THE CANCER LETTER

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NCCN in Transition

New Strategy to Examine Role of Informatics, Revenue Sources and International Programs

By Paul Goldberg

The National Comprehensive Cancer Network, a non-profit organization governed by a group of 21 cancer centers, is examining the future of its international programs and looking for new sources of revenue.

NCCN was organized twenty years ago, mostly as a means to help cancer centers adapt to the environment envisioned in the Clinton administration's ill-fated healthcare reform push.

For the past 15 years, the group was run by William McGivney, a former insurance company executive with a PhD in pharmacology. McGivney focused NCCN's efforts on guideline-making and outcomes measures. Most importantly, the network compiles a highly influential compendium, which determines how cancer therapies can be used on or off-label.

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Cancer Centers: Permanent Reinvention

UT Health System's Probe Finds Lapses At MD Anderson, CPRIT—But No Nepotism

By Paul Goldberg

A probe by the University of Texas System found deviations from standard procedures in the handling of MD Anderson Cancer Center's controversial proposal for an $18 million grant from the Cancer Prevention Research Institute of Texas.

The grant proposal—which listed Lynda Chin, wife of MD Anderson President Ronald DePinho, as the principal investigator—was submitted without review by the institution's provost and was accepted by CPRIT in a manner that deviated from its own standard procedures.

Chin is a scientist at MD Anderson.

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In Brief

Ozer Named Permanent Director Of UICC

HOWARD OZER was appointed director of the **University of Illinois Cancer Center**. He had served as interim director since January 2011, following the death of Gary Kruh.

Ozer will oversee the center's NCI grant application for formal cancer center designation.

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Guideline Making To Remain The Mainstay of NCCN Work

(Continued from page 1)

This compendium is continuously updated and used in coverage decisions by third-party payers.

Last December, McGivney departed from the organization as a result of what NCCN officials described as "differences in opinion about management style and the strategic direction for the organization."

According to the board, McGivney's successor would have to be a physician, preferably from a subspecialty involved in cancer treatment (The Cancer Letter, Jan 13).

NCCN is compiling a strategic plan, which is expected to be finished in November, officials said. Changes are occurring at a time when unrestricted funds from pharmaceutical companies are becoming more difficult to obtain. The organization reported $25.5 million in income in 2009, the most recent year for which tax filings are publicly available. This was a $4.3 million drop from the $29.8 million the organization raised in 2008. Tax documents show that in 2009, NCCN spent $3.4 million more than it raised.

In an interview, Thomas D'Amico, chairman of the NCCN board of directors, said the guidelines will remain the "the flagship program" of the organization. "I think one of the things we'd like to better define is what our international presence should be, when we have extensively interacted with nations all over the world," said D'Amico, chief of the Section of General Thoracic Surgery at Duke University.

Patricia Goldsmith, NCCN executive vice president and chief operating officer, said NCCN will likely carve out a greater role in clinical informatics systems. "Informatics and the ability to ensure that our content is able to be utilized in various systems, EHR systems, decision-assist tools, is increasingly very, very important to NCCN," she said. "And so I think the way our end users access our content will hopefully be different in the coming years in that it will be more readily accessible in EHRs and tools that they use in their everyday practice."

D'Amico and Goldsmith described their vision for next chapter in NCCN's history in an interview with The Cancer Letter.

A transcript of the conversation follows:

TCL: *What can you tell me about the strategic vision. How did you, as an organization, decide that it was time to rethink this strategic vision?*

TD: I think any organization has to re-evaluate itself on a regular basis, to reset goals and objectives, reset strategies for how to best succeed in achieving them. I don't think that NCCN is any different along those lines than any other organization.

It is a little different in how it's made. Its board of directors comes from 21 different cancer centers, being nonprofit, there are some unique things about it, we try to achieve some unique things, but as an organization I think we are ambitious, we have high goals, and periods of self-reflecting and realigning goals and objectives are what we should all be doing.

I don't think there's anything unique or different about that. We are in the process of doing that now, trying to determine what we want to be for the next five to 25 years.

TCL: *Was there anything that precipitated that reflection?*

PG: I think that when we looked at the organization, we recognized that we had never engaged in formal strategic planning process since its inception, number one.

Number two, you probably watched the remarkable growth in terms of programs at NCCN, and, number three, I would say that we certainly have been asked to do a whole lot of things, not only serve our members, but the greater oncology community.

And I think everyone has to prioritize and make sure that we're focusing our resources and efforts on those things that are important. I would say it was a combination of all of those things that said it is really

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time to focus with the greater oncology community, with our members, and understand their perspectives of us, and how we can best serve the membership and the greater oncology community.

