THE CANCER LETTER

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SPECIAL ISSUE

Revamping Cooperative Groups

NCI Boosts Funding For Groups by $25 Million, Cuts Overall Accrual By 20 Percent, to 20,000

By Paul Goldberg

The NCI Board of Scientific Advisors Nov. 7 unanimously approved a plan that would make massive changes in the institute's conduct of clinical research in cancer.

Eagerly awaited by some and intensely dreaded by others, the changeover will put an additional $25.6 million into the parched clinical trials cooperative groups system—and, in some cases, double the per-case reimbursement from $2,000 to $4,000.

To pay for this splurge at a time of fiscal near-starvation, the institute will cut overall accrual from about 25,000 to 20,000 patients per year.

(Continued to page 2)

Guest Editorial

Group Chairs Urge Implementation of NCI Plan, Next Step: Bioinformatics and Tissue Banks

By the Coalition of Cancer Cooperative Groups

The Cooperative Group Chairs support the Board of Scientific Advisors in its recent unanimous vote to approve the NCI proposal to revamp the federal mechanism through which we receive public funding for our cancer clinical research programs (U10 Cooperative Agreement).

These sweeping changes will impact nearly every clinical and translational investigator in the United States who receives NCI funding support. We congratulate NCI leadership for its methodical approach to invite—and indeed incorporate—input from multiple stakeholders and to utilize the process to more clearly align cooperative group and cancer center programs and leadership.

Likewise, we applaud the BSA subcommittee, under the leadership

(Continued to page 7)

In Brief

New Chair Golub Leads His First BSA Meeting; ACS Elects 11 Members to Board of Directors

TODD GOLUB conducted his first meeting as chair of the **NCI Board of Scientific Advisors** Nov. 7. Golub is the chief scientific officer and director of the cancer program at the Broad Institute of Massachusetts Institute of Technology and Harvard University.

(Continued to page 10)

NEXT WEEK:
The State of caBIG, NCI's Bioinformatics Program

NCI To Review Groups Simultaneously Using Uniform Criteria Proposed In RFA

(Continued from page 1)

Institute officials say that to make the once disparate clinical trials groups function as a single system, the new plan requires all groups to be reviewed at the same time, using the same review criteria, and emphasizing the same goal: integration.

In one fundamental change, investigators and their institutions would no longer need to be affiliated with a particular group in order to place patients on its studies.

NCI would give all but $4 million of the new $25.6 million total directly to group sites that accrue at a high level. This change moves money where it is needed the most—towards the reimbursement of site research costs, say institute officials.

Not all sites will see the doubling of per-case reimbursement. The institute will selectively reward better performing sites, and per-case raise will affect just under half of the patients enrolled annually,

"What do we really see the benefit being?" said Meg Mooney, chief of the Clinical Investigations Branch of the NCI Cancer Therapy Evaluation Program, presenting the RFA concept to the board.

"We do think that a smaller number of network group organizations that are fully integrated will actually help us integrate new agents much more rapidly into trials," Mooney said.

"An example is trials are already being developed with erlotinib, dasatinib and ipilimumab in earlier stages of lung cancer and melanoma, but they require screening of large populations, and having an entire network of all the groups working together will allow us to address these research questions much more rapidly and also be able to evaluate combining those agents optimally with surgery, radiotherapy and immunotherapy," Mooney said.

"We also think a large, integrated network will help us evaluate new agents in molecularly defined disease subsets much better," Mooney said. "Even in common diseases like breast cancer, the number of molecularly defined patient subsets is increasing, and there is a need for trial prioritization."

A guest editorial by chairs of the cooperative groups appears on page 1.

Mooney's slides, which represent all the information NCI has put on the table, are posted at http://www.cancerletter.com/categories/documents.

The board passed the concept unanimously, urging the institute to develop a standardized informed consent that would allow broad genetic and genomic studies. Also, the board urged the institute to make patient-level data from studies available to other investigators at the earliest possible time.

Change in the groups started last year, when the institute, responding to a report by the Institute of Medicine, said that it would fund no more than five cooperative groups. Children's Oncology Group was going to remain untouched while the nine cooperative groups focused on adults had to combine to form four.

By the time the BSA met to review the concept, this consolidation was finished.

The last group to join a federation was the Gynecologic Oncology Group, which became a part of a yet-to-be-named structure that includes the National Surgical Adjuvant Breast & Bowel Project and the Radiation Therapy Oncology Group (The Cancer Letter, Oct. 21).

Publically funded trials would focus on questions that either aren't aimed specifically at drug approval or would focus on indications that industry wouldn't find lucrative enough to pursue.

The RFA concept approved by BSA covers the clinical studies of the NCI Division of Cancer Treatment and Diagnosis as well as the Community Clinical Oncology Program of the Division of Cancer Prevention.

The clinical trials system will be further integrated with additional DCP studies and the NCI biorepositories program.

