THE CANCER LETTER

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NCI News

Needed Enhancement or Unfunded Mandate? New NCI Program to Merge CCOP, NCCCP

By Paul Goldberg

NCI is combining the programs it uses to engage community oncologists and hospitals.

The institute is merging the NCI Community Cancer Centers Program, the Community Clinical Oncology Program, and the Minority CCOP.

The new entity, which will be called the NCI Community Oncology Research Program, or N-CORP, is expected to be in operation in 2014. It will be housed in the Division of Cancer Prevention, institute officials say.

If all goes well, the consolidation could enable a community oncologist to enroll patients in clinical trials, collaborate with tumor registries at a cancer center a thousand miles away, and participate in health services research.

If things go badly, the new system will create unfunded mandates, driving away doctors by asking them to do more at a time when they are facing significant economic pressures on many fronts.

(Continued to page 2)

Cancer Centers

University of Kansas Cancer Center Receives NCI Center Designation

The University of Kansas Cancer Center was designated as a NCI cancer center.

NCI recommended the cancer center for the designation at a June 25 meeting in Bethesda, Md., endorsing a nearly decade-long effort by the center.

"The National Cancer Institute has recognized our scientific excellence, and the designation validates what we already knew—that research conducted at The University of Kansas Cancer Center is already helping to eliminate the burden of cancer," said Roy Jensen, the center's director.

(Continued to page 10)

FDA News

President Obama Signs User Fee Act Into Law

By Matthew Bin Han Ong

President Barack Obama signed the FDA Safety and Innovation Act July 9—enabling the FDA to collect about $6.4 billion in user fees over the next five years and expedite drug review and development.

The new law includes the Prescription Drug User Fee Act, or PDUFA V—the fourth reauthorization of FDA's user fee program. The Congressional Budget Office predicts FDA will collect $4.068 billion in prescription drug application fees over the next five fiscal years.

(Continued to page 5)

NCI Faces Challenge of Fusing Two Very Different Programs

(Continued from page 1)

Though they were designed to serve community oncologists, CCOP and NCCCP are very different, which makes fusing them a difficult task:

• Designed nearly three decades ago to boost accrual to clinical trials, CCOPs are proven to do just that, contributing over 12,000 patients—a third of the overall accrual—to NCI-sponsored clinical trials. The program, which spent $85.8 million in 2011, is administered through DCP. CCOP grantees usually match their NCI funds dollar for dollar.

• NCCCP was designed in 2009 with the broader—and critics say, more nebulous—goal of improving the quality of cancer care and broadening the reach of cancer research. NCCCP originally served 16 sites nationwide. After an infusion of money through the American Reconstruction and Recovery Act—a total of $75.7 million in fiscal 2009 and 2010—the number of sites went up to 30. Now, the program has been trimmed to 21 sites, and NCI officials said its 2012 current budget figures were unavailable. Often, the hospitals that take part in this program spend three for every one dollar they receive from NCI.

NCCCP is a legacy project of former NCI Director John Niederhuber, who chose to bypass review by the institute's advisors, instead funding the program as a subcontract of SAIC-Frederick. NCI Directors Niederhuber, Andrew von Eschenbach and Richard Klausner used the massive contract with SAIC to shield hundreds of millions of dollars worth of pet projects from being challenged by reviewers.

The mandate to merge CCOP and NCCCP came from the office of NCI Director Harold Varmus, and the project is overseen by Deputy Director Douglas Lowy, sources said.

The merger, once it's completed in 2014, would take NCCCP out of the protected cocoon of SAIC and place it into DCP, where the combined program will be headed by Worta McCaskill-Stevens, program director and acting chief of NCI's Community Clinical Oncology Program.

Now, NCI is conducting conference calls with stakeholders to help fuse the programs.

"The physicians come to the CCOP program with clear intention of accruing patients onto clinical trials, because that has immediate relevance to their practice," said Lori Minasian, DCP deputy director. "I think it's important that people look at the criteria for the new program and not require multiple additional other requirements without funds that are outside the scope of a practicing physician."

Many oncology insiders—those who favor the merger and those who are worried about it—note that change comes at a time when many community oncologists are assessing how much longer they would be able to remain independent practitioners. Profit margins in healthcare organizations have become so thin that additional unfunded mandates cannot be sustained, many insiders say.

Niederhuber, who was widely criticized for creating NCCCP outside standard peer review (see story on p. 5), said the merger indicates that his program was useful after all.

"It's certainly gratifying to know that the NCCCP program, which began as an experiment to see if we could bring clinical research and the latest cancer therapies closer to where more patients live, is today becoming part of the fabric of the National Cancer Institute," said Niederhuber, now CEO of the Inova Translational Medicine Institute at the Fairfax Hospital in Northern Virginia. "The true beneficiaries of this program are cancer patients: those who will receive outstanding care and those who will benefit from a more robust national cancer research system. I am grateful that Harold Varmus understands the strengths of the NCCCP and CCOP programs and that he has found a way to unite and strengthen both of them."

