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Report Calls For Stronger Peer Review, Prioritization, For Cancer Clinical Trials

By Kirsten Boyd Goldberg

The National Cancer Advisory Board voted unanimously June 7 to accept a plan for restructuring the government-funded cancer clinical trials system.

The Clinical Trials Working Group, appointed by Institute Director Andrew von Eschenbach in January 2004, proposed 22 initiatives that it said would "enhance the best of all the components of the NCI-supported clinical trials system."

Full implementation of the plan would take five years and $113 million,

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Despite Press Reports, No Settlement Date Set For Bristol's Pact With Federal Prosecutors

By Paul Goldberg

On June 6, The Wall Street Journal and The New York Times reported that Bristol-Myers Squibb Co. (NYSE: BMY) and the U.S. Department of Justice were on the verge of settling a criminal investigation of alleged accounting improprieties by the company.

Relying on unnamed sources, news reports indicated that Bristol would pay the government $300 million, and, according to the Journal, Bristol Chairman and CEO Peter Dolan would give up the board chairmanship.

The deal was to be announced on Tuesday or Wednesday, the Journal reported. Yet, Tuesday came and went, then Wednesday passed, and as Thursday wore on, the story of an imminent deal acquired the feel of an unfulfilled promise.

"There is no announcement pending concerning Bristol-Myers Squibb, and nothing is planned," Michael Drewniak, a spokesman for the U.S. Attorney's Office for the District of New Jersey, where the case is prosecuted, said to The Cancer Letter Thursday afternoon.

Drewniak has been saying the same thing publicly—and was dutifully quoted—since Monday.

BMS spokesman Brian Henry declined to comment. "There is nothing to talk about," he said.

How did an anonymous description of a yet-to-be-completed deal show up in the press?

"We don't know," Henry replied. "We don't have a comment on that."

Who would have leaked that story and why?

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Proposal Says $113 Million Needed To Implement Plans

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starting this fall at the beginning of fiscal 2006, the working group's report said.

The report endorsed the current system of NCI-supported clinical trials cooperative groups involving academic and community oncologists. NCI also supports trials through the Cancer Centers Program, the Specialized Programs of Research Excellence grants, the Community Clinical Oncology Program, Program Project grants, and investigator-initiated R01 grants.

"The strength of the current system is that it involves many institutions across the public, private, and academic sectors, as well as a broad cross-section of clinical investigators and other healthcare professionals," the report said. "The challenge is to bring these diverse institutions and individuals together into an integrated and efficient, but innovative and responsive, engine for moving therapies to patients."

The report recommended establishing a process for setting a national agenda for clinical trials. According to the report, this would require several new committees:

—An Investigational Drug Steering Committee to provide external scientific and clinical expertise for the design and prioritization of phase I and phase II trials with agents for which the NCI Cancer Therapy Evaluation Program holds the Investigational New Drug licenses. The committee would include the principal investigators of phase I grants and phase II contracts, senior CTEP staff, other experts as needed, patient advocates, and community oncologists.

—Scientific Steering Committees to address design and prioritization of phase III trials in each major disease area. The plan proposes to "leverage existing Intergroup, cooperative group, SPORE and cancer center structures" to form these committees, in effect, functioning much as the current Intergroup committees. All phase III trials funded by NCI would be peer reviewed through these committees, which would replace the existing Intergroups.

—A Clinical Trials Oversight Committee of the NCAB would be formed to advise the NCI director on conduct of clinical trials across the Institute.

Once the phase III steering committees are in place, NCI would determine whether to include all Institute-supported phase II trials in this prioritization process. "The ultimate goal is to coordinate prioritization of all clinical trials funded by NCI," the report said.

Also, the report said NCI should "develop a coordinated organizational structure… to manage the entire clinical trials enterprise supported by the Institute." Currently, the Division of Cancer Treatment and Diagnosis manages treatment trials, while the Division of Cancer Prevention manages prevention trials, and the Center for Cancer Research oversees intramural clinical trials.