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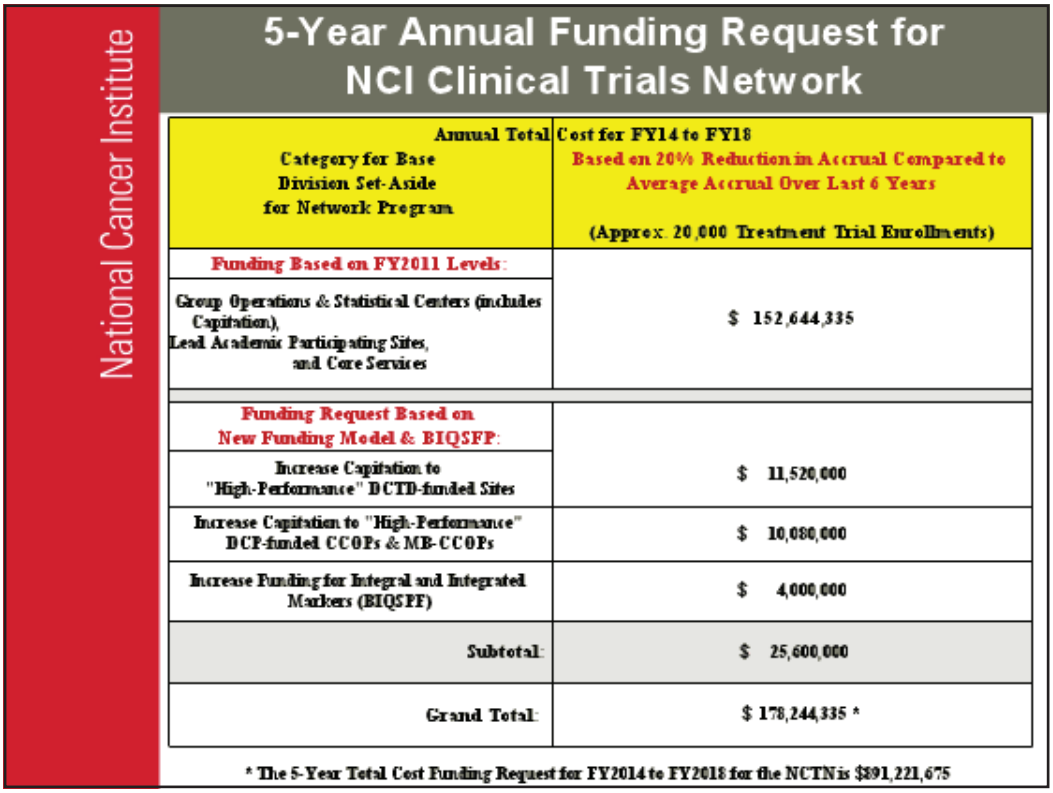
Earlier this year, BSA advised NCI to reconsider a plan for biorepositories, arguing that the clinical trials groups should be restructured before changes are made in the tissue banks.

"Part of this RFA is to have a collaborative management team with the network groups, so we can discuss how best to put a biospecimen collection and other collections into definitive trials," NCI's Mooney said at the board meeting.

"We will have separate funding for collection of biospecimens even when they are not integral to the study question.

"Part of the new RFA and having an integrative network and a collaborative network is for us to also have a collaborative management team to look and address where best to do those collections, and to make sure that they get done."



National Cancer Institute

5-Year Annual Funding Request for NCI Clinical Trials Network

Category for Base Division Set-Aside for Network Program	Annual Total Cost for FY14 to FY18 Based on 20% Reduction in Accrual Compared to Average Accrual Over Last 6 Years (Approx. 20,000 Treatment Trial Enrollments)
Funding Based on FY2011 Levels:	
Group Operations & Statistical Centers (includes Capitation), Lead Academic Participating Sites, and Core Services	$ 152,644,335
Funding Request Based on New Funding Model & BIQSFP:	
Increase Capitation to "High-Performance" DCTD-funded Sites	$ 11,520,000
Increase Capitation to "High-Performance" DCP-funded CCOPs & MB-CCOPs	$ 10,080,000
Increase Funding for Integral and Integrated Markers (BIQSFP)	$ 4,000,000
Subtotal:	$ 25,600,000
Grand Total:	$ 178,244,335 *

* The 5-Year Total Cost Funding Request for FY2014 to FY2018 for the NCTN is $891,221,675

A slide from the NCI staff presentation to the Board of Scientific Advisors Nov. 7 summarizes the institute's proposed increase in funding for clinical trials cooperative groups. The presentation, which represents all the information NCI has put on the table, is posted at: http://www.cancerletter.com/categories/documents.

New Review Criteria

Openness to participation by all sites is one of the new criteria for reviewing the groups.

"We are focusing the incentives of the review process on the incentives for a national system, so that trials would be open to all qualified sites that are members of any of the network groups, and any of these sites can credit an group to which they belong," NCI's Mooney said to BSA.

The institute would review the clinical trials network as a whole.

"We will for the first time be reviewing all the network groups and their components at the same time," Mooney said. "In the past, by looking at them individually at different points, it was very difficult for the reviewers to get a sense of the entire network and to actually provide the best review and advice in terms of how to go forward.

