of SSC-approved trials appropriately balanced across clinical domains in light of available resources, clinical needs, and scientific opportunities? If not, how should the SSCs adjust criteria and processes to achieve a more optimal balance across the system?

The strategic group would provide recommendations to individual steering committees, NCI, and groups about the portfolio in specific disease areas, and to NCI about the portfolio of the entire system across diseases. The strategic group would also report to CTAC about the functioning and needs of the system. Dr. Abrams noted that the makeup of the strategic group has yet to be decided; however, NCI anticipates that the group would comprise Cooperative Group chairs and statisticians, Cancer Center directors, CCOP principal investigators, patient advocates, translational scientists, CCOP research base principal investigators, SSC chairs, and CTAC members, with supporting representatives from NCI (DCTD, Division of Cancer Prevention [DCP], and CCCT).

The overall vision of the new Network is that it would be a system that provides essential infrastructure for trials in treatment, control, screening, diagnosis, and prevention, and an enabler of cutting-edge discoveries across all of NCI's clinical research programs. Approved trials must open rapidly and complete accrual according to defined guidelines by leveraging an integrated national network of performance sites. The user-friendly system should have harmonized processes available to the extramural cancer community—investigators, patients, advocates, and industry. In essence, the new system would offer the ability to perform large-scale tests of increasingly smaller subsets of molecularly defined cancers and efficiently answer critical questions not supported well in a commercial environment.

Questions and Discussion

Dr. Joel Tepper, Hector MacLean Distinguished Professor of Cancer Research, Department of Radiation Oncology, Lineberger Comprehensive Cancer Center, noted that one of the biggest problems is moving innovative ideas from the laboratory into trials. It is difficult to balance between one person's

innovative idea versus wild speculation without sacrificing potential advances. The Gastrointestinal Steering Committee attempted to address this problem by placing SPORE, P01, and R01 investigators on the Steering Committee and inviting scientists to present on different areas, in the hopes of stimulating interest. He added that CTAC should keep this in mind when developing metrics for the new Network.

Dr. Sandra Horning, Senior Vice President, Genentech, Inc., stated that the new structure will require a great deal of energy and monitoring to ensure diversity, balance of risk, and innovation in the consolidated Groups. The composition of the SSCs will be important; tenure of SSC members should be discussed to keep the Committees fresh. Dr. Abrams responded that there is a specific term of service, particularly for those who are not affiliated with Cooperative Groups. For the Cooperative Groups, the disease committee chair is the representative unless otherwise specified by the Group chair.

Dr. Richard Schilsky, Professor of Medicine and Associate Dean for Clinical Research, University of Chicago Pritzker School of Medicine, wondered whether the SSCs should continue their strategizing function. With the consolidation of the Groups and fewer and more closely networked disease committees, much of the strategizing would take place at the Group level. Also, the new oversight group would focus on strategy. The oversight group that evaluates the Cooperative Groups should not also be setting strategy; this would result in an inherent conflict if evaluations were tied to certain expectations regarding appropriate strategy. Dr. Schilsky suggested that once the new oversight committee is established, NCI should eliminate the strategy function of the SSCs but retain their evaluation function. Dr. Abrams responded that some strategy must reside in the SSCs, which replaced the previous Cooperative Group intergroup mechanism that allowed members of different Groups to network and strategize about shared protocol designs.

Dr. Peter Adamson, Chair of the Children's Oncology Group and Chief, Division of Clinical Pharmacology and Therapeutics, The Children's Hospital of Philadelphia, noted that someone must be accountable for strategy; if everyone is weighing in on strategy, it is not clear who is held accountable for successfully implementing the strategy. Ground-level strategy should come from the Groups. Dr. Abbruzzese countered that it is difficult to divorce the operational piece of the protocol evaluation and underlying scientific strategy, and that SSCs must be a part of creating that strategy. Dr. Tepper stated that "strategy" can mean many different things; the type of strategic planning performed by an SSC is likely different than the planning performed at the Cooperative Group level. It will be necessary to define "strategy."

Dr. Schilsky also noted that the IOM report explicitly recommended that NCI staff not be directly involved as scientific reviewers in the SSC review process. Dr. Abrams responded that the Network would be funded via Cooperative Agreement, which contains specific rules that the government have significant input into the research. NCI staff make up only a small percentage of the SSCs and serve to provide a voice about national needs across Groups. Without significant input from NCI staff, the system would not function well; reviews conducted by NCI staff are critical to the process. NCI staff help to manage conflict-of-interest issues and manage the work of developing consensus reviews.

Dr. Adamson asked about accountability within the new Cooperative Groups: If a site underperformed, would the lead Cooperative Group be accountable, or the Group whose trial was being conducted? Dr. Abrams stated that the site would be accountable to the Group running the trial for any protocol-specific data issues, but that the site's accrual performance would be evaluated by the Group(s) to which it belonged. NCI staff will help educate the Cooperative Groups about these kinds of issues; the monthly operational meetings of Group leadership will also help work out these problems.

Ms. Nancy Roach, Consumer Advocate, C3: Colorectal Cancer Coalition, commented that the position of the SSCs is biased; it would be helpful to include more surgeons, radiologists, etc. Also,

regarding whether changes in review criteria will foster a collaborative network—changes in funding will foster a collaborative network. People who are working well together should be funded; if they are not working well together, funding should decrease. These criteria should be explicit in the FOA. Dr. Abbruzzese responded that the CTAC Guidelines Harmonization Working Group has put forth a great deal of effort to assess and recommend changes to better harmonize through incentivizing collaboration. The review criteria are undergoing change; they are still evolving. Dr. Prindiville added that CTAC accepted the recommendations of the Guidelines Harmonization Working Group, and that these are being incorporated into the revisions of the SPORE, Cancer Center, and Cooperative Group guidelines.

