

# The National Institutes of Health: Public Servant or Private Marketer?

**Doctors have long relied on the NIH to set medical standards. But with its researchers accepting fees and stock from drug companies, will that change? A continuing examination by The Times shows an unabashed mingling of science and commerce.**

By David Willman  
Times Staff Writer

December 22, 2004

For 15 million Americans, it is a daily ritual: gulping down a pill to reduce cholesterol.

They do it because their doctors tell them to. Their doctors, in turn, rely on recommendations from the National Institutes of Health and its scientists, such as Dr. H. Bryan Brewer Jr.

Brewer, as a leader at the NIH, was part of a team that gave the nation new cholesterol guidelines that were expected to prompt millions more people to take the daily pill. He also has written favorably of a specific brand of cholesterol medication, Crestor, which recently proved controversial.

What doctors were not told for years is this: While making recommendations in the name of the NIH, Brewer was working for the companies that sell the drugs. Government and company records show that from 2001 to 2003, he accepted about \$114,000 in consulting fees from four companies making or developing cholesterol medications, including \$31,000 from the maker of Crestor.

Brewer was far from alone in taking industry's money: At least 530 government scientists at the NIH, the nation's preeminent agency for medical research, have taken fees, stock or stock options from biomedical companies in the last five years, records show.

NIH Director Dr. Elias A. Zerhouni has told Congress that outside work should be allowed if "the scientist is giving advice in an area ... that is not part of his official duties."

Information gathered by a congressional committee, in addition to company records and 15,000 pages of government documents obtained by the Los Angeles Times under the Freedom of Information Act, shows that NIH researchers have repeatedly crossed Zerhouni's line.

For example:

- Dr. P. Trey Sunderland III, a senior psychiatric researcher, took \$508,050 in fees and related income from Pfizer Inc. at the same time that he collaborated with Pfizer — in his government

capacity — in studying patients with Alzheimer's disease. Without declaring his affiliation with the company, Sunderland endorsed the use of an Alzheimer's drug marketed by Pfizer during a nationally televised presentation at the NIH in 2003.

- Dr. Lance A. Liotta, a laboratory director at the National Cancer Institute, was working in his official capacity with a company trying to develop an ovarian cancer test. He then took \$70,000 as a consultant to the company's rival. Development of the cancer test stalled, prompting a complaint from the company. The NIH backed Liotta.
- Dr. Harvey G. Klein, the NIH's top blood transfusion expert, accepted \$240,200 in fees and 76,000 stock options over the last five years from companies developing blood-related products. During the same period, he wrote or spoke out about the usefulness of such products without publicly declaring his company ties.

Announcing such ties is not required by the NIH. The agency has encouraged outside consulting, and has allowed most of its scientists to file confidential income disclosure forms.

Supported by the taxpayers at a cost this year of \$28 billion, the NIH oversees research with a mission to extend healthy life and to reduce "the burdens of illness and disability." The laboratories and offices of most NIH scientists are at the agency's woodsy, 300-acre headquarters in Bethesda, Md., nine miles north of the White House.

The scientists at the NIH — seen by many outsiders as neutral government experts — advise federal regulators and write hundreds of articles for influential medical journals. Some travel the world encouraging doctors to prescribe a particular medication.

The flow of drug industry fees and stock options to NIH scientists was disclosed in December 2003 in an article in *The Times*. The article also explained the bureaucratic means by which most of the payments had been kept secret from Congress, the public and the nation's doctors.

Subsequent inquiries this year by Congress have shown that even Zerhouni, the NIH's director, did not know the extent to which agency scientists were being paid by industry.

When leaders of the House Energy and Commerce Committee felt the NIH was not complying with a request to identify every drug industry payment, the panel went directly to 20 companies. Those responses revealed more than 130 consulting deals with industry that did not appear to have the required NIH approval. One of them was the \$508,050 relationship between Sunderland, the Alzheimer's researcher, and Pfizer.

