THE CANCER LETTER

Sept. 12, 2014 • www.cancerletter.com • Vol. 40 No. 34

Group Chairs Seek Role in Running NCTN

By Paul Goldberg

Is the new National Clinical Trials Network set up for success or heading for failure?

The National Cancer Advisory Board Sept. 9 attempted to review the early signals coming from the institute's revamped clinical trials system to determine whether it could use early tweaks.

The institute's new network, configured to conduct new-generation "smart" trials of targeted agents, creates new mandates and capabilities, but—overall—it provides no new money to the clinical trials system.

(Continued to page 2)

Tobacco Interests Contribute a Portion Of the $109 Million Raised by SU2C

By Matthew Bin Han Ong

Stand Up To Cancer, a non-profit cancer group that conducts televised fundraising events, raised over $109 million last weekend.

The group's triumphant Sept. 7 press release, awash with pictures of participating Hollywood celebrities, hailed this achievement. However, the group also became a target for criticism for failing to mention that three of its high-level donors have ties to the tobacco industry.

SU2C officials aren't denying the connection.

(Continued to page 7)

Guest Editorial

Learning from the Power Morcellation Fiasco: Government Must Do More to Regulate Devices

By Hooman Noorchashm

Following our discovery that my wife's occult uterine cancer was morcellated using a gynecological power morcellator, we initiated a vigorous campaign to protect others from this avoidable harm.

(Continued to page 9)

Varmus: Perhaps We Should Rethink Organ-Specific Groups

(Continued from page 1)

While new capabilities have been created, funding for the offices of group chairs and statistical centers sustained substantial budget cuts (The Cancer Letter, May 16).

At the NCAB meeting, the group chairs focused on the question of governance. Has the clinical trials system been reconfigured to carry out directives from the top down? Have the groups turned into clinical research organizations for NCI? Who gets to set strategy? And what is the governance process?

Presenters at the session included all "stakeholders" in the new clinical trials system: NCI officials, a group chair, a cancer center director, a chair of a coordinating committee, a community investigator, and operators of repositories of biospecimens.

The Question of Governance

"Is the new system meaningfully different from the old system?" asked Walter Curran, co-chair of NRG Oncology, executive director of the Winship Cancer Institute and the Lawrence W. Davis Professor and Chairman of Radiation Oncology at Emory University. "Is there better coordination? I think it's a little early to tell. This program is only six months old. But I do know that we need a clearer governance structure of NCTN, which really needs to be a partnership between [Cancer Therapy Evaluation Program], [Division of Cancer Prevention], and the leaders of the groups.

"Is it more cost-effective? Not clear. The funding is somewhat stable from the prior program to the current program, but the distribution of dollars is different. For the headquarters and statistical and data management sites, there have been reductions in the dollars going to those at the costs of going to some of the other initiatives you've heard about.

"There are good efficiency efforts in place. Are there more rare disease trials? The answer clearly is no to that. The only way the answer could be 'Yes' is if we look now at the molecular subtypes of common diseases, which is sort of the modern-day version of rare diseases, we are looking up more of that."

Curran cited his state as an example of lost opportunities in clinical research.

"Georgia's been a historic underperformer in enrollment in cooperative groups dating back decades," Curran said. "But in 2014 we did get a new lead academic participating site, U10 at Emory and the Winship Cancer Institute.

"There's a new minority [NCI Community Oncology Research Program site] between Georgia Regents University and Morehouse University, a large [NCORP-based site] across the entire state, and one hospital in Savannah participating in an NCORP based in South Carolina. Exciting news shared among the oncologists throughout the state. Particularly notable given that most sites in the state enroll over a third minority patients in trials and it's a growing state.

"But one of the challenges in this story is will this be a lost opportunity? We now in this state now have a tremendously expanded public clinical trials network. But are there enough NCTN trials? Are there enough patient slots in the NCTN trials? And already, the networks I noted are reaching or exceeding the target enrollment, but have much greater capacity to enroll. And what a lost opportunity we have here."

Curran's presentation triggered an exchange with NCI Director Harold Varmus:

VARMUS: "Do you have any recommendations on the governance issue?"

CURRAN: "Briefly, I think the governance has to be a partnership between the group leadership and the NCI."

VARMUS: "We can take that as a given—"

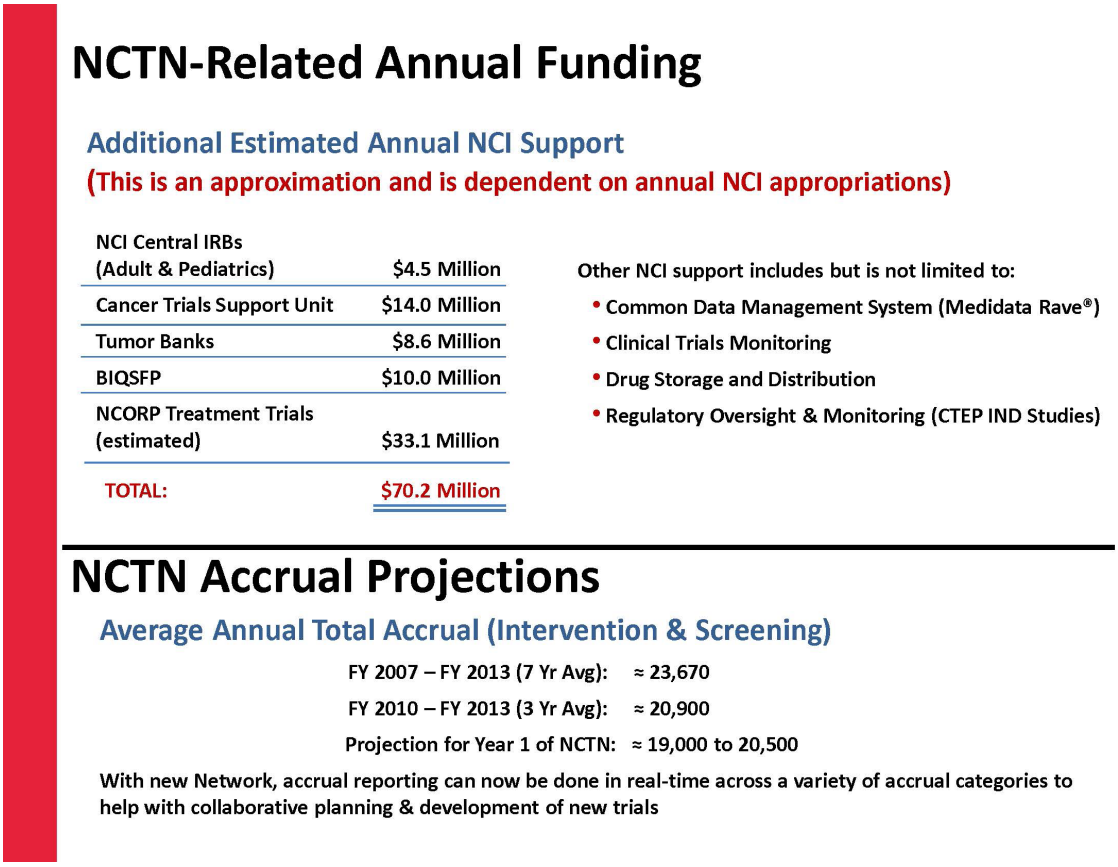
CURRAN: "But it has not been the case in the old system or the current system. While it's a given, it has not happened yet. And the system is six months