Dr. Daniel Sargent, Director, Cancer Center Statistics, Mayo Clinic Foundation, expressed concern that not enough time is built into the timeline for writing the grants; nine months are allotted for writing the FOA, while only four months are allotted for writing the grants themselves. Dr. Abrams noted that NIH regulations limit openness about what will be in an FOA and that NCI will be as open as possible. Nine months includes NIH review of the FOA and guidelines; this is out of NCI's control.

Dr. Deborah Bruner, Independence Professor in Nursing Education, School of Nursing, University of Pennsylvania, stated that after the pediatric Cooperative Groups merged, there were approximately five years of down time. She suggested that there may lessons learned from that process. Dr. Abrams responded that NCI has been speaking with Dr. Gregory Reaman, previous chair of the COG, in order to learn as much as possible from his experience. The intent is for Medidata Rave to increase communication among the Groups and remove some of the barriers related to CTSU registration; that communication is key. Dr. Monica Bertagnolli, Professor of Surgery, Harvard Medical School, stated that significant down time can be avoided as long as there is funding to help with the transition.

Dr. Bruner also encouraged the participation of CCOP and research base principal investigators. Dr. Abrams noted that Dr. Lori Minasian, Chief of the NCI Community Oncology and Prevention Trials Research Group, which manages the CCOP program, will be holding a CCOP meeting in the near future, one of the goals of which will be to bring all of the principal investigators up to speed on the new Network.

III. LEGISLATIVE UPDATE—MS. M.K. HOLOHAN

Ms. M.K. Holohan, Deputy Director, Office of Government and Congressional Relations, NCI, reported on the status of appropriations and gave an overview of the 112th Congress.

Fiscal Year (FY) 2011 Appropriations. On April 15, 2011 (seven months into FY 2011), the President signed a full-year Continuing Resolution (CR) to fund government operations through the remainder of FY 2011. The NIH budget received a 1 percent cut from the FY 2010 budget.

FY 2012 Appropriations. The President announced his FY 2012 budget on February 14, 2011, which included an allocation of $31 billion to NIH. Of that amount, NCI would receive $5.1 billion. On May 11, the Senate Appropriations Committee held a hearing to discuss FY 2012 appropriations for NIH. Dr. Francis Collins, NIH Director, testified and was accompanied by Dr. Varmus as well as other Institute/Center Directors, who were available to answer questions relevant to their Institutes' or Centers' research interests. Dr. Varmus was disappointed that the hearing was not more widely attended.

The Senate appropriations process is currently on hold pending outcomes of the debt limit discussions. The House cancelled its July 18-22 recess to work on debt negotiations. The House Committee on Appropriations is scheduled to vote on an appropriations bill on August 2. A letter to the

Senate appropriators, signed by 41 Senators (34 Democrat; 7 Republican), requested that a strong commitment to funding for NIH be maintained. Last week, the House Appropriations Committee marked up the Commerce-Justice-Science bill and continued the National Science Foundation budget at the same level as in FY 2011. This offers some encouragement that the NIH budget may stay at the same level as in FY 2011. Congress has shown interest in several issues relevant to NCI. These issues include clinical trials consolidation, Cancer Center funding, pancreatic cancer legislation, and pediatric cancer research.

New Legislation. Ms. Holohan briefly discussed new legislation and noted that a detailed report can be found in the CTAC board books.

Questions and Discussion

Ms. Roach commented that there would have been more attendees at the FY 2012 NIH appropriations hearing if it had been widely publicized. She noted that One Voice Against Cancer (OVAC) advocates effectively on the Hill.

Ms. Holohan stated that an appropriations bill will probably not be passed before the start of FY 2012 and that it is likely that the government will continue to operate on a CR.

IV. AACI-NCI CTRP STRATEGIC SUBCOMMITTEE REPORT—DRS. KEVIN CULLEN AND SHEILA PRINDIVILLE

Dr. Sheila Prindiville, Director, Coordinating Center for Clinical Trials, NCI, presented the recommendations of the joint Association of American Cancer Institutes (AACI)-NCI Clinical Trials Reporting Program (CTRP) Strategic Subcommittee. The CTRP is a comprehensive database being developed to provide regularly updated information on NCI-supported clinical trials. The AACI-NCI CTRP Strategic Subcommittee was formed in the fall of 2010 and is co-chaired by Dr. Prindiville and Dr. Kevin Cullen, Director of the University of Maryland Greenebaum Cancer Center. The committee was charged with reviewing the scope, current and future workload, and timeline for NCI awardees to provide data on trial registration, accrual, and outcomes to CTRP. In addition to Drs. Prindiville and Cullen, members include several representatives of the extramural community and an AACI liaison. Two of these members, Ms. Rhoda Arzoomanian and Ms. Alyssa Gateman, attended the presentation.

The need for CTRP predates the enactment of the Food and Drug Administration Amendments Act (FDAAA) of 2007. In 2005, the Clinical Trials Working Group (CTWG) recommended creating a comprehensive database containing information on all NCI-funded clinical trials to facilitate better planning and management. In 2010, the IOM report reiterated this need. Development of this comprehensive portfolio database will enhance NCI's ability to identify gaps in clinical research, prioritize trials, manage the clinical research process, and avoid duplicative studies. CTRP will facilitate required registration into ClinicalTrials.gov in an effort to avoid duplicate registration. It could also facilitate identification of toxicity trends across all NCI-supported trials if outcomes data were collected.