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CCOPs Budget (in thousands of dollars)

	CCOPs		Research Base		Subtotal		Minority CCOPs		Total	
FY	*Number*	*Amount*	*Number*	*Amount*	*Number*	*Amount*	*Number*	*Amount*	*Number*	*Amount*
2007	49	$34,891	13	$26,275	59	$61,166	14	$6,249	72	$67,415
2008	47	$39,200	13	$23,363	59	$62,563	13	$8,126	72	$70,689
2009	47	$39,165	12	$29,049	59	$68,214	14	$8,108	72	$76,322
2010	47	$37,150	12	$34,673	59	$71,823	16	$8,215	72	$80,038
2011	48	$39,152	13	$38,117	59	$77,269	16	$8,531	72	$85,800

Fear of Doing Less With More

In conversations with The Cancer Letter, the NCCCP grantees were more upbeat about the merger than CCOP constituents.

"Being a successful CCOP and being one of the original 14 NCCCPs, I can tell you that the scientific process of N-CORP will be a good thing," said Nicholas Petrelli. the Bank of America-endowed medical director of the Helen F. Graham Cancer Center at Christiana Care Health System of Wilmington, Del.

"Having done this from 2007 with NCCCP, I can tell you that one of the main differences, if not the main difference, between a CCOP and NCCCP is that NCCCP is a true network that shares best practices, allowing the institutions in the network to improve patient care throughout the continuum of care. CCOP's main priority is accrual to clinical trials," Petrelli said. "If you put a program together like N-CORP, where there is going to be a focus on the entire cancer continuum, this is going to be a very successful program."

CCOP grantees say they want to see the details before they start dancing in the streets.

"The problem is, you cannot keep adding more and more to be done with less and less," said Gary Morrow, director of a CCOP research base at the University of Rochester Wilmot Cancer Center.

Recently, Morrow, took part in an NCI conference call about the merger.

"It was not clear from what was presented to us that there was going to be balanced funding or balanced support for what appeared to be new requirements," Morrow said.

The money has to make sense to enable CCOP investigators to stay engaged. "The CCOP program works, because it has people who are dedicated to and interested in patient-generated research," Morrow said. "They are genuinely interested in advancing their field. A large number of CCOP affiliates either came from academia or were trained at NCI, and for one reason or another—in many cases, having to do with putting their kids through college—they went into private practice. They by-and-large are doing a lot of this out of conviction that the research and the science help move patient care and help move their profession forward.

"It's a unique group of very dedicated people that, frankly, I am privileged to work with."

Kremlinologists may note that it's not CCOP that's moving to the NCI Director's Office, where it would be overseen by SAIC staff. The opposite is the case: the merger will require NCCCP to move to DCP, where it will be combined with a popular, significantly larger program and subjected to ongoing, rigorous review.

NCCCP Budget (in thousands of dollars)

FY	Funding
2009	$7,235
2010	$5,263
2009/10 ARRA	*$75,671*
2011	$748

Though the N-CORP budget hasn't been announced, it will likely be lower than the sum of the CCOP and NCCCP budgets, insiders say. In part, this will be achieved from the increased efficiency from combining the two programs, sources said.

Changes envisioned by NCI will likely be significant. Doctors and hospitals that join N-CORPS will be expected to work on one of three levels, with amounts of NCI money going up as levels increase.

NCI officials say that some CCOP sites and some NCCCP sites would be able to hit the ground running and compete for designations.

"The CCOPs have a track record of successful performance in areas that play to their strength," said Barnett Kramer, director of the NCI Division of Cancer Prevention. "The intent is to build on those strengths.

"We have internally had intensive discussions, because we intend to develop a path to success for groups that have had their success in clinical trials, and now are going to attempt to branch out into other areas of research."

Though funding would depend on the level of research in which the new organizations engage, NCI will not expect all organizations to try to rise to the top level. "I am thinking that most, if not all, CCOPs should be able to succeed on at least one of the levels," Kramer said. "And each of the levels is stable. It's not as though you need to come in at Level 1, and you if don't successfully achieve Level 2 you will be dropped.

"Successful centers at Level 1 can be very stable and stay at Level 1. You don't need to move up. It's not like a farm team, where you are dropped if you don't make it to the next level.

McCaskill-Stevens said she has been assured by the administration that the clinical trials infrastructure will sustain these programs.

"In fact, having the various levels of eligibility gives a better assurance that we are not going to lose sites. Many sites are being bought up by hospitals. We have had examples within the CCOP program of sites having to consolidate," McCaskill-Stevens said to The Cancer Letter. The CCOPs are not going to go away."

Three Levels of N-CORP

A document describing the three levels was recently distributed to a limited number of participants in an NCI conference call, and was obtained by The Cancer Letter.

The institute's description of requirements for the three levels follows:

• A Level 1 site will participate in and support the NCI research agenda by conducting a range of clinical research, including cancer multi-modality treatment trials treatment and cancer control trials; epidemiology or case-control studies, across the cancer continuum, ranging from prevention, early detection, treatment, survivorship, and end-of-life research. The site will also participate in a co-investment arrangement with NCI, have an existing research infrastructure supporting NCI clinical trials, and a documented disparities commitment reflected by a practice that for any screening sponsored by or involving site, a patient with an abnormal finding and a diagnosis of cancer will be offered or referred for treatment. Level 1 sites will annotate biospecimens with quality clinical data and methods of diagnosis. Lay health navigator/community health educator or its equivalence to enhance awareness of and access to clinical services will be required.