Cover Photo: NRG's Walter Curran says group chairs should play a role in shared governance of NCTN.

Editor & Publisher: Paul Goldberg
Associate Editor: Conor Hale
Reporter: Matthew Bin Han Ong
Interns: Tessa Vellek and Will Craft

Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $405 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.



A slide presented by Meg Mooney at the Sept. 9 NCAB meeting.

in. So my view is that's an important priority for us to move forward in."

VARMUS: "The reason I make the comment about it being a given is because it's sort of an assumption, but what specific things do you want to see happen that would make it work as a partnership?"

CURRAN: "Part of it has to do with how do we use these resources. I gave you one example of a state that's geared up with people hungry to look at trials, how do we decide which trials we do? A lot of it should be based on opportunity.

"Is there a scientific opportunity in the next two or three years in melanoma? And lets not just do breast trials just to have a trial open if there isn't a good biologic imperative. And we're going to have to ask the hard questions and in reality I think it will be easier for group leaders and NCI to make those decisions together."

The impetus to hold the session focused on NCTN came from two NCAB members, Judy Garber, director of the Center for Cancer Genetics and Prevention at Dana-Farber Cancer Institute, and Mack Roach, chair of the Department of Radiation Oncology at the University of California, San Francisco Helen Diller Family Comprehensive Cancer Center.

For NCI, the session provided an opportunity to gain control of the narrative. Institute officials laid out the institute's NCTN-related expenditures, showing how the money is being directed, and—importantly—counter the notion that projected NCTN accrual would drop precipitously as a result of changes.

Accrual would be falling slightly below average over the past three years, NCI officials said. On the new NCORP program, NCI officials said the budget has been supplemented by $2.9 million, which came from the director's discretionary fund.

Nancy Davidson, director of the University of Pittsburgh Cancer Institute and UPMC Cancer Center and the Hillman Professor of Oncology at Pitt, agreed with Curran that NCI has transformed the culture of clinical research.

"For a long time, the cooperative groups have been a bit of a bottom-up, very dispersed decentralized," Davidson said at the NCAB meeting. "But that also has a lot of opportunity for fertile investigation. So I think we're going to have to look at the impact of this new system, which is clearly more centrally directed and more top-down than we've seen it in the past."

Davidson listed several potential "downsides."

"Wally talked about some of the unintended consequences," she said. "I think that one of them is

NCORP FY 2014 Budget

NCORP Funding

Grand Total: $97.0 Million

$91.1 Million allocation for NCORP grants

$ 2.0 Million from DCCPS for NCORP grants (Additional FY 2014 NCI Funding)

$ 93.1 Million

$ 3.9 Million allocation for contract support for NCORP

Details of NCORP grant funding

NCORP Component	No. of Sites	Clinical Trials $ Millions	CCDR Funding $Millions	FY 2014 Total
NCORP & NCORP-M/U Sites SUBTOTAL:	46	$42.7	$ 7.5	$50.3
NCORP Research Bases	7	$38.2	$ 4.5	$42.8

NCORP Supplemental Funding For Accrual

$2.9 M

A slide presented by Worta McCaskill-Stevens at the NCAB meeting.

that one of the reasons that we have been successful is that so many of our leaders were so invested in their disease areas and in their legacy cooperative groups, and I believe it's going to be a little bit of a challenge for us to transfer that focus and that loyalty from an area that has been historically very successful and channel that into success in the new cooperative groups.

"I think it's also going to be a challenge for us from some of our leaders to see them stay engaged in scientific leadership in the new cooperative groups and we really need to encourage them to do that. You heard from Wally, and I echo his concern that many of our clinical investigators, our clinical translationalists, got their start in the group system, and I think we're going to have to work very hard to encourage NCTN involvement for these young investigators, because there's not going to be as much an obvious way for them to lead going forward.

"And, finally, you also heard about the possibility that we worry about the financial penalties, not to mention the lost scientific opportunities for over-accrual, for a center that goes above the targets that have been set for us.

"I worry about some of the trials that we're trying to do and how easily they're going to be done in a small office in Johnstown, PA. Even with the re-engineering, I don't think we have fully worked out the interactions that are going to take place and the roles of these the component parts as we try to advance our clinical trials agenda."

Surgeon's Perspective on Steering Committees

John "Drew" Ridge, a surgeon at Fox Chase Cancer Center and co-chair of the Head and Neck Steering Committee, painted a bleak picture of the functioning of the selection process that determines which trials would go forward.

"What happened, to a great degree, is that we placed trial development into the hands of our academic competitors," Ridge said. "Now, that's not wrong. I think it was an unintended consequence. And it takes a while to work past that.