Information presently collected by CTRP includes: Summary 4 funding category, sponsor, program code, and anatomic site; identification of the NIH Institute/NCI Division associated with Investigational New Drug or Device Exemption contracts and grants; biomarker data (including assay type, use, and purpose; tissue specimen type; and collection method); protocol documents for abstraction by NCI staff; and patient accrual data (starting in 2012).

The scope of clinical trials registered in CTRP includes interventional trials conducted or funded by NCI that were open to patient accrual on or after January 1, 2009. Trials managed by CTEP's and DCP's Protocol Information Office are registered internally at NCI. Other trials are submitted by the awardee institutions that conduct the trials. NCI-designated Cancer Centers are required to complete trial registration by October 2011, and other awardees are expected to complete registration by January 2012.

Once trials are registered, investigators are asked to submit any amendments to the trials within 20 days of IRB approval. Amendments are changes that substantially alter the conduct of the trial, such as changes in the study design, treatment administered, or patient enrollment sites. Changes in trial status (active or closed) should be reported within 30 days. Cancer Centers are expected to have a process in place for reporting on amendments and status changes by March 2012. Other awardees should have a process in place by June 2012.

CTRP's accrual data elements are based on the Clinical Data Update System (CDUS) Abbreviated elements and are consistent with the standard Case Report Form Demography elements. These data elements are familiar to awardees as such data are already reported on CTEP and DCP trials through CDUS. Specifications for automated reporting on accrual will be finalized in September 2011 and quarterly reporting by Cancer Centers will begin by September 2012, or one year after the specifications are made available. Other awardees are expected to have begun reporting accrual by January 2013. The lead organization will report on accrual for all sites participating in a multicenter trial. Summary (cumulative) accrual for industrial trials will be submitted quarterly rather than at patient-level accrual.

The Subcommittee recommended deferring capture of outcomes data for three to five years. During that time, a group with extramural representation should work with NCI to develop outcomes data elements and a detailed proposal for implementation, including cost estimates and a timeframe for implementation.

NCI will continue to support NCI grantees and software vendors to facilitate registration and the reporting of accrual. Examples of NCI support include: funding supplements to NCI-designated Cancer Center grants to support startup costs of CTRP reporting requirements (supplement request issued in June 2011 with applications due July 22); professionally written abstracts following clinical trial registration and data files suitable for posting in ClinicalTrials.gov after review; and technical support to the CTRP community.

The Subcommittee identified several topics that require further consideration, including: inclusion of noninterventional trials (e.g., correlative and observational studies) after all interventional trials have been registered; development of simplified methods to record patient-level disease coding; the need to ensure that each Cancer Center's accrual to a study is appropriately counted (Summary 4 reports); provision of additional support (including more liberal timelines) for sites that lack compatible automated systems for clinical data management; and formation of a working group to evaluate future changes to registration and accrual specifications. Membership would include NCI staff, Cancer Center representatives, and Clinical Data Management System vendors.

Dr. Cullen noted that AACI began to work with NCI on this report because of concerns among AACI members about CTRP reporting requirements and the workload of Cancer Centers. AACI has become more comfortable with the process since it has been made clear that the burden on Cancer Centers will not be significant and that the automated process can be easily incorporated into established procedures. AACI was also pleased by the recommendation to postpone the addition of outcomes measures and the establishment of procedures for monitoring the process and modifying specifications.

Questions and Discussion

Dr. Adamson asked about plans for quality control. Dr. Prindiville replied that the Clinical Trials Reporting Office, which manages the CTRP, will examine at least 10 percent of submitted abstracts for quality control purposes. Dr. Doroshow noted that the automated systems used by Cancer Centers should ensure accuracy of data, but commented that there are no plans to audit the accuracy of information provided by the Centers. Dr. Linda Weiss, Director of the NCI Cancer Centers Program, added that standardization of data elements should reduce variability of reporting.

Ms. Roach suggested that correlative studies be incorporated into CTRP as soon as possible. She also asked whether NCI has discussed this initiative with advocacy organizations that provide clinical trial matching services for patients or considered whether this reporting program will interfere with patient-trial matching systems. Dr. Prindiville said that the Subcommittee has not communicated with those organizations, but she stressed that the CTRP will not disrupt existing NCI information resources designed to help patients find trials.

Dr. Bruner asked whether the definition of intervention trials includes those that focus on exercise. Dr. Prindiville replied that the definition of intervention trials includes both symptom management and behavioral interventions.

Dr. Lisa A. Newman, Professor of Surgery and Director of the Breast Care Center and Multidisciplinary Breast Fellowship Program, University of Michigan Comprehensive Cancer Center, suggested collecting information on the gender and race/ethnicity of principal investigators to help track the involvement of unrepresented populations in clinical research. Dr. Prindiville said that this topic has not been addressed by the Subcommittee but noted that it is an interesting question for future discussion. Dr. Paulette Gray, Director of the NCI Division of Extramural Activities, added that this information is not collected from grantees and that Dr. Newman's point is well taken.

Dr. Schilsky stressed the importance of organizing information in the database in a way that maximizes its usefulness for retrieval. Because data collection will add to the workload of investigators, it is essential to limit data collection to information necessary to meet the needs of stakeholders.

Dr. Sargent asked whether the fact that CTRP data elements are based on CTEP's abbreviated CDUS means that additional reporting is not required for sites using that system. Dr. Prindiville explained that data from sites currently using CTEP or DCP systems are transferred internally to CTRP.

