THE CANCER LETTER INTERACTIVE

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Cancer Clinical Trials System Needs Comprehensive Review, NCI Director Says

NCI Director Andrew von Eschenbach said he will appoint a panel to conduct a "comprehensive review" of the Institute-supported clinical trials system.

The panel will be formed in September, after the recruitment of a director for the Division of Cancer Treatment and Diagnosis is finalized, von Eschenbach said to the NCI Board of Scientific Advisors at its June 26 meeting.

The new group would conduct a "comprehensive and systematic review and assessment of our entire clinical trials system and infrastructure," von Eschenbach said. The review "will also integrate and

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In Brief:

Brian Kimes, Led NCI Centers Program, To Retire; NHLBI Director Lenfant, Also

BRIAN KIMES, director of the NCI Office of Centers, Training, and Resources, said he plans to retire Feb. 1. He will have served for 29 years at NIH, much of that time working with the Cancer Centers Program, one of NCI's largest, and oftentimes the most politically contentious, program. Kimes came to NCI in 1976, having had a year's training as an NIH grants associate. Kimes began as an assistant program director for tumor biology in the former Division of Cancer Research, Resources, and Centers. He became chief of the Cancer Biology Branch, and then was named associate director for extramural programs in the Division of Cancer Biology. Under NCI Director **Samuel Broder**, Kimes became chief of the Centers, Training, and Resources Program, where he developed the guidelines to implement Broder's idea for the Specialized Programs of Research Excellence grants. . . . **CLAUDE LENFANT**, director of the National Heart, Lung, and Blood Institute said he plans to retire Aug. 30. The longest-serving director of NHLBI, Lenfant assumed his position in July 1982. Previously, he was director of the NIH Fogarty International Center (1981-1982) and director of NHLBI Division of Lung Diseases (1971-1980). . . . **RANDALL TOBIAS** has been named by **President George W. Bush** to the newly created position of coordinator for international HIV/AIDS assistance. The position, which comes with ambassadorial rank, is intended to coordinate U.S. world-wide assistance. . . . **ROBERT CROYLE** has been appointed director of the NCI Division

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NCI, Dialogue Planning A "National" Tissue Bank

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dovetail into the larger NIH agenda to re-engineer our clinical research infrastructure nationwide," he said. "Both the clinical trials process and the clinical trials program is one that will be a major focus of attention in this next year."

The planned review, coupled with other recent actions, has left many chairmen of the 13 NCI-funded clinical trials cooperative groups wondering what von Eschenbach's plans are for future support of their organizations.

In May, NCI officials said there was no money in the Institute's $4.6 billion budget to provide a 3 percent cost-of-living increase promised to the cooperative groups. Overall, the Institute's budget increased this year by 10 percent, or $415 million, during the current year.

The budget for the groups is about $155 million in fiscal 2003, NCI Division of Cancer Treatment and Diagnosis Acting Director Ellen Feigal said to **The Cancer Letter**. Funds may become available later this year from lower-than-expected patient accrual to restore the 3 percent increase, she said.

Meanwhile, von Eschenbach has authorized double-digit increases in four NCI programs. Funding for cancer centers increased 19 percent, from $225 million in fiscal 2002 to $269 million in fiscal 2003. Specialized Programs of Research Excellence saw an increase of 30 percent, from $95 million to $123 million. Funding for NCI training programs increased by 14 percent, and bioinformatics increased by 14 percent.

Leadership of DCTD has been weakened by the lack of a permanent director, which led to an atmosphere in which other programs were able to claim more funds, sources said. Feigal became the acting DCTD director following the departure of Robert Wittes more than a year ago.

Even the tissue banks operated by the cooperative groups will get no new funds, despite strong support for the funding from NCI program staff. Institute officials are working with the National Dialogue on Cancer to develop plans for a "national tissue bank," Anna Barker, NCI deputy director for strategic scientific initiatives, said to the NCI Board of Scientific Advisors at its June 26 meeting.

It's unclear how the cooperative group tissue banks would fit in with the new program

Barker's remarks about the national tissue bank raises questions about the relationship between NCI and the Dialogue. Recently, that relationship became more formal, as the Dialogue became a 501(c)3 organization, and its steering committee became a board of directors. The conversion makes von Eschenbach vice chairman of the board of the Dialogue, and Barker a Dialogue board member.

The meetings of the Dialogue are not open to the public. Though von Eschenbach has maintained that the organization is not advisory to NCI (**The Cancer Letter**, May 16), it may take a court decision to determine whether the Dialogue is being used as a *de facto* advisory committee, lawyers say.

"These are private entities making decisions on public funds, and that's something that ought to be frowned upon, unless it's subjected to public scrutiny and transparency," said Tom Fitton, president of Judicial Watch, a Washington group that challenged the Clinton Administration on adherence to open meeting laws, and is challenging the Bush Administration on the same principles.

The group is suing the Administration over operation of the Energy Task Force, set up by Vice President Dick Cheney. The task force functioned as an advisory committee and should have been subject to open-meeting regulations, Judicial Watch asserts.

"There is nothing to prevent any government officials from seeking outside advice, but if they are

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going about it in a systematic way, if they have committees operating and policy being formulated, that outside advice needs to be given some public scrutiny and made transparent," Fitton said to **The Cancer Letter**. "That's because we are a democracy."

