CANCER RESEARCH

After Regime Change at the National Cancer Institute

Andrew von Eschenbach, who has been nominated to head FDA, is expected to step down soon as director of NCI after a controversial tenure. His successor will face a big budget squeeze and low morale

Robert Weinberg turned gloomy as he wound up an award lecture earlier this month in Washington, D.C., at the annual meeting of the American Association for Cancer Research. One of the founders of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, he flashed a slide of his lab team and gave a warning: Because investigator-initiated grants have become impossible to get, he said, these young researchers don’t have “much of a future.” Those “who determine funding … have lost sight of [the] most important element.” It is “not large research consortia, not new technologies, not cancer centers,” Weinberg said, but the young individual investigator. “We have deserted them.” His comments drew lengthy applause.

This complaint is echoing across the community as growth at the National Institutes of Health (NIH) comes to a halt. In cancer research, the largest chunk of U.S. biomedical funding, the situation is especially bad. The “payline,” or success rate, for bread-and-butter investigator grants (R01s) at the National Cancer Institute (NCI) this year, after peer approval, will drop to 11%, compared to 22% 4 years ago. Already, Weinberg and some other researchers are pointing to this as the main legacy of departing NCI Director Andrew von Eschenbach.

Justly or not, the former urologic surgeon at University of Texas M. D. Anderson Cancer Center in Houston, nominated last month to head the Food and Drug Administration (FDA), will likely be remembered as one of the most controversial NCI directors ever. The pet themes and management methods he adopted—as well as NCI’s budget problems—complicated his tenure. Says one leading cancer biologist and former member of an NCI advisory board, “He’s been a disaster.”

A three-time cancer survivor who came to NCI through connections with President George W. Bush’s family, von Eschenbach brought a passion for direct involvement with cancer patients to the $4.8 billion NCI. He introduced prayer to advisory committee meetings and a business model to NCI management. He set a startling goal of ending cancer deaths by 2015. He oversaw several major new technology initiatives to accomplish that. Paying for them, however, has added to the pressure on NCI’s budget, which has required painful cuts across NCI that have hit especially hard in the intramural program. One lab chief and 20-year NCI veteran says intramural morale “is as low as I’ve seen it.”

Other researchers are more upbeat. Von Eschenbach “has put a personal face to the problem of cancer,” says Robert Young, president of Fox Chase Cancer Center in Philadelphia, Pennsylvania. “That new, different outlook was refreshing and good.” John Mendelsohn, president of M. D. Anderson, praises efforts such as working with FDA to speed cancer drug approvals. “His vision is just beginning to be achieved,” he says. As for the current budget crisis, “I think it’s hard to lay the blame on him,” says molecular biologist Albert Fornace of Harvard School of Public Health in Boston, who left NCI’s intramural program last year: “It was the perfect financial storm.”

Through a spokesperson at FDA, von Eschenbach declined to be interviewed, pending the Senate’s vote on his nomination for his new position, but he responded to written questions. The initiatives he oversaw at NCI “will greatly accelerate cancer research” and “hold potential and promise for great advances,” von Eschenbach said. Asked about the declining grant award rate, he said NCI “is striving to be the best steward of all its resources” in tough budget times. He also dismissed the critics, saying “the research community has always and consistently been supportive of me and the NCL.”

Von Eschenbach is still director of NCI, although he also has been acting chief of the FDA since September. A spokesperson for the Department of Health and Human Services (HHS), NIH’s parent agency, says von Eschenbach will leave NCI “soon.” This would resolve an apparent conflict, in that he now heads two agencies—one a developer of drugs and the other a regulator. Anticipating a change, leaders in the cancer field have quietly circulated an appeal to the White House for a national search for the next NCI director. (The NIH and NCI directors are both nominated directly by the president.) Whether there will be a search is not known, but this much is clear: The new NCI chief’s first challenge will be to solve the agency’s massive budget gridlock.

Optimism

Picking the right person to lead cancer research 5 years ago was a high priority for Bush. He named von Eschenbach NCI chief in December 2001, less than 3 months after the departure of former director Richard Klausner, a cell biologist. Von Eschenbach, head of prostate cancer research and later executive vice president at M. D. Anderson, praises efforts such as working with FDA to speed cancer drug approvals. “His vision is just beginning to be achieved,” he says. As for the current budget crisis, “I think it’s hard to lay the blame on him,” says molecular biologist Albert Fornace of Harvard School of Public Health in Boston, who left NCI’s intramural program last year: “It was the perfect financial storm.”

