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Von Eschenbach To Serve Dual Role: Acting FDA Commissioner, NCI Director

By Paul Goldberg and Kirsten Boyd Goldberg

President Bush has combined unprecedented powers—and unexplored conflicts—in the hands of a fellow Texan and family friend Andrew von Eschenbach.

On Sept. 23, the urologist who pledged to put an end to "suffering and death due to cancer" by the year 2015 was named acting FDA commissioner and allowed to keep his job as NCI director.

As people familiar with NCI and FDA were trying to understand how one man can serve in this dual role, von Eschenbach offered an answer: he would delegate. "It is the strong professionalism of the management and staff at both organizations that will enable me to carry out the dual roles,"

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Von Eschenbach Faces Triple Conflict As Leader Of NCI, FDA, and C-Change

By Paul Goldberg

The duties of Acting FDA Commissioner Andrew von Eschenbach will likely include regulatory oversight of NCI Director Andrew von Eschenbach.

Self-regulation is the most startling aspect of a tangle of conflicts the administration's appointee will face as he combines his two jobs. Also, the appointment compounds the seriousness of von Eschenbach's existing conflict of interest, which stems from his role as vice chairman of the board of C-Change, a non-profit group headed by George and Barbara Bush.

Von Eschenbach, formerly a urologist at M.D. Anderson Cancer Center, is credited with bringing the Bushes into the organization. Four years ago, when von Eschenbach was named NCI director, HHS officials gave him a waiver to continue to function as a C-Change fiduciary.

Legal experts interviewed by The Cancer Letter said von Eschenbach is facing three sets of conflicts:

--His duties at NCI vs. his duties at FDA,

--His duties at NCI vs. his duties at C-Change, and

--His duties at FDA vs. his duties at C-Change.

"If this were a horse race, Dr. von Eschenbach would be a 'trifecta' pick for conflicts of interest by adding the FDA to his NCI and C-Change affinities," said Michael Clark, a former federal prosecutor who is now an attorney with the Houston law firm of Hamel, Bowers & Clark and editor of LJN Bioethics Legal Review.

"It seems to me, Dr. von Eschenbach is wearing three hats, and none

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FDA Job Is An "Interim Role," NCI Director Tells Advisors

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he wrote in an email to members of NCI advisory committees. Von Eschenbach described his FDA job as an "interim role."

The message made no mention of the conflicts inherent in running the two institutions. NCI has vested interests in many compounds and works in partnership with pharmaceutical companies. FDA has the power to stop trials to protect patients from unwarranted risk. Most importantly, the agency approves drugs.

"While the missions of the NCI and FDA are very different, the purpose is the same—to bring patients the full benefits of molecular medicine," von Eschenbach wrote.

FDA officials are reviewing the conflicts, said Julie Zawisza, a spokesman for the agency. "We obviously have to be mindful of that," she said. "We don't know yet what the scope of his activities will be with respect to the oncology drugs, but it's being looked at."

In addition to running NCI and FDA, von Eschenbach is vice chairman of the board of C-Change, a coalition of cancer groups heavily funded by pharmaceutical companies and headed by former President George Bush and his wife Barbara Bush. Peter Dolan, CEO of Bristol-Myers Squibb Co., and Gary Reedy, a vice president at Johnson & Johnson, also hold board seats.

"It is difficult to be a regulator and a regulated at the same time, or to be with a group funded by industry, when you are regulating that industry," said J. Mark Waxman, a healthcare lawyer at the Boston firm of Foley & Lardner.

Von Eschenbach's appointment has attracted a new level of scrutiny to his stewardship of NCI. (See story on page 5).

Now, von Eschenbach's critics are pondering the implications of his new power. "At this point, he is no longer just Andy; he is the President's Andy," said an oncologist who spoke on condition that his name would not be used. "He is the Cancer Czar, God help us."

Von Eschenbach's dual role is a triumph for the predominantly conservative groups that demand lowering the bar for drug approval.

This movement operates outside the mainstream of oncology and is separate from the pharmaceutical industry. It is led by the financier and cancer survivor Michael Milken, a von Eschenbach ally, and the editorial board of The Wall Street Journal (The Cancer Letter, Aug. 5).