"We have increased the information exchange at an early stage of trial development. It's not clear to me that this has really increased the efficiency of clinical trial evaluation. We've certainly put in place an organization that will do that formally. But, frankly, I think it was going on pretty well before the disease-specific steering committees were rolled out.

"I don't think we've reduced trial redundancy, because I don't think it was really that bad. But we have a mechanism to do that now.

"So, in the main, I think that we are meeting the

articulated goals that were put in place, and that with experience, the disease-specific groups are increasingly effective. I don't think that this will be affected adversely by the decline in groups, but that because the diseases are different, we are very vulnerable to a one-size-fits-all prescription."

During discussion, several NCAB members and others proposed formulating scientific questions—and conducting clinical trials—based on molecular targets, as opposed to disease sites.

"I wonder whether we are at the point where we ought to rethink the idea that we have organ-specific disease groups," Varmus said. "Maybe they should be pathway-based, or gene-profile-based, or, when we take on the MATCH program, then all hell breaks loose, because every patient is a potential entry into a MATCH-type clinical trial. I just wonder whether these boundaries are now increasingly artificial… Maybe we need a UN of disease groups. Maybe the UN is not the best model, but…"

Ridge cautioned about that approach.

"I wanted to offer a brief counterpoint," he said. "Not to the idea that it would be good to cure everything based on our understanding of its pathway—it certainly would. As a surgeon, I am engaged in the pursuit of a 150-year-old modality.

"But the very same advances in the computing power—in science—that allow us to use combinatorial chemistry rationally to design drugs and intensity-modulated radiation to reduce the morbidity of radio-therapeutic treatment made it possible to do operations with far less morbidity.

"And if we lose track of the ability to employ old modalities in modern ways, we are not employing everything at our disposal. I have to treat patients now. I have to treat them in the next five years. Despite my enthusiasm for modern drug design and the new trial approaches that we are taking, I don't think we should ignore the disease-specific features of care and the nature of patients' diseases that may be amenable to modern approaches.

"Right now, we are engaged in the search for a robot, in prospective trials, to figure out if we can reduce the morbidity of treatment that used to require us to cut people's throats open and stop them from eating, and it's no longer necessary. We need to know whether it's as good or better than radiation, and we will not find that out if we give up the disease-based studies.

"Compelling as the scientific arguments are, I think there are issues of feasibility and need right now that we cannot ignore as a therapeutic community."

Varmus agreed.

"You and I don't disagree," he said to Ridge. "I was speaking mainly of drug-based therapeutics, and I often feel that in NIH-supported science, and in thinking about cancer therapy in general, we often ignore the fact that we do cure cancer often, and we cure it because people like you go in and do surgery. As someone who has run a hospital when I was at Sloan-Kettering, a lot of our efforts went into trying to improve the way we do surgery. That obviously requires a different organization to the oversight of trials."

RIDGE: "Trials are necessary."

VARMUS: "They are critical."

The Bar for Phase II vs. the Bar for Phase III

The new NCI clinical trials system is limiting opportunities for young investigators, said Peter Adamson, chair of Children's Oncology Group and the Alan R. Cohen Endowed Chair in Pediatrics at the Children's Hospital of Philadelphia.

"I think the issue with young investigators is a critically important one," Adamson said. "Despite major strides forward in efficiencies, one thing we haven't really addressed well is the concept of failing late.

"The system still is systematically designed to fail late," Adamson said. "For a young investigator, it's one thing to invest four to six months of their time developing a single concept and having it fail. It becomes a very different issue when they invest two to two-and-a-half years of their time.

"It has to succeed at the committee level within the group, within the group, and then at the steering committee level. That probably impacts the young investigators the most. There are areas where we address it. I think in the drug development area, in the team approach, it's beginning to work…

"Certainly, phase III is not a place to build a career for a young person. Phase II is more feasible. But that remains a challenge across the groups…

"Are we doing the best trials? I think that's the wrong question. The problem is, if we try to do the best trial, every committee will look at it and say it's not the best trial, and they will try to tweak it. I think the bar for phase III, which is a huge investment, has to go up. Too high a failure rate; we have to raise the bar. But the bar for phase II, I think, needs to be lower.

"If it's interpretable, if it's feasible, I believe we learn in the clinic, and if we take so long to move it forward, guaranteed the science will be old.

"It's just a matter of time.

"I don't think we should strive for the best trial. I

think we should strive to learn in the clinic. Make sure it's interpretable, make sure it's reasonable. Phase III—let's raise it. But phase II, if it takes us that long, we're never going to have the best trial just from a time factor.

VARMUS: "I don't see necessarily why it has to take a long time to make a choice. We're not making a definitive assessment, but it seems to me that if you're comparing several potential phase II trials, where your resources are limited, you can get a bunch of people together and say what makes the most sense."

ADAMSON: "But I can tell you that the time it is taking to make a decision on a trial…"

VARMUS: "Sure. The bar should be lower, I agree with that. But I think the answer to that is, you know, 'Make up your fucking mind.'"

Varmus's choice of words triggered nervous giggles from the audience and a question by an unidentified individual at the NCAB table: "What did he just say?"

At this moment, Robert Comis, co-chair of ECOG-ACRIN, came up to the microphone to pose a question about NCI's strategy for working with disease groups, which raise money and spend it on research focused on specific diseases.

COMIS: "I'd like to follow up on a comment that was made about interacting with other organizations. All of our investigators have deep ties into all the disease and other types of foundations. I think that as resources have become more and more constricted and we have limits on how much we can accrue and we can't go over this number or that number, we are going to be much more flexible about how we are interacting with other organizations.

"There are disease organizations that are doing deep sequencing. We have studies that are of tremendous interest to them. And I think we have to be very flexible about how we engage these opportunities. There is a new [American Association for Cancer Research] opportunity, there is a new [Multiple Myeloma Research Foundation] opportunity. They are all over the country. I think we have to be very flexible in understanding how we can capitalized on those things. We aren't going to get additional resources. We all know that. But we can magnify the resources that are available if we can be flexible about how we approach these interactions."

