



Pfizer Broke the Law by Promoting Drugs for Unapproved Uses

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By David Evans



Nov. 9 (Bloomberg) -- Prosecutor **Michael Loucks** remembers clearly when lawyers for **Pfizer Inc.**, the world's largest drug company, looked across the table and promised it wouldn't break the law again.

It was January 2004, and the attorneys were negotiating in a conference room on the ninth floor of the **federal courthouse** in Boston, where Loucks was head of the health-care fraud unit of the U.S. Attorney's **Office**. One of Pfizer's units had been pushing doctors to prescribe an epilepsy drug called **Neurontin** for uses the **Food and Drug Administration** had never

approved.

In the **agreement** the lawyers eventually hammered out, the Pfizer unit, Warner-Lambert, pleaded guilty to two felony counts of marketing a drug for unapproved uses.

New York-based Pfizer agreed to pay **\$430 million** in criminal fines and civil penalties, and the company's lawyers assured Loucks and three other prosecutors that Pfizer and its units would stop promoting drugs for unauthorized purposes.

What Loucks, who's now acting U.S. attorney in Boston, didn't know until years later was that Pfizer managers were breaking that pledge not to practice so-called off-label marketing even before the ink was dry on their plea.

On the morning of Sept. 2, 2009, another Pfizer unit, Pharmacia & Upjohn, agreed to **plead guilty** to the same crime. This time, Pfizer executives had been instructing more than 100 salespeople to promote Bextra, a drug approved only for the relief of arthritis and menstrual discomfort, for treatment of acute pains of all kinds.

Record High Fine

For this new felony, Pfizer paid the **largest criminal fine** in U.S. history: \$1.19 billion. On the same day, it paid \$1 billion to settle civil cases involving the off-label promotion of Bextra and three other drugs with the U.S. and 49 states.

"At the very same time Pfizer was in our office negotiating and resolving the allegations of criminal conduct in 2004, Pfizer was itself in its other operations violating those very same laws," Loucks, 54, says. "They've repeatedly marketed drugs for things they knew they couldn't demonstrate efficacy for. That's clearly criminal."

The penalties Pfizer paid this year for promoting Bextra off-label were the latest chapter in the drug's benighted history. The FDA found Bextra to be so dangerous that Pfizer took it off the market for all uses in 2005.

Across the U.S., pharmaceutical companies have been pleading guilty to criminal charges or paying

penalties in civil cases when the U.S. **Department of Justice** finds that they deceptively marketed drugs for unapproved uses, putting millions of people at risk of chest infections, heart attacks, suicidal impulses or death.

\$7 Billion in Penalties

Since May 2004, Pfizer, **Eli Lilly & Co.**, **Bristol-Myers Squibb Co.** and four other drug companies have paid a total of \$7 billion in fines and penalties. Six of the companies admitted in court that they marketed medicines for unapproved uses.

In September 2007, New York-based **Bristol-Myers** paid \$515 million -- without admitting or denying wrongdoing -- to federal and state governments in a civil lawsuit brought by the Justice Department. The six other companies pleaded guilty in criminal cases.

In January 2009, Indianapolis-based Lilly, the largest U.S. psychiatric drug maker, pleaded guilty and paid \$1.42 billion in fines and penalties to settle charges that it had for at least four years illegally marketed **Zyprexa**, a drug approved for the treatment of schizophrenia, as a remedy for dementia in elderly patients.

In five company-sponsored clinical trials, 31 people out of 1,184 participants died after taking the drug for dementia -- twice the death rate for those taking a placebo. Those findings were reported in an October 2005 article in the **Journal of the American Medical Association**.

'Don't Respect the Law'

"Marketing departments of many drug companies don't respect any boundaries of professionalism or the law," says **Jerry Avorn**, a professor at Harvard Medical School in Boston and author of **"Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs"** (Random House, 2004). "The Pfizer and Lilly cases involved the illegal promotion of drugs that have been shown to cause substantial harm and death to patients."

The widespread off-label promotion of drugs is yet another manifestation of a health-care system that has become dysfunctional.

"It's an unbearable cost to a system that's going broke," says Avorn, who heads the pharmacology economics unit of **Brigham and Women's Hospital** in Boston. "We can't even afford to pay for effective, safe therapies."