• A Level 2 site will participate in and support the NCI research agenda by conducting a range of clinical research, including: NCI phase III clinical trials and early phase trials; and population-based, behavioral, and health services research across the cancer continuum, ranging from prevention, early detection, treatment, survivorship, and end-of life research. Sites at Level 2 are required to demonstrate the capability of collecting and maintaining standardized data in collaboration with other participating sites on selected project initiatives, including implementation, outcomes and dissemination research at the site and N-CORP network level with data sharing agreements. Sites also will be involved in practice and program self-assessment initiated through participation in network quality improvement initiatives (e.g. COC RQRS, ASCO QOPI or their equivalent) to target potential research opportunities for the program. As with Level 1 sites, sites will participate and report their co-investment arrangement with NCI. Similarly, as with Level 1, it is expected that a documented disparities commitment reflected by practice that for any screening event sponsored by the site, a patient with an abnormal finding and a diagnosis of cancer will be offered or referred for treatment. The research to be conducted will require sites to have plans to implement Electronic Health Records and the capacity to support disparities research (e.g., OMB classification data collection for all program activities.) Sites should demonstrate experience in delivering prospective multi-modality multidisciplinary care.

• A Level 3 site will participate in and support the NCI research agenda by conducting a full range of clinical research, including NCI clinical trials and population-based, behavioral, health services, and outcomes research across the cancer continuum, ranging from prevention, early detection, treatment, survivorship, and end-of-life research. Research at this level will include more complex multi-site studies, such as cost-effectiveness studies, detailed comparative outcomes research and longitudinal patient-level and organizational-level studies. This will require integration of clinical, cost, utilization, and patient characteristic data across cancer providers and with primary care providers to support site and N-CORP network level projects, including participation with the network research partners (i.e. COC RQRS, ASCO QOPI, CMS or their equivalent). As in Level 2, sites also will be required to have experience in delivering prospective multi-modality, multidisciplinary care and navigation services. The sites will participate in a co-investment arrangement with the NCI and will have disparities research partnerships (e.g., NCI, CNP, NCI-designated cancer center disparities research initiatives.)

An NCI document describing the three levels can be found at: http://www.cancerletter.com/categories/documents.

Hartford Hospital's Experience

After first learning about the opportunity to join NCCCP, Andrew Salner had to sell the administration of his institution, Hartford Hospital, on the idea.

"We went into this recognizing that we were going to need to make a commitment bigger than what we would get back from NCI," said Salner, director of the Helen and Harry Gray Cancer Center and chief of the Department of Radiation Oncology. "The persuasive argument I made to our hospital was: these are things we want to do anyway.

If we are going to move toward being the kind of comprehensive center we should be, when we grow up, we are going to need to make a financial commitment to support programs, and survivorship, and outreach.

"It's added value."

Hartford is a large, urban teaching hospital that sees 3,000 new cancer patients a year. It's not a part of a university, and it doesn't do basic research.

"We wanted to have multiple linkages with NCI-designated centers, so we could participate in translational medicine," Salner said to The Cancer Letter. The NCI program helped it restructure its cancer services, broadening the scope of its clinical research, Salner said.

The hospital receives about $500,000 under an NCI subcontract. But it has matched NCI funds roughly 3:1, counting both financial and in-kind investment.

The investment is worthwhile, Salner said.

"Cancer represents 20 to 25 percent of our hospital business," he said. "It's an important service for us to render to the community. It's also a service that brings people back for other parts of their healthcare. If we do it well, and we do it comprehensively, then we also serve our patients well, and that pays dividends back to the hospital, and it's a really good investment.

"It's a nice edge to have, and it's nice to have the NCCCP logo on our letterhead. It's interesting that we haven't marketed that as much as we have the actual substance of our programs."

The NCI designation has helped with fundraising, too.

"Since we started this work, we received $2 million or $3 million in donor funds over three years that I am convinced we wouldn't have gotten had we not been focused on the areas that NCCCP brought us," Salner said. "I think the donors saw that we had visibility in the community, saw that we had a linkage with NCI that added credibility to the work we did, and really thought that it merited support."

Soon after Hartford Hospital started to work with NCCCP, researchers from H. Lee Moffitt Cancer Center called.

"They said, 'We understand you've joined NCCCP. You have a very high volume of cancer patients. Would you be willing to collaborate with us, because we are doing some really interesting genomics research?

"They are 1,000 miles away. It's not like a local university. We are much closer to New Haven, Boston and New York. One would think we would be doing this work with Yale or Dana-Farber or Memorial Sloan-Kettering. But if you are taking tissue from a patient who has been generous enough to participate in this research study and you are putting it in the overnight mail, it doesn't matter whether it goes to Boston or Tampa."

The collaboration has been productive. "The Moffitt opportunity enabled us to develop a biospecimens program and hire some staff, and we have sent over 3,000 fresh-frozen tissues and fully annotated clinical information to Moffitt as part of this program," Salner said.

"It never would have happened without NCCCP."

BSA Slammed NCCCP in 2006, What The Cancer Letter Wrote:

John Niederhuber, NCI director at the time, didn't really have to ask the Board of Scientific Advisors what it thought of his proposal for the NCI Community Cancer Centers Program.

After all, the Request for Proposals for what was then a $9-million, three-year pilot project was issued by SAIC-Frederick Inc. Niederhuber's predecessors often used the contractor to shield their favorite projects from peer reviewers.

Yet, on Nov. 2, 2006, Niederhuber presented the project to a board. Certainly, Niederhuber had to have realized that the fact that the board wasn't asked to approve the project was going to make its members even more indignant.