TCL: *I guess the history of NCCN is that things sort of just happened. The needs were there, the needs of the organization just grew with that, based on changing visions. So this is really the first time of looking at this thing strategically, isn't it?*

PG: That's right. I would say obviously there's a lot of strategy involved in terms of our growth with respect to for example, developing the drugs and biologics compendium and getting that recognized by CMS, working with payers, now increasingly working with employers.

But I don't think that any organization can be all things to everybody. And so best focusing our efforts and resources in terms of what's going to make the greatest difference seems very logical.

TCL: *How will this organization differ from what it is today, or what it was a few months ago? Is there any sort of specific standout feature that you could highlight?*

TD: There are several things that we are specifically considering. I don't think we are going to change the major mission and the several things that we do really well.

The guidelines being the flagship program, the oncology research program being very productive, our involvement in the compendium, our work with the foundation, all those, I think, are going to stay mainstays in our mission, I think one of the things we'd like to better define is what our international presence should be, when we have extensively interacted with nations all over the world.

But how do we better interact with Asia, for example, or the Middle East, where there could be relationships that improve cancer care in those regions? And how we optimize the database, our outcomes database in terms of not only setting parameters for care, which the outcomes database can do, but also how do we get the most research potential out of it. So those are just two of the things I think we'd like to better define for the future.

TCL: *Are you considering a different informatics approach?*

PG: I think that informatics and the ability to ensure that our content is able to be utilized in various systems—EHR systems, decision-assist tools—is increasingly very, very important to NCCN. And so I think the way our end users access our content will hopefully be different in the coming years in that it will be more readily accessible in EHRs and tools that they use in their everyday practice.

I also think that one difference is quite obvious, that someday in the near future, hopefully, we will have an MD CEO, which will be the first MD CEO that NCCN has had, and I think one additional piece is that we have begun to work much more closely with employers through our collaboration with the National Business Group on Health, which has been extremely successful for us, and I think to figure out the path forward to meet the demands of employers who are coming to NCCN and asking them to help with their benefit design, with the network quality of the providers that serve their members and making the right decisions will also be an increasing emphasis for NCCN.

TCL: *So far, from what you told me, I'm not seeing a different in strategic direction. Is there one thing that we may not have gotten to?*

PG: Nothing that jumps out at me.

I think it's more refinement and optimizing what we do and ensuring that we continue to be very relevant as opposed to a very dramatic change in direction, where we might say, gosh, we're now going to start moving into cardiology.

The guidelines really are the heart and soul of NCCN and they will remain that way, and a focal point of much of what we do.

TCL: *I'm also seeing that, in the 2010 990 forms, there is a relatively small deficit. How did the financials look in 2011?*

PG: The financials in 2011 had a very, very small deficit.

TCL: *On the same magnitude? Or higher?*

PG: In my recollection, it was around a $170,000

TCL: *That's very small, compared to 2010, which was about $3 million, so things have improved on which side? On the cost side, or on the money-in side?*

PG: I would say it's a combination of both, obviously looking at and managing costs is critical to any organization, we're no different, and we really are beginning a strategy of licensing our content to various companies to be able to utilize them and embedding them in EHRs, decision-assist tools.

You may have just seen a large announcement by

McKesson yesterday that talks about their InterQual tool and enhancements, and the InterQual tool will be using our drugs and biologics compendium as the source for determining appropriate utilization on-label and off-label, of drugs and biologics. So that's just one example of a number of them where we are trying to move forward with this strategy of having our content embedded in systems and generating fees to support that.

TCL: *Just looking at the 990 [tax report], dues from member institutions are fairly small portion of that NCCN takes in. How do you stay focused on keeping the interests of these institutions first? Because that is the board.*

PG: The institutions and their 21 names down the side of the letterhead are the organizations that created us, and we exist to serve them in a variety of programs, such as the oncology research program, some of our efforts in the foundation supporting young investigators at our institutions and so I really characterize the member institutions as the driving force at NCCN and why we exist.

TCL: *But how do you keep their interests first? Is this what triggered this change in direction? Because the institutions are really crucial here, and I don't think that these institutions would have really thought of taking NCCN where it went, or not immediately. I'm sure they were all in it.*

TD: I think you're off-base there. The institutions are committed to the NCCN, and since Duke has been a member there has been no wavering on the board of any of the activities of the NCCN, in fact, we turned people who wanted to join the NCCN.

I think the NCCN has been very successful at capturing the missions of the 21 centers and being very productive with it.

TCL: *I guess I'm sort of lost about why now? Why rethink it now? I was looking at the 990 [federal filings] and thinking that the institutions are a very small financial contributor [to the NCCN budget].*

PG: Oh not at all. You are just looking at just the member dues.