Through a spokesperson at FDA, von Eschenbach declined to be interviewed, pending the Senate’s vote on his nomination for his new position, but he responded to written questions. The initiatives he oversaw at NCI “will greatly accelerate cancer research” and “hold potential and promise for great advances,” von Eschenbach said. Asked about the declining grant award rate, he said NCI “is striving to be the best steward of all its resources” in tough budget times. He also dismissed the critics, saying “the research community has always and consistently been supportive of me and the NCL.”

Von Eschenbach is still director of NCI, although he also has been acting chief of the FDA since September. A spokesperson for the Department of Health and Human Services (HHS), NIH’s parent agency, says von Eschenbach will leave NCI “soon.” This would resolve an apparent conflict, in that he now heads two agencies—one a developer of drugs and the other a regulator. Anticipating a change, leaders in the cancer field have quietly circulated an appeal to the White House for a national search for the next NCI director. (The NIH and NCI directors are both nominated directly by the president.) Whether there will be a search is not known, but this much is clear: The new NCI chief’s first challenge will be to solve the agency’s massive budget gridlock.

Optimism

Picking the right person to lead cancer research 5 years ago was a high priority for Bush. He named von Eschenbach NCI chief in December 2001, less than 3 months after the departure of former director Richard Klausner, a cell biologist. Von Eschenbach, head of prostate cancer research and later executive vice president at M. D. Anderson, praises efforts such as working with FDA to speed cancer drug approvals. “His vision is just beginning to be achieved,” he says. As for the current budget crisis, “I think it’s hard to lay the blame on him,” says molecular biologist Albert Fornace of Harvard School of Public Health in Boston, who left NCI’s intramural program last year: “It was the perfect financial storm.”

Through a spokesperson at FDA, von Eschenbach declined to be interviewed, pending the Senate’s vote on his nomination for his new position, but he responded to written questions. The initiatives he oversaw at NCI “will greatly accelerate cancer research” and “hold potential and promise for great advances,” von Eschenbach said. Asked about the declining grant award rate, he said NCI “is striving to be the best steward of all its resources” in tough budget times. He also dismissed the critics, saying “the research community has always and consistently been supportive of me and the NCL.”

Von Eschenbach is still director of NCI, although he also has been acting chief of the FDA since September. A spokesperson for the Department of Health and Human Services (HHS), NIH’s parent agency, says von Eschenbach will leave NCI “soon.” This would resolve an apparent conflict, in that he now heads two agencies—one a developer of drugs and the other a regulator. Anticipating a change, leaders in the cancer field have quietly circulated an appeal to the White House for a national search for the next NCI director. (The NIH and NCI directors are both nominated directly by the president.) Whether there will be a search is not known, but this much is clear: The new NCI chief’s first challenge will be to solve the agency’s massive budget gridlock.
Cancer, a private group funded by ACS and co-chaired by George H. W. Bush. The Cancer Letter, a newsletter in Washington, D.C., relentlessly criticized von Eschenbach’s ties to the group (now called C-Change) as a conflict of interest. Von Eschenbach resigned from it last September after he became acting chief of FDA. The Cancer Letter had reported that C-Change’s board members included drug company executives.

Still, von Eschenbach’s message of bolstering links between “the three Ds: discovery, development, delivery” was welcome at a time when the NIH budget was booming, says cancer biologist Thomas Curran of St. Jude Children’s Research Hospital in Memphis, Tennessee. Von Eschenbach’s ties to the Bush family, some suspected, was a strange thing to hear from the director of NCI. “Politics, some suspected, was involved in the selection from extramural scientists.”

The new chief’s style, however, took scientists by surprise. He introduced a moment of silence for cancer patients at NCI’s National Cancer Advisory Board (NCAB) meeting. According to one scientist, at a private meeting, von Eschenbach said he was “on a mission from God.” The scientist adds: “That was a strange position from the director of NCI.” Politics, some suspected, was involved in one early incident. A few months into his tenure, several congressional Republicans complained about a fact sheet on NCI’s Web site stating that abortion does not raise a woman’s risk of breast cancer. Von Eschenbach ordered it removed. He then held a scientific workshop to investigate; it came to the same conclusion—and the evidence did not support a link—and the fact sheet went back up.