Other documents obtained this year by *The Times*, including programs of industry meetings for physicians that featured NIH scientists as speakers, reveal dozens more relationships not reported as approved by the agency.

The companies, in marketing their products, have frequently cited the NIH's reputation for high scientific standards. The cholesterol guidelines, for example, have been widely circulated by makers of anticholesterol drugs.

Dr. Curt D. Furberg, a former head of clinical trials at the National Heart, Lung, and Blood Institute and now a professor at Wake Forest University in North Carolina, explained how such information reached physicians: "The [company] reps tell the doctors, 'You should follow these guidelines,' implying that you're not a good doctor if you don't follow these guidelines."

Often NIH involvement is featured, while the government researchers' links to the companies go unmentioned.

When Brewer, the cholesterol researcher, praised Crestor in a medical journal in 2003, the article

identified him as an NIH scientist, not as a paid consultant to the manufacturer. In marketing Crestor to doctors, the company cited Brewer's findings without mentioning that he was on its payroll.

As leader of the NIH, Zerhouni has acknowledged that some past deals have been improper. But he has also argued for allowing most agency scientists to consult privately for industry. Close government-industry cooperation, he says, can help bring important products to market. He has also said that the supplemental income from industry fees can help the NIH retain talented scientists.

Others disagree. Dr. Marcia Angell, the former editor of the New England Journal of Medicine, said in an interview that doctors and patients counted on NIH scientists for "their critical, scientific, dispassionate judgment."

"When they have financial ties to the companies that make the products that they're supposed to be impartial about, we can't assume that," Angell said.

Dr. Philip R. Lee, who served Presidents Lyndon B. Johnson and Bill Clinton as an assistant secretary of Health, said that every NIH scientist should be prohibited from taking industry money.

"Damn it, if you work for NIH, you're not working for a drug company, you're working for the public," Lee said. "When you have people who have a split allegiance, undisclosed to the public, to me it is just unthinkable."

### **'Should Have Mentioned It'**

As chief of the National Heart, Lung, and Blood Institute's molecular disease branch since 1976, Brewer is one of the nation's leading experts on cholesterol.

With his rimmed glasses and shock of sandy hair, he has the bearing of an accomplished scientist and the credentials to match. Born in Casper, Wyo., he gained his medical degree from Stanford University and received further training at Massachusetts General Hospital. Now 66, Brewer has a manner that is both authoritative and plain-spoken.

But when Brewer wrote a medical journal article in 2003 helping to introduce Crestor, he did not inform doctors about a potentially lethal safety risk.

The product was about to be launched in the United States by AstraZeneca, a British company that had put Brewer on a scientific advisory board and paid him \$31,000 from 2001 through 2003, according to NIH records.

In the Aug. 21, 2003, American Journal of Cardiology, Brewer wrote that Crestor "produced markedly greater reductions" in cholesterol levels than three established competitor drugs tested in clinical trials. That was true. But Brewer also concluded that Crestor's "benefit-risk profile ... appears to be very favorable," and that proved to be questionable.

Brewer assured doctors there was no basis for worry about a muscle-wasting side effect called rhabdomyolysis, which can cause kidney failure and death. (Another anticholesterol drug, Baycol, was removed from the market in 2001 after at least 31 deaths related to rhabdomyolysis were reported.)

Brewer wrote: "No cases of rhabdomyolysis occurred in patients receiving [Crestor] at 10 to 40" milligrams.

But eight cases of rhabdomyolysis were reported during clinical trials of Crestor. One of the case reports cited a patient who took the drug in 10-milligram doses, according to records filed with the

Food and Drug Administration and reviewed by The Times under the Freedom of Information Act. Sales representatives for AstraZeneca have routinely provided copies of Brewer's journal article about Crestor to doctors nationwide, a company spokeswoman confirmed last week.