"We Are Going To Have Another Meeting"

Several group chairmen publicly expressed surprise at von Eschenbach's plan for a clinical trials system review.

In the past eight years, the groups have gone through two reviews. The reviews—first, by a committee led by James Armitage, professor and chairman of the Department of Internal Medicine at University of Nebraska Medical Center, then, by an implementation panel of outside experts—resulted in several pilot projects designed to speed the implementation of clinical trials, add more rigor to protocol review, and make trials available to more cancer patients.

The work of these committees has been presented to the NCI Board of Scientific Advisors and the National Cancer Advisory Board. Also, the National Cancer Policy Board of the Institute of Medicine, is working on a report that deals with aspects of the clinical trials system, said Roger Herdman, staff director of the Policy Board. The report is scheduled to be completed later this year. Armitage serves on the IOM committee writing the report.

The report, which will be titled, "Shortening the Timeline for New Cancer Treatments," will examine "ways to realize more efficiently and rapidly the new potential for developing targeted cancer therapies depending on recent advances in genomics and other basic science," according to a summary of the board's work. "It focuses on developing drugs for children, cancer vaccines, tissue resources, the FDA, the NCI, clinical trials, intellectual property, and reporting quality-of-life outcomes in trials."

At the BSA meeting, board member Richard Schilsky, chairman of the Cancer and Leukemia Group B, asked von Eschenbach to elaborate on his plans for yet another review of the clinical trials system.

"We have had several large committees that have undertaken to review that program in the last eight years or so, and it may be premature to ask you what the charge to the group will be, but maybe you could give us a general sense of what the goals are," Schilsky asked.

The clinical trials system remains suboptimal, von Eschenbach said.

"I will probably turn the question around and ask you, in spite of the fact that there have been significant number of reviews in the past eight years with regard to clinical trials, is there general agreement that our clinical trials infrastructure is working, functioning as optimally, as efficiently, as effectively as it should?" von Eschenbach said. "I haven't had anyone tell me that that is so overwhelmingly the case that we need not do any more.

"Until we have a clinical trials program and process that I believe is achieving its greatest impact, output, cost efficiency, and is in fact as effective as you want it to be, and as the community demands and expects it to be, I'm afraid, Rich, we are just going to have to have another meeting," von Eschenbach said.

"It's our responsibility to carry out these programs and be certain we are meeting the needs and expectations of the community," von Eschenbach said. "But we want to do this in concert with you, and with the community. Unfortunately, you specifically. Your name is already on the list. There are others who we are very anxious and want to be a part of this process. I fully intend for us to have milestones and outputs."

"What's The Story Here?"

Cooperative group chairmen have argued for years that their groups work efficiently and as intended when given appropriate funding.

In a famous example, the Southwest Oncology Group in 1990 and 1991 responded to then-NCI Director Samuel Broder's demand to increase patient accrual. The group was on track to double its accrual in 1991, but that effort suddenly created financial problems for the group's operations office and statistical center, which were overwhelmed with data.

Despite pleas from the group, NCI declined to provide additional funding, so SWOG Chairman Charles Coltman Jr. raised $270,000 from pharmaceutical companies and delayed the activation of new protocols so that accrual could "come in for a soft landing," to the group's funded level at the time of about 6,000 (**The Cancer Letter**, Oct. 10, 1997, Vol. 23 No. 39).

Last month, NCI's budget priorities came in for scathing commentary at a meeting of the group chairmen.

"There is always a message in a budget," said Robert Comis, chairman of the Eastern Cooperative Oncology Group and president and chairman of the Coalition of National Cancer Cooperative Groups. "Is the senior leadership basically saying that they don't want this system to survive or thrive? Is the senior leadership basically saying that they don't care about the phase III system? If that's the case, they don't understand it…. What's the story here?"

"I can give you a brief story," answered DCTD Director Feigal at the June 13 meeting. "The groups' budget is being held flat not for lack of advocating for an increase in budget from the division. It's a very high priority. What happened this year is that there were a certain number of funds available. Dr. von Eschenbach had competing priorities being presented to him."

The groups shouldn't get the message that NCI is no longer interested in phase III trials, Feigal said. "There is a commitment to running clinical trials and there is also a realization that if we are going to get to the 2015 goal, we have to get it through conducting clinical trials," she said, referring to von Eschenbach's goal to "eliminate the suffering and death from cancer" by that date.

"So it does seem like a mixed message," Feigal said. "There are going to be some tremendous challenges, but I suppose you can also think of them as opportunities to think of ways to get the important clinical trials done without compromising the system."

In 1998, NCI began what officials said would be a three- to four-year process to close an estimated $70-million funding gap between the amount that peer reviewers say cooperative groups should receive and the amount the Institute actually provides. Then-NCI Director Richard Klausner said that having completed a review of the system, the Institute would make a commitment to "correct the historic under-funding of the clinical trials program" (**The Cancer Letter**, Nov. 13, 1998, Vol. 24 No. 43).

Funding for the groups has increased by $62 million, or 66 percent, from the 1998 level of about $93 million to the current $155 million, Feigal said to **The Cancer Letter**.

During that time, a new group was funded, the American College of Surgeons Oncology Group, and four separate pediatric oncology groups merged to form the Children's Oncology Group.