The Journal editorialists described von Eschenbach's appointment as a "regime change" at the agency. "FDA has long needed to recognize that there are valid modes of science beyond the randomized clinical trial," the paper said in an editorial Sept. 27.

FDA should abandon the requirement that cancer drugs demonstrate efficacy, Milken wrote in an opinion article for the Journal two years ago. Last week, Milken wrote a "guest commentary" for the NCI Cancer Bulletin, the Institute's weekly newsletter. "For the first time in history, we hold the potential of eliminating cancer's burden," he wrote.

"The FDA has become a tall barrier to that progress," said Steven Walker, a patient activist and frequent contributor to the Journal who opposes the agency's reliance on randomized clinical trials. "Dr. von Eschenbach knows what change is needed, he realizes that change requires goal-setting and holding people accountable for achieving those goals, and he will not be afraid to take on the FDA's bureaucratic resistance to change that has rendered it an archaic and ineffective stumbling block in the war on cancer and other serious and life-threatening diseases."

"They Get It" on Capitol Hill

"A lot of people on Capitol Hill are very upset about this. They get it," said Merrill Goozner, director of the Integrity in Science Project at the Center for Science in the Public Interest. "They understand this is fundamentally flawed."

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In separate letters, Sens. Charles Grassley (R-Iowa) and Sen. Edward Kennedy (D-Mass.) asked the White House to name a full-time FDA commissioner.

"No single person, no matter how able or dedicated, can do both of these vital full-time jobs on a part-time basis," Kennedy said in a statement.

The plan "ain't going to work," Sen. Christopher Dodd (D-Conn.) said in a press interview. "I don't care who the guy is—he could be Jonas Salk—he's not going to do both jobs."

The dual appointment "looks like a conflict" and "given the problems at the agency, that's not a prescription in my view for turning things around," said Sen. Ron Wyden (D-Ore.).

Von Eschenbach is an "excellent choice" who will provide "strong, certain leadership" to FDA, said James Greenwood, president and CEO of the Biotechnology Industry Organization.

Von Eschenbach's "leadership, and the expertise of dedicated veteran FDA regulators, will allow the agency to continue its important work until a new commissioner is nominated and confirmed," said Billy Tauzin, president and chief executive of the Pharmaceutical Research and Manufacturers of America.

First Pledge; First Blunder

The circumstances of von Eschenbach's appointment are unclear.

On Friday, Sept. 23, at 3:38 p.m., FDA Commissioner Lester Crawford announced that just two months after confirmation by the Senate, he would resign, because "it is time at the age of 67, to step aside."

The following day, The New York Times and The Wall Street Journal cited a confidential source who said Crawford's resignation stemmed from failure to disclose financial information. Crawford and members of his family dispute this allegation, stating that the commissioner had indeed made a sudden decision to retire, effective immediately.

As Crawford's email bounced out of the agency Friday afternoon, another rumor emerged: von Eschenbach had the inside track to replace him.

At 6:15 p.m., the White House announced that von Eschenbach would indeed be named acting commissioner. Why would the Administration announce this change at 6:15 p.m. on a Friday, as the country was riveted to the news of an approaching Category 4 hurricane? Why didn't the White House devote a few days to considering candidates and assessing their potential conflicts?

What came next was the biggest surprise. On Saturday, von Eschenbach told reporters that he had no plans to leave NCI. In an interview with The New York Times, von Eschenbach said he had a "100 percent commitment" to both jobs.

This pledge may have been his first blunder in the new role.

"The nominee the President selects to serve [should] demonstrate a clear understanding of the importance of this position, and a willingness to dedicate 100 percent of his or her talents and energy to the FDA," Grassley wrote in a Sept. 26 letter to the White House.

"I expect that whoever is named commissioner—either acting or confirmed—will know that it's not possible to give the FDA the kind of strong new leadership that is needed to reinvigorate the agency on a part-time basis."

HHS Acknowledged Conflict With C-Change—And Waived It

(Continued from page 1)

of them fit very well," said Alan Milstein, a health care attorney with the firm of Sherman, Silverstein, Kohl, Rose & Podolsky, in Pennsauken, N.J.

At C-Change, von Eschenbach's fellow board members include executives from Bristol-Myers Squibb and Johnson & Johnson.