V. MAKING THE INFORMED CONSENT DOCUMENT MORE CONCISE: REVISING THE NCI INFORMED CONSENT TEMPLATE—MS. JEANNE ADLER

Ms. Jeanne Adler, Nurse Consultant, Cancer Therapy Evaluation Program, NCI, gave a brief background on the NCI informed consent template and an overview of the current revisions of the document.

In 1997, both research participants and investigators voiced concerns about informed consent documents (ICDs) for cancer treatment trials—the forms were too long and difficult to understand. In response to these concerns, an Informed Consent Working Group was formed by NCI, the Office for

Protection from Research Risks (OPRR), and the U.S. Food and Drug Administration. The efforts of the Working Group resulted in the creation of the NCI informed consent template, which is used by authors and institutional review boards. The template was written in lay language using NIH plain language principles and includes all federally required elements. A Web site was also established with recommendations for the informed consent process as well as the informed consent document itself. Minor revisions were made to the template in 2004 and 2009.

Despite the efforts of the 1997 Informed Consent Working Group, the ICDs have again become too long and complex. Many sources in the literature highlight issues with ICDs.

> *Among the problems...are excessive length, complexity of wording (Albala, 2010).*

> *The length of patient information and consent forms...is increasing with time. QuIC-A scores [which rate participants' objective knowledge of the clinical trial] were significantly higher for trials in which the...page count was seven or less (Beardsley, 2007).*

In 2009, the Agency for Healthcare Research and Quality (AHRQ) found ICDs to be "long and written at a reading level beyond the capacity of most potential subjects." Letters from IRB chairs from Illinois, Maryland, and Ohio reiterated that consent forms were too long. Patient advocates, investigators, clinical research associates (CRAs), colleagues from the Association of American Medical Colleges and IOM, and NCI staff members all shared the same concerns regarding the documents. Immediate actions were taken to address the ICD issues. CTEP conducted a "snapshot" audit of the length of ICDs for Phase III treatment trials—97 studies were reviewed, and ICD page lengths ranged from 5 to 35 pages; the median page length was 16 pages. NIH Institutes were surveyed on their approaches to ICDs. It was found that many NIH Institutes used the NCI informed consent template, which validated the idea to revise the template and continue its widespread use. A literature search was conducted for general and specific guidance on ICD format and content. This search resulted in a table of evidence. Patient advocate organizations were also contacted for recommendations on ICDs. The information gathered from all of these actions was used to develop a background document to provide a rationale for revision of the NCI ICD.

The next step in the process of revising the ICD was drafting a concise template. A "blank slate" approach was taken to draft the template. "Basic" and "additional" required elements of informed consent (per Office of Human Resource Protection [OHRP]) and FDA regulations) were addressed. The goal of the draft ICD template was attaining brevity without sacrificing key concepts about a trial that might affect a patient's decision to participate. Plain language principles were retained, including: writing for the reader; using common, everyday words (short words, sentences, and paragraphs); and displaying material correctly (e.g., question-and-answer format of template titles and responses). Additionally, repetitive information was eliminated from the revised template. The draft concise template was applied to three ICDs from existing CTEP-sponsored Phase III trials in breast, lung, and lymphoma. These three trials were chosen based on the length of their ICDs—16 pages (the median length from the "snapshot" audit). The application of the draft concise template to these three trials reduced ICD length by more than half.

With the success of the early draft, a planning committee was assembled to develop an approach to rewriting the current template so it would result in more concise and shorter ICDs. The committee included representatives from NCI Divisions collaborating with CTEP on treatment trials, as well as those conducting prevention studies, with representatives participating from the Office of the NCI Director, the Center for Cancer Research, and the DCP, among others. Federal advisors from OHRP and FDA were also included on the committee. The recommended approach consisted of constituting five working groups, each co-chaired by two individuals with specific expertise. The working groups included key

stakeholders: patient advocates, IRB chairs, Cooperative Group regulatory and protocol development staff, nurses, CRAs, and investigators.

Each working group was tasked with addressing specific sections of the existing template, including considering how companion studies should be presented and whether or not informational attachments would provide added value for study participants. The planning committee nominated qualified individuals to serve as co-chairs and working group members. The planning committee met with working group co-chairs in March to outline tasks, goals, deliverables, and questions to consider. Each working group drafted its assigned section of the ICD template to be more concise and developed responses for the questions provided. Working Group 1 worked on the beginning of the template (background, required tests, intervention sections). Working Group 2 focused on the risks and benefits sections. The alternatives, privacy, injury, costs, rights, and signature sections were covered by Working Group 3. Working Group 4 was in charge of the possible attachments section. Lastly, Working Group 5 focused on the companion studies section.

A face-to-face meeting was held June 28-29, 2011, with the planning committee, regulatory advisors, and all working group members. Working group co-chairs presented their assigned drafts at the meeting. Some of the recommendations for the ICD were to: include a lay title and brief description of standard treatment to set the stage for study discussion; focus on how the study is different from standard treatment rather than using limited space to describe standard treatment; take measures to avoid drifts in document length over time (i.e., implement page counts, word counts, or reading time estimates); and create attachments that are informative and optional. Working Group 2 felt that risks should be formatted into tables in the risks section, with different tables for experimental and standard arms. Risks should be grouped by body system, keeping descriptions at a general level, such as "heart attack," "irregular heartbeat," or "kidney damage" instead of including details often provided about specific abnormalities, like "ventricular tachycardia" or "nephrotic syndrome." Risks should be described by how study participants might experience them, rather than including laboratory findings such as hypokalemia or hypercalcemia. OHRP suggested making risk descriptions meaningful by stating how effects of the study intervention are different from standard treatment. Working Group 2 also recommended developing a repository of side effects of commercial drugs. The final revised template is currently being prepared. Once all of the changes are included, the revised template will be vetted by the planning committee. Additional comments on the final version will be solicited from OHRP, FDA, working group members, and others.