A new diagnostic imaging group, the American College of Radiology Imaging Network, was started in 1999, but that group's budget is separate from the cooperative group U10 line, Feigal said. The ACRIN base funding was about $2 million in 1999 and $4.2 million in 2003.

Group chairmen say under-funding is still a fact of life for their organizations.

The Children's Oncology Group budget, peer reviewed for about $56 million in fiscal 2003, is expected to receive $29 million from NCI this year, a $27-million shortfall, COG Chairman Gregory Reaman said to **The Cancer Letter**.

"We began as an NCI-sponsored organization, much of what we do is in collaboration with NCI, yet we are expected to find sources of funding outside NCI and the federal government to actually do the work they would like us to do," Reaman said. "I really think there needs to be some special attention to pediatric cancer, and particularly translational research in pediatric cancer, because our plans and efforts to accomplish that through COG have been made nearly impossible with a flat budget."

A group of COG investigators specializing in acute leukemia have submitted an application for a SPORE grant to NCI. "Ninety percent of children with acute leukemia are treated on trials of COG," Reaman said. "COG is uniquely poised to be the cancer center without walls for pediatric acute leukemia."

Most of the groups contribute to research funded through other NCI grants, Comis said. "In ECOG alone, we have 21 R01s that are supported by the tissue bank that basically nurture the national system," he said. The NCI-supported programs are interdependent, and the group system should not be penalized for primarily conducting phase III trials, because the work of the groups contributes to all areas of cancer research, he said.

NCI may be able to restore some or all of the 3 percent increase later this year, Richard Kaplan, chief of the Clinical Investigations Branch in the NCI Cancer Therapy Evaluation Program, said at the meeting of the group chairmen.

The Institute held back a proportion of the budget for patient accrual so that the funds could be distributed as needed throughout the groups, Kaplan said. The groups expect to enroll about 1,000 fewer patients this year than last year, due to the closing of some large studies.

"The other major, major thing we wanted to have funding for was the tissue banks," Kaplan said. "We didn't get money for that this year, despite the fact that Sheila Taube lobbied for it very hard from

the Cancer Diagnosis Program, and we lobbied very hard for it from CTEP. That money has not been forthcoming."

"We are going to try again to get some end-of-year funding specifically for the tissue banking effort," CDB Director Taube said to the group chairmen. "We are also trying to think of more creative and innovative ways to provide stable funding for the tissue bank effort that doesn't get plowed into the cooperative group line, and we will come back to you with those ideas as we develop them."

NCI-NDC National Tissue Bank

At the BSA meeting June 26, NCI's Barker said the national tissue bank concept "is a collaborative effort between the NCI and the National Dialogue on Cancer."

The group in charge of developing the concept is co-chaired by Paula Kim, president of the Pancreatic Cancer Action Network, and Jeffrey Trent, director of the Division of Intramural Research in the National Human Genome Research Institute.

A "national" tissue bank is needed, because most tissues currently are not collected or stored in a manner compatible with genomic analysis, Barker said at a June 26 meeting of the NCI Board of Scientific Advisors. Also, existing tissue banks have "ownership barriers" that impede tissue sharing among researchers, she said.

Barker said additional details would be presented to BSA in the fall.

"At a recent meeting of the cooperative group chairs, we were told there would be no additional funds for cooperative group tissue banking activities, despite strong advocacy for those funds from some members of NCI staff," CALGB Chairman Schilsky asked. "I'm curious as to how that reconciles with your view of the importance of tissue acquisition, and if it's not going to be through the cooperative group mechanism, where we obtain the most highly annotated specimens, what do you view as the better mechanism?"

BARKER: It's not clear yet where the resources for this would come from, but it likely would not be funded solely through the NCI. It would probably be funded, and would have a governance structure that would involve national agencies. I suspect we would be the lead in that.

Legacy systems would continue. This would be a new resource just for this issue of genomics and proteomics that we are trying to underpin. It's a challenge to fund these resources.

SCHILSKY: I'm sure you are aware that the clinical specimens are almost useless by themselves without annotation data, so you need to obtain the specimens in the context of well-annotated clinical data.

BARKER: That is the sole objective of this whole resource, is to collect and annotate specimens, as well as to underpin it with technology. We would see this through a virtual network using a lot of our current resources, but working on a common set of standards.

FREDERICK APPELBAUM, BSA CHAIRMAN: Is the view that this would look more like Napster [the peer-to-peer file sharing software]?

BARKER: I think, probably. It's in process. The business model needs to be worked out.

"Coke vs. Pepsi"

Von Eschenbach doesn't appear to favor the cooperative groups.

Associates say they have come to expect the NCI director to say "Coke vs. Pepsi" when he hears about group trials comparing cancer therapies.

Two weeks ago, von Eschenbach, a urologist and a prostate cancer survivor, passed up the opportunity to address a nationally covered press conference announcing the results of the Prostate Cancer Prevention Trial, led by the Southwest Oncology Group. Only minor shuffling of schedules and a short cab ride would have been required for von Eschenbach to speak at that event (**The Cancer Letter**, June 27).

Von Eschenbach's predecessors have used such press conferences to affirm the capability of clinical trials to improve health care.

"Coke vs. Pepsi is total misrepresentation of the system," said a group chairman, who spoke on condition that his name would not be used.