As the board attacked his legacy projects, Niederhuber sat quietly, taking a beating.

Excerpted from The Cancer Letter, Nov. 10, 2006:

Starting the discussion, BSA member Raymond DuBois, director of the Vanderbilt Ingram Cancer Center, said the program might help cancer centers link to non-profit hospitals outside their immediate area.

"This concept has a lot of potential to reach out into the community in a very positive way, but I guess

some of that really depends on what the ground rules are for establishing these community centers," DuBois said. "We've had some experience in our community dealing with for-profit hospital groups that don't tend to see anybody that's not covered by insurance. They send those people our way. I wonder if the ground rules could be put together in such a way that we could reach out into the community, like Knoxville or Chattanooga, and bring some of those non-profit people on board with these kinds of concepts?"

"I think you and I are thinking exactly the same way," Niederhuber replied.

But BSA member Patricia Ganz wondered whether the project would duplicate existing NCI programs.

"I happen to work in a cancer center where we have extensive outreach for early-phase trials in our community, as do several of the cancer centers," said Ganz, director, Division of Cancer Prevention and Control Research, Jonsson Comprehensive Cancer Center, University of California, Los Angeles.

"Accessing state-of-the-art trials is not necessarily always a problem in the community practices. Secondly, for most of those who do population science work, the laboratory is the community, and we are looking at these issues scientifically. Is this a demonstration project or is this science? I have concerns that there is research that is going on in various institutions where helping leverage some resources might do as much and create more infrastructure. Many of our community hospitals already have multidisciplinary tumor boards and so forth. Are we reinventing the wheel, or do you think you are going to reach people who are not interested in the Commission on Cancer?"

NIEDERHUBER: "I think this will incentivize places to do that. Hopefully, we will be able to reach into communities where these programs don't, and in as robust a manner as we would like. I think there are many areas in this country where individuals are at great distances, four or five hours away, from major cancer hospitals, lots of rural areas in this country, in the Southeast and Southwest. Even in the city of Washington, there are some major issues of access where a program like this might address."

JAMES WILLSON, director, Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center: "I, too, agree that dissemination of discovery is very laudable and this is a great time to be doing this, because of where science and treatment and control is. I've been impressed over the last five years in looking at cancer centers, how well many cancer centers are beginning to do dissemination, and I want to second Patty's comments and to raise a concern. That concern is that as you talk about the science of this initiative, you truly have set a very high bar in areas of dissemination, in areas of tissue procurement, and early-phase clinical trials that are challenging the very best of our cancer centers to do this well, and I think there are some models out there that are doing quite well, but they are still striving to improve.

"Maybe this is turned around. Maybe the initiative of dissemination really belongs with the NCI-designated cancer centers looking out into the community with opportunities which you recognize and cancer centers recognize. It should be focused."

NIEDERHUBER: "As I tried to stress at the beginning, I know that many of our cancer centers are doing this and working very hard at it. This isn't in competition with that. This is, hopefully, in addition to and in parallel with. What we are doing is creating another program, another rim, if you will, that I hope will add to what is going on in the cancer centers program."

HEDVIG HRICAK, chairman, Department of Radiology, Memorial Sloan-Kettering Cancer Center: "I'm worried about the quality control... specifically for pathology and radiology. We know how often the diagnosis is changed, the stage is changed, as we receive outside films and outside pathology. So, you may have the best new drug that's given for a disease. Are you going to have some ground rules?... Before you put those places on site, there has to be some kind of quality control that they do have dedicated radiology related to cancer care."

NIEDERHUBER: "I think we can ignore that and leave it as it is, or we can get our feet on the ground and our hands dirty and get into the community and see if we can change that. I don't know how to change that unless we get involved in the community. We can't solve those problems—we're not going to change that unless we get there are work with them. When we bring clinical research into a setting, whether it's in this country or some of the underdeveloped countries, we change the quality of care."

HRICAK: "That's exactly what I meant. Can we build in some ground rules for competence that they have to demonstrate, for example, that they have radiology that specialize in oncology, that reads certain number of cases?"

NIEDERHUBER: "I don't know that we want to be that specific on ground rules for entering into this system, but we certainly have built into this metrics and are continuing to evolve the metrics for how we are going to gauge the success."

LELAND HARTWELL, president, Fred Hutchinson Cancer Research Center: "We've heard a lot of comments around the table about programs that are going on at various cancer centers and community involvement, and a lot of comments about the problems associated with them. I would think that one of the most useful things that NCI could do would be to collect that information and disseminate it to us at cancer centers—case studies of what works and what doesn't."

"A Challenging Model, To Be Sure"

The cooperative groups also view the project as duplicative, Young said. He summarized a statement sent to him by BSA member Richard Schilsky, chairman of Cancer and Leukemia Group B.

"Rich Schilsky had to leave early, but he sent me some comments, and I think it expresses a concern that certainly would be present throughout the whole cooperative group structure," Young said. "He emphasizes, as others have, that the project is very diffuse, and the infrastructure required to accomplish the goals is, therefore, hard to delineate. He points out that the goals call for doing early-phase clinical trials in community settings, and for improving accrual of minority patients to clinical trials—and the strategies for accomplishing those are very different and would be challenging in any setting, let alone a community setting...He mentions that it's likely that the only community sites that would qualify for this initiative are likely to be CCOPs or large hospitals already participating in cooperative groups, and he said, 'I think it's surprising to commit $9 million to this program at a time when the cooperative group budget is being cut by 10 percent.' In his mind, this is money to create an infrastructure to duplicate something that already exists."