"The NCI director will appoint an internal committee composed of senior leaders of all divisions who are responsible for clinical trials to develop detailed recommendations for restructuring the internal NCI management of clinical trials to achieve the objectives of the CTWG initiatives and to provide ongoing integration and oversight of clinical trials supported by NCI," the report said.

The report recommended establishing a funding mechanism and providing a budget to support correlative science and quality-of-life studies in conjunction with clinical trials, as well as creating a "comprehensive database containing information on all NCI-funded clinical trials," changing NCI's incentives to promote collaborative team science, and developing standard electronic case report forms.

"Fifty years ago, NCI had the foresight to initiate support for networks of investigators and institutions engaged in clinical trials who could speed the development of new cancer therapies," James Doroshow, co-chairman of the working group and director of the NCI Division of Cancer Treatment and Diagnosis, said to the NCAB. "Over the next half-

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century, with enhanced commitment of time an scientific expertise from extramural investigators, physicians, and advocates, as well as the new investment called for by this restructuring, it is our expectation that NCI, in collaboration with the entire clinical trials community, will lead the process of translating extraordinary advances in cancer biology into the clinical trials that materially improve the outcome of cancer patients everywhere."

About 75 percent of the new funding would consist of direct support for extramural activities, the report said. NCI would use 10 percent of the funds to develop a comprehensive clinical trials database, 10 percent to run the new committees required under the proposed trials prioritization process, and 5 percent would support NCI management.

The CTWG presented its preliminary report to the NCAB earlier this year (The Cancer Letter, Feb. 25). Doroshow presented a brief overview of the plan at the American Society of Clinical Oncology annual meeting May 14 (The Cancer Letter, May 20).

Reactions Mixed: Relief, Suspicion

Reaction to the proposals among cooperative group investigators was mixed. Some endorsed the recommendations, while others continued to worry that NCI's ultimate goal would be to gradually consolidate and centralize the 12 independently-governed cooperative groups.

"I'm quite pleased with the way this report came out," Richard Schilsky, chairman of Cancer and Leukemia Group B, said to the NCAB. "If everything can be implemented the way we envision it, I think it will profoundly influence for the better the way we do clinical trials in cancer in this country."

Schilsky served on the working group.

"I am relieved by what I have read so far," said Richard Goldberg, chairman of the CALGB Gastrointestinal Committee, head of the Colon Cancer Task Force of the Gastrointestinal Cancer Intergroup, and associate director for clinical research, UNC Lineberger Comprehensive Cancer Center. Goldberg wasn't involved in the working group.

"Many of us were concerned that there would be an attempt to deconstruct the cooperative groups and reconstruct them as a single huge organization," Goldberg said to The Cancer Letter. "While the current mechanism has its flaws, in my opinion, cooperative group trials have accomplished a tremendous amount in the U.S., and their funding by NCI has been a real advantage. Having groups with different flavors adds diversity to the process. In Europe, the vast majority of studies are funded and the data controlled by pharmaceutical companies. The U.S. system adds important objectivity to the evaluation of agents."

Other observers said the wording of the report is vague in places, and the document could provide cover for consolidation of group functions. Statisticians have been concerned that NCI may merge the cooperative group biostatistics centers under the Institute's Cancer Bioinformatics Grid, which Institute officials say will eventually become a massive Web-based repository of cancer research data.

The concern about consolidation was fueled by von Eschenbach's public and private statements critical of the groups. Also, two years ago, NCI tried unsuccessfully to put the groups' biorepositories under contract to the Institute. That arrangement would have eroded the groups' control over the tissue banks, group leaders said at the time.

In his remarks to the NCAB earlier this week, von Eschenbach said his charge to the working group "wasn't simply to fine-tune the system, but to start with a blank sheet of paper and look ahead to 2015 at what the reality will be like and what it would take to get there."

"One thing that I think emerged out of the process is trust," von Eschenbach said. "There was a lot of concern as to what was this effort about, what was its purpose and goal, yet people trusted that there was an effort to forge a new opportunity."