"So here you have companies who are bringing products before FDA, and he is sitting on the board of a non-profit organization with them; what more do you have to say?" said Merrill Goozner, director of the Integrity in Science Project at the Center for Science in the Public Interest.

"It's a conflict of interest for the same reason that we don't allow the head of the Securities and Exchange Commission to own stock in the companies he is auditing," Goozner said.

Von Eschenbach's drug approval agenda, which emerged during his years at NCI, emphasizes post-market surveillance and reliance on databases as an alternative to randomized clinical trials.

In 2003, von Eschenbach's top political operatives shopped around a plan for development of cancer prevention drugs that would be given to healthy people to treat conditions believed to be pre-cancerous.

The plan included reform of product liability laws to shield drug companies from injury claims, and reliance on FDA post-market surveillance and NCI's epidemiology database to monitor whether these

interventions do harm.

"It's shocking to see NCI associate its name with anti-science," said a member of the cancer prevention committee of the American Society of Clinical Oncology, which reviewed the proposal. "Whom is this for?" asked another member of the ASCO committee that withheld endorsement of the plan (The Cancer Letter, May 30, 2003).

Attorney Milstein said he fears that the lives of cancer patients would be imperiled as a consequence of von Eschenbach's conflicts.

"Human subjects will be left without the protection of the government," said Milstein, who represented the family of Jesse Gelsinger, who died in a gene therapy trial at the University of Pennsylvania. "When you are talking about cancer patients in trials, who are desperate for a cure, they are a vulnerable population. These are a class of subjects who need protection from overzealous and conflicted researchers."

The only thing worse than a conflicted researcher is a conflicted head of two institutions, Milstein said. "Here you got the researcher and the cop," he said.

This conflict cannot be remedied with any sort of a Chinese Wall that would restrict von Eschenbach's participation in the affairs of either NCI or FDA, ethics experts say.

"This is the head of the FDA!" said Milstein. "If you need to set up a mechanism by which this guy avoids conflicts of interest, then he shouldn't be there."

Steven Walker, an activist with Abigail Alliance, a patient group that demands early access to cancer drugs and argues against reliance on randomized trials, said he doesn't share such concerns.

"The goals of the two agencies have to be at least well enough aligned to allow real progress to reach real patients in real time—meaning when they are still alive," Walker said. "Presently, that is not happening, and the FDA is the ever-increasingly lethal reason for that."

Von Eschenbach's Waiver

Top HHS officials recognized von Eschenbach's conflict with C-Change, but allowed him and his deputy Anna Barker to act as fiduciaries of the organization.

No one would have objected to von Eschenbach or Barker taking part in C-Change as rank-and-file members or as ex officio members of the board.

The HHS waivers allow the two NCI officials to play a greater role as fiduciaries of an organization that includes parties that have business before HHS. Also, the waivers place von Eschenbach and Barker safely out of range of new NIH ethics rules that prohibit service on such boards if this is done outside official duties.

The Cancer Letter obtained copies of the waivers. The most recent document that covers von Eschenbach's conflict at C-Change—which at the time was called the National Dialogue on Cancer—is posted at http://www.cancerletter.com/archives/post.html?http://www.newslettersonline.com/user/user.fas/s=292/fp=3/tp=18?T=open_article,901522&P=article.

Legal experts who were asked to review that document said they were struck by its failure to spell out the rationale for granting the waiver and to state how the government expects to benefit as a result of allowing the NCI director to serve as a C-Change fiduciary.

"This is not like any kind of a waiver of a conflict of interest that I am familiar with, and I have spoken quite a bit on this subject," said Milstein. "If there is a conflict of interest—a true conflict, like this is—it's not something that can be waived or remedied by simply acknowledging it.

"Typically, the way these documents are worded, they emphasize that the conflict is not a real conflict," Milstein said. "What's unusual about this document is that it says there is a conflict, but we don't care. The purpose of this document is to allow him—with conflicted interests—to serve both posts, and it doesn't justify anything."

J. Mark Waxman, an attorney with the Boston firm of Foley & Lardner, agreed that the document contains no justification for granting the waiver.