"In addition, the scientific evaluation will shift to evaluating the groups' role in the national system and its overall strategy and innovation in quality of its trials rather than focusing on the very routine review of each individual committee within a group.

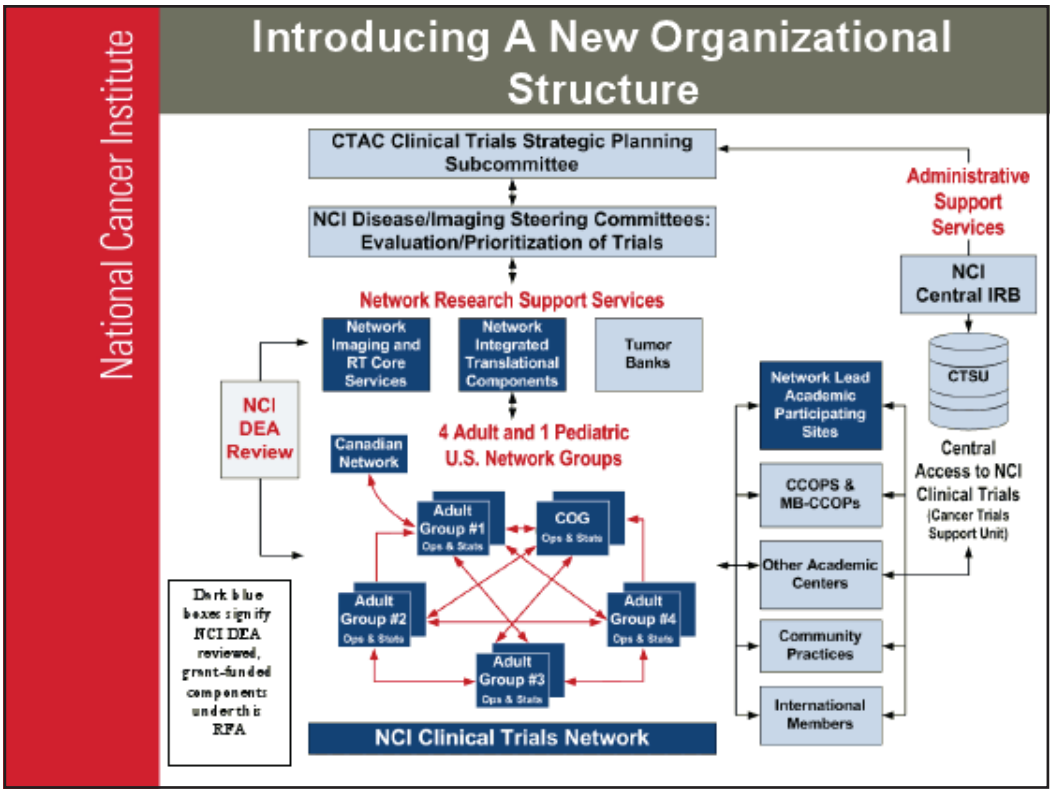
"Lastly, the review criteria will focus on operational efficiency and collaborative management of the network, and that would include coordination with other NCI groups and NCI programs including not just the CCOPs, but also cancer centers SPOREs, early drug developers, R01 and P01 investigators."

The review criteria for participating sites will change, too.

"In the past, the U-10s for large institutions were [awarded based upon a] relationship to one group, with the accrual associated with that one group," Mooney said. "Instead, these will be for institutions that participate in trials across the network. And so the accrual will be based on accrual on every network trial regardless of what group leads it."

The RFA is broken into six "Funding Opportunity Announcements." They are:

- Group operations centers;
- Group statistical and management centers;
- Canadian collaborating network;
- Integrated translational science awards;
- RT and imaging core services;
- Lead academic participating sites.



These FOAs would fund as many as 58 grants that would be renewed every five years. Now, cooperative groups are funded through six-year grants.

Review will determine who will benefit from the boost in per-case reimbursement.

"We estimate that with this additional funding and accrual reduction that we will be able to provide increased funding for approximately 46 percent of all the accrual to the network on an annual basis," Mooney said.

Greater Role for Cancer Centers

"We were particularly pleased to see the emphasis on accrual from all groups, regardless of an institution's alignment to any particular group—and then uniform peer-reviewed evaluation discussed," said BSA member Michael Caligiuri, CEO and director of the Ohio State University Comprehensive Cancer Center, who headed a board subcommittee that worked with the institute on developing the concept.

"Also, [we support] the emphasis on the late phase II, presumably randomized, and phase III trials, delegating earlier trials to other groups, such as SPORES, P01, C01 and N01s," Caligiuri said. "U-10 grants to individual institutions put a fiscal incentive to accrue well to both therapeutic and correlative science trials, placing much more accountability on an investigator at an individual institution and less on the network central office.

"And we felt the RFA addressed the concern that—imaging radiology, radiation oncology—that these somehow not be lost."

BSA member Robert Diasio concurred with the NCI plan to review the entire clinical trials network at once.

"This needed to be reviewed at the same time," said Diasio, director for the Mayo Clinic Cancer Center and a member of the BSA subcommittee that worked with NCI on the RFA. "That's a very important aspect of assuring that the same quality is looked for in each of the applications."