VARMUS: "Couldn't agree more. Maybe Dr. [Douglas] Lowy [NCI deputy director] would like to comment. He's been bringing in a number of those advocacy groups to think about interaction with the NCI. And, frankly, we're feeling very flexible about this, and I'm not sure all those organizations are so flexible."

LOWY: "Well, the hour is late. But the NCI certainly would be open to hearing from groups that are interested in working closely with us. And we are quite flexible in our orientation."

VARMUS: "There are many of them in the room, and from my perspective, not a whole lot of progress was made in flexibility."

On Sept. 23, the group chairs, network statisticians and chairs of Imaging and Radiation Oncology Cores are scheduled to meet with Varmus and James Doroshow, director of the NCI Division of Cancer Treatment and Diagnosis.

Expletive Deleted By NIH From NCAB Webcast

By Paul Goldberg

At the Sept. 9 meeting of the National Cancer Advisory Board, NCI Director Harold Varmus used an expletive in a way that may be considered tolerable in hallway conversations and in behind-closed-door settings.

Varmus appeared to suggest that steering committees and investigators quickly reach decisions on proposals to launch phase II studies and move on.

Even though this choice of words is exceedingly rare at meetings of advisory committees, under normal circumstances, the story would have ended on Sept. 9, triggering no more than a single line in a news story.

However, two days later, on Sept. 11, the archived version of the video recording of the meeting posted on an NIH website was altered to exclude the Varmus expression and the laughter it triggered. Tampering with record of a public meeting by the staff of a federal agency created the obligation for any reporter to investigate.

"It seems to me that the only rule with a recording of a government meeting should be that they be accurate," Gregg Leslie, legal defense director of the Reporters Committee on Freedom of the Press, said to The Cancer Letter. "To take out a word like that would be entirely inappropriate."

Amos Gelb, director of Washington Media Institute, agrees.

"Public record is a public record; it is not that 'part of a public record minus that part of the record someone arbitrarily thinks appropriate,'" said Gelb, former director of broadcasting at Northwestern University's Medill School of Journalism. "It is the entire public record, written or broadcast, even if the written regulation has not caught up. The barrier is simply higher for public organizations and officials, particularly someone as important and influential as the NCI director. It goes to the core of public transparency

and is the same rationale that would justify deleting the famous 18 minutes of Nixon's recording.

"The response to dismiss this case as a minor issue misses the point that the advisory hearings are public and transparent for a reason, and all public records have to be unvarnished reflects of that," Gelb said. "The question it raises is 'if this, what else?'"

Why was the video of an advisory committee edited? By whom? Were any other parts of the recording tampered with? Is this common practice at NIH?

Contacted by The Cancer Letter, NIH officials said the law requires only that written minutes of meetings covered be the Federal Advisory Committees Act. "It doesn't say anything about video," said John Burklow, an NIH spokesman.

After investigating, Burklow provided the following account: "The technician who was taping it heard it, and flagged it for the folks who post the video, and they decided to take it out. They did it on their own. I am guessing they heard the word and thought, 'Let's take it out.' I don't think they are editing at will. This was a unique situation."

Asked whether such actions are appropriate, Burklow said that the event suggests the need for NIH policy on editing video recordings of meetings. "We will be having that discussion," Burklow said. "Ultimately, I think people running videocasts would appreciate guidance in these cases."

Burklow said the video would remain on the NIH website in edited form.

"The segment added color to the proceedings, [but] it didn't add substance, so I have decided to keep it out."

SU2C Praises Companies Related to Tobacco in Telethon

(Continued from page 1)

These donors—called "partners" in SU2C parlance—promote cancer through the sale of tobacco products, said Alan Blum, director of the University of Alabama Center for the Study of Tobacco and Society and the Gerald Leon Wallace, MD, Endowed Chair in Medicine at the University of Alabama School of Medicine.

"It is shameful that after decades of efforts to end the leading cause of cancer, the organizers of this cause would welcome the participation of manufacturers, promoters and sellers of cigarettes," said Blum, editor of the Medical Journal of Australia and the New York State Journal of Medicine, and former head of the physicians' anti-smoking group Doctors Ought to Care.

The trio identified by Blum is: SIEMENS, Safeway Foundation and the Steve Tisch Foundation.

Stand Up To Cancer has received over $260 million in pledged funds since its inception in 2008.

SU2C's most recent telethon aired Sept. 5 on major television networks in over 170 countries, featuring celebrities such as Robert Downey Jr., Gwyneth Paltrow, Pierce Brosnan and others.

One hundred percent of donations received from the public go to cancer research programs, the organization says. The group is backed by a variety of donors—pharma companies, philanthropic foundations, and advocacy organizations.

SU2C's Tobacco-Friendly Donors

SIEMENS manufactures cigarette-making machinery and barcode-tracking technology for improved efficiency of cigarette distribution. Its customers include Philip Morris USA, the maker of Marlboro.

The SIEMENS website describes the Simotion Motion Control System. At top speed, a single machine can make up to 1.2 million cigarettes, or 60,000 packs, per hour.

"SIEMENS is one of the chief manufacturers of tobacco-making machines," said Joel Dunnington, a recently retired professor of radiology and previous section chief of diagnostic radiology at MD Anderson Cancer Center. "They're very big. From what I understand, they are the gold standard."

SU2C recently announced that it accepted over $1 million in donations from SIEMENS.

The company didn't respond to an inquiry from The Cancer Letter.

The Safeway Foundation is funded by Safeway Inc., now the second-largest supermarket chain in the U.S. following its acquisition in July by Albertsons. In contrast to CVS, Wegmans, Target and other retail chains that have ended the sale of tobacco products, Safeway continues to sell cigarettes in more than 1,330 stores nationwide.

The Safeway Foundation didn't respond to an email from The Cancer Letter.

The Steve Tisch Foundation derives its funds from the Tisch family, which was involved in the manufacturing and sale of cigarettes. Between 1967 and 2008, the Tisch family-run Loews' Corp. controlled the nation's third leading cigarette manufacturer, Lorillard.