The trials of high-dose chemotherapy and bone marrow transplantation were of greater significance than a soft drink taste test. Those trials ended a highly toxic, expensive, and ineffective treatment, the group chairman said. The PCPT results were not trivial, either. The trial established the proof of principle that prostate cancer can be prevented, raised questions about the value of screening with the Prostate Specific Antigen test, and established vast banks of pathology samples for future research.

Given von Eschenbach's ties to the Dialogue, it may be useful to consider the Dialogue's vision of

NCI.

That vision—described in the bill by the Dialogue vice chairman, Sen. Dianne Feinstein (D-Calif.)—establishes cancer centers as the foundation of the new cancer plan. The centers would be enhanced, geographically distributed, and linked to the pharmaceutical industry and to the public health functions coordinated by Centers for Disease Control and Prevention.

The legislation states that the centers would be involved, together with cooperative groups, in all phases of clinical research. Currently, centers do not conduct phase III trials (**The Cancer Letter**, June 13).

Unlike cancer centers, which are formidable brick-and-mortar structures that appeal to civic pride, the groups are elusive voluntary associations of physicians and scientists involved in clinical research.

Yet, in the coming battles, the groups are likely to demonstrate that their willingness to resist is greatly underestimated, while the Institute is bound to learn—once again—that its power has limits, cooperative group leaders and legal experts said.

A decade ago, the fight over the National Surgical Adjuvant Breast and Bowel Project resulted in Congressional hearings, damage to distinguished careers, public confusion, lawsuits, and—ultimately—a financial settlement from the Institute.

"Tread carefully. That, to me, is the major lesson of NSABP," said Robert Charrow, an attorney with the Washington law firm of Greenberg Traurig, who represented former NSABP Chairman Bernard Fisher in a suit against NCI. "Tread carefully, and think strategically. At the time, NCI did neither."

Chairmen of several groups said they would fight back. "NCI would be making a big mistake," said one group chairman. Another group chairman said he is waiting for NCI to put all the cards on the table. "We need to hear from them what they have in mind, and have a chance to promote our cause and our case," he said.

"I am confident that the cooperative groups are developing a broad-based Washington strategy," said John Engel, an attorney with the law firm of Engel & Novitt, who represented NSABP eight years ago. "By the same token, I would anticipate that the NIH legal advisor's office is seriously evaluating the legal and regulatory ramifications of any effort to undermine, much less eliminate, the groups or their independence."

Group chairmen know that their data are valuable. With genomic analysis, even data and pathology samples obtained decades ago provide insight on a variety of tumors.

"The groups will do everything they can to retain the possession of the pathology specimens, that have been collected as part of cooperative group trials, and that are central to the research mission of the groups," a group chairman said.

If the Institute managed to gain control of the groups' data and tissue banks, it would have to turn around and build another structure that would perform the same functions as the groups.

"There is no other government-funded system that can do or has done randomized, definitive phase III trials," a group chairman said. "Our national network puts 20,000 to 25,000 patients on study a year, has a 150,000 patients in follow-up, and is recognized everywhere outside NCI as one of the treasures of cancer research in the world."

The Institute has heralded the accomplishments of the groups whenever this serves its needs, maintaining a 134-page document listing the group studies initiated between 1986 and 2001: http://ctep.cancer.gov/forms/accomplish2.doc.

The complexity of the groups may be their greatest strategic asset, attorney Engel said. "The databases and tissue banks that have been disparagingly referred to as 'legacy systems' are safe from attacks," he said. "The law and the policies that have governed the cooperative groups for decades are unambiguous. The data and the tissue samples belong to the groups. Indeed, in its guidelines on industry collaboration with the groups, NCI expressly eschews any attempt at control over these fundamental research resources."

NCI will face legal challenges on three levels, Engel said. The cooperative groups, the institutions holding the grants, and individual researchers could file legal actions.

Often, the groups' biostatistical center, administrative offices and tissue banks are located in different institutions, which could mean a multitude of suits.

"If the government—NCI or any third party—tried to get control of the tissues, the only way the tissues would be of any value would be if they were accompanied by the clinical data, which would require that the control be wrested from more than one institution," a group chairman said. "It would be enormously complicated, and cumbersome, and unpleasant."

Also, many researchers at cancer centers are staunch allies of the groups. Many enroll patients in group trials in order to provide state of the art treatment, advancing science and their own academic careers. Will these scientists behave as cancer center constituents, or as leaders of the cooperative groups? Will the patients come to the aid of clinical researchers? Will the national press and Congress get involved?

Ultimately, everyone stands to lose if the groups are damaged, a group chairman said.

"The damage to cancer research would be enormous and irreparable, because the specimens that are collected in cooperative group repositories are the highest quality research specimens that we have available in this country, because they are collected in the context of clinical trials, they are all completely annotated, and accompanied by clinical outcomes," he said.

"If these repositories were destroyed or scattered to the four winds, we would lose an extraordinary resource."

Group Chairmen Point To NCI As Source Of Problems

The leaders of the cooperative groups point to NCI as the cause of many of their most persistent problems.

The Institute reserves the right to approve every study, makes it difficult for the groups to shift funds among budget categories, and prevents the groups from setting per-case reimbursement fees for accrual.