Diasio said the low per-case reimbursement, which hasn't gone up in over a decade, has prevented many institutions from taking part in NCI-sponsored trials.

"It has become increasingly difficult for any academic institution [to participate] due to the costs of actually doing a clinical trial, which is absolutely prohibitive at $2,000 per case," Diasio said at the BSA meeting. "This eliminates a number of active centers that need to be a part of this program.

"The response here—in terms of decreasing accrual, putting more attention on the protocols that are going to be accepted for evaluation in this system, and then paying more for the cases, and particularly paying more for the centers that are truly interested in this type of trials—is a step forward.

"The bottom line of all of this is that it puts the cooperative group system sponsored by NCI as being much more responsive to the future needs of doing clinical trials."

NCI's per-case reimbursement hasn't gone up from $2,000 in over a decade.

Meanwhile, per-patient costs, estimated in a 2006 report, are $8,450 for phase II trials and $4,700 for phase III trials. Some industry trials cost $15,000 per patient or more.

Overall, the participating institutions and investigators contribute $100 million worth of unreimbursed goods and services annually when they take part in cooperative group clinical trials.

National Cancer Institute

Overview of RFA: Cooperative Agreement FOAs and Estimated # Grants

Network Component	Mechanism (Duration)	Est. Max. # Grants	Frequency New Application Accepted?	Multiple PI Option?
Group Operations Centers	U10 (5 Yrs)	5	Every 5 Years	Yes
Group Statistical & Data Mgt Centers	U10 (5 Yrs)	5	Every 5 Years	Yes
Canadian Collaborating Network	U10 (5 Yrs)	1	Every 5 Years	Yes
Integrated Translational Science Awards	U10 (5 Yrs)	1 to 5	Every 5 Years	Yes
RT and Imaging Core Services	U24 (5 Yrs)	1 to 2	Every 5 Years	Yes
Lead Academic Participating Sites	U10 (5 Yrs)	30 to 40	Any Year	Yes

Informed Consent and Data Availability

Several BSA members said informed consent procedures in the new clinical trials system should be standardized to make genomic data broadly available

"I wonder whether we are missing an opportunity here to be bolder in terms of defining the role of genomics in the context of the clinical trials," said Andrea Califano, director of the Columbia Initiative in Systems Biology, director, Sulzberger Columbia Genome Center, and associate director of the Herbert Irving Comprehensive Cancer Research Center.

"I've seen the word biomarkers appear several times in presentations, but if it's presented that way, you would get whatever people submit in proposals, and not the patient-level data that is necessary" Califano said. "I think that you have to be a little bit more specific in the role that genomics can have in this type of studies.

"Because otherwise the data would be fragmentary. For instance, one thing that is now emerging very clearly is that having a non-responder arm in a clinical trial is extremely valuable and it's extraordinarily difficult to get access to that kind of data," Califano said. "If it's in the RFA, people will adapt to it. Otherwise some people will do it and some people will not do it. There is potential here for better defining the role of genomics."

Joe Gray, a BSA member and director of the Oregon Health and Science University Center for Spatial Systems Biomedicine, said the NCI informed consent should anticipate advances in science.

"Anticipating that five years from now we will know how to do a complete genomic analysis out of paraffin, how are patients being consented?" Gray said. "That's [question] number one, and number two, are you making any comments about data availability policy?"

Jeff Abrams, acting director for clinical research at DCTD and associate director at CTEP, said the institute is trying to institute broader consent forms.

"I think part of this comes at the behest of the new rules that are being put out for public comment by the FDA and OHRP [Office for Human Research Protection]," Abrams said. "We are actually going through the NCI-wide process of changing the informed consent template and making sure that we incorporate the ability to collect tissue for all the different genomic tests. We agree with you that this is critical and we have to address this upfront so we don't run into problems and have to go back and get the consent. So this is going to be done prospectively."

While NCI's goal is to make the patient-level data available, this isn't always possible, NCI officials said.

"We have a requirement to have data sharing," said Mooney. "What complicates it is that occasionally on some trials we have industry partners and they may be making a licensing indication and going forward with

an FDA marketing application.

"We are committed to making sure that we do have databases and data-sharing of trials as soon as we can make them publicly available. I think that is something we have to address and sort out going forward. It would be much easier to do that with an integrated network and with everybody at the table than in the past, when each group set out their own data sharing policy."

While NCI is often expected to complete trials with the same speed as the pharmaceutical industry, the institute's trials are different from those conducted in the private sector, said the new BSA chair Todd Golub, chief scientific officer and director of the cancer program at the Broad Institute of Massachusetts Institute of Technology and Harvard University.

"I think there is an inherent tension in the dual roles of increasing operational efficiency, getting trials open more quickly than historically, and at the same time increasing scientific innovation, which will add a significant degree of complexity, which one would imagine, slows things down," Golub said. "How do you manage to balance these opposing forces?"