Young continued, speaking for himself: "I would second the comments that Jim Willson made. I was very interested in this, because we've had an extensive program and we've put probably 600 patients a year on clinical trials through a very extensive network that's taken 20 years to build.... The description [of the project] is that the principal investigator must be in a hospital that has at least 1,000 cancer patients, but less than $2 million in peer-reviewed funding. So, that defines large community hospitals with no historical involvement/interest in research or clinical trial activities. It then requires that group, which has historically been somewhat estranged from the rest of us, to link up closely with cancer centers, to presumably provide that clinical trial infrastructure, research infrastructure, to make this thing work.

"It seemed to me that that's a challenging model, to be sure," Young said. "Maybe Jim's right. Maybe the driver ought to be thrown back into the cancer centers environment, and tell them, if they haven't already done it, 'show me how you're going to do it.'"

Niederhuber didn't respond to Young's statement.

Kathleen Foley, a neurologist at Memorial Sloan-Kettering Cancer Center, asked how the project's success would be measured. "Would it be 1,000 more patients enrolled by these institutions in clinical trials, or the program is just up and running?" she asked.

"I think it's much more than that," Niederhuber said. "It's how effective they've been in getting electronic medical records into this environment. How effectively they have been in creating a cohort across sites. It's about how effective they have been in education among populations which would benefit from education about cancer prevention and screening. It's about how effective we have been in bringing new advances, targeted therapies as an example, biomarkers research as an example—how effective they have been in bringing that to a community setting."

Foley also asked whether centers would have any incentive to work with the hospitals. "There is a level of technology transfer that you are attempting to create in this system," she said. "What would be the incentive for the cancer center to help them with this technology transfer? Usually, it will require time, energy, money—and that's been a problem in the CCOP program. All of us trying to do research in the community know how hard this is to do. There need to be some incentives for the cancer centers to help this technology transfer, so is there money built in to this pilot project to do this?"

Niederhuber said the pilot didn't include incentive money for cancer centers.

Susan Curry, director, Institute for Health Research and Policy at University of Illinois at Chicago, asked whether the pilot sites would be representative of the hospitals where most cancer patients are treated. "Sometimes, for any study we are doing, you kind of recruit the best you can get, and you wind up really not learning a whole lot about what you're doing in general care," she said. "There are a lot of national organizations involved in the quality of care and have a lot of influence on how health care is delivered. If this is a serious initiative, you want to somehow be bringing them in."

"We actually did," Niederhuber said. "A number of those large groups came to visit with us and spent the day discussing this program with us. A lot of them have innovative programs to change the way things are

done in their system...

"There is a lot of opportunity for us for a very small amount of money to leverage for a very big impact," Niederhuber said. "That's a little hard to stand up here and explain to you, unless you've kind of been out there talking and seeing how just the opportunity to say, 'We are connected to the National Cancer Institute,' how much that means in a community setting, and how much they are willing to put resources into programs. I happen to think that's important."

The "Third D," But Wrong Mechanism

Referring to former NCI Director Andrew von Eschenbach's use of the phrase "discovery, development, and delivery" to describe the phases of cancer research, BSA member Jane Weeks, chief of the Division of Population Sciences, Dana-Farber Cancer Institute, said she favored research on health care delivery, but had concerns about this project.

"I'm delighted to see that the third 'D' is getting some attention, and nobody's more enthusiastic about that than I am," Weeks said. "But, I share the concern expressed by essentially everybody that this may not be the right mechanism with which to do that.

"I think about the history on the cancer treatment side, and we really learned the hard way that it's better to understand the mechanisms first and then develop therapies and interventions to target those mechanisms," Weeks said. "On the delivery side, I'm not sure we understand well enough what the structures are that lead to poor quality versus good quality. The little bit of literature that does exist on this I don't think would necessarily support the components of this plan as the ideal way to get optimal cancer care into the community."

Some pieces, yes. Some pieces, probably no. "Nine million dollars is not a lot of money, but, boy, would it be a lot of money to begin to answer that question, and it's really painful to see funds that could be used to answer those questions really being used to replicate what I think many of the cancer centers, my own included, are already doing." Niederhuber didn't respond to her comment. BSA member Shelton Earp III, director of the Lineberger Comprehensive Cancer Center at University of North Carolina, Chapel Hill, said he favored a program that would focus on a specific area, such as "six inner-city hospitals that concentrate on African- Americans" or filling in parts of the U.S. far from NCI-designated cancer centers. "You talk about how the hospital systems are interested in putting resources into this so they will have an NCI designation," Earp said. "That's, of course, nothing, compared to what our institutions are putting into the NCI. So, I worry about the structure."

Niederhuber didn't respond to his comment.

Young asked whether the project would emphasize accrual to phase I or phase II trials. Many cancer centers that have outreach programs are accruing patients to phase II trials, he said. "Phase I trials, however, are a very different breed of cat," he said. "We, for instance, in 20 years, have not done it, nor are our community hospitals interested in doing it when they find out what is involved with having to deal with it."