Additional discussions have been held to determine how to roll out the new template. The working groups suggested that a subcommittee plan the roll-out and dissemination of the new template. The tentative plan is to prepare a memorandum to IRB chairs that provides the rationale for the shorter ICD. Engaging OHRP and FDA to support the new template was encouraged. The working groups suggested giving presentations on how the new template was developed and the expertise of those involved to Cooperative Group Annual Meetings; Public Responsibility in Medicine and Research; and the Association for the Accreditation of Human Research Protection Programs (AAHRPP)—the primary accrediting body for IRBs. It was suggested that a national IRB chair conference call might aid in providing rationale for why shorter ICDs are better in the long run. The working groups also recommended not mandating the use of technology during the informed consent process as it could be too resource-intensive for some sites; use of technology should be considered on a per-trial basis. Additionally, the working groups discussed how the template should be used to address ICD differences between early- and late-phase trials and treatment and prevention trials. This issue was addressed by including sample language in the template to address different phases/types of trials and permit those with special trial types to include additional text or deviations from the template.

NCI's Office of Market Research and Evaluation (OMRE) is conducting two evaluations of the revised template. The formative evaluation will be conducted during the next six to eight weeks and will entail gathering input from advocates during development of the revised template. This evaluation will be supported through existing OMRE contract mechanisms. The outcome evaluation will be conducted prior to implementation of the template. This evaluation will involve randomizing cancer survivors to ICDs written using the current template versus the revised version. IRB and Office of Management and Budget clearances will be obtained for this study, which will be funded through NIH set-aside evaluation funds.

In closing, Ms. Adler presented CTAC members with a number of questions: Does CTAC support the effort to reduce page length from 16 to 6-7 pages? Does CTAC feel that page limits on ICDs are an effective way to ensure against future length "drift"? Also, while there is compelling evidence that lengthiness of the consent form is a major hindrance to patient comprehension, how can IRBs be convinced that shortening the form is beneficial?

Central IRB Model Change. Ms. Adler also gave a brief update on the CIRB model change. In the current CIRB model, regulatory responsibility is shared between the NCI CIRB and local IRBs. The CIRB's primary responsibility is initial and continuing review of studies, including amendments and other study-specific documents distributed by the Cooperative Groups. The local institutions' primary responsibility is consideration of local context and oversight of conduct of the trial. During "facilitated review," the local IRB reviews the CIRB-approved study for local context considerations. The proposed new model would grant all regulatory responsibilities to the NCI CIRB. The CIRB would continue to review study-specific documents and take on review of local context considerations for new studies—the facilitated review would no longer be necessary. The CIRB would be the sole IRB of Record when investigators use the CIRB.

A significant number of institutions have requested a CIRB model change. The changed model should increase CIRB enrollment and utilization. It would also position the CIRB well for AAHRPP accreditation—an indicator of quality to the IRB community. Eliminating the need for facilitated review in the new model would save institutions time and effort. Local IRBs would have no review responsibilities. The current level of human subjects protection review would continue under the new CIRB model. The CIRB would be informed of local context considerations via an Annual Institution Worksheet (containing descriptions of state and local laws) and an Annual Principal Investigator Worksheet (providing research activity descriptions). A principal investigator could open a new study by submitting a Study-Specific Worksheet directly to the CIRB. Any study-specific unanticipated problems and/or serious or continuing noncompliance would be reported to the CIRB. When applicable, the PI/institution would submit a management plan, and the CIRB would make a determination and report to FDA or OHRP.

A pilot study of the new CIRB model will be conducted to learn about the impact on local institutions, feasibility for the CIRB Operations Office, and best practices for new model operations. Twenty institutions are currently enrolled to participate in the pilot, and five institutions that are not currently enrolled will be invited to participate. The pilot should be operational by early September 2011 and last 9 to 12 months. An evaluation will be conducted consisting of surveys of different levels of site personnel. An analysis of the completed surveys will be done, and a report of the findings will be available in late summer of 2012. NCI plans to make a decision regarding the CIRB model change in late 2012. The IOM report and ASCO letter recommend that sites use NCI's CIRB for multi-institutional Cooperative Group trials. Ms. Adler asked CTAC members for suggestions for additional strategies that would accomplish this. Many sites in the CIRB initiative feel that a switch to an independent model would be beneficial. Do CTAC members have any suggestions about this new approach?

Questions and Discussion

Dr. Abbruzzese asked whether the final revised template was applied to the three ICDs from existing CTEP-sponsored Phase III trials to see whether the page length of the documents increased at all. Ms. Adler responded that the analysis of the three test cases occurred before the working groups did their work. Dr. Abrams also noted that such an evaluation has not been conducted formally but they are confident the page lengths are not increasing.

Dr. Adamson asked whether the revised template applies to pediatric studies. Ms. Adler clarified that the new template does not include pediatric studies. The Children's Oncology Group has its own informed consent template for pediatric trials. Ms. Adler communicated with COG during the start of the revised template effort, and COG developed what it felt was its own concise template using the standard practice to format risks, which was used to inform the efforts of the working groups.

Dr. Adamson also commented that a page limit is necessary or this effort will quickly fail. He stated that the real challenge exists in taking current ICDs that are 35 pages long and cutting them down. This will be much more difficult than decreasing the page limit of 16-page ICDs.