The FDA received 78 reports of rhabdomyolysis among patients taking Crestor during its first year on the market, FDA records show. Two of those patients died.

In contrast to Brewer's opinion in August 2003, an editorial two months later in the Lancet, the prominent British medical journal, said: "Physicians must tell their patients the truth about [Crestor] — that, compared with its competitors, [Crestor] has an inferior evidence base supporting its safe use."

In March of this year, a U.S. consumer group, Public Citizen, called for banning Crestor based upon several cases of kidney failure or muscle damage. AstraZeneca defended its drug as safe and effective in print and television ads this fall, adding that FDA management agreed. But on Nov. 18, senior FDA epidemiologist Dr. David J. Graham told a Senate committee that the safety of Crestor needed reassessment.

After Dr. Sidney Wolfe of Public Citizen questioned Brewer's ties to AstraZeneca and his depiction of Crestor's safety, Brewer sought to explain himself in a July 9 memo to NIH Director Zerhouni.

Brewer told Zerhouni that he had not mentioned seven of the rhabdomyolysis cases because those patients had received doses of Crestor higher than the approved level. As for the patient who took the drug at 10 milligrams, "it was not possible to definitively conclude" that Crestor had caused her rhabdomyolysis, Brewer wrote. Other medical experts said reviewers should report such a serious event regardless of possible cause.

"Baycol had already been pulled for exactly that same side effect and it was a matter of great concern," said Angell, the former editor of the New England Journal of Medicine. "If he knew about it, he should have mentioned it."

Zerhouni sought to distance his agency from the controversy in a written response to Wolfe, suggesting that the NIH had no responsibility for omissions in Brewer's article about Crestor. Brewer had produced it in his "private capacity" as a consultant to AstraZeneca, Zerhouni wrote. That the article identified Brewer as an NIH employee and directed reprint requests to the NIH was "most unfortunate," Zerhouni added, acknowledging that it "gives the reader the impression that it was done in his Government capacity."

Zerhouni's letter added: "Dr. Brewer has been counseled about these requirements." A spokeswoman for AstraZeneca, Emily Denney, said that Brewer had remained a consultant to the company until April of this year.

AstraZeneca was not the only client of Brewer's who made use of his NIH title. Agency rules have long instructed employees not to use their NIH affiliations for outside consulting work. Nonetheless, Lipid Sciences Inc. of Pleasanton, Calif., listed Brewer by his title on the company website — and displayed video clips of Brewer that showed the entrance to his federal workplace, the NIH Clinical Center.

In the clips, Brewer appeared in his white lab coat, telling viewers, "Currently, there are a number of excellent new drugs that have come out." In late November, after The Times submitted questions to Brewer about his role with the company, Lipid Sciences removed the video clips and all references to Brewer from the website.

The company, which is developing a product that would remove cholesterol from human cells, paid Brewer \$83,000 from 2002 through 2003. As of September 2003, his consulting contract with

Lipid Sciences was to pay him \$125,000 annually plus stock options, according to a filing with the Securities and Exchange Commission. The company reported in March that Brewer, who until recently served on its board of directors and scientific advisory board, held 411,927 stock options.

Brewer also has taken consulting fees from Pfizer, the maker of Lipitor, the nation's biggest-selling cholesterol pill. >From 2001 to 2003, Pfizer paid Brewer fees totaling \$55,500, according to NIH records. Brewer has been among the many agency employees whose annual financial reports were kept confidential by the NIH.

Brewer's other duties have included serving with the agency-sponsored National Cholesterol Education Program, which issued aggressive guidelines for reducing cholesterol in 2001, and revised them in July of this year to call for even wider use of cholesterol drugs.

Eight of the nine authors of the guidelines, including Brewer, had financial ties with companies that marketed cholesterol drugs — but their connections were not mentioned in their report, published in July by the medical journal *Circulation*. Following criticism from consumer advocates, the NIH posted on its website a listing of the authors' financial ties.