"You point out something that is a burden on NCI-sponsored trials," responded Abrams. "We view it as an opportunity. I think the cooperative groups have done this quite nicely. We have to work together that much harder to get these trials open on time. It isn't worthwhile to have a great correlative science question if it takes you two years to open a trial.

"We have to show to our industry partners that we can open these trials in the same timeframe as they would if they were running the trial. And yet we can add some science to it that hopefully will ask more questions about where to go next.

"We haven't gotten to our 'efficiency' targets yet. However, we've cut our timeline already by 50 percent and with more innovation and use of technology we can hopefully achieve the targeted reduction."

National Cancer Institute

Budget History for Components of NCI Clinical Trials Network

Base Divisional Set-Aside for Network/Group Program *	FY2006	FY2007	FY2008	FY2009	FY2010	FY2011 (Estimated)	Grand Total (Over 6 Yrs)	% Grand Total
Group Operations & Statistical Centers (including Capitation for Majority of Accrual)	$128,853,204	$126,516,480	$126,141,046	$126,380,185	$127,127,666	$120,304,563	$755,383,144	78.7%
Participating Site U10s	$ 12,532,773	$11,375,647	$11,074,808	$11,241,179	$11,823,333	$10,839,407	$ 68,887,147	7.2%
Core Services for Imaging & RT (RPC, QARC)	$ 4,185,608	$4,302,227	$ 4,271,987	$ 4,224,437	$ 4,307,091	$ 4,131,527	$25,422,877	2.6%
Subtotal	$145,551,585	$142,194,354	$141,487,841	$141,845,801	$143,258,090	$135,275,496 **	$849,613,167	
Estimated CTSU Capitation	$ 4,000,000	$ 3,779,781	$ 4,289,927	$ 5,162,362	$ 5,174,165	$ 5,040,808	$ 27,446,235	2.9%
Subtotal	$ 149,551,585	$145,974,135	$145,777,768	$147,008,163	$148,432,255	$140,315,496	$877,059,402	
ACRIN	$7,082,444	$15,442,854	$13,129,762	$13,509,478	$12,816,778	$10,612,813	$ 72,513,329	7.6%
ATC	$1,644,551	$ 1,749,999	$ 1,716,026	$ 1,716,026	$1,716,030	$ 1,716,026	$ 10,258,658	1.1%
Grand Total	$158,198,580	$163,166,188	$160,623,556	$162,233,667	$162,965,863	$152,644,335	$959,831,389	100.0%

* Does not include ARRA funding and special "one-time" supplements (e.g., transition supplements) or funding provided by other NCI/NIH Programs for Special Initiatives (e.g., complexity funding)

** Base funding was decreased by FY2011 general budget cuts

A "Mundane" Question

The institute's efforts to review all the entire clinical trials network concurrently could make it difficult to find a sufficient number of reviewers who would have the expertise and be clear of conflicts of interest, said Nancy Davidson, director of the University of Pittsburgh Cancer Institute and a member of the NCI Clinical Trials Advisory Committee.

"A mundane question: what's the review process going to look like after all those applications come into Bethesda a year from now?" asked Davidson at the Nov. 9 meeting of CTAC, when that committee was asked to discuss the NCI RFA. "Because you have nice evaluation criteria, but who's going to apply them?"

"We've had some preliminary discussions with the Division of Extramural Activities about how best to do this," said Mooney. "It's a big country, so within the United States, we do feel that we will be able to have review panels.

"We will have to place greater attention on conflicts of interest, because all the groups will be coming in together. We do have the opportunity to get the reviewers from other countries as well. But we do believe that even within the United States there are adequate numbers of reviewers without conflicts, and we've had some preliminary discussions of how to

do that, how to roll it out, and the types of reviewers that we need."

The institute's plan is to publish the FOAs next July. Applications would be completed in the winter of 2012 and reviewed by the summer of 2013. The National Cancer Advisory Board would review the program in December 2013, and the awards would be rolled out in March 2014.

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Guest Editorial

Group Chairs: Cuts In Accrual Come When Opportunities Abound

(Continued from page 1)

of Dr. Michael Caligiuri, for a strong understanding of the role of the groups in the NCI's translational research continuum and their integration with other federally funded research programs, most notably the cancer centers, SPOREs, and P01s. We believe that the new RFA to come will enhance cooperative group clinical and translational research, will lead to improved therapeutic outcomes for patients with cancer or at risk for cancer, and will improve our understanding of the biological basis of cancer and its treatment.

Previously, the Cooperative Group Chairs publicly endorsed the April 2010 report from the Institute of Medicine entitled A National Cancer Clinical Trials System for the 21st Century. We again acknowledge the IOM for listening to many stakeholder groups and for handling concerns and issues in a responsible, responsive way that has led us to where we are today.

For many years, cooperative group leadership has focused on increasing efficiency and collaboration.

Among the notable examples: creation and maintenance of the regulatory support service that provides centralized investigator and institutional regulatory information for the Cancer Trials Support Unit (CTSU), creation of standards for a common data management system now being implemented across the groups via Medidata's RAVE informatics solution, standardized data collection forms, and full participation in the development and implementation of the Operations Efficiency Work Group's guidelines to reduce time to protocol activation.