Let me talk to you just in one context about the institutions being a monumental contributor, for the last several years, we have actually quantified the volunteer effort on the part of the 21 institutions and the 900 physicians that contribute to the development and maintenance of the clinical practice guidelines.

That was approximately 18,900 hours of volunteer time from the clinicians in our institutions, just to develop and maintain the guidelines.

If you were to multiply that out by a factor of $200-300 an hour, do the math, and you can see the magnitude of the contribution let alone the volunteers on our board of directors, there is extremely active engagement on the part of the institutions, far outside the dues that they pay.

TCL: *Why are you looking for an MD instead of a businessperson when it comes to leading NCCN?*

TD: I think there are enough examples of MDs that are successful businesswise. But I think we've had medical directors in the past and it was helpful to have someone who was a medical director to help guide decision-making—regarding the guidelines, the outcomes, the oncology research program, the database. This was a relatively unanimous decision among the board. It would be a better fit for future strategy development and future business accomplishment if we could find the proper CEO that not only had a background in executive administration, a background in policy, as well as a medical degree—and, ideally, a background in oncology.

TCL: *Well, that's really fascinating.*

PG: We call ourselves a clinical and scientific organization, and when you think about the guidelines driving the standard of care medical practice, and increasing coverage, who better than an MD to lead that type of an organization?

TCL: *It just wasn't a requirement before. I'm just wondering why is that really necessary when you could, in principle, hire someone who is more of a business person, with more of an industry background and working with and MD. It must have been a very interesting decision to seen having been made. There are many ways to skin a cat of course.*

PG: Of course. But we believe that this is the best way.

TCL: *In your recruitment ad, you say this has to be someone that has a high understanding of academic values and cultures. I can see the rationale for it, but I don't want to be guessing. Why is that necessary?*

PG: I think that gets back to what we said earlier, the 21 names down the side of the letterhead and the significant investment, time, resources, and money that these institutions have made.

The NCCN was created to serve them, certainly, it does serve the broader oncology community, our members are made up of solely academic NCI comprehensive or equivalent comprehensive cancer centers. Having a deep understanding and appreciation of the academic environment in which they live, I think, is extremely important to the position.

And having coming out of that environment myself for 20 years before joining NCCN I can say it's very,

very different from the community environment. So a deep understanding of that helps serve our members.

TCL: *I was thinking more industry environment, where it's basically a CEO or president makes a decision and then everybody falls in line. Academia is usually more consensus-building. The understanding of these 21 names and what they want is very different way of thinking than, say, a businessperson would think.*

TD: I think that in the cancer community specifically, and in the medical community—that the chancellor of our hospital is an MD with an MBA, the president of our hospital is an MD with an MBA, the CEO of our hospital is a nurse with an MBA, the COO has a medical background and also a financial background—so it's natural to me that leadership in any kind of medicine would include a medical background, and I think that this is going to be a better fit as we go forward.

TCL: *There is also some discussion in your recruitment ad of new sources of revenues. What other sources of revenues are out there to be had?*

PG: Some of it gets back to what I said before, in terms of growing this business of licensing of content in a variety of systems, that's a relatively new source of revenue for us. We do think there are opportunities to secure grant funding for some of the work of NCCN, possibly other entities funding NCCN and then our foundation is relatively new and I think that our strategic plan will suggest the growth of the foundation's resources of philanthropic support will be extremely important to NCCN as well.

TCL: *Have these licensing fees been quantified? Is that something that you could discuss?*

PG: We are too early into the plan to talk about numbers, so, unfortunately, I don't have anything that I can quantify.

TCL: *So it doesn't exist yet, it's something that will exist.*

PG: Yes, I believe so. I think that we will have goals. Just as we do every year, financially, we will have goals in terms of what we want to accomplish. Some of those may be governed by confidentiality agreements, etc., but I'm sure we will meet to quantify those goals, and understand the investments that we can finance with respect to NCCN going forward.

TCL: *And when will the plan be completed and made public?*

PG: We are hoping that the plan will be finalized no later than November.

And this really is a process that I should say has active involvement from a number of stakeholders that we engaged at the beginning of March, an executive that owns her own firm, Marion Jennings, to work with NCCN to facilitate—and I think facilitate is the operative word here. Meaning that this plan is really the plan of the executive committee and the board of directors of NCCN.

Basically what we wanted her to do was facilitate the process. She actually conducted 66 interviews as part of this process, with a variety of stakeholders—from all of our board members, to CMS, to foundation board members, to private payers, and to a variety of other stakeholders—to really understand their perspectives of NCCN, the value of NCCN, and what they want from NCCN. That is all being brought together with a traditional analysis and this plan will be worked with the executive committee in a series of retreats; and then with the board of directors, beginning in June; and then throughout the summer—with every objective of having a final plan to present to the board of directors to adopt at our November board meeting.