Niederhuber said he developed a program at Wisconsin that brought rural patients in for phase II studies. "At that time, in watching that program and learning from it as we were doing phase II, there were certainly elements of phase I—especially as we are moving into this new era—where I bet we could do some phase of that in community settings.... Not everything, certainly not our first-in-man study that we do in the Clinical Center, for example.

"I'm not sure that sometime over the next five or six years, that phase I, phase II, phase III will be [outmoded as terms] of clinical trial nomenclature," Niederhuber said. "We are moving into a different era. Most of us recognize that our major cancer centers grew up in order to manage toxicity. We had very toxic therapies, and we needed those big centers and all those resources, and all the ancillary divisions within the medical center—infectious disease, cardiology, and all of those programs that actually helped us manage. This is changing, and I think it's going to change even more dramatically over the next four years, five years, to a decade."

FDA News

PDUFA V Allows Collection Of User Fees From Generics

(Continued from page 1)

PDUFA V is projected to fund 2,599 full-time equivalent staff members who will work towards FDA's commitment to review and act on 90 percent of standard applications within 10 to 12 months from the date of filing, and on 90 percent of priority submissions within six to eight months. By some estimates, this funding could help decrease the time it takes to review applications by 33 percent by the end of the program's fifth year.

For the first time, the law allows FDA to collect fees for biologic and generic drugs, giving the agency

resources to quickly review generic drug applications and fund the new approval pathway for biosimilar biologics created by the Affordable Care Act.

The generic user fees are expected to generate $1.575 billion, and the biosimilar fees will generate $128 million.

"The historic user fee legislation will provide FDA with additional resources and ensure all participants in the U.S. generic drug system, whether U.S.-based or foreign, comply with our country's strict quality standards," said Ralph Neas, president and CEO of Generic Pharmaceutical Association. "Very importantly, the programs will make certain that all Americans receive timely access to safe, effective and affordable generic drugs."

To help combat drug shortages, the law requires manufacturers of certain drugs to notify FDA when they experience circumstances that could lead to a potential drug shortage, said Kathleen Sebelius, secretary of the Department of Health and Human Services.

Oncologists have experienced a growing number of shortages of therapies the past two years, said Michael Link, immediate past president of the American Society of Clinical Oncology. The majority of these treatments are old, off-patent chemotherapy drugs, and the enactment of this law makes significant strides in addressing a crisis in public health and reduces the number of drug shortages, he said.

"While we are glad that the law requires drug manufacturers to notify the FDA six months in advance of an anticipated shortage, fines or similar penalties are needed to ensure that manufacturers comply," Link said. "ASCO will continue to advocate for legislation adding this enforcement mechanism."

Link also urged Sebelius to include biologics in the drug shortage provisions immediately, because biologics are already first-line treatments for numerous cancers.

"The pace and bipartisan fashion [in] which the House and Senate moved this legislation shows their keen understanding of the need for enhanced scientific capacity at the FDA, and the urgency that patients across the United States have for new lifesaving treatments for diseases like cancer," said Ellen Sigal, chair of Friends of Cancer Research.

Other provisions include changing FDA's inspection policy from a mandatory inspection of domestic plants every two years to inspections on both domestic and overseas manufacturing plants based on risk-to-patient safety. The law also reauthorized two pediatric drug measures set to expire this year and increased staffing for rare disease programs.

Capitol Hill

OVAC Asks for $2 Billion Raise For NIH; $280 Million for NCI

By Matthew Bin Han Ong

Cancer advocates from 15 healthcare groups met on Capitol Hill to demand an appropriation of $32.7 billion for NIH and $5.36 billion for NCI over the next year—$2 billion and $280 million increases, respectively.

The groups met July 9 and 10 for the One Voice Against Cancer Lobby Day.

Participants scheduled nearly 160 meetings with Congressional representatives to urge lawmakers to support funding for cancer research and prevention programs, citing biomedical sector inflation and a greater need for research funds as reasons for appropriating a 6.5 percent increase for NIH and a 5.5 percent for NCI.

The Senate Committee on Appropriations recently recommended a fiscal 2013 appropriation of $30.7 billion for NIH and $5.08 billion for the institute—basically a flat budget compared to 2012 (The Cancer Letter, June 22). The House has yet to decide, but cancer advocates are nervous about news of a lower budget allocation despite, the Senate numbers.

"Clearly the fiscal situation isn't ideal, so most organizations will likely be delighted to stay level," said Chris Hansen, president of the American Cancer Society Cancer Action Network. "But we are hoping to see an increase—I think that there is a 50-50 chance that the Congress will listen to us."

ACS CAN helped found OVAC in 2000, which includes representatives from a number of active organizations, such as the American Association of Cancer Research and the Pancreatic Cancer Action Network. A total of 36 national and community cancer organizations are represented in the coalition.

"There could be an appropriations bill this year, but the problem is they are getting so late to kicking the can around," said Hansen.

Participating organizations in this year's lobby day were:

- American Cancer Society Cancer Action Network
- American Academy of Dermatology Association
- American Association for Cancer Research
- American College of Surgeons Commission on Cancer
- American Society for Radiation Oncology
- Fight Colorectal Cancer

• International Myeloma Foundation
• LIVESTRONG
• Men's Health Network
• National Brain Tumor Society
• National Coalition for Cancer Research
• Oncology Nursing Society
• Pancreatic Cancer Action Network
• Preventing Colorectal Cancer
• Susan G. Komen for the Cure Advocacy Alliance

Cancer Centers

University of Kansas Center Receives NCI Designation

(Continued from page 1)

"We are extremely proud of what this designation means—and it's a dream that could not have become a reality without the commitment and enthusiasm shown by thousands of our closest friends," said Jensen.