Currently, investigators are paid about $2,000 for every patient accrued, about a third of the fees paid by pharmaceutical companies.

"If we want to get the questions answered quickly, we have the flexibility to increase the per-case reimbursement, but it will be at the expense of something else," Ellen Feigal, acting director of the NCI Division of Cancer Treatment and Diagnosis, said June 13 at the meeting of the cooperative group chairmen. "My sense is the mission is not to accrue as many patients as possible. It's to answer the critical questions quickly."

CALGB Chairman Richard Schilsky said the lack of funding will drive investigators and their institutions away from the groups. "I suspect if the per-case reimbursement is not increased, that we actually will see a progressive downturn in accrual," he said. "Accrual is already way down in 2002. It's not looking much better in 2003.

"I think our institutions are completely demoralized by the consistent flat-funding of the cooperative group system at time when their expenses are going up," Schilsky said. "They are turning more and more to industry studies, of which there are many more available, some of which include agents that are not available through the cooperative groups, and considerably more interesting.

"Unless the per-case reimbursement comes up—it will never come up to a level that will adequately cover our costs—but if it doesn't come up as an indication that the Cancer Institute is serious about supporting clinical trials, we are just going to see institutions flocking to other sources of studies," Schilsky said.

Last year, CALGB proposed a per-case reimbursement of $3,600 for its trials, but NCI program staff opposed the plan, saying reimbursement had to be the same across the group system, Schilsky said.

"We do need to be equitable across the system," Cancer Therapy Evaluation Program Director Michaele Christian said. "We need a global way of addressing this problem. We have gone forward every year requesting $3,000 or $3,500, and we have the dollars that we have."

NCI is interested "in looking at how we can better integrate clinical trials resources, including work being done in the SPOREs and the centers," Christian said.

Richard Kaplan, chief of the NCI Clinical Investigations Branch, said the low reimbursement may not have been the reason for declining accrual.

"If you really analyze what's happened to our accruals, it's the closure of some big breast and colon studies," Kaplan said. "There are some very attractive studies that are about to come online. I think that we will probably do quite a bit better in accrual next year, which means the budgetary crunch is more critical."

Schilsky said industry trials are looking more interesting to group members.

"I don't disagree with that analysis, but while there have been a number of gaps in the cooperative group portfolio, there also have been a number of industry trials that have come online in the same patient populations that have captured people's attention, both because the trials are available while the groups haven't had trials, and because they are paying two and three times the rate," Schilsky said. "A lot of institutions have committed to the industry

trials, and we may not see an immediate impact on the new cooperative group trials coming on."

If the groups want to increase per-case reimbursement, they will have to develop some method of prioritizing their trials, Feigal said.

"What people aren't willing to do at the leadership end is have an open-ended commitment," Feigal said. "Because, presumably, an increase in reimbursement will increase your accrual, which will increase the budget."

Besides, having a list of important studies that can't be funded is a compelling argument for funding, Christian said.

"I personally think that the strongest argument we can make is to go forward with important questions—questions that we all agree are important—that we are not able to address because of limitations of accrual," Christian said.

If NCI declines to support an across-the-board increase on capitation, the Institute should consider allowing rates to be set at a higher level for studies deemed to be the most important, or technically complex, Schilsky said

"We have been paying the same rate for every treatment study, regardless, which is basically what we have been told to do," Schilsky said. "But obviously, there are some studies that are higher priority, asking more important questions, than others, that all of us can identify in our groups. If those are the studies we really want to get accrued, nothing stimulates accrual like money."

Kaplan agreed. "We have always felt we would like to have some sort of sliding scale in terms of capitation, but we didn't have a truly national system of equal access of patients to those trials, and we now do," he said. "That's the reason why it wouldn't be an acceptable solution for just CALGB to capitate its members for $3,000 for the same study that other people could access, but only at $2,000 within their group.

"We have committed to the principle that trials that are highly important need to be available to everybody, and that means that we need to have a system that can capitate them evenly across the country," Kaplan said. "I think that can be done. I think there are ways we can raise the capitation consistently across the country, if we make some hard decisions on prioritization, and among those, if we could make some relative value decisions on a national basis, as well."

Cooperative group protocols must be approved by CTEP's Concept Review Committee, comprised of NCI staff. Kaplan presented a proposal for assignment of priority scores to protocols. Also, he proposed the addition of two external reviewers and a patient representative to the committee. The protocols would be reviewed for "clinical significance," "scientific innovation," and "approach."

Protocols Already Prioritized, Groups Say

Group chairmen pointed out that their organ site committees review all protocols before sending them to NCI for approval.

Bruce Hillman, chairman of the American College of Radiology Imaging Network, said the proposal seemed like "an attempt to move decisions more centrally."

Jan Buckner, chairman of the North Central Cancer Treatment Group, said the addition of reviewers may slow the protocol review process. "One of the criticisms now is the slowness with which trials are put in place," Buckner said. "In our experience with protocol development, the more people we bring in, the slower it goes."

"We will find reviewers who can meet our timeline," Christian said.

"I don't think the groups just scribble down ideas and send them in," Schilsky said. "We can probably do a more stringent review to ensure that we only send the best concepts forward. We all need to exercise a greater degree of rigor."