Von Eschenbach stunned the community in February 2003 when he announced that NCI intended “to eliminate the suffering and death from cancer by 2015.” This “challenge goal,” reminiscent of President Richard M. Nixon’s 1971 launch of the “War on Cancer,” was embraced by ACS and some other advocacy groups. But among researchers, it became “a point of some ridicule for Andy and this Administration,” says oncologist Richard Schilsky of the University of Chicago in Illinois.

As a manager, von Eschenbach described himself as a corporate CEO. He created four new deputy director positions to run the institute. These deputies became part of a new top level for decision-making, rather than an executive committee that included division directors. This “changed the culture” by adding a new layer of management, says Dinah Singer, director of NCI’s Division of Cancer Biology, although she sensed no change in the “commitment of leadership” to her division. And new initiatives often came from these deputies, not from the program staff.

Leading these efforts was one of von Eschenbach’s first hires, Anna Barker, former CEO of a biotech company and a C-Change leader. Barker, who has a Ph.D. in immunology and microbiology, had no recent experience as a researcher. She was put in charge of starting new technology initiatives—and soon ran into opposition from extramural scientists.

An idea that ran into early trouble, a national biopspecimen network, had first been proposed by C-Change. The ambitious plan was to create a new shared resource of tumor samples with attached patient information. But it was vague on details and disregarded existing tissue banks collected through clinical trials for decades, critics said. It also raised concern that NCI’s ideas were coming not from its scientific public advisers but from a group that met behind closed doors. The proposal reflected “ naïveté on the part of some of the NCI leadership,” says Schilsky. It now survives as a small pilot project collecting prostate cancer specimens.

A second big idea, a $187 million nanotechnology initiative, got a tongue-lashing from skeptics at the June 2004 meeting of NCI’s Board of Scientific Advisors (BSA). The reviewers said NCI leaders had failed to demonstrate the scientific promise of nanotech, had not shown that the private sector couldn’t carry the ball, and had overlapped with another nanomedicine component launched by NIH Director Elias Zerhouni. BSA soon approved a $144 million, 5-year nano initiative, however.

Two other big initiatives fared better: a proteomics effort to identify proteins in blood and other biomarkers that might work as early warning signs of cancer, and the most recent: a human Cancer Genome Atlas. The latter, presented by Eric Lander of the Broad Institute in Cambridge, Massachusetts, would systematically sequence tumor samples for mutations involved in cancer to speed up the search for new drugs and diagnostics. Some have criticized the Atlas as an employment project for genome centers. Its projected price tag of $1.5 billion over a decade was whittled down to a 3-year, $100 million pilot, to be split between NCI and the National Human Genome Research Institute.

Unlike Barker, who had a contentious beginning, other top recruits enjoyed a relatively gentle welcome. James Doroshow, who oversees the Division of Cancer Treatment and Diagnosis, has made progress with better coordinating clinical trials, says Schilsky. And Mark Clanton,
deputy director for cancer care and delivery, started “important” new outcomes research programs, Fox Chase’s Young notes. Von Eschenbach never filled a fourth position for basic science deputy.

The crunch
The new projects might have been less controversial had more money been available. But von Eschenbach was working with an ever-tightening NCI budget, much of it tied up in continuing grants and activities. For example, just before von Eschenbach arrived, NCI had agreed to fund a now—$350 million screening trial to see if spiral computed tomography (CT) scans could detect lung tumors missed by x-ray imaging in former smokers. The hope is that by detecting tumors earlier, CT screening could save many lives. The study is controversial: Critics suggest it will lead to a huge increase in biopsies of benign tumors in healthy people, with a relatively minor decline in overall mortality, Curran notes. And the technology is expensive.

Although NCI’s budget rose 81% during the 5-year NIH doubling that ended in 2003, the brakes hit hard in 2004, translating into a slight $2.7 million cut in NCI’s operating budget after paying grants, salary raises, and contributions to trans-NIH activities. It has been falling in real terms since (see graph, right). To fund the new initiatives and help maintain the payline, von Eschenbach has cut the intramural program 4.4% since 2003.