The committee determined that the system needed "renovation," von Eschenbach said. "Some parts have served us well in the past, but are not suitable or adapted for the future. Those needed to be demolished and replaced. Some parts needed adaptation… and some parts needed to be reoriented so they fit more effectively."

NCI will begin to implement the plans immediately, von Eschenbach said. "Everyone has the commitment of the Institute that this work will not be one more report. This report will change the future of clinical research in this country.

"One of the greatest things we will see come out of this is elimination of the waste of the human capital," von Eschenbach said. "So many people in this community expend such enormous amounts of energy and effort trying to make that incremental progress. Everyone who has been involved in the clinical research enterprise is fatigued by the enormous amount of effort that's required to get an outcome. What this report will realize is our ability to eliminate some of that waste. It

isn't just about fine-tuning things, it's much more about creating a new, streamlined pathway that will bring efficiencies…. We are going to see our talent, energy, and effort result in more lives saved."

GI Intergroup As Model

The proposed network of Scientific Steering Committees "represents significant restructuring in current procedure for selecting phase III trials," Doroshow said to the NCAB. These committees will conduct state-of-the-science meetings to develop priority areas for phase III clinical trials.

"We hope to roll out a small number of the steering committees, perhaps four in the first two years, and then do an evaluation to see whether we are on the right track," Doroshow said.

Intergroup committees within the cooperative group system were models for the proposed steering committees, particularly the Gastrointestinal Cancer Intergroup, Schilsky said to the NCAB.

"A proposed reorganization of the GI Intergroup, that is supported by all the cooperative group disease committee leaders and the cooperative group chairs, looks remarkably like what Jim presented for these disease-specific strategy committees," he said. "I'm very encouraged by the fact that the investigator community itself, as represented by the GI Intergroup, has already begun to think about how to do these things somewhat differently, so that we get better coordination, better collaboration, we bring in content experts as appropriate, bring in representatives of SPOREs, cancer centers, and other funding mechanisms, so that within the realm of GI cancer, we have a very comprehensive approach.

"I'll be frank with this group, there is concern that has been expressed among the cooperative groups about whether this prioritization process will in some ways make the internal prioritization process that typically goes on within the cooperative groups somewhat superfluous," Schilsky said. "If that were the case, then there's a concern that it may diminish interest on the part of investigators in participating in the cooperative groups as currently structured.

"I personally don't think that that needs to be a concern," Schilsky said. "I think that there will continue to be a role, and an important role, for the debate that occurs at the level of individual cooperative groups. That's where a much broader swath of expert investigators reside than on one of these individual strategy committees.

"However, it clearly will be important to have this national prioritization process," Schilsky said. "There are lots of questions, lots of agents, too few patients and too few dollars, to be able to do everything that needs to be done. These things, in my view, can be complementary, and if the system works well, should really ensure that only the very best trials go forward."

Many of the same participants on the Intergroup committees would be involved in the steering committees, said James Abbruzzese, chairman of gastrointestinal oncology and digestive disease at University of Texas M.D. Anderson Cancer Center, and a member of the CTWG. "In a complex group of diseases like GI, there would be working groups with specific diseases assigned," he said. "This process is beginning to work in GI. We can envision this process functioning extremely well. We hope this process will reduce duplication and improve collaboration between cooperative groups and, ultimately, provide the best trials."

"NCI has no interest in micro-managing these committees," Howard Fine, chief of the NCI Neuro-Oncology Branch and co-chairman of the CTWG, said to the board. "It's our intent that each individual committee will self-organize. Each disease type has its own particular way of doing business, has its own interests relative to the disease. It's our intent to allow each disease committee to put together the best organizational structure for their own purposes."

CALGB's Goldberg said he agreed with the report's proposed system of prioritization. "There is a need for a group with some authority to set the national agenda for treatment trials in a given disease," he said. "That has been largely lacking in the system to date."

Until recently, NCI hasn't tried to prioritize trials, Goldberg said.