TCL: *Will that be public once that's adopted?*

PG: I don't think there's going to be any secrets. It will become very clear as to what the direction of NCCN is. I guess I hadn't really thought about it, whether it's fully in the public domain. This is not something where we're developing the world security strategy in a secret way. It's designed to chart our direction and our investments.

TCL: *This is just a pro forma question, there are places that do not make their strategic plans public. What can you tell me about the international programs, is this something that NCCN needs to do, is there support for this?*

TD: I think that's one of the things that we're investigating now. What we can do with the relationships that we have now.

As you know, the guidelines are already translated into multiple languages. We have relationships with many of the oncology societies within other countries and representatives from some of these countries have expressed an interested to be part of the NCCN in some way.

And we haven't decided what the best way that is, what would be the best fit, for us to bring value to them and vice versa. So I think we're in the process of trying to determine what our best relationships would be.

TCL: *And that's an open question right now?*

PG: I think it is. We literally have had cancer centers across the world ask for membership in NCCN. We've had cancer centers ask to participate in our outcomes database. We've had cancer centers ask to

participate in our oncology research program.

So there's a desire for a closer alignment, but the question is: what's the best path forward.

And strategically, I think our international work, historically, has been that we've gone where we've been asked to go, and we've worked with the experts and the leaders in various countries to adopt the guidelines. Or adapt the guidelines I should say, to their standards of care based upon population and based upon availability of technology, drugs and biologics and then translate those guidelines into modern languages.

But we're going to continue dealing with requests for that, as well membership and other participation in other programs, we just have to strategically see what the best focus is.

TCL: *Plus you're turning away some potential members in the U.S.*

PG: We've had a moratorium on membership for a number of years, yes.

TCL: *So that must be a really profound question.*

PG: It is!

TCL: *It's my own question, but it's fundamental to what the organization would look like.*

PG: That's right.

TCL*: I didn't understand that immediately. I guess another question is even broader and more complicated. What is the value--and I'm asking this neutrally--of consensus guidelines for treatment.*

I am not asking about prevention. That would be another question. Is that something that is essential today, consensus-based guidelines, as opposed to evidence-based? And I know that this is something that NCCN got into as it evolved. It's not something that was predetermined from the outset.

PG: I have to jump in and say that if you're characterizing our guidelines as solely consensus-based is wrong.

They are evidence-based using consensus where evidence does not exist. I think the best way that I can characterize that is that we could all wish that there was the gold standard of evidence in randomized, controlled, clinical trials for every single point of decision making along the way, but that doesn't exist.

But that doesn't negate the fact that there are thousands of patients every day presenting in clinicians offices that need to have a decision made that day—and in some circumstances that information doesn't exist. But that's the beauty of the system that we put in place, because we gathered the world's leading clinicians who treat only that disease, who participate in the trials and often construct the trials, and truly are leaders that can help put out the best decision making.

And the last point I'll make, in terms of what is the value of the guidelines, I think if you could ask the 1.5 million unique visitors per year that come to our website and use the guidelines— many of them self-reporting that they use them on a weekly basis, or increasingly well in clinical at point of care with patients—they could probably articulate the value of the guidelines even better than I could.

Dr. D'Amico was an architect of one of the guidelines so, please, weigh in.

TD: I agree. To take it a point further, we update the guidelines at a minimum of every year, and that's because they need to be updated. In most cancers it's fortunate that these are dynamic and can get better.

We are in the third version of the non-small cell lung cancer guidelines, the third 2012 version. They're updated at minimum once a year, but we'll probably get into the fifth or sixth version because things come along and we make changes so there's a need for oncologists across the country to be current with the changes, and they're accessed millions of times a year by healthcare professionals.

TCL: *Do you foresee any changes in the process of guideline making? I'm not saying that there should be.*

TD: I think we use evidence when the evidence exists. As evidence grows in certain fields we try to add the evidence in and when it doesn't, when there aren't specific clinical trials that give an answer to a question, we try to use the best available evidence, systematic reviews, meta-analyses, etc.

I think the process that we have which is to distribute the guidelines in their current form to all the members of the committee to take back to their institutions and share with their oncologists there, so you have 21 members or so in each committee, and they go back and share with 8 or 10 oncologists, so now you have 200 people that have looked at the guidelines critically to say how can we make them better and then to meet either in person or over the phone after all of those institutional reviews have been done I think is a pretty sound process.