The company, which is about to merge with the number-two cigarette maker Reynolds-American, produces Newport, the top-selling menthol brand and the leading cigarette smoked by African-Americans.

In 1994, at a U.S. House of Representatives hearing on cigarettes, Lorillard CEO Andrew Tisch, the first cousin of Steve Tisch, famously testified under oath that he did not believe either that nicotine is addictive or that cigarette smoking causes lung cancer.

Blum said that many of SU2C's media partners also accept advertisements for tobacco products. These partners include Sports Illustrated, TIME, Entertainment Weekly, People, WIRED, Vanity Fair, Playboy, The National Enquirer, and Cosmopolitan.

The role of retailers in the sale of tobacco came into focus earlier this year, when the CVS drug chain said it would stop selling tobacco products in its 7,600 pharmacies.

SIEMENS gave $1 million to SU2C. At top speed, a single SIMOTION Motion Control System machine can produce up to 60,000 packs of cigarettes an hour.

At the SU2C telethon, newscaster Katie Couric said: "And by the way, another new donor in the Stand Up To Cancer movement is CVS Health. This year they made the extraordinary decision to stop selling tobacco, one of the leading causes of cancer deaths worldwide. CVS, I'm buying my toothpaste from you! Now they're taking it a step further. Starting in November they're raising funds for critical cancer research. Thank you, CVS pharmacies, for joining the fight."

Blum said this tribute is excessive. "I don't think we should be congratulating CVS for finally stopping a practice that it should never have engaged in," he said. "To really clear the air, I believe CVS should apologize for having sold the leading cause of cancer for so long."

SU2C Declines to Disclose Standards

SU2C officials didn't respond substantively to questions from The Cancer Letter.

The questions were intended to establish whether SU2C has a review process to screen corporate donors for ties to the tobacco industry and whether it works with tobacco-related donors and organizations to decrease their affiliation with tobacco.

Instead of responding to specific questions, Kathleen Lobb, co-founder and spokesperson for SU2C, said in a statement to The Cancer Letter:

"The mission of Stand Up To Cancer is to accelerate the pace of collaborative, translational research and get new life-saving therapies to patients quickly. To do so, we've galvanized a broad range of supporters—companies, foundations, philanthropists, organizations, and individuals.

"Because of the generosity and profound commitment of these donors, SU2C has supported 12 Dream Teams, two Translational Research Teams, and 26 Innovative Research Grants. These grant recipients include more than 800 researchers, representing 112 unique institutions in six countries.

"Collectively, these investigators have planned, launched, or completed 141 clinical trials, in which more than 5,700 patients have enrolled. Stand Up To Cancer funded research has also resulted in over 350 papers in peer-reviewed journals.

"The results are tangible, and benefiting patients: work by SU2C-supported researchers has led to the development of a new combination treatment for pancreatic cancer, which is now a first-line therapy, as well as promising new drug for the treatment of the most common subtype of breast cancer."

Asked whether SU2C would like to address this reporter's aforementioned questions directly, Lobb said, "I don't have anything to add."

The American Association for Cancer Research, the scientific partner of SU2C, declined to comment on the group's choice of donors.

"As the Scientific Partner of Stand Up To Cancer, the AACR's role is to provide peer review, grants administration, and scientific oversight of team science and individual grants in cancer research," Rick Buck, senior director of communications and public relations at AACR, said to The Cancer Letter.

By accepting money—and, apparently, having no explicit standards for defining tobacco interests—SU2C is making these donors look good.

"Stand Up To Cancer has all these 'partner' companies who have forever advertised tobacco with the media outlets," Dunnington said to The Cancer Letter. "As long as they keep helping them, and they keep allowing them to be good guys instead of being bad guys, we're never going to win this cancer war."

Blum said that the American public should expect better of SU2C, which isn't denying that it is in "cahoots" with companies and foundations that have helped promote cancer through the manufacture, sale, and marketing of cigarettes.

"By covering up for several of their sponsors who manufacture or promote the leading avoidable cause of cancer—cigarettes—the Stand Up To Cancer organizers are saying, 'Who do you believe, us, or your own eyes?'" Blum said. "Here we have proof that Stand Up To Cancer is related to tobacco by only one degree of separation, and they are not denying it."

Guest Editorial

Noorchashm: Government Must Regulate Devices Better

(Continued from page 1)

It is now increasingly clear that one in 350-500 women with symptomatic fibroids have occult or missed uterine cancer lurking in what a majority of gynecological surgeons have assumed to be benign tumors. This assumption of benignity has proven deadly to many women for over twenty years because it allowed the upstaging of aggressive, but early stage and potentially curable, gynecological cancers. Additionally, morcellation, particularly power morcellation, is known to cause the spread of benign uterine tissues leading to highly morbid non-cancerous disease—so-called, parasitic leiomyomatosis and endometriosis. Of course this careless gynecological practice of morcellation rests at the core of a very high volume and revenue-rich procedure. Likely over 100,000 minimally invasive hysterectomy and myomectomy operations are performed using morcellation in the United States alone.

We reported the deadly oncological hazard of gynecological morcellation, and power morcellators, to the FDA and CDC for the first time in December 2013. Our alarm led to an FDA advisory issued on April 17, 2014 and a FDA hearing on July 10-11, 2014. Subsequently, Johnson & Johnson, the largest world-wide manufacturer of power morcellators, withdrew the device from market. And several large insurance carriers in the US have stopped covering the procedure. However, strikingly, the gynecological societies (ACOG, AAGL, and SGO) and a large

number of individual gynecologists continue to defend the practice. And several device manufacturers have refused to withdraw their product from the market. In fact, the manufacturer whose device was used to upstage my wife's cancer had the tenacity to recently threaten us with legal action if fail to cease our campaign to ban morcellation and power morcellators from surgical practice.