Dr. Curt Civin, Director, Center for Stem Cell Biology and Regenerative Medicine, commented that part of the reason ICDs are so long is that they often try to incorporate every possible patient question. A solution to this is having a frequently asked questions (FAQs) section. He suggested that the FAQs be available as part of a living, real-time document housed online that could continue to be annotated.

Dr. Scott M. Lippman, Professor and Chair, M.D. Anderson Cancer Center, stated that it is very important that the template is usable in various settings (i.e., treatment versus prevention trials).

Dr. Lee Helman, Deputy Director, Center for Cancer Research, NCI, commented that IRBs always seem to assume that the ICD covers every possible issue and that the document is the end of the informed consent process—which is not the case. He asked whether there was any discussion about what is required in an ICD versus how the informed consent process is covered. If the informed consent process is organized and streamlined, the ICD can be kept to a minimum. Ms. Adler responded that this is an important issue that will be included in the justification letters to IRB chairs. Dr. Abrams added that the process of informed consent was the underlying impetus for starting the ICD revision. In revising the template, education and roll-out of the document were considered in order to effectively communicate these changes to the community.

Dr. Stephen S. Grubbs, Chief of Oncology, Medical Oncology Hematology Consultants, noted several pitfalls associated with beginning the document by outlining standards of care. The standard of care may not apply to a particular potential participant, or it may change over time. He also commented that probabilities of toxicity and other potential side effects must be included.

Dr. Newman asked which sections of the ICD lost the most space when shortening the document. Ms. Adler said that reformatting the risks section contributed most to the decrease in page length.

Dr. Bruner commented that formatting toxicities in a way that patients can understand and that outlines how patients experience the symptoms has great implications for patient-reported outcomes. NCI has funded studies that test the words used to describe toxicities. She suggested that this work should be part of the revised informed consent document.

Dr. Mitchell D. Schnall, Matthew J. Wilson Professor, University of Pennsylvania Medical Center, commented that the use of imaging in therapeutic trials creates particular issues for informed consent, especially when dealing with radiation risk. He also commented that the management of study-related problems is a challenge for large academic medical centers. Other institutions have a coordinated compliance effort (e.g., the IRB or OHRP) to manage trial-related problems as they arise.

Ms. Roach stated that local IRB review of national trials is almost unethical and should not be allowed from a patient perspective.

VI. RECOGNITION OF RETIRING MEMBERS—DR. JAMES DOROSHOW

Dr. Doroshow thanked seven members who are retiring from the Committee. Drs. Nancy Mendenhall, Edith Perez, James Wade, Deborah Bruner, Stephen Grubbs, Sandra Horning, and Richard Schilsky were recognized for their contributions to CTAC and service to NCI. They will receive plaques by mail.

VII. CTWG EVALUATION WORKING GROUP REPORT—DRS. PETER ADAMSON AND DANIEL SARGENT

Drs. Adamson and Sargent presented the final report of the CTWG Evaluation Working Group. The goal of the planned CTWG evaluation is to assess the performance and impact of CTWG initiatives on the effectiveness of the overall NCI clinical trials enterprise. The objectives of the CTWG Evaluation Working Group were to refine the evaluation plan and establish a timeline for implementation. An interim report was presented to CTAC in March 2011. The Working Group's final report was completed in May 2011, and the purpose of this presentation is to present final findings, describe proposed next steps, and obtain CTWG approval of the final plan.

The Working Group focused on trials under the purview of Scientific Steering Committees. The evaluation plan contains four primary evaluation components: system outcomes performance metrics; status of disease steering committees; status of the Investigational Drug Steering Committee (IDSC); and measures of collaboration among Cooperative Groups, SPOREs, and Cancer Centers.

The Working Group proposed a variety of quantitative measures to assess trial quality. Evaluating the scientific merit and clinical relevance of trial results will require qualitative measures and expert judgment. The proposed plan calls for convening an expert panel to pilot proposed qualitative measures for a recent year of clinical research. If this process proves feasible, evaluations should be done on an annual basis. The interim CTWG Evaluation Working Group report included FDA approval as a qualitative measure of clinical relevance; the final report adds adherence to the National Comprehensive Cancer Network guidelines. Centers for Medicare and Medicaid Services (CMS) coverage determinations were deleted from the final report. Dr. Sargent noted that the pilot analysis revealed data collection from CMS was not feasible for this purpose and that the final report also adds new measures to the efficiency of trial conduct.

For evaluation of SSCs, there are measures for overall system outcomes, such as scientific importance and clinical relevance of trial results. Measures for individual disease SSCs include the quality of the concept evaluation, whether it influenced concept development, and whether enhanced

collaboration among Cooperative Groups was encouraged. Task force and SSC members, as well as NCI staff, should be interviewed.

The final report adds a recommendation that evaluation of collaboration should be guided by definitions of collaboration developed by the Guidelines Harmonization Working Group of the CTAC ad hoc Coordination Subcommittee. Since under the proposed NCTN all trials would be open to all Groups, contributing to accrual would not by itself signify collaboration. Proposed next steps for this evaluation effort include: initiating database analysis in 2011 for measures relying on data already available in NCI databases; convening an expert panel in 2011 or 2012 and piloting proposed measures; beginning annual evaluations in 2013 (if measures prove feasible); developing methodology in 2011 for document analyses; beginning annual analyses in 2012 (if methodology proves feasible); evaluating each disease steering committee five years after inception and every five years thereafter; evaluating the IDSC in 2011-2012 and every five years thereafter; analyzing program guidelines in 2012 when the current Cooperative Group guidelines revision is completed; and conducting database analyses of collaboration measures in 2011-2012 and every three years thereafter.