"They had to get a waiver, because, as they said, obviously there is a conflict issue, and they decided to waive it," Waxman said. "What the document doesn't point out is why they needed to waive it. They say it's justified because he would serve as an assigned official duty activity. Well, why do they need that at all? Why is that necessary? He could have been an invited guest."

In a footnote, the document states that funding applications from C-Change would be subjected to the same level of peer review as other projects funded by NCI and NIH. "While Dr. von Eschenbach may figure heavily into the priority setting activity of the Dialogue and the NCI, all NCI resource allocation decisions are subject to review by committees of outside experts constituted under the Federal Advisory Committee Act, as well as by NCI Executive Committee, the operating committee for the NCI," the document states. "Therefore, it is highly unlikely that Dr. von Eschenbach could unilaterally take action to affect the financial interests of the Dialogue."

Waxman doesn't find this convincing.

"So they say he is unlikely to take unilateral action.

Well, that's not the issue," he said. "The issue is, could there be a very strong influence on both sides by virtue of singularity of interests? He is one guy."

This is not a hypothetical situation. After von Eschenbach took over the Institute, he asked C-Change to develop a plan to centralize collection of tumor tissues.

The development work was formally sponsored by C-Change, but the proposal included the results of a RAND Corp. study which NCI funded through a sole-source contract. Constella Health Sciences, a contractor paid at least in part by NCI, coordinated the work.

By outsourcing development of this program instead of directing NCI staff to draw up a plan, von Eschenbach evaded the open-doors requirements of the Federal Advisory Committee Act and the Freedom of Information Act.

When the work was done, C-Change proposed that tissue banking should be taken out of the public sector and given to another entity—C-Change (The Cancer Letter, Aug. 8, Dec. 12, 2003). The plan has since been scaled down and is yet to be implemented.

"If you have a situation where you have a government agent on one side giving money to an entity where they are on the board, that raises issues with respect to conflicts of interest and public perception," Waxman said.

Flaws notwithstanding, a mere declaration by HHS that von Eschenbach's conflicts have been waived is probably all that's needed to allow the urologist to sit on the C-Change board, ethics experts say.

"The question is whether an appointment is appropriate given the private relationship, even if there is a waiver," said Geoffrey Hazard, Trustee Professor of Law at the University of Pennsylvania Law School. "That is a policy and politics question."

Von Eschenbach's NCI: From "Humility" To Grandiose Plans

By Kirsten Boyd Goldberg

At his swearing-in ceremony as NCI director on Feb. 4, 2002, Andrew von Eschenbach said he "humbly" accepted his new job.

"What an incredible privilege to be a public servant and join the ranks of so many talented and dedicated individuals who have sacrificed in order to serve others," said the former urologic surgeon from M.D. Anderson Cancer Center.

Despite presenting himself as a humble servant, von Eschenbach has aggressively promoted a triumphant, grandiose, and, scientists say, blatantly unachievable vision to the public. Away from public view, his tenure as NCI director has been marked by secrecy, consolidation of power in the hands of a few selected individuals, a decline in the R01 payline, and a shifting of emphasis to "big science" projects.

One year after his acceptance of public service, von Eschenbach declared that NCI's mission would be nothing less than the "elimination of suffering and death due to cancer" by the year 2015.

This goal is "realistic," he said at the time. "It is like putting a man on the moon in a decade. We can make it a reality." (The Cancer Letter, Feb. 14, 2003).

The 2015 goal was developed as part of a one-year strategic planning process with the NCI leadership, von Eschenbach said.

However, NCI sources said consensus was reached on only the first part of the goal, the "elimination of suffering and death due to cancer."

NCI staff advised the director against setting a specific date, sources said. This would be an unrealistic, they cautioned.

Advocates for cancer research have a long history of promising cancer cures. Indeed, the claim that cures would arrive by 1976 helped encourage support for the National Cancer Act of 1971, which enhanced NCI's role and budget authority.

In the 1980s, then-NCI Director Vincent DeVita set a "Year 2000" goal of a 50-percent reduction in cancer mortality, but the goal soon became an embarrassment and NCI stopped mentioning it.