10 Million Prescriptions

About 15 percent of all drug sales in the U.S. are for unapproved uses without adequate evidence the medicines work, according to a study by **Randall Stafford**, a medical professor at **Stanford University** in Palo Alto, California.

He estimates that doctors write more than 10 million such prescriptions each year.

As large as the penalties are for drug companies caught breaking the off-label law, the fines are tiny compared with the firms' annual revenues.

The \$2.3 billion in fines and penalties Pfizer paid for marketing Bextra and three other drugs cited in the Sept. 2 **plea** agreement for off-label uses amount to just 14 percent of its \$16.8 billion in revenue from selling those medicines from 2001 to 2008.

The total of \$2.75 billion Pfizer has paid in off-label penalties since 2004 is a little more than 1 percent of the company's revenue of \$245 billion from 2004 to 2008.

\$36 Billion in Revenue

Lilly already had a criminal **conviction** for misbranding a drug when it broke the law again in promoting schizophrenia drug **Zyprexa** for off-label uses starting in 1999. The medication provided Lilly with \$36 billion in revenue from 2000 to 2008.

That's more than 25 times as much as the total penalties Lilly paid in January.

Companies regard the risk of multimillion-dollar penalties as just another cost of doing business, says **Lon Schneider**, a professor at the University of Southern California's **Keck School of Medicine** in Los Angeles.

In 2006, he led a **study** for the **National Institute of Mental Health** of off-label use of drugs, including Zyprexa, for the treatment of Alzheimer's disease.

"There's an unwritten business plan," he says. "They're drivers that knowingly speed. If stopped, they pay the fine, and then they do it again."

Shareholders Unmoved

Schneider has been paid both by Lilly as a consultant and by plaintiffs suing the company.

Big Pharma's off-label transgressions didn't trigger a rush for the doors by **shareholders**. From Jan. 26, when Pfizer announced that it would pay billions in penalties, to Oct. 12, Pfizer's share price increased 9.3 percent, just shy of the 11.2 percent rise in the Standard & Poor's 500 Health Care Index.

From Oct. 21, 2008, when Lilly said it would pay its penalties, to Oct. 12, the company's stock value went up 0.6 percent; the **S&P** index gained 6.9 percent in that time.

In pushing off-label use of drugs, companies find ready and willing partners in physicians. Under the fragmented system of medical regulation in the U.S., it's legal for doctors to prescribe FDA-approved drugs for any use.

The FDA has no authority over doctors, only over drug companies, regarding off-label practices. It's up to the 50 states to oversee physicians.

"I think the physician community has to take some ownership responsibility and do their own due diligence beyond the sales and marketing person," says Boston's former U.S. Attorney **Michael Sullivan**.

Off-Label Benefits

Loucks says prosecutors realize that patients can benefit when doctors use drugs for off-label purposes based on science and not on false marketing claims.

Doctors generally don't tell people that they're prescribing drugs pitched to them by pharmaceutical salespeople for unapproved treatments, says **Peter Lurie**, deputy medical director of **Public Citizen**, a Washington-based public interest group.

Most physicians don't keep track of FDA-approved uses of drugs, says Lurie, a physician who has published articles in "The Lancet" and the "**Journal of the American Medical Association**."

"The great majority of doctors have no idea; they don't even understand the distinction between on- and off-labeling," Lurie says.

Pharmaceutical companies have showered doctors with cash to persuade them to use drugs off-label, according to their guilty pleas.

'Buying Access'

Pfizer's marketing program offered doctors up to \$1,000 a day to allow a Pfizer salesperson to spend time with the physician and his patients, according to a whistle-blower **lawsuit** filed by John Kopchinski, who worked as a salesman at Pfizer from 1992 to 2003.

"By 'pairing up' with a physician, the sales representative was able to promote over a period of many hours, without the usual problems of gaining access to prescribing physicians," Kopchinski says. "In essence, this amounted to Pfizer buying access to physicians."

Pfizer spokesman **Chris Loder** says the company stopped what it calls "mentorships" in 2005. He says Pfizer paid doctors \$250 per visit.

It used to be legal for companies to promote drugs for any use in the U.S. Congress banned the practice

in 1962. The catalyst was **Thalidomide**, a morning sickness drug taken by pregnant women outside the U.S. that caused severe birth defects.