TCL: *I'm just curious to establish what are the*

constants and might change in terms of the strategic vision of the organization. In prevention, many other organizations, particularly the American Cancer Society, are moving toward evidence based guidelines, and what can NCCN in any shape thinking about moving to specifically evidence based guidelines in the strictest medicine based definition of the word. Is that something NCCN is considering?

TD: I'm not sure exactly what you mean. Most of the guidelines we have are treatment, follow-up, but we have specific guidelines on breast cancer screening or colon cancer screening, on lung cancer screening, so their early detection, I don't know if there are guidelines on preventing cancer.

TCL: *That's what I mean, early detection guidelines*.

TD: We already have these early detection guidelines. They've been in place. The newest one is the lung cancer screening and that was just waiting for the completion of the lung cancer screening trial which is published in the New England Journal [of Medicine] last year. But the thought process for having a screening panel was in the last four five years. But we have early screening and early detection panels in place and have had them for years.

TCL: *Are you leaning towards a role in this? What I'm really thinking about doing is comparing your panels and your process and it's really all about process to say the panels and the process of the U.S. Preventive Services Task Force, where you do not have experts who treat the disease on the panel and its experts in evidence were making the recommendations. Is that a direction that you are thinking of going?*

The American Cancer Society is moving in that kind of, heavily pre-specified, procedure-based approach that excludes people who are actually treating the disease from membership on the guideline-writing panels, which is exactly the opposite of the way you do it.

TD: I don't really foresee that as being in our future. I don't think it would take advantage of the strengths that we have at NCCN to go to a non-expert-based guidelines process.

TCL: *I was referring to something that was more non-specialist based.*

TD: I understand, but we do have a lot of the world's experts, and I think we are going to rely on that expertise.

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Permanent Reinvention

Probe: "No Delibrate Attempt" To Circumvent Procedures

(Continued from page 1)

Submission of a grant proposal without review by the provost is highly unusual since the provost manages the academic mission of an institution, which includes signing off on all grant applications. This deviation from standard procedures, first reported in this publication (The Cancer Letter, May 25), was the sole focus of the UT System's "compliance review."

Deviations notwithstanding, the UT System's rapidly conducted review concluded that there was no evidence of conflicts of interest or nepotism in the handling of the grant application, attributing the lapses to missteps on the part of new, lower-level employees and an "internal breakdown at CPRIT in its grant acceptance and handling process."

In parallel attempts to put the matter to rest, CPRIT announced that it would create the position of a "compliance officer," and MD Anderson officials said they would resubmit the grant proposal to CPRIT for another level of review.

"The UT System review concluded that there had been no deliberate attempt by anyone to circumvent MD Anderson's procedures," UT System's Chancellor Francisco Cigarroa said in a statement June 14. "Furthermore, no conflicts of interest whatsoever were identified in the review, and absolutely no acts of nepotism occurred between Dr. Chin and her husband, MD Anderson President Ron DePinho."

The statement by Cigarroa indicates continuing support for DePinho, whose actions have sparked controversy on several occasions in recent weeks. In addition to the CPRIT matter, DePinho recommended the stock of a company he co-founded during an appearance on CNBC (The Cancer Letter, June 1). The UT System didn't investigate this matter, and DePinho, who is an employee of the state of Texas, offered a mea culpa for giving investment advice, especially advice that would boost the value of his holdings.

The UT System's 27-page report, obtained by The Cancer Letter under the Texas Public Information Act, is posted at http://www.cancerletter.com/categories/documents.

The report, by Larry Plutko, the UT System compliance officer, confirms that the grant application bypassed standard procedures at MD Anderson and CPRIT, and was submitted directly by Eric Devroe, executive director for strategic alliances at the Institute

for Applied Cancer Sciences, an MD Anderson unit where Chin serves as the scientific director.

The report shows that MD Anderson officials preparing the application were in contact with Jerry Cobbs (Chief Commercialization Officer) at CPRIT, who worked directly with IACS in coordinating preparation of a proposal which would merge with the incubator proposal submitted earlier by Rice University with the IACS scientific projects.

Since the incubator was defined as a commercialization project, its scientific component didn't undergo any review. Only a brief business plan was requested. This is a stunning departure from CPRIT's standard peer review, which is conducted by top-level scientists from outside the state. Ultimately, the decision to fund the incubator led to the resignation of CPRIT's Scientific Director Alfred Gilman, a Nobel laureate.

"Hard to know what to attribute this to, but the document certainly reads as a defensively postured document," said Arthur Caplan, director of the Division of Medical Ethics at NYU Langone Medical Center.

The UT System report confirms that Raymond DuBois, the MD Anderson provost, was only partially involved in handling the application. He had circulated information about the award to MD Anderson staff, but was not asked to review the final application.