I am writing this letter for the public record - specifically because the defense of morcellation by the gynecological industry and device manufacturers represents a severe system failure in patient-safety and medical ethics. The morcellator disaster is a litmus test, which has diagnosed a very serious threat to the integrity of our healthcare institutions and government. To dispel any notion that my statement is overblown, I will remind the reader that over the course of twenty years hundred, if not thousands, of women world-wide have been irreversibly harmed or killed by gynecological morcellation resulting in cancer upstaging. And, incredibly, many gynecologists and device manufacturers had known about this harm and accepted the collateral damage, because the practice was convenient and the revenue flow abundant.

There are three lines of argument the gynecological societies are posing in defense of morcellation. The device manufacturers are, of course, following in suit. I will dissect and deconstruct these arguments here.

First, a large number of minimally invasive gynecological surgeons are claiming that the majority of their patients benefit from morcellation because it permits them to perform small incision surgery. This is more comfortable for the patient. It permits same day discharge from the hospital and may reduce the chances of wound infections. It has also been argued that performing open operations may increase the mortality risk, though the data in this regard are far from clear. Certainly, it is defective reasoning to equate morcellation with minimally invasive surgery – it is possible to perform small incision surgery without the use of a morcellation, as all other subspecialties in surgery do. What is certain, is that when an occult or missed cancer of the uterus is emulsified (i.e., morcellated) inside a woman's body, cancer is upstaged and outcomes are dramatically worsened. So, it appears that the gynecological surgeons and device manufacturers are willing to accept an avoidable mortality hazard to a minority subset of their patients for the presumed "benefit of the majority". This argument has been voiced by formal representatives of the ACOG, AAGL and SGO in formal statements to the FDA and to the press following the start of our campaign. Of course, this argument is a clear violation of the bed-rock principle of medical ethics known as "non-maleficence", which most people know of as "First, do no harm". Nowhere in medical ethics, or in our American social value system, can we accept the avoidable sacrifice of a minority subset of lives for the benefit of the majority. Perhaps in other societies and in other times this concept would be acceptable, but in 21st century America, this is a fundamental violation of our social construct and professional ethics.

Second, many gynecologists and industry advocates have stated that morcellation must remain available to gynecological surgeons as a matter of "women's choice." Of course, the public and all bioethicists agree that bad medicine should never be in the arsenal of choice offered to patients, most of whom are not doctors and trust doctors not to expose them to avoidable hazards. That the gynecological specialty is willing to defend a dangerous practice by invoking the principle of "patient autonomy" and "women's choice" is a reckless attempt at using rhetoric to defend a grave wrong – after all, what could be so bad about women choosing?

Third, many gynecological surgeons have argued that "informed consent" is the solution to the problem of morcellation. That is, if a patient gives the surgeon permission to morcellate, it is justified to proceed. This suggestion also reeks of liability management. How does informed consent protect a woman with an occult or missed uterine cancer from upstaging using morcellation? It does not. If a doctor offers a woman a morcellation operation, he/she does not think the patient has cancer. If a patient accepts the risk of morcellation, she does not believe herself to have cancer. But if, in reality, the patient does have a cancer, the "informed consent" obtained does nothing to protect her. Therefore, "informed consent" in this case is only a medico-legal vehicle to protect gynecologists and hospitals from liability in a courtroom – it is not a mechanism to ensure patient safety. Proposing that "informed consent" could justify exposing women to the hazard of morcellation is, therefore, itself an act of professional negligence.

But why are the gynecological specialty and the corporations manufacturing these devices mounting such a vigorous defense against our campaign to ensure patient safety? I hope the reader can accept my analysis that the answer lies in the corporate takeover of American healthcare. When the volume of practice, technology, revenue and liability concerns

come anywhere near guiding physician and hospital behavior, the primary mission of our healthcare establishment is corrupted. Indeed, when confronted with the possibility of these primarily financial interests being compromised, physicians themselves will accept the collateral damage to their patients by using arguments of "majority benefit" and "patient choice" to justify harm. Make no mistake, the problem we have identified here is that leaders of American healthcare seem to have deviated from being guided primarily by good science and the bed-rock principles of medical ethics: non-maleficence, beneficence, autonomy and justice. No, we seem to be fueled by volume, revenue, liability, and industry. And this driving force corrupts our profession's hard-earned ideology and will bankrupt us spiritually and financially – but most importantly, as we found when our profession's ideals take a back seat to corporate interests, our patients will be harmed unchecked.

Unfortunately, the problem of corporate ideology corrupting ethics is not isolated to medicine. It has also seeped into our federal government and is corrupting the halls of the United States congress away from the remarkable ethical achievement that framed the government of the United States. I am also compelled to explain this dimension of the problem, for the record.

The power morcellator device that has caused the unnecessary or premature demise of hundreds, if not thousands, of women world-wide for nearly two decades bears a seal of approval from the United States Food and Drug Administration. Of course, a superficial look at this fact may lead one to say, "no regulatory system is perfect and mistakes happen". But, in the case of the FDA's mechanism for approval of medical devices in the US, the power morcellator disaster is no accident. A large number of medical devices in the United States are approved through a federal legislation known as 510(k). This is a "streamlined" approval process to get potentially life-saving devices to market quickly. Of course, industry enjoys this relaxed checkpoint, because it is good for business. But the unfortunate reality is that 510(k) is entirely impotent in empowering the FDA to require adequate pre-market safety testing or post-market outcomes surveillance. It is such that power morcellators went on causing advanced stage cancers for twenty years and FDA continued to approve generation after generation of this device with its 510(k) "rubber stamp" but no one bothered to report a deadly oncological complication back to the FDA, until December 2013. The critique of our government is even more powerful given the fact that in 2011, after an exhaustive review of the 510(k) legislation, the Institute of Medicine (IOM) concluded and testified to the United States Senators of the Health, Education, Labor and Pensions (HELP) committee that "510(k) cannot ensure patient safety". The senators of the HELP committee listened to this IOM testimony and chose to either remain complacent or to protect industry interests over patient safety. In fact, even after the morcellator disaster has come fully into public view, only two United States Senators (Schumer and Gillibrand of NY) have been willing to go on the record publicly and demand that the FDA step up and regulate this deadly hazard to American lives. Certainly, no member of congress has yet called loudly for a revision of the 510(k) legislation, which has likely allowed other dangerous devices into the medical marketplace. Why? Is it that corporate interests and industry lobby power in the halls of the United States congress carry more weight than individual American lives and livelihoods? Is it that industry lobby power has been capable of even corrupting our federal government whose framing mission was to defend the right to "life, liberties and pursuit of happiness" for every American person? Is it that industry lobby has the power to deviate our federal representatives to accept collateral damage to American lives? If this is the case in the year 2014, the immortal words of Thomas Jefferson may prove prescient: "The chief purpose of government is to protect life. Abandon that and you have abandoned all." When the United States senators of the HELP committee heard from the IOM chairman, Professor David Challoner, in 2011 that 510(k) cannot ensure patient safety and chose not to correct this public health hazard, they abandoned their "chief purpose" in government. I can only conclude that the 2011 senators of the HELP committee were guided by industry lobby more powerfully that by the principles that framed their responsibility to the people from their seats in American government—unless, of course, the senators did not believe the Institute of Medicine's analysis and warning.