Most recently, group chairs voluntarily partnered to create the organizational framework for four adult groups.

Despite these accomplishments, we are just starting to take advantage of the potential to bring scientific discovery into the clinical setting. Ultimately, the success of the new approach and restructuring will be dependent upon harmonizing the activities across the entire system, including the cancer centers, SPORES, and other translational research-oriented programs.

We urge the NCI to rapidly implement proposed changes to the Cancer Center Support Grant and SPORE review guidelines, both of which provide greater incentives for proposing and accruing to cooperative group trials. Such attention to synchronization represents the first step taken down the path toward a truly integrated translational research network.

Increased collaboration among cancer center investigators and cooperative group trials will speed

the conduct of innovative trials so that we can provide answers to important questions more quickly. Moreover, incentives to cancer center laboratory investigators will speed the conduct of translational research, providing the basis for future trials by the groups, which are the integrated hub for phase III and large phase II studies in the NCI's translational research continuum. In that regard, the new RFA provides an additional $4 million in resources for bench-related translational research through the new Integrated Translational Science Awards.

We echo many of the concerns and cautionary themes raised by BSA members in its meeting this week, such as improving greater access among researchers to group-based biorepositories. Standardization and integration of biospecimen collections across the cooperative groups is still nascent. We are prepared to work collaboratively to develop the informatics systems and tissue processing standards that are vital to high-quality translational research.

Adequate support for this important endeavor must be the next major priority for enhancing the national network. On a related note, we concur with the BSA that language in informed consent documents must be upgraded so as to better inform patients about the use of bio-specimens for research opportunities beyond the trial.

The BSA rightly noted that the new funding guidelines not lose sight of the specialty research that is such a rich and meaningful component of the group culture; namely the surgical, radiation oncology, imaging and other approaches beyond medical oncology.

Unfortunately, just when opportunities abound to impact the survival and quality of life of cancer patients and those at risk, fiscal austerity has resulted in a reduction in patient accrual to publicly-funded clinical cancer research.

In these times, it is unusual to present a funding plan that is anything more than a zero-sum game. The additional $25 million in the proposal this week speaks to the importance of the program and the steadfast commitment of the NCI director to advancing this program in spite of "hard times."

Furthermore, we fully support NCI leadership's realistic approach to the funding situation, which acknowledges the sheer magnitude of the group re-organization and the fact that we will incur significant costs during the first five years before beginning to realize operational efficiencies. In fact, NCI has started to fund each of the new groups as we incur the costs of planning and developing our new scientific and operational structures.

Nearly all ($21.6 of the $25.6 million) of the requested increased cooperative group budget will support research costs to accrue patients to trials. This will allow the base-case reimbursement rate to increase from $2,000 to $4,000 for "high-performing" academic and community sites. Additional resources will be required to do the imaging and laboratory research associated with cutting-edge clinical trials. It should be noted, though, that some of the additional funds will result from capping accrual at about 20,000 cases/year overall, which translates into about 15,000 adult cases/year. Once again, we accept that fiscal realities require adjustments across the board.

Whenever funding priorities are considered in the future, however, it will be critically important both to identify ways to diminish costs and to maintain sufficient funding so that NCI-supported clinical cancer research will remain fiscally viable.

One way to reduce costs is to make a concerted effort to reduce the regulatory burden on investigators and institutions. We believe there are several opportunities to do so.

For example, in anticipation of the network strategy, NCI should immediately reorganize audit procedures so that institutions are audited for participation in all NCI-funded trials at a single visit, rather than by multiple visits from multiple groups. Also, in the phase III trial arena, we could eliminate the requirement to report physician speculation as to whether or not an adverse event was related to investigational intervention, co-morbid conditions or disease.

Two reports from the Cooperative Groups have demonstrated that such speculation is unreliable. Investigators were as likely to attribute adverse events to a placebo intervention as to the some other cause. Investigators, FDA, OHRP, NCI, and industry collaborators should all carefully monitor patient safety, but current data collection procedures need to be evaluated, and those practices that add little or no value should be eliminated. Perhaps the savings would allow increased patient accrual to trials.

The NCI's language regarding consolidation states that in the future it will fund one pediatric and *up to four* adult groups. To that end, our previous nine adult Groups have already been compressed into four entities, each of which are proceeding with all due haste—and in good faith—towards the development of new organizational structures so that we can be ready to apply in Summer 2012 when the new funding announcement is released.

In summary, the group chairs continue to promote,

above all else, the principle that patients are best served by having strong scientific programs.

The BSA support of the cooperative group program is welcome news. The groups are committed to collaboration with each other, with cancer centers, industry partners, patient advocates, and philanthropic organizations to conduct innovative, cost-effective clinical and translational research.

We also recognize that these collaborations require that the groups and NCI both provide incentives to a broad cadre of investigators and institutions in order to sustain the mission. We have significant work ahead to improve informatics systems for data and biospecimen collection. We also must be continually alert to opportunities to eliminate waste and improve efficiency. But we can do it.