The report states:

Dr. DuBois indicated that information on the Texas Life Sciences Incubator Infrastructure Award had gone out under his auspices on February 21, 2012, to all faculty and departments including the process for submission to CPRIT.

This communication did go to IACS, including Drs. Chin and [Guillo] Draetta [IACS Director]. Dr. DuBois forwarded an email to me, dated April 18, 2012, from Eric Devroe to [staff members], which states:

"As you have certainly gathered, this entire CPRIT engagement was likely an exception to standard rules and channels. I am attaching documents that I sent directly to Jerry Cobbs (Chief Commercialization Officer) at CPRIT."

This documentation is attached to this report but the above excerpt is noteworthy, according to Dr. DuBois, for it points out that Mr. Devroe did interpret the overture from Jerry Cobbs as an exception to submitting the proposal through the CPRIT web portal.

Dr. DuBois clearly pointed out that he did not see any deliberate or malevolent intent present, but attributed it to Mr. Devroe's newness at IACS combined with "Guilio, Lynda, and Mr. Devroe getting caught up with the advice of Jerry Cobbs." Dr. Dubois also feels that CPRIT needs to clarify why IACS was not expected to follow the web portal protocol pointing to a procedural breakdown at CPRIT.

However, Mr. Devroe's email does indicate he knew there was a standard protocol but it was not followed in this case. Dr. DuBois was unaware of any instructions from CPRIT to Mr. Devroe to submit the incubator grant proposal directly by email…

It appears that in the rush to respond and as directed by Jerry Cobbs, IACS, through Mr. Devroe, submitted the business plan for the commercialization grant to CPRIT by direct email with attachments and did not employ the official CPRIT web portal with use of standard CPRIT forms and Application Signing Official (ASO) attached.

This procedure resulted in a departure from the customary CPRIT grant submission process and, accordingly, notice of the grant's submission failed to reach the Provost's Office.

CPRIT did not reject the email application from Eric Devroe and it did not make a follow-up request to submit the same through the CPRIT web portal.

This points to an internal breakdown at CPRIT in its grant acceptance and handling process and brings into question why CPRIT did not have checks and balances in place to redirect the submission process.

UTMDACC did not receive any notice from CPRIT that anything was amiss or inappropriate about this commercialization proposal and it was reasonable for UTMDACC personnel to assume it was an appropriate submittal process for a commercialization grant proposal as opposed to a research grant.

No Nepotism Alleged, No Conflicts Found

The MD Anderson policy on conflicts of interest states:

"It is the policy of The University of Texas MD Anderson Cancer Center that an MD Anderson employee may not have a direct or indirect interest, including financial and other interests, engage in a business transaction or professional activity, or incur any obligation of any nature that is in substantial conflict with the discharge of the employee's duties."

The UT System compliance officer's report argues that the CPRIT grant controversy doesn't meet this bar.

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Excerpted text of the report follows:

This reviewer questioned each person about allegations of conflicts of interest and whether they could identify actions or activities, which constitute conflicts of interest, including the presence of nepotism. No conflicts of interest were identified in this review and there exists no basis to reasonably allege such conflicts exist.

No documents reviewed pointed to any type of conflict of interest, including nepotism…

Despite the fact that no conflicts of interest internal to UTMDACC were found, we suggest a review of all policies to guard against outside influences causing UTMDACC to make decisions, which interfere with the objective exercise of its official and public duties and responsibilities.

The UT System has recently reviewed and updated policies governing financial interests, management, and reporting of individual financial conflicts of interest in research.

This reviewer recommends that UTMDACC and all UT System institutions conduct a review of institutional conflicts of interest policies so that our institutions can effectively manage the complexities of ensuring right relationships with all outside organizations. The goal is to be transparent at all times and maintain the public trust.

DePinho's View

After the completion of the UT System report was announced, DePinho sent out an email blast to the cancer center's staff, making another in a series of efforts to accept partial responsibility for some missteps and trying to explain others.

The text of the email follows:

You likely have seen news coverage concerning MD Anderson in newspapers, journals and other venues recently. Two topics have been covered, sometimes together, sometimes separately.

First, I personally made a mistake during a live interview on CNBC May 18. Near the end of my interview with Maria Bartiromo, she asked me what biotech companies I would recommend to people for investment. I cited Genentech first, then suggested AVEO, a biotech company I co-founded and in which I still hold stock. As a public official in the state of Texas, my suggestion of AVEO was inappropriate. For that, I owe you all an apology. It will not happen again.

Second, some of the articles are about controversy over a Cancer Prevention and Research Institute of Texas (CPRIT) incubator infrastructure award, for which MD Anderson applied with Rice University.