Recouping Investments

The 1962 law required pharmaceutical companies to prove their drugs were safe and effective for specific uses. Before that, a drug company could market an approved medicine for any illness.

If the law is clear, why do drug companies keep breaking it? The answer lies in economics. Pharmaceutical companies spend about \$1 billion to develop and test a new drug. To recoup their investment, the companies want doctors to prescribe their drugs as widely as possible.

Pfizer's Neurontin is a case in point. The FDA approved the drug as a supplemental medication in treating epilepsy in 1993. Pfizer took in \$2.27 billion from sales of Neurontin in 2002. A full 94 percent - \$2.12 billion -- of that revenue came from off-label use, according to the prosecutors' 2004 Pfizer sentencing memo.

Pfizer, which bought Wyeth on Oct. 15 for \$68 billion, put itself at the center of illegal off-label drug marketing with an acquisition frenzy a decade earlier. From 1995 to 2005, Pfizer purchased more than 20 companies.

Guilty Pleas

Since 2004, companies that are now Pfizer divisions have pleaded guilty to off-label marketing of two drugs. Pfizer continued off-label promotions for these medications after buying the firms, according to Pfizer's Sept. 2 guilty **plea** and FDA correspondence with Pfizer.

Pfizer first stepped into an off-label scheme in 1999, when it offered to buy Morris Plains, New Jersey-based **Warner-Lambert Co.** Prosecutors charged that Warner-Lambert marketed Neurontin off-label between 1995 and 1999.

Warner-Lambert admitted doing so for one year in a May 2004 guilty plea for which Pfizer paid \$430 million in fines and penalties.

Neurontin, which was invented by Warner-Lambert, was first tested in humans in 1987. When the FDA approved it in 1993 to be used only along with other epilepsy drugs, the agency wrote that a side effect of the drug can be that it induces depression and **suicidal thoughts** in patients.

Whistle-Blower

Much of what prosecutors learned about Warner-Lambert's marketing of Neurontin comes from a former employee.

David Franklin, who holds a Ph.D. in microbiology from the **University of Rhode Island**, left his job as a pediatric researcher at Harvard University's **Dana-Farber Cancer Institute** in 1996 to work for the Parke-Davis unit of Warner-Lambert in Boston.

He says he hoped the salary boost -- to \$55,000 annually from \$18,000 -- would help him pay off student loans and better support his family.

Franklin's title at Warner-Lambert was medical liaison. He says he soon realized his new employer viewed his doctorate as a badge that would allow him to strike up conversations with physicians.

Franklin, 48, says his job involved more salesmanship than science. He told doctors that Neurontin was the best drug for a dozen off-label uses, including pain relief, bipolar disease and depression.

'What I Did Was Wrong'

"Technically, I had responsibility for answering physician questions about all of Parke-Davis's drugs," Franklin says. "In practice, my real job was to promote Neurontin for off-label indications heavily -- to the exclusion of just about everything else."

Franklin, whose wife is a lawyer, says he knew such uses of the drug had no scientific support for effectiveness and safety.

"I was actually undermining their ability to fulfill the Hippocratic oath," Franklin says, referring to a physician's pledge to "first, do no harm."

Franklin says he was horrified when he learned from a doctor that a child had a behavioral outburst at school for the first time after taking Neurontin.

"Don't we have an obligation to tell physicians about this?" Franklin says he asked his manager, Phil Magistro. His boss tried to reassure him, Franklin says.

'Total Disregard'

"Don't worry about this stuff," he says Magistro told him. "It can never get back to us."

Franklin was stunned.

"I realized at that moment, looking into his eyes, that there was an absolute total disregard for the patient," he says.

Magistro, who now works at drug marketing adviser **Atom Strategic Consulting LLC** in Randolph, New Jersey, didn't return calls seeking comment.

Franklin saved phone messages from Magistro to his sales team urging them to market Neurontin for off-label uses, including pain relief. During one such call, on May 23, 1996, at 5:48 p.m. in Boston, Magistro told his staff, "You're supposed to be pushing on Neurontin," according to a **transcript** of the tape filed in federal court.

"When we get out there, we want to kick some ass. We want to sell Neurontin on pain," Magistro said. "All right?"