"NCI looked at each protocol on its own merits and either didn't have the authority or didn't take the approach that it should prioritize among competing groups," he said. "There could be three to five phase III trials active in advanced colorectal cancer in the U.S. at one time, all of which either doom each other to failure, or slow the speed of accrual to the point where the question being answered lacks relevance when the trial gets to the analysis stage."

As chairman of the Colon Cancer Task Force of the GI Intergroup, Goldberg holds monthly conference calls with representatives from all of the groups, patient advocates, and ad hoc experts. "Ideas are discussed, modified, and sometimes put on the back burner for a while until we can get to some consensus," he said. "We keep track of the studies as they progress (or don't) through the various bureaucracies that they must traverse before they open to accrual.

"By the time an idea emerges from the task force, it has been vetted, and all of the groups take some ownership," Goldberg said. "If groups choose to compete, they know what each other are doing. In some cases, we have interrupted an attempt to compete and pressured groups to rejoin our top priority. There is an attempt to balance studies across groups to use the data collection and statistical resources efficiently.

"Once an idea surfaces, it is owned by its promoter, and we would shun any attempt by a more powerful opinion leader to spirit it away, a phenomenon that I observed to happen with some regularity in the early years of my intergroup involvement," Goldberg said.

"As an example of an attempt to serve a national agenda, recently we made a deliberate decision to have two adjuvant trials, one with chemo + bevacizumab and the other with chemo + cetuximab in colorectal cancer, because we felt that the field and the patients were best served by evaluating both monoclonals simultaneously," Goldberg said. "I think that this system has had its moments of great success. Sometimes, when we have been mired in lack of consensus, we lost time. However, when we came out the other side, we did all own the output.

"What I hope will happen is that the new system will allow the engagement of some additional individuals with different perspectives, so that we see the full potential of each trial," Goldberg said. "However, this is going to be work, and it will need to be taken seriously by those involved. NCI should also devote some resources to support whomever is leading each group. The leaders need to be carefully chosen, or this could become a dictatorship.

"I am cautiously optimistic," Goldberg said. "I also feel some sense of personal pride that I believe my colleagues on the Colon Cancer Task Force will share, because the GI Intergroup is credited as having beta-tested this new paradigm."

Board Discussion

At the NCAB discussion, board member Carolyn Runowicz, director of the Carole and Ray Neag Comprehensive Cancer Center, University of Connecticut, asked Doroshow whether the cooperative groups had read the report. "How much input will they have in changing or modifying the document, or is it a done deal?" she asked.

"I felt that it would be inappropriate to send out this document before you all had a chance to look at it," Doroshow said. "They have not seen the document. They have seen all of the slides from our ASCO presentations and our presentation [to the NCAB] in February. I personally called each cooperative group chair over the past week to update them on what we were about and what would be in this document. I'm the guest of honor at the cooperative group coalition meeting [June 20]."

"This has not been done in secret," said NCAB Chairman John Niederhuber, professor of oncology and surgery, University of Wisconsin-Madison.

Board member Lydia Ryan, of Children's Healthcare of Atlanta, asked whether pediatricians were involved in the working group and what role they would play in the plan's implementation.

"The pediatricians, as in most things, are ahead of the adult oncologists," Doroshow said. "There has been a lot of consolidation already. They can certainly participate, but they are starting at a place that is much more organized than the rest of oncology."

Peter Adamson, chief of clinical pharmacology and therapeutics, Children's Hospital of Philadelphia, and a member of the CTWG, noted that the four pediatric groups merged several years ago to form the Children's Oncology Group. "Many aspects of this report will impact us," Adamson said. "In some ways we are a few steps ahead, but we still have some distance to go."

Board member David Koch, executive vice president, Koch Industries, asked if the working group considered combining phase II and phase III trials. "If you could do that, it could save an enormous amount of money and time," he said.