The UT System Compliance Office has just completed an external review of the process we followed in applying for the award. (See UT System news release.) The review confirmed that "there had been no deliberate attempt by anyone to circumvent MD Anderson's procedures. Furthermore, no conflicts of interest whatsoever were identified in the review, and absolutely no acts of nepotism occurred between Dr. Chin and her husband, MD Anderson President Ron DePinho."

However, two procedural missteps were made, which we've acknowledged. First, the application should have been reviewed and authorized by an MD Anderson official before submission. Second, the proposal was not submitted using the online portal provided for that purpose, but rather was sent via an email directly from our Institute for Applied Cancer Science (IACS) team to CPRIT.

The IACS leadership team was in regular communication with CPRIT throughout the proposal-writing process. Even though we made those two errors in submitting the grant, CPRIT did not ask us to resubmit through the portal or reject the application. As a corrective step to ensure that this doesn't happen again at MD Anderson, all commercialization grants will now be reviewed by our Research Administration and Business Affairs offices. We must hold ourselves to the highest procedural standards to maintain the public trust.

It should also be understood that even though the incubator infrastructure award was announced, no contracts had been negotiated between CPRIT and MD Anderson, and no funding had been distributed. This allowed us all to hit the pause button and forge a new course for this novel type of CPRIT grant.

We volunteered to resubmit the proposal and CPRIT has accepted our proposed solution. We continue to stand behind the IACS plan and welcome any review process CPRIT chooses. IACS is a solution to help solve the 95% failure rate in cancer drug development and an engine for creating new biotech companies and alliances with biopharma companies.

Various articles have suggested that a conflict of interest exists with my wife, Dr. Lynda Chin. However, under strict written guidelines from Dr. Kenneth Shine, executive vice chancellor for health affairs at UT System, I'm prohibited from being involved in any decisions about Dr. Chin's employment status, resources or compensation. Additionally, conflict of interest disclosures for me and Dr. Chin are

reviewed by a multi-institutional UT System conflicts committee comprising representatives from other UT health care universities. It includes no MD Anderson representatives when our disclosures are reviewed.

We must not lose focus on the most important challenge before us. Texas had the vision and courage to establish CPRIT on the premise that Texas could contribute considerably toward reducing mortality and suffering from this devastating disease. That is also our mission. Much progress will be made as a result of the programs funded by CPRIT to our colleagues and to us. Texas, and certainly UT, is fortunate to have so many outstanding academic medical centers. It will take all of us to make the difference.

We cannot let our patients down. We have a great deal of work to do.

Ronald DePinho, M.D.
President

In Brief

Ozer Named Permanent Director of UI Cancer Center

(Continued from page 1)

Previously, Ozer was the Eason chair and section chief of hematology/oncology at the University of Oklahoma Health Sciences Center. He served as center director from 2000 to 2005 and received a cancer center planning grant from NCI.

He was an associate professor of medicine at Roswell Park Cancer Institute before moving to the University of North Carolina at Chapel Hill as division chief of oncology, professor of medicine, and associate director for clinical affairs of the Lineberger Comprehensive Cancer Center. He was director of the Winship Cancer Center at Emory University as well as director of the cancer center at Hahnemann University Hospital.

GERALD DAL PAN was appointed permanent director of the FDA's **Office of Surveillance and Epidemiology** within the Center for Drug Evaluation and Research.

Dal Pan was director of the OSE since 2005 (then known as the Office of Drug Safety) and held the position of acting director of the reorganized "super office" since June 2011.

The reorganized office houses two new subordinate offices: the Office of Medication Error Prevention and Risk Management and the Office of Pharmacovigilance & Epidemiology. The office grew from a staff of 116 to 250 over the past five years.

Dal Pan first joined FDA in July 2000 as a medical officer in the Division of Anesthetic, Critical Care, and Addiction Drug Products.

DARUKA MAHADEVAN was named director of the Phase One Clinical Trials Program and associate director of research with The West Clinic, as well as full professor in the division of hematology/oncology at the **University of Tennessee Health Sciences Center**.

Previously, Mahadevan was associate professor of medicine and director of Phase I, New Drug Program Development at the University of Arizona Cancer Center.

Mahadevan's major interests in clinical research is in pancreatic cancer, gastrointestinal stromal tumors, myelodysplastic syndromes, non-Hodgkin's lymphoma, and chronic lymphocytic leukemia.