Patients will have access to clinical trials that are available only to NCI-designated cancer centers, said Jensen. The center will also be able to apply for exclusive federal research grants.

Through efforts initially led by the Kansas Masons, hundreds of private donors have given more than $107 million to the KU Endowment Association in support of the effort to attain NCI designation.

The Kansas legislature has included annual appropriations to support the cancer center since 2007.

The Kansas Bioscience Authority helped fund drives to recruit research faculty. Local financial support has also been generated from the 1/8-cent Johnson County Education and Research Triangle sales tax to support the KU Clinical Research Center in Fairway, where scientists are conducting early-stage clinical trials of cancer drugs developed by KU researchers.

In 2011, The University of Kansas Cancer Center merged with Kansas City Cancer Center.

Obituary

Gastroenterology Pioneer Joseph Kirsner, 1909-2012

Joseph Kirsner, the Louis Block Distinguished Service Professor of Medicine at the University of Chicago, died from kidney failure at his home in Chicago July 7. He was 102.

Kirsner was a leader in understanding the immunology and genetics of inflammatory bowel disease and one of the first to show the increased risk of colon cancer in patients with ulcerative colitis.

"Few if any physicians have had a broader and more positive impact than Joe Kirsner on thousands of patients, students and professional colleagues," said Kenneth Polonsky, dean of the Division of the Biological Sciences and the Pritzker School of Medicine and executive vice president of medical affairs at the University of Chicago. "His legacy at the University of Chicago will persist for generations. We are truly fortunate to have been able to call Joe a friend and colleague and a member of our faculty."

Every gastroenterologist should feel "at least slightly indebted to Joe Kirsner," said Stephen Hanauer, the Joseph B. Kirsner Professor of Medicine and section chief of gastroenterology at University of Chicago Medicine.

After coming to the University of Chicago in 1935, Kirsner helped transform the field of gastroenterology from what was, in his words, "speculative, impressionistic, anecdotal, almost mystical at times," into a science.

Kirsner helped found the American Gastroenterological Association, the American Society for Gastrointestinal Endoscopy and the American Association for the Study of Liver Diseases. He was also key in the creation of the original General Medicine Study Section, a voluntary group of experts who advise NIH on the merits of grant applications.

"He was among the first to demonstrate that stomach acid was necessary for ulcer development, and he drew attention to the complex relationships between bacteria in the gut and the immune system in the development of inflammatory bowel disease," said Hanauer.

"He was also an extraordinary mentor, albeit a demanding one," he said. "He was entirely devoted to the care of the patient and he expected that same level of passion and commitment from the entire team."

As a central figure in the evolution of what was

once a small specialty, Kirsner has received every major award in his field but one—for which he is not eligible—the American Digestive Health Foundation's Joseph B. Kirsner Award. The Crohn's and Colitis Foundation gave him their lifetime achievement award twice, in 1991 and 2002.

"He was here for two lifetimes," said Eugene Chang, the Martin Boyer Professor of Medicine at the university. "He's an icon in the field. Everyone knows him. He's been a key player nationwide for so long that even those who have worked with him for decades only know pieces of his career. I'm not sure where the field would be without him. He was at the beginning of everything."

Kirsner also taught generations of medical students and young physicians the importance of combining competence with compassion when treating patients.

"Although he was a devoted scientist, taking care of patients was always at the core of his thinking," said David Rubin, associate professor of medicine and co-director of the Inflammatory Bowel Disease Center at the university. "He was a bulldog when it came to fighting for his patients, and he transmitted that tenacity to everyone on his team."

In 1976, at the recommendation of Donald Fredrickson, then the director of NIH, Kirsner was asked to take care of King Hassan II of Morocco, who had complex digestive issues. Over the next 22 years, Kirsner made 55 trips to Morocco, providing care to more than 200 patients, including the king and many members of the royal family.

The oldest of five children, Joseph Barrett Kirsner was born in Boston Sept. 21, 1909, to Ukrainian Jewish parents who had immigrated to the U.S. He grew up in Boston's East End neighborhood. Throughout his adolescence, Kirsner held multiple jobs, delivering newspapers, stocking a grocery store and working as a library clerk. He then worked his way through a six-year program at Tufts University that combined college and medical school.

He entered medical school in 1929, the week the stock market crashed. "My thought was to go through medical school as quickly as possible and start earning a living," he recalled in a talk he presented at an IBD conference in 2004. He graduated near the top of his class in 1933 and, planning a career as a general practitioner, moved to Chicago for a two-year internship at Woodlawn Hospital, with free room and board plus a salary of $25 a month.

One of his patients, however, had grander ideas. Minnie Schneider, a young dancer with an ear infection, was hospitalized at Woodlawn. "She was a ballerina," Kirsner recalled. "I fell totally in love with her."

She pushed him to choose a specialty soon after they were married in 1934.

So he began attending lectures at the University of Chicago. Walter Palmer, who had established the first academic gastroenterology unit in the United States in 1927, particularly impressed Kirsner. In August 1935, an entry-level faculty job opened up and Kirsner joined the hospital staff as an assistant in medicine with an annual salary of $1,000.