In the 1990s, NCI's leadership abandoned the war metaphor, and with it, the goal-setting for cancer incidence and mortality. Then-NCI Director Samuel Broder spoke in genuinely humble phrases about what the Institute could accomplish. Cancer research and treatment is all about "incremental progress," he said. It was important for NCI to maintain a "balanced portfolio" to pursue a variety of research leads.

Meanwhile, other organizations were clamoring for a renewed "war on cancer."

In 1995, the American Cancer Society conducted a "Futures Symposium," led by futurist Clement Bezold, inviting leaders of cancer organizations to envision the world in 2015 and establish goals for reducing the burden of cancer. Afterward, ACS issued a "challenge goal" to the federal government and cancer organizations to achieve a 50-percent decline in cancer mortality by 2015. This would require a variety of cancer control strategies, ACS said.

Also in 1995, the financier and prostate cancer

survivor Michael Milken held a "summit," where he presented a plan for a renewed assault on cancer. He suggested recruiting the commanders of the Persian Gulf War to lead the troops.

Richard Klausner, the NCI director at the time, didn't promote the war theme or endorse the ACS goal. He said he was guided by a microbiologist's vision of the potential of "molecular medicine." Research on cancer cells and genetics would find all the steps in the progression of healthy cells to cancer, and this would ultimately provide multiple targets for new therapies, Klausner promised.

The combination of political pressure and promises from scientists convinced Congress to double the NIH budget over five years. But as the new funds began to flow into NCI, proponents of the new war on cancer clashed with Klausner over how the money should be spent and called for legislation to establish an office of a federal "cancer czar."

In a public debate with Klausner, former NCI Director DeVita claimed that cancer research had reached "critical mass," enabling a shift of funding to cancer control. Klausner warned against forsaking basic research and making false promises to the public (The Cancer Letter, Sept. 22, 2000).

DeVita was representing the National Dialogue on Cancer, a group established by ACS funding, and founded by von Eschenbach. Two years ago, the Dialogue changed its name to C-Change.

The group's key white paper, titled "Conquering Cancer: A National Battle Plan to Eradicate Cancer in Our Lifetime," used the word "war" 20 times in 59 pages (The Cancer Letter, Sept. 28, 2001).

With the help of the Dialogue, von Eschenbach rose to prominence in the cancer community as the group attempted to develop a new National Cancer Act and sought more cancer control funding for the Centers for Disease Control and Prevention.

In 2002, von Eschenbach was slated to serve as president of ACS. Instead, President Bush appointed him NCI director.

It was nothing less than a victory for the warriors.

2015 Goal: Jaws Drop

One year after he became NCI director, von Eschenbach introduced a new version of the ACS 2015 goal. He gave it what public relations professionals call a "soft rollout."

Von Eschenbach made the announcement in the middle of routine remarks to the National Cancer Advisory Board. Jaws literally dropped around the table. It was a complete surprise to the Presidentially-appointed board.

In recent years, NCAB members have tended to avoid publicly challenging the NCI director. Most belong to institutions that receive grants and contracts from NCI. Others are politically connected with the Administration, or represent patient advocacy groups that work with NCI and must maintain a good relationship with the director.

Moreover, von Eschenbach had begun to foster a climate of fear among NCI staff and advisors, sources said. He shut down the Institute's traditionally open discussion of is budget priorities.

Few within NCI's circle of advisors and grantees have publicly questioned the 2015 goal, with one major exception. Harold Varmus, president of Memorial Sloan-Kettering Cancer Center and former NIH director, called the 2015 goal unrealistic. "We have a long way to go before we beat cancer," Varmus said at the 2005 annual meeting of the American Society of Clinical Oncology. "We're not going to do so before 2015."

Those outside NCI's influence view the goal as calculated public relations tool. "It was little more than aggrandizement for the purpose of ensuring continuous generous public support of NCI initiatives for the next decade," said Fredric Cohen, president of Pharma Growth Strategies, a pharmaceutical management consultant and former senior director for drug development at Johnson & Johnson.

The stunned NCAB didn't iimmediately jump on the 2015 bandwagon, and neither did other NCI advisors, patient advocates, and cancer professional organizations. Von Eschenbach went on the offensive.