"I really think this would be demoralizing," said Philip DiSaia, chairman of the Gynecologic Oncology Group. "Why do we need this? Why do we need another layer?"

"It's not a new level of oversight," Kaplan said. "All we are doing to change the system is adding a few people who will probably come from the groups themselves."

Groups conduct "a number of trials that are keeping the engine running" until new agents or better ideas come along, Kaplan said. "'There isn't a better idea at this time' is not an argument to do a trial. This system is so strained that we shouldn't be paying for those trials."

Gregory Reaman, chairman of the Children's Oncology Group, said his group is "increasingly frustrated that we can't do some studies," due to budget constraints.

"We do prioritize our trials," Reaman said to **The Cancer Letter**. "They are all high priority, but we recognize that some are more high priority than

others. Given our limited resources, we have concluded that we can't do some studies in relatively rare pediatric cancers, or in pediatric cancers where the outcome is already very good, because our priority has to be on high-risk cancers or reducing the impact of long-term effects of treatment."

COG, formed by the recent merger of four pediatric oncology groups, has gone through a process of becoming more efficient, Reaman said.

"We recognized that we could gain some economies of scale and become more efficient by eliminating duplication and sacrificing some of the healthy competition," Reaman said. "We have gone through a time of difficult rebuilding, but we feel strongly that we can operate as a lean and mean machine."

Sam Wells, chairman of the American College of Surgeons Oncology Group, said group chairmen are operating in a time of uncertainty, which makes them all feel nervous about the NCI clinical trials system review, as well as the pilot project establishing the Cancer Trials Support Unit, a centralized system for phase III trial support and accrual.

"ACOSOG is the newest group, started in 1998, and we are just getting off the ground, so we feel equally if not more nervous than the other groups," Wells said.

"I think this happening in concert with the CTSU has created some apprehension about how the groups are going to be operated and how they are going to be operated in the future," Wells said.

The Institute's budgetary problems are going to get worse, NCI officials said to the group chairmen.

The Institute is expecting smaller increases over the next several years, based on the Bush Administration's budget proposal for fiscal 2004 for a 3 percent increase for NCI.

"One of the main issues that's coming out is prioritization of the questions being asked across the large clinical trials system," Feigal said to the group chairmen.

"I think that since the purse is not going to increase, there is going to have to be some serious work, working together," Feigal said. "This isn't an us-versus-you situation. We are all in this together. This is the engine for phase III clinical trials.

"The cancer centers and SPOREs are components of a much larger system which conduct the early phase, but it's really the cooperative groups that the conduct the multicenter phase III clinical trials," Feigal said.

NCI News:

Cancer.gov Web Site Knocked Offline By Network Router Theft

Computer equipment at an NIH off-campus building at 6116 Executive Boulevard, in Rockville, Md., was stolen earlier this week, causing a network outage to the building and disrupting NCI's Web site for most of a day.

NIH employees discovered that the equipment was missing the morning of July 9.

The stolen equipment was described by Montgomery County police as network routers, worth about $7,500 each.

It had not been determined how many routers were stolen, a police spokesman said.

The NCI Web site, www.cancer.gov, hosted on one of the routers, was offline for most of the day, sources at the Institute said.

An NCI spokesman said Institute officials could not discuss the theft or its impact on the Web site.

"Because this is an ongoing investigation by the Montgomery County police, we can't say anything about it," said Peggy Vaughn, of the NCI Mass Media Office.

Cancer.gov is a popular Web site. The site had 383,000 page views during April, the most recent month for which data is available, Vaughn said.

No Off-Site Back Up?

NCI's Office of Communications does not have emergency procedures in place for Cancer.gov, such as off-site back up, a source at the Institute said to **The Cancer Letter**.

"It is 'tech 101' practice to have an off-site back up for major Web sites for just these types of events," the source said.

County police are investigating the theft, Officer Joyce Utter said. A Wells Fargo bank in the same building was broken into at the same time and a computer scanner was stolen, she said.

"No personal information could be obtained from these routers," Utter said.

The routers, taken from various floors of the building, did not store information, she said.

Building 6116 houses the NCI Cancer Information Products and Systems Program and its Information Management Branch, which is responsible for the NCI Web site. The Cancer Information Service offices also are located at the building.

Six Cancer Centers Win Grants To Study Barriers To Trials

NIH has awarded grants to six cancer centers for research on overcoming barriers to early phase clinical trials.

The grants are funded through a partnership between the Friends of Cancer Research, NCI, the Foundation for the National Institutes of Health, and five pharmaceutical companies: Aventis, Bristol-Myers Squibb, Eli Lilly and Co., GlaxoSmithKline and Novartis.

NCI provided $3 million to fund the grants. The companies provided $2.7 million.

Institutions receiving funding include: Massachusetts General Hospital, University of Colorado Health Sciences Center, Washington University, St. Louis, University of Pittsburgh Cancer Institute, University of California, Davis Cancer Center and Ohio State University Comprehensive Cancer Center.

HHS News:

PHS Commissioned Corps To Be "Revitalized," HHS Says

HHS officials said they plan to expand and strengthen the Public Health Service Commissioned Corps by recruiting more health care professionals and better preparing those professionals to respond to emergency health needs around the country.

The Commissioned Corps, begun in 1889, needs revitalization to become a more effective medical health unit, HHS officials said.