"I am very interested in collapsing the process down, getting drugs into patients much earlier than we do now, using smaller numbers of patients, if we have the appropriate pharmacodynamic, molecular tools to do that." Doroshow said. "I think it may well be, in the future, possible to do trials with 200, 300, 400 patients, not randomized, in diseases in which the response rates in unselected patients are so low, that if we have the appropriate markers, we would be able to get a result that will allow the application to go forward to the FDA. Absolutely, we would be poised to do that, but that requires the availability of real-time correlative science dollars to be appended to the prioritization process."

Richard Pazdur, recently named director of the FDA Office of Oncology Drug Products, representing the agency on the NCAB, asked Doroshow to describe how the reorganized system would work with industry.

"Obviously, since the last time we restructured clinical trials in the U.S.—or structured them—there have been some fundamental changes in the way industry does trials," Pazdur said. "There is an increasing internationalization of clinical trials. Companies

have hired many of our brightest and best people, so they do have the manpower, the intellectual power to develop their own drugs. There have been criticisms levied against working with government in the sense that sponsors lose control of trials, they are not done in an expeditious fashion, and hence, drugs would be delayed. There are several problems that I see. How do you determine which companies and which drugs specifically that you want to work with? How to you get companies to work together on common issues; for example, developing the science of the disease, target assay validations? These are fundamental issues that need to be addressed, because you have two different structures here. You have the government and you have industry, and how you mesh these two, I think, are vitally important to getting drugs out there. Obviously, the private sector has their own sets of desires, a that's to get their particular drug out there. We, as a government entity, may have different interests, and that is the science of developing an entire field. These don't necessarily have to be mutually exclusive, but they are different interests."

DOROSHOW: "That's a very, very large question—"

PAZDUR: "Sorry."

DOROSHOW: "—Some of which is not really related to the CTWG, in that the issue of developing biomarkers is something that the government has to do a better job of. We all certainly have to figure out better ways to work with industry, because there is a lot of intellectual property that is not available publicly. That's not something that we addressed, but it is something we are interested in. I think everyone on our committee would agree that David [Parkinson, of Amgen] and Steve [Averbuch, of Merck] played a critically important role in making sure that these issues that transcend individual companies, that are critical for the overall clinical trials process, were integral to our thinking."

AVERBUCH: "Merck obviously didn't hire the best and the brightest…. Clearly, there will always be elements that remain in the private sector, as long as we have that system, and there will be private interests driven by industry. The thrust of this report was identifying the domains where there is a private-public partnership, and trying to make those processes much more efficient with respect to setting up these dialogues. Although industry is not explicitly involved in the prioritization process, there's no doubt that will impact on the direction of industry as we will be listening to those steering committees to help us identify where the greatest areas of medical need are, where the science is going, and how to respond to that. I think there will be a lot of integration, both explicit, where there are specific trial activities going on between NCI and industry, where FDA is going to be much more engaged in dialogue, but also indirectly by our looking from the outside in at this prioritization process."

KOCH: "I'm not clear exactly to what extent the FDA was involved in the development of the plan and whether the FDA wholeheartedly buys into the report. Obviously, the FDA has to agree with the validity of the results that will come from these revised clinical trials, and if they don't, then, gosh, this whole effort would have been in vain."

PAZDUR: "I signed page 2. We were involved."

DOROSHOW: "Dr. Pazdur was a member of the committee."

PAZDUR: "What we are talking here are structural changes, not anybody saying we are going to decrease the level of evidence or the proof of what we need to approve a drug. The issues here are streamlining and making a product better. We would be more than happy to take a look at smaller trials that basically show better results. You don't need thousands and thousands of patients if you have a 90 percent response rate. That's a lot different than a 5 percent response rate. Your confidence in approving a drug is much different. I think we are open, through the Critical Pathway [an FDA strategic plan], to look at novel designs for clinical trials, statistical approaches, that will reduce some burdens, and also regulatory burdens of auditing. We are fundamentally interested in impressive results and drugs that work, rather than laborious efforts at trying to prove that minor effects are there. I don't think there are any fundamental issues with this report that the FDA would have a problem with."