Dr. David L. Brown, chief of cardiology at the State University of New York at Stony Brook, said the interpretations of data in the cholesterol recommendations should not be trusted because the NIH panel was "in the pocket of the drug companies."

Brown was among 22 physicians who wrote to Zerhouni in September, questioning the 2001 guidelines and the revisions this year. NIH officials said they stood behind the recommendations.

Brewer, whose annual government salary is \$187,305, referred questions submitted by *The Times* to an NIH spokeswoman, Diane Striar, who said Brewer's paid consulting arrangements for four drug companies had been approved in advance.

As of this month, Brewer "no longer serves on any advisory boards of pharmaceutical companies," Striar said, adding that the agency would not comment further. Brewer, after accepting consulting payments from companies for several months this year, had stopped doing so by this fall, records show.

Meanwhile, anticholesterol pills are the biggest-selling category of prescription drugs in America, with sales last year of \$14.7 billion. Under the current guidelines, the number of Americans taking the medications may more than double, to 35 million, according to NIH estimates.

### **Winning Over Its Critics**

The pharmaceutical bonanza that has swept the country in the last decade has created one of the most influential lobbies in Washington. A total of 3.5 billion prescriptions — medicating about 129 million Americans — were filled last year. Drug industry revenue in the U.S. tops \$231 billion annually. The drug companies donated \$41 million to candidates for federal offices in the last four years, according to the Center for Responsive Politics.

"The pharmaceutical industry has never been more powerful than now," said Rep. Henry A. Waxman (D-Los Angeles). "The companies have made investments in the people who have power in Washington. And they've gotten a very good return on those investments."

In the last 12 years, the companies have secured passage of legislation that fast-tracked FDA approvals of new drugs and transformed the agency into a more compliant partner of industry.

And when congressional critics surface, the industry has a way of winning them over: This year's top two recruits had recently launched a congressional investigation of conflicts of interest at the NIH.

Rep. W.J. "Billy" Tauzin (R-La.), as chairman of the House Energy and Commerce Committee, had cited "secret consulting fees and stock options from drug companies" to NIH scientists as a reason for requesting that the agency produce documentation of all the payments. Tauzin, who did not seek reelection, was hired this month to be the president of the Pharmaceutical Research and Manufacturers of America, the group that represents the nation's largest drug companies.

Rep. James C. Greenwood (R-Pa.), who led three hearings this year on NIH conflicts of interest, had criticized the agency for allowing its scientists to use "a swivel chair" to make government decisions while taking drug company fees. In July, Greenwood announced that he would give up his position as chairman of the Energy and Commerce subcommittee on oversight and investigations and retire from Congress to become president of the Biotechnology Industry Organization — a group that urged policymakers this year not to prohibit NIH scientists from paid consulting deals.

In the face of such industry influence, leading the NIH has become more complicated. Zerhouni, the agency's director, is an expert in magnetic resonance imaging. He also knows the value of moonlighting: While serving as executive vice dean of the Medical School at Johns Hopkins University, he cofounded a Maryland company that developed and marketed devices to enhance the usefulness of MRI scans.

He was trained as a physician in his native Algeria. With a gently accented English and a propensity to say that he agrees with members of Congress even when they pose pointed questions, Zerhouni, 53, has projected affability while addressing the NIH's conflicts of interest.

When he was appointed by President Bush in March 2002, Zerhouni inherited an agency whose scientists were avidly pursuing private consulting.

Although historically separate from industry, the NIH by the late 1980s was allowing some limited outside arrangements. In November 1995, the consulting gate was swung wide open by then-Director Harold E. Varmus in an internal memo, which was first made public in December 2003 by The Times.

The Varmus memo "immediately" lifted all limits on outside income, reversed the prohibition against taking stock or stock options, and freed the top leaders — the directors of the research institutes and centers — to start making personal deals with companies.