The revitalization aims to create a flexible and "truly deployable" force that is ready to respond to public health and emergency needs across the country or around the world, HHS said.

"This is an exciting time for the Public Health Service Commissioned Corps," U.S. Surgeon General and Commander of the Commissioned Corps Richard Carmona said. "This first step will lead to a stronger and more versatile corps that will be able to respond to any public health emergency."

As part of the transformation, the Commissioned Corps will:

—Create scholarships to recruit 1,000 nurses and 100 doctors per year to work in medically underserved areas.

—Identify PHS officers who can assist in reducing staffing shortages in clinical settings in the Indian Health Service and the National Health Service Corps, as well as assist with President Bush's plan to increase Community Health Center capacities throughout the nation.

—Recruit at least 275 new officers to support the IHS by Sept. 30, 2004.

—Improve and expand training and deployability of PHS officers into areas where primary care services are lacking.

—Phase out the existing Commissioned Corps Readiness Force structure, and replace it with a revised system designed to bring the status of the Commissioned Corps to 100 percent deployability by the end of 2005.

—Create additional short term duty missions and "rolling deployments" to address Presidential and Secretarial initiatives directed toward serving critical needs through the use of active duty and reserve officers who will be called to temporary active duty.

—Provide a modernized reserve component system that can marshal resources for deployment at the local level for needed public health initiatives.

—Establish a ready reserve corps that will supplement the efforts of the Commissioned Corps.

—Open new opportunities for registered nurses and other credentialed health personnel who hold an associate degree and appropriate credentials.

* * *

Food Labels to Include Trans Fat Contents: Food labels will be required to list the amount of trans fatty acids, or trans fat, to give consumers better information when choosing their foods, HHS said.

The new requirement through FDA will mean that manufacturers of most conventional foods and some dietary supplements will have to list in the Nutrition Facts panel the trans fat content of the product, in addition to the information about its overall fat content and saturated fat content.

Trans fat, saturated fat, and cholesterol are associated with an increased risk of heart disease.

Under the new FDA regulations, by Jan. 1, 2006, consumers will be able to find trans fat listed on food nutrition labels directly under the line for saturated fat. The new information is the first significant change on the Nutrition Facts panel since 1993.

Trans fat occurs in foods when manufacturers use hydrogenation. Also, dietary supplement manufacturers will need to list trans fat, saturated fat, and cholesterol, on the Supplement Facts panel when their products contain more than trace amounts (0.5 gram) of trans fat.

Funding Opportunities:

Lymphoma Research Foundation Grants

Two-Year Fellowships*:* $105,000

Deadline: Sept. 15, 2003

The fellowship encourages applicants to pursue careers in lymphoma basic, translational and clinical research. Research can be laboratory or clinic based, but the results and conclusions must be relevant to the treatment of lymphoma.

Three-Year Clinical Investigator Career Development Award*:* $225,000

Deadline: Sept. 15, 2003

The 3-year grant funds training clinicians to design and administer clinical studies in lymphoma and to take on the primary responsibilities for clinical trial design, protocol writing, Institutional Review Board submission, and publication. The grant provides support to spend at least half of their time implementing clinical studies in lymphoma. A Career Development Plan is required as part of the grant application. Applications and further information may be downloaded from www.lymphoma.org or email: researchgrants@lymphoma.org.

Inquiries: Lymphoma Research Foundation, 111 Broadway; 19th Floor; New York, NY 10006, phone 212-349-2910; Fax 212-349-2886.

NCI Program Announcements

PAR-03-149: Established Investigator Award in Cancer Prevention, Control, Behavioral, and Population Sciences

The award, part of the NCI Strategic Training Plan, provides investigators protected time for their research and to mentor new investigators and junior faculty members. Examples of disciplines relevant to this PAR include any aspect of human cancer prevention (health promotion, modifiable risk factors, new animal models and extrapolation of these models to human cancer, genetic predisposition to cancer, detection of precursor lesions, chemoprevention trials in human populations, behavioral research and behavioral intervention trials), epidemiology (classic, genetic, molecular), biostatistics, human cancer genetics, human nutrition, health services and health policy research, medical decision analysis, survivorship and quality of life as they relate to cancer, and basic and applied research in the behavioral sciences that independently or in combination with biomedical approaches, reduces cancer risk, incidence, morbidity, and mortality over the lifespan and across the entire process of carcinogenesis from primary behavioral prevention in youth, to screening, treatment, and survivorship.

The PAR will use the NIH K05 award mechanism. The Established Investigator Award in Cancer Prevention, Control, Behavioral and Population Research is a special NCI modification of the NIH Senior Scientist Award or K05 grant mechanism. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PAR-03-149.html.

Inquiries: Maria Agelli, Cancer Training Branch, NCI, Bldg. 6116, Rm 7021, Bethesda, MD 20892, Rockville, MD 20852 (express courier), phone 301-496-8580; fax 301-402-4472; e-mail ma215e@nih.gov

PA-03-147: Age-Related Changes in Tissue Function: Underlying Biological Mechanism

The PA will consider projects that have a clear relevance to aging and encourage those which focus on molecular aspects, as well as cellular aspects of tissue aging. Projects that emphasize molecular and cellular changes that are common among tissues with aging are also encouraged, as are projects that compare mechanisms of aging change in different tissues.