KOCH: "I think it's great we have that on the record."

SCHILSKY: "The privately-funded and publicly-funded clinical trials... are very much complementary and need to remain so. Industry has a critical role to play in developing drugs and bringing them to the marketplace where they can benefit patients. The publicly-funded system has historically been largely an investigator-initiated system, and needs to remain as such. A fundamental goal in the publicly-funded system, in addition to generating new knowledge, is figuring out how to integrate new therapies into medical practice.

"Herceptin was based on research done in university laboratories, developed by a company, brought to market by a company, but we saw the real impact of Herceptin at this last ASCO meeting in two

large clinical trials done in the publicly-funded system, in the adjuvant setting, with p-values of 3 times 10^{-12} showing an improvement in disease-free survival. That story exemplifies the complementary relationship between what industry does and what our publicly-funded system does, to make life better for all of our patients."

ANNA BARKER, NCI deputy director for advanced technologies and strategic partnerships: "Was there any discussion of how to bring more new ideas to the table?"

MARK RATAIN, associate director for clinical sciences, Cancer Research Center, University of Chicago, and a CTWG member: "I would argue that there's a big pipeline out there. There are probably 500 cancer drugs currently in clinical trials, and probably about another 1,000 drugs out there being developed by the pharmaceutical industry that are ready to go to the clinic. The issue is getting them through the system. Right now the success rate for oncology drugs that enter the clinic—success defined as FDA approval—is 8 percent. We need to do a better job of prioritizing which drugs we want to take to phase III trials. Focus on critical issues in phase I, phase II, such as the right dose, the right schedule, the right patients to treat. We have many opportunities, and by having a better public system, more companies will want to work with it."

The report, "Restructuring the National Cancer Clinical Trials Enterprise," is available at http://integratedtrials.

Next: Translational Research

NCI Director von Eschenbach said he would now form a Translational Research Task Force to examine the "entire landscape" of translational research, similar to the CTWG's review of the clinical trials system.

Ernest Hawk, director of the NCI Office of Centers, Training, and Resources, will serve as chairman of the task force. The group will report to the NCAB Cancer Centers Subcommittee.

BMS Made Early Disclosure Of 2003 Deal With State AGs

(Continued from page 1)

"It probably would be best to ask the reporters," he suggested.

Premature disclosure of details in pending deals is a standard public relations strategy companies use to steal the thunder by preempting the prosecutors' news releases. By being the first to break the story, a company creates the illusion of being in control, and the government's announcement—which comes later—becomes old news and the impact on stock price is minimized.

"Going to the court of public opinion in legal cases is a high-risk strategy," said Sheldon Rampton, research director at the Center for Media and Democracy and an expert on the PR industry. "You have to be pretty confident that something like this will break your way before you make an announcement."

In January 2003, during similar negotiations, Bristol stunned state attorneys general by unilaterally announcing an "agreement in principle" to pay $670 million to settle claims related to the company's efforts to block generic competitors from the market for the cancer drug Taxol and the anxiety drug BuSpar.

According to state prosecutors, Bristol made that disclosure after working out the financial terms of the settlement, but before concluding negotiations on limitations on its future conduct (The Cancer Letter, Jan. 10, 2003).

"We don't have an agreement in principle," Meredyth Smith Andrus, an assistant attorney general in Maryland, one of the states that led the litigation, said at the time. "For government prosecutors [injunctive relief] is of paramount importance."

A deal with Justice this week would have allowed Bristol to conclude a lingering investigation of its acknowledged past practice of building up wholesalers' inventories and diverting operating income to enhance dividends and create the illusion that the company was achieving its ambitious growth goals.

Bristol set the stage for full resolution of this matter by settling the remaining lawsuits by shareholders, those who chose not to take part in last year's settlement of litigation pertaining to accounting irregularities and the company's relationship with ImClone Systems Inc.

Under a deal announced June 1, the plaintiffs' claims would be dropped in exchange for $89 million.