He was scheduled to present the 2015 goal in remarks to the 2003 annual meeting of the American Association for Cancer Research, in Toronto. When the meeting was cancelled due to the SARS virus, von Eschenbach quickly promised the group $2 million to help fund a rescheduled meeting.

In the past, such funding decisions generally would be discussed and debated by the NCI Executive Committee, or go through formal peer review. The funding for AACR was presented to the committee as a *fait accompli*. No discussion was allowed (The Cancer Letter, June 20, 2003).

At the rescheduled AACR meeting, held that July in Washington, D.C., von Eschenbach's place on the agenda had moved up to keynote speaker. AACR issued a press release supporting the 2015 goal. Also at the meeting, NCI announced its plan, developed with the

National Dialogue on Cancer, for a multi-billion-dollar National Biospecimen Network, a biorepository.

Whether AACR needed government funding to put on its meeting is questionable. The group had $12 million in a reserve fund. Two years later, it received insurance coverage for most of its costs from the Toronto cancellation (The Cancer Letter, April 15, 2005).

The 2015 goal has pervaded NCI communications. Von Eschenbach rarely misses a chance to talk about it. NCI staff know that to propose a new program, they must include a sentence or two on how the project will help reach the 2015 goal.

Invoking the goal also is a not-so-subtle way to pressure for action or funding.

Anna Barker, NCI deputy director for advanced technologies and strategic partnerships, regularly makes the 2015 appeal. At an NCAB meeting earlier this month, she presented a plan to establish standard operating procedures for biorepositories. "We're not going to be able to move toward 2015 until we harmonize and resolve some of these issues," she said.

Survival Vs. Mortality

When von Eschenbach speaks about the goal to "eliminate suffering and death due to cancer" by 2015, he relies on five-year survival data to define progress.

The five-year survival rate measures how many people diagnosed with cancer are alive five years later.

Improvements in five-year survival are strongly related to changing patterns of diagnosis, experts say. Increasing cancer awareness and screening may lengthen the time between diagnosis and death, and may diagnose more people with early cancer, but may not affect mortality rates.

In testimony to the Senate Labor-HHS-Appropriations Committee earlier this year, von Eschenbach said "two out of three patients" diagnosed with cancer today "can look forward to being a cancer survivor." This was, indeed, an accurate statement based on current five-year survival data (The Cancer Letter, July 29, 2005).

"What is going to happen by 2015 as you project it?" Sen. Arlen Specter (R-Penn.) asked von Eschenbach.

"No one who hears the words, 'You have cancer,' will suffer or die from the disease," von Eschenbach said. "We will prevent and eliminate the outcome."

"So you will move from two out of three survivors to all three?" Specter asked.

"Yes, sir," von Eschenbach said.

By not mentioning the difference between the cancer survival rate and cancer mortality, von Eschenbach appeared to equate the two.

A study published in JAMA in 2000 of trends since 1950 found no relationship between changes in five-year survival and changes in mortality for the most common cancers in the U.S.

"To measure true progress in the 'war against cancer,' physicians and policymakers should focus on mortality," wrote the paper's authors, Steven Woloshin, Lisa Schwartz, and H. Gilbert Welch, of the VA Outcomes Group, VA Medical Center, White River Junction, Vt.

It is unclear what von Eschenbach means by "suffering." Two years ago, he said NCI would develop a method for measuring it, but it appears that this work hasn't been completed.

Senior Management Team vs. EC

Other profound changes have transpired at NCI during von Eschenbach's tenure, sources said.

NCI traditionally has been managed by an Executive Committee of about 11 senior executives: the director, deputy director, seven division directors, the deputy director for management, and the associate director for budget.

Over the years, von Eschenbach has increased the committee to 16 members, adding three new deputy directors. Also added to the EC were the directors of two offices that report to von Eschenbach: the Center to Reduce Cancer Health Disparities and the Office of Centers, Training and Resources.

Even as the EC expanded to include his hires, von Eschenbach moved most major decision-making from the EC to a "senior management team," sources in NCI said. This team includes the new deputy directors, the management and budget directors, and Dorothy Foellmer, his special assistant for program coordination.

Except for Foellmer and budget director John Hartinger, the senior management team has substantially fewer years of NIH experience than the full EC. David Elizalde, whom von Eschenbach hired from HHS as deputy director for management, left for the Surgeon General's office earlier this year.