By upstaging early stage and potentially curable cancers, power morcellators have devastated many American lives for nearly two decades, and many more globally. This disaster is a result of professional deviation from the basic ethical principles that must govern the practice of medicine. It is the result of corporations not acting responsibly and not alerting the FDA to a deadly hazard they very clearly knew about. It is the result of the United States Congress not acting decisively to protect patients, citizens and

residents of the United States. And all three of these problems are fueled by corporate interests overriding the fundamental principles of medical ethics and American government.

The morcellator disaster has provided an opportunity for a specific correction to be made to our professional ethics and to federal legislation governing medical devices - because good must be made from the suffering of the many innocent families and unsuspecting mothers, wives, daughters, and sisters harmed by FDA approved power morcellators. Medicine cannot become a business and the people's voice must guide American federal government to remain steadfast in its primary framing principle to serve and to protect every American's right to life, liberty, property and the pursuit of his/her ideals. American federal government cannot be permitted to deviate towards protecting industry and corporate gains over lives.

I ask the reader to write his/her congressmen and senators and demand that FDA approved power morcellators be banned from the marketplace and that the 510(k) legislation governing medical device approval be corrected to ensure patient safety.

The author is a cardiothoracic surgeon at Thomas Jefferson University.

AACR Urges FDA to Regulate High Risk Lab-Developed Tests

By Will Craft

The American Association for Cancer Research urged FDA to regulate high-risk laboratory-developed tests, a category of assays that has escaped scrutiny because of loopholes in the regulatory process.

Normally, FDA requires that diagnostic tests developed by manufacturers adhere to three measures: analytic validity, clinical validity, and clinical utility. However, laboratories can get around this requirement by using laboratory-developed tests, or LDTs.

LDTs are designed and manufactured for use in a single laboratory, but can go to market without obtaining FDA approval as long as the laboratory meets other requirements—called the Clinical Laboratory Improvement Amendments, which are unrelated to the manufacturing and testing of the LDTs.

The loophole persists because FDA chooses not to actively regulate LDTs, the AACR said in an article published Sept. 9 in Clinical Cancer Research.

"The FDA chose not to exercise its regulatory authority in the past largely because LDTs were typically well-established diagnostic test procedures (e.g., urine analysis, microbiology cultures, blood analysis). However, some LDTs being developed today run the risk of being ineffective and exposing patients to inappropriate clinical decision-making if they are not subject to the same scrutiny given to FDA-approved tests," wrote authors Charles Sawyers and Laura van't Veer.

Sawyers is chair of the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering Cancer Center and a former president of AACR. Van't Veer is leader of the Breast Oncology Program and associate director of applied genomics at UCSF Helen Diller Family Comprehensive Cancer Center.

The paper stresses the need for regulation of LDTs, but recognizes the limit of FDA resources, saying that the agency should focus on certain high-risk LDTs.

"Implementation of a risk-based framework by the FDA that would provide for evaluation of all high-risk molecular diagnostic tests would balance the need for encouraging innovative medical product development with the need for ensuring patient safety," the authors wrote.

"A focus on high-risk tests would also help channel the FDA's limited resources toward those products that pose the greatest health risks for patients… Therefore, a single regulatory standard for high-risk diagnostic tests is key to ensuring the safety and efficacy of molecular diagnostic tests."

The policy statement comes a month after FDA officials announced their intent to release a draft guidance on the regulation of LDTs (The Cancer Letter, Aug. 1). Under the FDA Safety and Innovation Act of 2012, the agency has to notify Congress 60 days before issuing guidance or any regulation that affects LDTs.

"FDA's policy of enforcement discretion over LDTs was acceptable when these tests were mostly routine laboratory procedures; however, as LDTs have evolved in complexity, the risk posed to patients has also increased," Sawyers said in a statement. "It is therefore vital that all diagnostic tests used to make high-risk treatment decisions be FDA-approved, so patients and physicians can be assured of the test's safety and accuracy."

Follow us on Twitter: @TheCancerLetter

Funding Opportunity

PanCAN Offering $4.1 Million In Research Grant Funding

THE PANCREATIC CANCER ACTION NETWORK announced more than $4.1 million in research grant funding for 2015. Investigators at all points in their careers are invited to apply for research grants aimed at improving patient outcomes and pancreatic cancer survival rates.

Some of the grants offered include:

• The Research Acceleration Network Grant: providing $1 million in funding to support team projects aimed at doubling pancreatic cancer survival rates by 2020. It is offered as a partnership between the Pancreatic Cancer Action Network and the American Association for Cancer Research.

• The Fredrick National Laboratory for Cancer Research KRAS Fellowship: a one year, $45,000 fellowship for a postdoctoral or clinical research fellow conducting research on inhibiting the activity of mutated KRAS proteins. The fellowship is offered as a partnership with the National Cancer Institute, and will be linked to the NCI's RAS Program.

In Brief

Lasker Foundation Names 2014 Award Winners

THE ALBERT AND MARY LASKER FOUNDATION announced its 2014 award winners.

• **Mary-Claire King**, of the University of Washington, received the Lasker-Koshland Special Achievement Award for her contributions to medical science and human rights.