Last year, Bristol agreed to pay $300 million to settle class action suits from shareholders and another $150 million in civil claims by the Securities and Exchange Commission (The Cancer Letter, Aug. 6, 2004).

If Bristol settles with Justice by paying a $300 million penalty, the company will have paid a total of $840 million to settle the accounting irregularities and ImClone-related matters. It's unclear whether former and current Bristol executives would face separate charges.

No Evidence FDA's Crawford Had Affair, Investigation Finds

By Paul Goldberg

The HHS Office of the Inspector General said it found no evidence of an extramarital affair between FDA Acting Commissioner Lester Crawford and a female subordinate.

Government investigators concluded that Crawford and the subordinate whose name was blacked out in the investigation report had a "collegial, close personal, or 'father-daughter' relationship."

The OIG report, dated June 7, was released by Sen. Mike Enzi (R-WY), chairman of the Senate Health, Education, Labor and Pensions Committee. Enzi asked for the investigation two months ago after receiving an anonymous letter when his committee was reviewing Crawford's candidacy for heading FDA. Enzi said he would now move to have Crawford confirmed.

According to the OIG report, investigators reviewed over 5,700 e-mail messages between Crawford and the woman, finding no sign of impropriety. "Both Dr. Crawford and [the woman] denied having an affair," the report states. "Both submitted signed statements to that effect."

OIG found no evidence to corroborate the allegation that the woman's elevation to the Senior Executive Service was based on an improper relationship. However, investigators found that Crawford may have helped the woman in her application for the SES position. The acting commissioner was the "selecting official" for the SES post.

"Dr. Crawford… stated that [the woman] was selected, in part because of a recommendation made to him by an administrator within the Commissioner's office," the report states. "During an interview with us, this administrator stated that he made no such recommendation and that he had previously expressed concern about [the woman's] qualifications to join SES."

The report notes discrepancies in Crawford's and the woman's accounts of his role in her preparation of her SES application. The woman said Crawford provided "some assistance with her application," but the acting commissioner said he gave "moral encouragement."

The investigators corroborated the anonymous report that the woman was tardy in paying her credit card bill and that in one instance she used a government card to pay for a personal item while on travel. Those matters were resolved when FDA officials told the woman "to pay her bill to avoid administrative action" and "provided her with guidance on the proper use of the card."

A Notch-Signaling Pathway Inhibitor in Patients with T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL)

An investigational study for children, adolescents and adults with relapsed and refractory T-cell acute lymphoblastic leukemia/lymphoma is now accruing patients at various centers around the country.

This study's goal is to evaluate the safety and tolerability of a Notch inhibitor as a rational molecular therapeutic target in T-ALL, potentially uncovering a novel treatment for these cancer patients.

Eligibility criteria and treatment schema for the study include:

Notch-Signaling Pathway Inhibitor in Patients with T-ALL	
Eligibility Criteria	Patient must be = 12 months with a diagnosis of T-cell acute lymphoblastic leukemia/lymphoma AND must also have: • Relapsed T-ALL • T-ALL refractory to standard therapy • Not be a candidate for myelosuppressive chemotherapy due to age or comorbid disease ECOG performance status =2 for patients >16 years of age OR Lanksy performance level >50 for patients 12 months to =16 years of age Fully recovered from any chemotherapy and >2 weeks from radiotherapy, immunotherapy, or systemic steroid therapy with the exception of hydroxyurea or intrathecal therapy Patient must be >2 months following bone marrow or peripheral blood stem cell transplantation No treatment with any investigational therapy during the preceding 30 days No active or uncontrolled infection
Treatment Plan	Open label and non-randomized, this study is conducted in two parts. Part I is an accelerated dose escalation to determine the maximum tolerated dose (MTD), and Part II is a cohort expansion at or below the MTD. MK-0752 will be administered orally. Plasma concentrations will be measured at defined time intervals.

For information regarding centers currently open for enrollment, please contact 1-888-577-8839.

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