*Key excerpt from IOM Repor*t: "The committee concluded that a robust, standing cancer clinical trials network is essential to effectively translate discoveries into clinical benefits for patients…it is imperative to preserve and strengthen the unique capabilities of the cooperative group program as a vital component in NCI's translational continuum."

This week's action is a good step forward.

Signed,

Monica Bertagnolli, Jan Buckner, and Heidi Nelson, for the Alliance for Clinical Trials in Oncology; *Peter Adamson,* Chair, Children's Oncology Group; *Robert Comis, and Mitchell Schnall,* for the ECOG-ACRIN Cancer Research Group; *Philip DiSaia, Walter Curran, Jr., and Norman Wolmark,* for the consolidating RTOG/GOG/NSABP; and *Richard Fisher,* Acting Group Chair, SWOG.

FDA Approvals

Seven Approvals Place Cancer Ahead of Other Therapeutic Areas

Thirty-five new drugs have been approved by the FDA within the past year, making it the second-highest yearly total in the past decade (following 37 approvals in 2009), the agency said.

The period spans October 2010 to September 2011.

Seven of the 35 approvals were cancer medications, an approval record placing oncology and hematology in the lead over other therapeutic areas.

The following cancer drugs approved this year include:

• **Yervoy** (ipilimumab) for metastatic melanoma. Yervoy is sponsored by Bristol-Myers Squibb.

• **Caprelsa** (vandetanib) for the treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease. Caprelsa is sponsored by AstraZeneca.

• **Zytiga** (abiraterone acetate) is for metastatic castration-resistant prostate cancer patients who have received chemotherapy with docetaxel. Zytiga is sponsored by Janssen Biotech Inc.

• **Xarelto** (rivaroxaban) for prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism in adults undergoing hip and knee replacement surgery and stroke prophylaxis in patients with non-valvular atrial fibrillation. Xarelto is sponsored by Janssen Pharmaceuticals.

• **Zelboraf** (vemurafenib) for unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. Zelboraf is sponsored by Genentech.

• **Adcetris** (brentuximab vedotin) for two indications: (1) the treatment of patients with Hodgkin lymphoma after failure of autologous stem cell transplant or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates, and (2) the treatment of patients with systemic anaplastic large cell lymphoma after failure of at least one prior multi-agent chemotherapy regimen. Adcetris is sponsored by Seattle Genetics Inc.

• **Xalkori** (crizotinib) for locally advanced or metastatic non-small cell lung cancer that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. Xalkori is sponsored by Pfizer Inc.

"Thirty-five major drug approvals in one year represent a very strong performance, both by industry and by the FDA, and we continue to use every resource possible to get new treatments to patients," FDA

Commissioner Margaret Hamburg said in a statement.

The approvals were enabled due to a combination of expedited approval authority, flexibility in clinical trial requirements, and resources collected under the Patient Drug User Fee Act, officials said.

"Before the PDUFA program, American patients waited for new drugs long after they were available elsewhere," said Janet Woodcock, director of the FDA Center for Drug Evaluation and Research. "As a result of the user fee program, new drugs are rapidly available to patients in the United States while maintaining our high standards for safety and efficacy."

Two of the approvals—one for melanoma and one for lung cancer—are seen as advances in the personalization of cancer treatment. They were both approved with a companion diagnostic test which identifies patients who would benefit most from the medications.

A breakdown of the thirty-five approvals shows:

• Nearly half were "significant therapeutic advances" over older treatments of heart attack, stroke and kidney transplant rejection.

• Ten were for orphaned diseases. Sixteen were approved under priority review.

• Two-thirds were approved in a single review cycle.

• Three were approved under accelerated approval.

• Thirty-four were approved on or before FDA-administered review time targets.

• Three cancer drugs were approved in less than six months.

Cancer Act, 40 Years Later

ASCO Publishes "Blueprint" On Accelerating Progress

By Lucas Thomas

The American Society of Clinical Oncology released the report "Accelerating Progress Against Cancer: ASCO's Blueprint for Transforming Clinical and Translational Cancer Research."

The the 32-page report revisits the National Cancer Act of 1971, and advises oncology researchers and policymakers on how to build on the advances that have been made in the field in the past forty years, as the current period of cancer research goes through "a period of revolutionary change."

ASCO identifies the need to refocus cancer research to become "more targeted, more efficient, and more effective" by addressing three components.

The first is to establish a new approach to therapeutic development using new technologies.

The second is to design smarter, faster clinical trials that can more quickly benefit the patient.

The third priority is to harness advances in health information technology, making clinical research more accessible by integrating the expansive supply of cancer information into easy-to-access mediums.

The report was developed by Mark Kris, of Memorial Sloan-Kettering Cancer Center; Neal Meropol, of University Hospitals Case Medical Center & Case Western Reserve University; and Eric P. Winer, of the Dana-Farber Cancer Institute.

"Advances in cancer prevention, detection and treatment have already extended the lives of millions of adults and children living with cancer—but the critical question is, 'Where do we go from here?'" ASCO President Michael Link said in a statement. "With the cancer burden growing rapidly around the globe, millions of future patients are depending on the answer. This report aims to set us on a path to deliver the new therapies that patients urgently need."