Because so much of NCI’s intramural budget is tied up in salaries, the effect has been severe. The Center for Cancer Research, the main division, is down 43 principal investigators (PIs) to 275, says CCR Director Robert Wiltrout. About 10 labs have been shut down, other PIs have retired, and still others—including several scientific standouts—have left on their own. NCI’s advisers recommended cutbacks, but some say without any effort to define the program’s mission. Fornace says one reason he left was that remaining labs have lost staff positions; others complain of having no money to refurbish equipment. Von Eschenbach remained “pretty distant,” says Fornace, never showing much interest in the labs. The study is controversial: Critics suggest it will lead to a huge increase in biopsies of benign tumors in healthy people, with a relatively minor decline in overall mortality, Curran notes. And the technology is expensive.

Even so, the cuts haven’t been enough to stave off a slide in the portion of basic R01 grant applications that are funded during each round of reviews. The drop in the payline to 11% this year is the lowest level since at least the early 1990s. NIH officials caution that it’s not as bad as it seems: The number of applications has been rising, which pushes the success rate down. The total number of funded grants has been fairly steady, roughly 5150 in 2005. Still, the number of new grants dropped by about 200 last year, grants are getting smaller, and some long-term and even midcareer grantees are not being funded. Most worrisome is that young, creative researchers are leaving the field.

Are the big new initiatives to blame? Mendelsohn doesn’t think so. “If you eliminated all of the new projects, I don’t think it would have solved this problem,” says Mendelsohn, noting they only add up to “a few hundred million” dollars spread over several years. Even $100 million annually would only be 2% of NCI’s overall budget.

Slippery slope
Worse may be yet to come, however. Paylines are expected to slip to single digits next year when NCI faces a $40 million cut. The sense of crisis is bringing new scrutiny of NCI’s large projects, that Congress and the public will assume is deliverable,” Young says. “My concern is the potential ramifications if it’s not reached.” A task force of cancer center directors is working on a modified timeline that will be “numbers and data driven,” Mendelsohn says. It will look at concrete goals, such as reducing smoking, and may revise what can be achieved by 2015, he says.

Despite the ongoing budget slide and lack of a permanent chief, scientists within NCI seem to be breathing a bit easier lately. “Everybody feels as if … the dust and feathers have settled,” says one lab director. Funds freed up by the many departures will allow CCR to recruit some new hires for key positions such as radiation oncology, says Wiltrout. He also hopes to hire a dozen or so “young, smart,” tenure-track scientists in the next 2 years.

Some NCI staff members also seem at ease with the person running NCI now, John Niederhuber, deputy director for clinical and translational science. A former director of the University of Wisconsin Cancer Center and NCAB chair, Niederhuber was named NCI’s chief operating officer in charge of day-to-day operations when von Eschenbach became acting head of FDA last fall (Science, 30 September 2005, p. 2142). Within NCI, Niederhuber has been a “stabilizing force,” Wiltrout says. Some are encouraged that he has started a small lab. It shows a “commitment to science,” Singer says.

The enormous challenges ahead will require great skill and stamina of the next NCI chief. Many researchers are hoping the White House will conduct a national search for the director. In an unusual step, about 60 prominent cancer researchers sent Bush a letter in March emphasizing the importance of the position and offering their help with finding candidates. Zerhouni, according to an NIH spokesperson, is in touch with HHS and the White House about the position, and the White House “is committed to conducting a broad search so as to identify the best qualified candidates for the president’s consideration.”

Whether the government can recruit a star is an open question. Any newcomer will have to come to terms not only with the most dismal NCI budget scenario in 3 decades but also with stringent new rules on owning pharmaceutical stock; and because this is a presidential appointment, the director might have less than 2 years to serve. But the hope, says molecular oncologist Michael Kastan of St. Jude, is that there just may be an altruist out there interested in taking on the job.

—JOCELYN KAISER

Hard landing. As NCI’s budget flattens out and falls short of inflation, the institute is struggling to maintain research grants, centers, and the intramural Center for Cancer Research.
After Regime Change at the National Cancer Institute
Jocelyn Kaiser

Science 312 (5772), 357-359.
DOI: 10.1126/science.312.5772.357