Excluded from top-level decisions are the division directors, most of whom are longtime NCI employees.

"[Von Eschenbach] is walled off from the professional staff," an NCI staff member said. "He never discusses the budget in open meetings [with advisors],

or even in closed meetings with staff. We just see the [investigator-initiated grant] payline going down."

Von Eschenbach originally planned to hire four new deputy directors who would be "arrayed across the realm of the discovery, development, and delivery continuum" and "help to organize and orchestrate the entire NCI portfolio."

His first hire was Barker, who ran a small company that developed products to treat "diseases of oxidative stress," and co-founded a start-up—that never got off the ground—to sell dietary supplements (The Cancer Letter, May 30, 2003).

At NCI, Barker has led the development of several controversial and expensive initiatives, including the biospecimen network, a nanotechnology project, and a proteomics initiative.

These projects don't go through the same internal scientific peer review as projects proposed from within NCI divisions, sources said. Questioning the merit of these projects is seen as disloyalty, insiders say.

It took von Eschenbach about a year to hire two other deputy directors, Karen Antman and Mark Clanton. Antman, former director of the Herbert Irving Cancer Center at Columbia University, served as deputy director for clinical and translational sciences for one year. She left NCI last May for Boston University.

Clanton, a former president-elect of ACS and chief medical officer of Blue Cross and Blue Shield of Texas, is deputy director for cancer care delivery systems.

The fourth deputy von Eschenbach planned to hire, for "integrative biology and molecular oncology," hasn't been recruited.

"The Situation"

NIH and NCI staff members were surprised by the White House announcement of von Eschenbach's appointment. "If you look carefully at how he's done one job, it's poor," an NIH staff member said.

Others worried that NCI would suffer under inattentive leadership, because of the political challenges FDA faces. "It will at some level divert his focus from NCI and won't bring the stability that FDA needs," a cancer center official said. "It's not an encouraging development for anybody. It's hard to imagine that this could be a successful long-term strategy."

Some NCI staff members said von Eschenbach's new duties at FDA probably wouldn't affect their day-to-day work. "He wasn't around much anyway—he does a lot of traveling," a staff member said.

In fact, von Eschenbach prides himself on his big-picture management style, which he calls "flying at 30,000 feet," sources said.

In some NCI offices, the atmosphere von Eschenbach created at NCI is referred to as "the situation."

"We're just trying to do our jobs and wait for the next three years to pass," an NCI staff member said. Presumably, the winner of the 2008 Presidential election would appoint a new NCI director.

Staff morale under the situation is mixed. "Some say, 'Let's hang in there and get the work done.' Most people here are dedicated," an NCI staff member said. "But there is a lot of worry about how NCI is going. You slide down too far, and it takes years to recover."

One Voice

In NIH Building 31, where the NCI director's office has occupied one end of the top floor for decades, von Eschenbach has gradually taken over two floors for senior management and his office staff, sources said.

Many of the offices contain growing numbers of communications experts, many of them on contract to NCI. Much of what they do is troubling to longtime NCI employees.

"The theme of our communications has always been, 'Let's be credible and open,' " an NCI staff member said. "That's changed to, 'Let's have a party line and speak with one voice.' "

In 2003, after The Cancer Letter's coverage of the biospecimen network, the Dialogue, and Barker's first actions in NCI—which won awards from the Society of Professional Journalists—von Eschenbach decided to establish a Web page for weekly messages to advisors and staff.

"There are so many things I would like to tell you," he said to the NCAB. "It's regrettable sometimes that these kinds of stories and these kinds of activities do at times get reported, but they may not necessarily get reported accurately, or get reported from the perspective of what is truly, fully involved in the initiative." (The Cancer Letter, Sept. 26, 2003).

Von Eschenbach didn't stop at establishing a Web page. In January 2004, he started a weekly, federally-funded newsletter, the NCI Cancer Bulletin, which looks conspicuously similar to The Cancer Letter.

The Bulletin's tag line reads: "Eliminating the suffering and death due to cancer." The first issue featured a photo of von Eschenbach on page 1. The most recent issue described von Eschenbach as a "renowned urologic oncologist."

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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