An excerpt from one section of the report, titled "ASCO's vision and recommendations for the future," follows:

1. Establish a new approach to therapeutic development, driven by our more thorough understanding of cancer biology and the advent of new technologies.

• Identify and prioritize the molecular targets that have the greatest promise to improve survival

• Incentivize collaboration to encourage industry and researchers to pursue high-priority targeted therapies and diagnostics in combination

• Ensure more aggressive and timely development of biomarkers and diagnostic tests to guide treatment decisions and speed research

2. Design smarter, faster clinical trials to provide evidence for effective treatments targeted to patients most likely to benefit, sooner:

• Prioritize trials with the greatest potential benefits for patients, or that address clear unmet needs; shift away from trials that promise only marginal improvements in care

• Develop shared standards for flexible trial designs that allow researchers to demonstrate results with smaller populations defined by specific molecular characteristics

• Select trial participants primarily based on molecular characteristics, to ensure that only those who are most likely to benefit are included, and that patients aren't excluded from trials because of health conditions

that aren't relevant

• Revitalize the National Cancer Institute's Clinical Trials Cooperative Group Program, which has been instrumental in much of the progress achieved against cancer to date. ASCO supports the continued efforts by the NCI, the Groups, and other stakeholders to fully implement recommendations issued by the Institute of Medicine in 2010 to revitalize this essential component of the nation's cancer research system

3. Harness advances in health information technology to seamlessly integrate clinical research and patient care:

• Use HIT tools, including EHRs and "rapid learning" systems, to allow researchers to draw upon the wealth of real-world patient information that is now locked away in file cabinets and unconnected computer systems

• Standardize EHRs by defining functional requirements, harmonizing data fields and ensuring secure patient and provider access to information at any time

• Develop industry standards for working with, storing and capturing information from biospecimens (tissue and blood samples), which are essential to identifying and evaluating new therapeutic targets

• Ensure that advances in HIT protect patients and researchers by examining the need for revised standards for patient privacy, information sharing and intellectual property protections to support HIT innovation

The report is posted at: http://bit.ly/vTwPlP

In Brief

Golub is New Chair of NCI BSA; ACS Elects 11 New Board Members

(Continued from page 1)

The group includes the following new members:

• **Francis Ali-Osman**, the Margaret Harris & David Silverman Distinguished Professor of Neuro-Oncology Research, professor of surgery and director of experimental therapeutics at Duke Comprehensive Cancer Center.

• **Sangeeta Bhatia**, the John H. and Dorothy Wilson Professor at the Division of Health Sciences and Technology and Electrical Engineering and Computer Science at the Massachusetts Institute of Technology.

• **Brian Druker**, director of the Oregon Health and Science University Knight Cancer Institute, associate dean for oncology at the OHSU School of Medicine, and the JELD-WEN Chair of Leukemia Research.

• **Karen Emmons**, deputy director of the Center for Community Based Research at Dana-Farber Cancer Institute and professor and associate dean for research in the Department of Society, Human Development and Health at the Harvard School of Public Health.

• **Stanton Gerson**, the Shiverick Professor of Hematological Oncology; director of the Case Comprehensive Cancer Center at Case Western Reserve University; director of the National Center for Regenerative Medicine; and director of the University Hospitals Seidman Cancer Center.

• **Theodore Lawrence**, the Isadore Lampe Professor and chair of the Department of Radiation Oncology at the University of Michigan Medical School.

• **Luis Parada**, chairman of the Department of Developmental Biology, the Southwestern Bell Distinguished Chair in Neuroscience Research, director of the Kent Waldrep Center for Basic Research on Nerve Growth and Regeneration, and the Diana & Richard C. Strauss Distinguished Chair in Developmental Biology at the University of Texas Southwestern Medical Center.

• **Lincoln Stein**, director of the Informatics and BioComputing Platform at the Ontario Institute for Cancer Research.

• **Gregory Verdine**, the Erving Professor of Chemistry in the Department of Stem Cell and Regenerative Biology at Harvard University.

THE AMERICAN CANCER SOCIETY elected 11 new officers to its 2011-2012 **National Board of Directors**.

Chair **Cynthia LeBlanc** will preside over the board. LeBlanc has served on the society's California Board of Directors since 1994, has received the St. George medal, and is a Road to Recovery volunteer, legislative ambassador, and National Leadership Development Program coach.

Leading the organization's National Assembly will be newly elected President **W. Phil Evans**, director of the Center for Breast Care and professor of radiology at the University of Texas Southwestern Medical Center. He is also a recipient of the St. George medal and has served on the National Board of Directors since 2004.

Other officers elected are: **Gary Reedy**, chair-elect; **Vincent DeVita**, president-elect; **Pamela Meyerhoffer**, vice chair; **Tim Byers**, first vice president; **Douglas Kelsey**, second vice president; **Daniel Heist**, treasurer; **Robert Kugler**, secretary; **Edward Partridge**, immediate past president; and **Stephen Swanson**, immediate past chair.