At the same time, arcane rules wielded by NIH administrators were allowing more and more of the deals to remain confidential.

Following The Times' report, Zerhouni was summoned to Capitol Hill on Jan. 22 by the Senate appropriations subcommittee for health issues.

Zerhouni initially told the panel that the NIH had "not identified any situations where outside activities resulted in undue influence" on official decisions. The subcommittee's chairman, Sen. Arlen Specter (R-Pa.), warned Zerhouni that far-reaching, internal investigations would be needed to ensure that conflicts of interest did not exist.

Zerhouni said he would impose tighter controls. Henceforth, he said, the consulting deals of all NIH employees would be subjected to "independent peer review" by a newly created ethics committee.

He also said he was appointing a blue-ribbon committee to "completely review" the NIH's policies on conflicts of interest. But Zerhouni added that "instead of having a complete one-size-fits-all rule, I think the rules should be different" depending on the employee's rank or authority to oversee research grants.

Zerhouni's position sought to keep the agency's many influential laboratory or branch chiefs, such as Brewer, Sunderland, Liotta and Klein, eligible for outside consulting.

Two months later, Zerhouni's blue-ribbon panel recommended what he wanted. It called for barring the institute directors and their top administrators from outside consulting — while allowing 5,000 or more staff scientists, including all the laboratory and branch chiefs — to take payments from industry. The panel also recommended, and Zerhouni said he supported, an agencywide ban on taking stock or stock options from biomedical companies.

Most NIH scientists should be allowed to consult, Zerhouni said, because such arrangements helped "translate" discoveries from NIH labs into products that could help patients.

"You can have a policy that says, 'All right, all prohibited.' But how does that help the public, in terms of translating the discoveries in our laboratories into real things?" Zerhouni told reporters.

For years, the agency has had procedures for formal collaborations with industry — but they prohibit NIH scientists from taking the companies' money. The formal agreements have resulted in at least 1,300 collaborations with biomedical companies over the last 20 years, agency records show.

On the other hand, the public record is bereft of products "translated" from NIH labs to patients through private consulting contracts. No such evidence was presented during days of testimony this year before the NIH blue-ribbon panel or congressional subcommittees.

By midyear, the failure of the NIH to produce a full accounting of its ties to industry had spurred bipartisan criticism in the House. On May 12, the new chairman of the House Energy and Commerce Committee, Rep. Joe Barton (R-Texas), warned Zerhouni to lift the agency's secrecy and to relinquish all records documenting drug industry payments to NIH scientists.

The panel's senior Democrat, Rep. Peter Deutch of Florida, told Zerhouni at the same hearing: "I would urge you in the strongest possible terms to end the practice today of NIH researchers taking anything of value from a drug or a biotech company."

Zerhouni endorsed some additional restrictions, including ceilings on compensation that employees could accept from industry and the amount of time they could devote to outside activities. While NIH employees could still accept fees to sit on companies' scientific advisory boards, they would be barred from serving on boards of directors.

But a July report by the U.S. Office of Government Ethics concluded that the NIH was beset by a "permissive culture." The office found that 40% of the 155 outside payments to NIH employees it sampled randomly had not been approved in advance or accounted for within the agency.

Zerhouni proposed another compromise: a one-year "moratorium" on industry consulting. Details of the moratorium have not been completed.

Last month, nearly 200 NIH researchers said in a letter to Zerhouni that a permanent ban would make the scientific staff — who are paid between \$130,000 and \$200,000 a year by the government — "second-class citizens in the biomedical community."

Dr. Raynard S. Kington, a deputy NIH director, said Tuesday that the agency had "moved actually quite fast" to carry out tougher restrictions. Yet he acknowledged that unless new rules were put into effect, perhaps in the new year, the scientists were free to continue collecting stock options and consulting fees from drug companies.

"Fundamentally," Kington said, "we are operating under the same rules."

*Times researcher Janet Lundblad in Los Angeles contributed to this report.*