Questions and Discussion

Ms. Roach noted that the role of the Patient Advocate Steering Committee is not accurately described in the report—promoting awareness of clinical trials is not the mission of the Committee. She offered to work with the Working Group after the CTAC meeting to correct this section. Dr. Adamson agreed to revise this section of the Report.

Ms. Roach asked whether previous reviews of task forces and SSCs have produced useful findings. She expressed concern about the ability to obtain meaningful qualitative information on past activities. Dr. Adamson responded that piloting the measures will provide an opportunity to refine those measures and determine the most appropriate timeframe for questions. Dr. Sargent added that asking questions immediately following concept reviews may elicit emotional reactions.

Dr. Schilsky asked whether the Working Group discussed the possible outcomes of the evaluation in terms of proposed actions. Dr. Adamson replied that the Working Group proposed to analyze and summarize data and report to CTAC, which will have responsibility for interpreting the findings and planning action steps in response to those findings.

Dr. Newman asked about evaluation of subcommittees within Cooperative Groups that focus on the needs of special populations. She expressed concern that these subcommittees need to survive the Cooperative Group reorganization. Dr. Schilsky explained that this effort is a system evaluation, not an evaluation of individual Cooperative Groups. These issues could be incorporated into system outcomes measures. Dr. Prindiville noted that the report cites a CTWG recommendation related to recruitment of underserved populations (Other CTWG Initiatives, Section A.4. Initiatives Recommended for Separate Evaluation Studies, page B-59).

Dr. Schilsky asked whether the proposed expert panel would be related to the proposed CTAC Clinical Trials Strategic Planning Subcommittee. Dr. Adamson said that this potential relationship will be discussed during implementation of the evaluation.

Ms. Roach stressed the importance of bringing the voices of the translational community, oncologists, and advocates to the table in addition to Cooperative Groups and NCI.

Dr. Helman observed that while some measures, such as the number of trials that answer their primary scientific questions, present challenges, any data are better than no data. He stated that the proposed evaluation plan should produce useful results.

Motion. A motion was made to accept the CTWG Evaluation Working Group Final Report with a stipulation that the section on the Patient Advocate Steering Committee be revised. The motion was seconded and approved unanimously.

VIII. POTENTIAL CTAC SUBCOMMITTEES AND WORKING GROUPS—DR. SHEILA PRINDIVILLE

Dr. Prindiville gave an overview of two potential CTAC Subcommittees and elicited members' feedback.

CTAC Clinical Trials Strategic Planning Subcommittee. The scope of authority of the Clinical Trials Strategic Planning Subcommittee would cover analysis of the clinical trials portfolio, evaluation of clinical trials activities, and strategic advice on the overall NCI clinical trials program. The Subcommittee's responsibilities would be to assess the priority of these tasks and the need for working groups in the following areas: portfolio analysis; evaluation; and Cooperative Group/CCOP strategic analysis. If working groups were convened, the Subcommittee would review their findings/ recommendations, oversee their activities to avoid duplication of effort, and report to CTAC on all working group activities and recommendations.

Portfolio analysis tasks would entail reviewing the initial (2006) clinical trials portfolio analysis data and methods and recommending whether periodic clinical trials portfolio analysis should begin in 2012. If future clinical portfolio analysis were approved, the Subcommittee would recommend improvements in methodology, recommend analysis frequency and scope, oversee the analysis process and review the results, and recommend changes in NCI clinical trials funding priorities, as appropriate.

Evaluation tasks would include overseeing: analysis of measures relying on data currently collected in NCI databases and prioritizing data elements to be added in the future; expert panel processes for evaluating scientific importance and clinical relevance of trial results; evaluation of IDSC and Disease and Symptom Management Steering Committee operations and processes, making recommendations as necessary; and evaluation of the extent of collaboration in NCI-funded clinical trials. Strategic analysis of the Cooperative Group/CCOP program would encompass reviewing the scientific effectiveness of steering committees—including the quality of concepts they approve, the scientific importance and clinical relevance of trial results, contributions to development and refinement of trial concepts, standards for judging scientific merit and clinical importance of concepts, and contributions of committee activities in identifying new strategic priorities—and recommending needed improvements to increase scientific effectiveness. Strategic analysis would also involve reviewing the quality of the Cooperative Group/CCOP trial portfolio and making necessary recommendations by examining trial quality and scientific importance/clinical relevance of trial results and the balance of trials across diseases and modalities in light of scientific opportunities and clinical needs. The Subcommittee would recommend new overall strategic priorities and directions, as needed.

Dr. Prindiville asked CTAC members to decide whether a Clinical Trials Strategic Planning Subcommittee is warranted by considering whether the scope of authority as outlined is correct, with clear and appropriate responsibilities. She also asked whether the Cooperative Group and CCOP clinical trials

portfolio is of sufficient importance to warrant a working group dedicated to their strategic scientific oversight. Perhaps other working groups of this Subcommittee should be planned at this time?

If the Subcommittee is approved, the next steps will be to establish its charge, membership, and chair; determine whether working groups are needed; assign initial tasks and responsibilities to the Subcommittee and working groups, as appropriate; and initiate deliberations in fall 2011.

Questions and Discussion

Dr. Abbruzzese commented that the CTAC Strategic Planning Subcommittee could consist of both CTAC and non-CTAC members.