FDA News

FDA Approves Perjeta Therapy In HER2-Positive Breast Cancer

FDA approved **Perjeta** in combination with Herceptin and docetaxel chemotherapy for the treatment of people with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

The combination of Perjeta (pertuzumab), Herceptin (trastuzumab) and chemotherapy is the only regimen to have shown a significant improvement in PFS compared to Herceptin plus chemotherapy in people with previously untreated HER2-positive metastatic breast cancer.

The approval was based on data from a phase III study which showed that people with previously untreated HER2-positive mBC who received the combination lived a median of 6.1 months longer without progression compared to Herceptin plus docetaxel chemotherapy (median PFS 18.5 vs. 12.4 months). The study enrolled 808 people with previously untreated HER2-positive mBC or that had recurred after prior therapy in the adjuvant or neoadjuvant setting.

Perjeta is a personalized medicine that targets the HER2 receptor, and is believed to work in a way that is complementary to Herceptin, as the two medicines target different regions on the HER2 receptor.

With the approval, Genentech has agreed to post-marketing commitments related to the manufacturing process for Perjeta. These include FDA review of data from the next several productions of the medicine.

"We expect to meet demand for Perjeta following today's FDA approval. We recently identified a cell growth issue that might affect our future supply of the medicine," said Patrick Yang, head of Genentech Pharma Global Technical Operations. "We take this very seriously and are working with the FDA to ensure a consistent manufacturing process that maintains drug supply for the people who need it."

In the study, the most common adverse reactions seen with Perjeta in combination with Herceptin and docetaxel were diarrhea, hair loss, low white blood cell count, nausea, fatigue, rash and peripheral neuropathy. The most common Grade 3-4 adverse reactions were low white blood cell count, low white blood cell count with fever, decrease in a certain type of white blood cell, diarrhea, peripheral neuropathy, decrease in red blood cell count, weakness and fatigue.

Herceptin has two approved uses in metastatic breast cancer: in combination with the chemotherapy drug paclitaxel, for the first-line treatment of HER2-positive mBC; and Herceptin alone for the treatment of HER2-positive mBC in patients who have received one or more chemotherapy regimens for metastatic disease.

The Roche Group has also submitted a Marketing Authorization Application to the European Medicines Agency for Perjeta in combination with Herceptin and docetaxel chemotherapy. This application is currently under review by the EMA.

FDA approved the **Ventana Companion Algorithm p53 (DO-7) image analysis application**, which uses the iScan Coreo Au scanner and Virtuoso software developed by Ventana Medical Systems Inc., a member of the Roche Group.

The p53 (DO-7) image analysis algorithm assists pathologists in the detection and semi-quantitative measurement of p53 (DO-7) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue.

When the p53 (DO-7) algorithm is used in conjunction with the CONFIRM anti-p53 (DO-7) Primary Antibody, it may be used as an aid in the assessment of p53 expression in breast cancer patients, but is not the sole basis for treatment.

The FDA clearance includes all of the components of the Ventana laboratory workflow system, including the BenchMark XT slide stainer, p53 clone DO-7, iView and ultraView DAB detection systems, iScan Coreo Au slide scanner, and Virtuoso image management software.

FDA is seeking public comment on a proposal encouraging manufacturers to consider the safety of children in the design of new X-ray imaging devices.

In the draft guidance, FDA recommends that manufacturers design protocols and instructions that address use on pediatric patients.

The guidance also proposes that manufacturers who do not adequately demonstrate that their new new X-ray imaging devices are safe and effective in pediatric patients should include a label on their device that cautions against use in pediatric populations.

FDA is collaborating with the Alliance for Radiation Safety in Pediatric Imaging and manufacturers, through the Medical Imaging and Technology Alliance, to develop pediatric imaging radiation safety training materials.

The FDA has also launched a pediatric X-ray imaging website that provides recommendations for parents and health care providers to help reduce unnecessary radiation exposure, and information for manufacturers of X-ray imaging devices.

A workshop scheduled for July 16, 2012, will bring together industry, X-ray imaging equipment users and patient advocates to discuss FDA's draft guidance.

The **Reagan-Udall Foundation** received $900,000 in funding from **FDA** to support its operations and infrastructure. The foundation is an independent, non-profit organization, created by Congress in 2007 to study regulatory science initiatives.

The foundation employs experts, consumer advocates and research scientists to cultivate scientific evidence relevant to the development, manufacturing and use of medical products. The law requires FDA to provide between $500,000 and $1.25 million each fiscal year.

"Genomic science, biomarker research, and biomedical information technology are examples of areas of rapid scientific progress that have the potential to help improve the safety and effectiveness of FDA-regulated products," said Mark McClellan, chair of the foundation's board of directors and former FDA commissioner.

In 2011, the foundation received a grant from Susan G. Komen for the Cure to support a pilot project to better understand treatment toxicity in a specific cancer population.