• **Kazutoshi Mori**, of Kyoto University, and **Peter Walter**, of the University of California, San Francisco, received the Albert Lasker Basic Medical Research Award for research into a key quality-control system in the cell, the unfolded protein response.

• **Alim Louis Benabid**, of Joseph Fourier University, and **Mahlon DeLong**, of Emory University, for clinical research for developing a surgical technique that reduces tremors and restores motor function in patients who have advanced Parkinson's disease.

"Walter and Mori zeroed in on the molecular machinery that senses excessive unfolded proteins, and they exposed the process by which cells correct that problem; DeLong pinpointed a region of the brain that plays a central role in Parkinson's disease, and Benabid applied a novel technique to that region and alleviated symptoms; and King discovered that certain women with early-onset breast cancer owe their disease to a harmful version of a particular gene, BRCA1," said Joseph Goldstein, chair of the Lasker Medical Research awards jury.

ANDREAS HOCHHAUS and **ROBERT GALE** were named co-editors-in-chief of Leukemia.

Hochhaus is interim head of the Department of Hematology and Medical Oncology at University Medical Center Jena. Gale is visiting professor of hematology at the Imperial College London.

They will succeed **Nicole Muller-Bérat Killmann**, co-founder and editor of Leukemia, who passed away in February. She founded the journal with her husband, **Sven-Aage Killmann** in 1987, and became editor-in-chief after his death.

Hillard Lazarus, professor of medicine at Case Western Reserve School of Medicine and director of Novel Cell Therapy at University Hospital Case Medical Center, and **Mohammed Mohty**, professor of hematology and head of the Hematology and Cellular Therapy Department at the Saint-Antoine Hospital and University Pierre and Marie Curie, have taken over as co-editors-in-chief of the journal Bone Marrow Transplantation.

Lazarus and Mohty will succeed the late **John Goldman**, who founded the journal with Gale in 1984. Goldman was emeritus professor of Leukemia Biology at Imperial College London. He passed away in December 2013.

GEORGETOWN LOMBARDI COMPREHENSIVE CANCER CENTER received a five-year, $11.25 million P30 Cancer Center Support Grant and renewal of its designation as a comprehensive cancer center.

With MedStar Health, center director **Louis Weiner** led an expansion of the cancer center by starting the MedStar Georgetown Cancer Network.

An area that received a particularly high rating from NCI reviewers was the center's cancer prevention and control program, which conducts population-based and translational research, ranging from early detection to lifestyle intervention to survivorship.

LOUIS DEGENNARO was named president and CEO of the **Leukemia and Lymphoma Society**.

DeGennaro joined the society in 2005, was appointed chief medical officer in 2009, and has served

as interim president and CEO since February. Prior to joining the LLS, DeGennaro served as senior director of molecular genetics at Wyeth Pharmaceuticals.

While at LLS, DeGennaro was the architect of the LLS Therapy Acceleration Project, a philanthropic initiative that funds projects related to speeding up the development of blood cancer treatments.

In 2012, DeGennaro was appointed as a member of the National Center for Advancing Translational Sciences Advisory Council and the Cures Acceleration Network Review Board at the NIH. He is also on the board of BioTheryX, an early-stage biotech firm, as well as the Health Research Alliance, a group of non-profit research funders.

MAYO CLINIC and **IBM** announced plans to use Watson, the IBM cognitive computer, to match patients more quickly with appropriate clinical trials. The proof-of-concept phase is underway, with the intent to introduce it into clinical use early next year.

A version of Watson will be designed for Mayo Clinic. As it progresses in its tasks and matures through this collaboration, it will learn more about the clinical trials matching process, become even more efficient and likely more generalizable. Watson also may help locate patients for hard-to-fill trials, such as those involving rare diseases.

Mayo researchers are working with IBM to expand Watson's knowledge base to include all clinical trials at Mayo Clinic and trials in public databases such as ClinicalTrials.gov. The Watson system is being trained to analyze patient records and clinical trial criteria in order to determine appropriate matches.

INFINITY PHARMACEUTICALS Inc. and **ABBVIE Inc.** entered into a global collaboration to develop and commercialize duvelisib (IPI-145), Infinity's oral inhibitor of phosphoinositide-3-kinase (PI3K)-delta and PI3K-gamma, for the treatment of patients with cancer.

The companies said duvelisib has shown clinical activity across a broad range of blood cancers, including indolent non-Hodgkin lymphoma and chronic lymphocytic leukemia. Infinity is conducting registration-focused trials evaluating the safety and efficacy of duvelisib, including DYNAMO, a phase II study in patients with iNHL, and DUO, a phase III study in patients with CLL.

Under the agreement, Infinity will receive an upfront payment of $275 million and is eligible to receive up to $530 million in additional payments for the achievement of development, regulatory and commercial milestones, including up to $405 million for the achievement of milestones through the first commercial sale of duvelisib.

In the U.S., the companies will jointly commercialize duvelisib and will share equally in any potential profits. Outside the U.S., AbbVie will be responsible for the conduct and funding of commercialization of duvelisib, and Infinity is eligible to receive tiered double-digit royalties on net product sales.

As part of the collaboration, the companies will share responsibility for the conduct of specific trials specified within an agreed-upon global development plan, with each company leading the development of certain trials within the plan. For the initial global development plan agreed to by the companies, Infinity will fund the trials it conducts and the companies will share equally the funding of trials conducted by AbbVie. The agreement includes plans to launch multiple phase II and phase III studies of duvelisib in hematologic malignancies over the next several years.

STANFORD UNIVERSITY began an online **Genetics and Genomics Certificate** program, available through the university's School of Medicine and School of Engineering. Courses will be taught by faculty from the Department of Genetics and guest lecturers.

Participants may take individual courses within the program, or earn a professional certificate in genetics and genomics by completing two core courses and four elective courses in topics such as biotechnology, stem cells, cancer, gene therapy, pharmagenomics, and biology. Details about the online certificate program can be found at http://geneticscertificate.stanford.edu.