Dr. Sargent made a comment regarding the CTAC Strategic Planning Subcommittee's scope of authority: Providing strategic advice on the overall NCI clinical trials program is a huge responsibility that should lie with CTAC, not with a Subcommittee. Dr. Prindiville responded that the Subcommittee would have to report back to CTAC on all activities and recommendations. She further clarified that the intent would be to focus on the portfolio of clinical trials coming out of the current restructuring activities and that looking at the overall NCI clinical trials portfolio might not currently be the highest priority.

Dr. Schilsky stated that the scope-of-authority language is confusing. From previous CTAC presentations, he understood that there is a need to form an overarching subcommittee to provide strategic advice on late-phase trials that are predominantly being performed by the Cooperative Groups. Dr. Abbruzzese commented that the NCI clinical trials program also includes Phase I and II trials and the funding mechanisms that support them. The initial deliberations of the CTAC Strategic Planning Subcommittee would be to determine what pieces of the clinical trials portfolio need strategic advice. There needs to be oversight of scientific output of the late-phase trial program and another authority assessing the overall clinical trials portfolio.

Dr. Schilsky commented that the CTAC Strategic Planning Subcommittee should be charged with the review of NCI's late-phase clinical trials portfolio so that they can ensure that the priorities are correct and that funds are spent optimally.

Dr. Horning stated that one of the important aspects of late-phase development is providing visibility for early-phase development. She suggested that in conducting a portfolio analysis, a mapping exercise be done to show the "landscape" to make sure that those doing late-stage development are aware of the connections with earlier development phases.

Dr. Gray clarified several differences between a subcommittee and a working group. Subcommittee meetings are open to the public, must be published in the *Federal Register*, and can include non-CTAC members. Working group meetings are not open to the public, which allows for frank and open discussion. Additionally, a working group does not have to develop a consensus opinion on issues—it is a fact-gathering body.

Dr. Abbruzzese stated that there is some benefit to having a subcommittee responsible for portfolio analysis, oversight of the clinical trials program, and evaluation of clinical trials activities (e.g., Steering Committees)—this may not require three separate working groups. Dr. Schnall suggested creating two separate subcommittees or working groups—one to focus on strategic advice and evaluation of the overall clinical trials portfolio and one to focus on the Cooperative Group/CCOP portfolio.

Ms. Roach expressed support for the need to have frank and open discussions that can be conducted privately, but that the process should also be transparent. She agreed with the suggestions that working groups should be created to collect data and formulate recommendations for CTAC.

Dr. Kenneth Cowan, Director, Eppley Cancer Center, concurred that a working group must determine what data are needed for CTAC to make decisions, but there should be oversight of and regular reporting by the working group(s).

Dr. Abbruzzese clarified that the purpose of the discussion is to request CTAC's approval to form a Clinical Trials Strategic Planning Subcommittee and that there would be further discussion at a later date on how the Subcommittee should be organized (e.g., formation of two working groups) and the scope of its authority.

Motion. A motion to establish a CTAC Clinical Trials Strategic Planning Subcommittee was approved unanimously.

CTAC Clinical Trials Informatics Subcommittee. The scope of authority of the Clinical Trials Informatics Subcommittee would be to evaluate informatics initiatives requiring user/stakeholder input from the clinical trials community. The Subcommittee would focus on implementation of the following CTWG informatics initiatives: the CTRP database; common case report forms for NCI information systems; and development of a credentialing repository (e.g., electronic 1572 forms). Two additional areas relevant to the Subcommittee would be implementation of a common clinical trials data management system for the Cooperative Groups and adverse event reporting systems (AdEERS/cAERS).

The Subcommittee's responsibilities would be to review progress on implementation of the aforementioned informatics activities and provide advice on topics needing additional consideration as identified by the AACI-NCI CTRP Strategic Subcommittee Report. These topics include outcome reporting, reporting of noninterventional trials in CTRP, Summary 4 report design, patient-level disease coding for accrual, and the process for changing CTRP technical specifications.

Questions and Discussion

Dr. Sargent asked whether the CTAC Clinical Trials Informatics Subcommittee would replace the caBIG Clinical Trial Management System Steering Committee. Dr. Prindiville clarified that the CTAC Clinical Trials Informatics Subcommittee would specifically focus on the CTWG informatics initiatives.

Dr. Adamson commented that he would like to see biobank informatics initiatives included under the purview of the CTAC Clinical Trials Informatics Subcommittee. Dr. Schilsky added that an inventory of NCI-funded biobank materials—informatics or imaging—are very important issues moving forward. Dr. Doroshow agreed that this would be a good home for these discussions.

Motion. A motion to establish a CTAC Clinical Trials Informatics Subcommittee was approved unanimously.

IX. NEW BUSINESS—DR. JAMES ABBRUZZESE

Dr. Abbruzzese commented that his goal is to make the work of CTAC as effective and relevant to NCI as possible. He asked members to contact him if they have suggestions regarding the Committee's function. Dr. Abbruzzese also mentioned that a substantial amount of time is spent developing the agendas for CTAC meetings. If an issue is not included on the agenda, it will not be discussed at the meeting. He noted that one issue brought up at today's meeting that perhaps should be included as a future agenda item is the clinical aspects of NCI's intramural program. If CTAC members would like to suggest an agenda item(s), or if they would like to participate in the agenda planning process, it was noted that they should contact Dr. Prindiville or Dr. Abbruzzese.

X. ADJOURNMENT—DR. JAMES ABBRUZZESE

There being no further business, the 14th meeting of the CTAC was adjourned at 2:20 p.m. on Wednesday, July 13, 2011.