NCI is interested the similarities and differences in the aging stroma and the stroma associated with malignant epithelial cells both in early and later stages of the malignancy. Within the context of changes in tissue with age that lead to, or are permissive of tumorigenesis, areas that are of interest to NCI include: the extracellular matrix and cell adhesion molecules, properties or behavior of stroma of various tissues such as the breast, prostate, brain, gastrointestinal tract, bone etc., aberrant expression of growth factors and/or their receptors in the stroma, altered expression of protease as well as tissue inhibitors of proteases, response of aging/premalignant stroma to hormonal regulation, and changes in the migratory properties of epithelial or stromal cells.

The PA will use the NIH R01 award mechanism. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-03-147.html.

Inquiries: For NCI— Suresh Mohla, chief, Tumor Biology and Metastasis Branch, Division of Cancer Biology, NCI, NIH, DHHS EPN, Suite 5000, Bethesda, MD 20892, phone 301-435-1878; fax 301-480-0864; e-mail mohlas@mail.nih.gov.

In Brief:

Croyle Named DCCPS Director; Stiff To Direct Loyola Center

(Continued from page 1)

of Cancer Control and Population Sciences. He has been acting division director since November 2002, and is former associate director of the division for behavioral research. . . . **PATRICK STIFF** was named director of the Loyola Cardinal Bernardin Cancer Center. Stiff is a professor in the Department of Medicine, division of hematology/oncology at the center. He served as director of the Bone Marrow Transplant Program at Loyola University Health System since 1986, said **Stephen Slogoff**, dean, Stritch School of Medicine. The center also named **Brian Nickoloff** to the position of deputy director, and director of the Loyola University Chicago Stritch School of Medicine Oncology Institute, which oversees research at the CBCC. He is professor and vice chair, Department of Pathology. . . . **LOMBARDI Cancer Center** at Georgetown University received a $7 million Department of Defense grant to establish a multi-institution Breast Cancer Center of Excellence. The center, which will be looking at the relationship between alcohol and breast cancer risk, will be lead by Lombardi researchers working with investigators at the State University of New York, at Buffalo, NCI, the Washington Hospital Center and Catholic University. **Peter Shields**, professor of medicine and director of cancer genetics and epidemiology at GUMC, is the principal investigator. The center will use both experimental and epidemiology studies, looking at Caucasian and African-American women, some with cancer and some without for the epidemiological studies. Experts in cancer, epidemiology, basic science, biomarkers, biostatistics, radiology, medical oncology, and transgenic models will collaborate in the research study. . . . **RICHARD CHENEY** was appointed chairman of the Department of Pathology & Laboratory Medicine at Roswell Park. Cheney has been interim chairman since March 2002. . . . **LANGDON MILLER** has joined PTC Therapeutics as chief medical officer. He was vice president of global clinical research in oncology at Pharmacia Corp. He will be responsible for establishing and managing the PTC clinical development programs in genetic disorders, oncology and infectious diseases. Miller developed and led numerous clinical research programs, including those culminating in the successful registration of epirubicinin as adjuvant therapy for early breast cancer and irinotecan as first-line therapy for metastatic colorectal cancer. Miller was primary or senior author of eight new drug applications and led six presentations before the FDA Oncologic Drugs Advisory Committee. Miller was a senior investigator at NCI. . . . **LANCE ARMSTRONG**, a member of the President's Cancer Panel and Tour de France champion, is collaborating with Bristol-Myers Squibb for a 3000 mile cross-country journey from Oct. 11-18. During the week-long Tour of Hope, Armstrong will lead 20 cyclists on an mission of public cancer education. His fellow cyclists will include nurses, physicians, survivors, caregivers and researchers. The Tour will begin in Los Angeles and end in Washington, D.C. Further information is available at www.tourofhope.org. . . . **SIDNEY KIMMEL** Cancer Research Scholars ere recognized with a grant of $200,000 from the Sidney Kimmel Cancer Foundation. A list of awardees is available at www.upci.upmc.edu/internet/news/upci_news/2000/050300_kimmel_award.html. . . . **THOMAS JEFFERSON UNIVERSITY** announced two appointments. **Steven McKenzie** was named vice president for science policy and technology transfer. McKenzie, professor of medicine and pediatrics at Jefferson Medical College, is director of the Cardeza Foundation for Hematologic Research and the Division of Hematology at Jefferson Medical College. He is also a member of Jefferson's Kimmel Cancer Center. **James Keen** has been named dean of the Jefferson College of Graduate Studies. Keen is professor of microbiology and immunology at Jefferson Medical College and associate director of the Kimmel Cancer Center. He succeeds **Jussi Saukkonen**, who is retiring later this year. Both appointments are effective July 1. . . **INTERNATIONAL Cancer Research Portfolio,** an on-line database, has become available at www.cancerportfolio.org. The ICRP contains details of cancer research funded by NCI and the U.K. National Cancer Research Institute member organizations. The ICRP holds 13,000 records, providing information on the funding organization, awardee institution, principal investigator, and research abstract. . . . **CORRECTION**: In the In Brief section of the June 21 issue of **The Cancer Letter**, one of the funding sources for the Roswell Park Cancer Institute's $1.6 million tobacco grant should have been listed as the American Legacy Foundation.

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