He began working with Palmer, who was doing pioneering studies in stomach and intestinal disorders. He also began a PhD program in biology, which he completed in 1942. His wife gave up dancing for secretarial work to help with expenses.

Kirsner's early research involved peptic ulcers, stomach-acid secretion and body chemistry, which led to an unusual research collaboration. A penniless, homeless young man, known as Edwin R., enrolled in one of Kirsner's research studies. Edwin badly needed treatment. He also needed a job and a place to live, so Kirsner kept him hospitalized for an entire year as a patient and research subject and trained him to be a technician.

"It would be difficult to gain approval for such an arrangement today," Kirsner acknowledged, even though none of the studies put Edwin at risk, "but it was acceptable to him, and he helped me start some of my research. Everybody was happy."

In the late 1930s, Kirsner began shifting his focus to inflammatory bowel diseases: ulcerative colitis and Crohn's disease. Working initially with Palmer, Kirsner developed new methods to manage IBD patients. In the 1940s, he showed that patients with IBD, even mild cases, lost high levels of protein, a discovery that placed new emphasis on nutrition. He developed the first animal models of IBD, demonstrated the influence of the immune system and genetics on this disease, and documented the increased risk of colon cancer in patients with IBD.

World War II forced Kirsner to put his research on hold. In 1943, he joined the U.S. Army as a physician. In August 1944, about 10 weeks after D-Day, his unit landed at Utah Beach, Normandy. They established bases at various hospitals in France and Belgium, one of which was hit by a German V-2 rocket. Over the next six months, Kirsner cared for U.S. soldiers with

severe battle wounds, captured German officers, and survivors of the Nazi concentration camps who had complex nutritional issues.

Soon after VE Day, he was transferred to the Pacific Theater, where he advised on the rehabilitation of more prisoners of war, including a group of badly burned Dutch prisoners who were being held captive in Nagasaki in August 1945 when an atomic bomb obliterated much of the city. He was discharged in 1946 at the rank of major, with three battle stars.

Back at the University of Chicago, Kirsner continued his research in IBD and rose steadily through the academic ranks. He became an associate professor in 1947, professor in 1951, chief of gastroenterology in 1960, and the Louis Block Distinguished Service Professor of Medicine in 1968. In 1971, he was named the chief of staff and deputy dean for medical affairs.

He published more than 750 scientific papers and 18 books, including six editions of his authoritative textbook, "Inflammatory Bowel Disease." He continued to see patients until age 95; even then, former patients continued to call him for advice.

Kirsner also helped raise funds for gastrointestinal studies. In 1962, a collection of his grateful patients formed the Gastro-Intestinal Research Foundation, which has provided nearly $30 million to support gastrointestinal research at the university, including $2 million for the university's 17,000-square-foot Joseph B. Kirsner Center for the Study of Digestive Diseases, which opened in 1986.

"In my opinion, and the opinion of most people involved with GIRF, without Dr. Joe, this group would ever have been possible," said Sy Taxman, a long-time member of the GIRF board. "He leaves us all with a strong traction and big shoes to fill."

His wife of 64 years, Minnie, died from complications associated with Parkinson's disease and stroke in 1998.

Kirsner is survived by his son, Robert Kirsner, professor of linguistics at the University of California at Los Angeles, and his wife Elaine; their son Daniel and daughter Rachel Kirsner Schneider and her husband, Steve; and four great grandchildren: Yaron, Gilad, Amira and Eden Schneider.

FDA Approvals

FDA Approved Erbitux Therapy For KRAS Wild-Type mCRC

FDA approved Erbitux in combination with the FOLFIRI chemotherapy regimen for first-line treatment of patients with KRAS wild-type, EGFR-expressing metastatic colorectal cancer. The agency also concurrently approved the first KRAS companion diagnostic test, the Therascreen KRAS diagnostic kit.

Erbitux is the first and only FDA-approved therapy for KRAS mutation-negative patients. Erbitux is not indicated for the treatment of KRAS mutation-positive colorectal cancer.

The new indication is based on data from the CRYSTAL trial, a phase III, open-label, randomized, multicenter study conducted outside the U.S. that used European Union-approved cetuximab as the clinical trial material.

The study's primary endpoint was progression-free survival and compared patients treated with cetuximab plus FOLFIRI versus FOLFIRI alone.

A statistically significant improvement in PFS was observed for the cetuximab plus FOLFIRI arm compared with the FOLFIRI-alone arm (median PFS 8.9 vs. 8.1 months, HR 0.85 [95% CI, 0.74-0.99], p value= 0.0358).

Additionally, the median overall survival in each arm was 19.6 months (95% CI, 18-21) and 18.5 months (95% CI, 17-20), respectively (HR= 0.88; 95% CI, 0.78-1.0). The objective response rate in each arm was 46% (95% CI, 42-50) and 38% (95% CI, 34-42), respectively.

Serious infusion reactions occurred with the administration of Erbitux in approximately 3 percent of patients in clinical trials, with fatal outcome reported in less than 1 in 1000.

Erbitux is a monoclonal antibody (IgG1 Mab) designed to inhibit the function of a molecular structure expressed on the surface of normal and tumor cells called the epidermal growth factor receptor.

Erbitux is approved for several therapies for head and neck, and colorectal cancers. Erbitux is sponsored by Eli Lilly and Co. and Bristol-Myers Squibb; the diagnostic kit was developed by QIAGEN.