Quit the Job

After working for Warner-Lambert for three months, Franklin grew concerned about his own liability. He quit the job and talked with Boston attorney Thomas Greene, who helped him file a **lawsuit** against the company.

Franklin acted as a whistle-blower, suing on behalf of taxpayers to recover money the government paid for illegally promoted drugs. Under federal and state whistle-blower statutes, he stood to collect as much as 30 percent of any settlement the company made with the government.

Franklin had to wait four years -- until 2000 -- before the Justice Department began a criminal investigation. In November 1999, Pfizer made its public offer to buy Warner-Lambert. In January 2000, a federal grand jury in Boston issued subpoenas to Warner-Lambert employees to testify about the marketing of Neurontin.

That March, Warner-Lambert's annual report disclosed that prosecutors were building a criminal case. Undeterred, Pfizer bought Warner-Lambert in June for \$87 billion. It was the third- largest merger in U.S. history.

'Misleading and in Violation'

A year after the acquisition, the FDA discovered that Neurontin was still being marketed off-label. In a **letter** to the company on June 29, 2001, the agency wrote that Pfizer's promotion of the drug "is misleading and in violation of the Federal Food, Drug and Cosmetics Act."

The agency asked Pfizer to stop such promotions of Neurontin. The FDA said Pfizer had distributed brochures -- known as "slim jims" because they're small enough to put in a jacket pocket -- improperly claiming that the drug could improve energy levels and memory.

"Immediately discontinue the use of this slim jim and any other promotional material or practices with the same or similar messages," the FDA wrote.

Pfizer marketed Neurontin off-label after receiving that letter, agency records show. For 2001, Pfizer reported revenue of \$1.75 billion from Neurontin sales, making it the company's fourth-largest-selling

drug that year, ahead of impotence pill Viagra, which Neurontin topped for four years.

Marketing Violated Rules

As Neurontin sales soared to \$2.27 billion in 2002, the FDA found that Pfizer was improperly claiming that the drug was useful for a broader range of brain disorders than scientific evidence had established.

The agency sent a [letter](#) dated July 1, 2002, that said the company's marketing practices were in violation of FDA rules. It asked Pfizer to stop using misleading promotions. Pfizer reported \$2.7 billion in revenue from Neurontin in 2003. Overall, the drug has provided Pfizer with \$12 billion in revenue.

In a response to Bloomberg News, Pfizer spokesman Chris Loder said, "Regarding the 2001 and 2002 FDA letters, we do not believe that they were suggestive of any continuing off-label promotion."

For blowing the whistle on his employer, Franklin collected \$24.6 million under the False Claims Act.

Prosecutors Loucks and Sullivan got involved in the case after Franklin filed his suit, relying on information from Franklin and their own investigation. Before 2004, prosecutions for off-label marketing were rare.

'Everybody Does It'

"Until a couple of these cases became public, companies were probably saying, 'Everybody does it this way,'" Sullivan says.

Loucks had a track record in off-label prosecutions. He gave up private practice at [Choate Hall & Stewart LLP](#) in Boston in 1985 to join the U.S. Attorney's Office.

In 1994, he negotiated a \$61 million settlement with Murray Hill, New Jersey-based C.R. Bard Inc., which pleaded guilty to promoting off-label use of a heart catheter that led to patient deaths.

In 2002, he co-authored, with Carol Lam, "Prosecuting and Defending Health Care Fraud Cases" ([BNA Books](#)).

In the January 2004 settlement negotiations with Loucks, Sullivan and two other prosecutors, Pfizer's lawyers assured the U.S. Attorney's Office that the company wouldn't market drugs off-label.

'Those Promises'

"They asserted that the company understood the rules and had taken steps to assure corporate compliance with the law," Loucks says. "We remember those promises."

What Pfizer's lawyers didn't tell the prosecutors was that Pfizer was at that moment running an off-label marketing promotion using more than 100 of its salespeople. They were pitching Bextra, a Pfizer sales manager admitted when she pleaded guilty to [misbranding](#) a drug on March 30, 2009.

[Jeff Kindler](#), who became Pfizer's general counsel in 2002, supervised the lawyers who made the promises to prosecutors. By 2004, Kindler increased the compliance budget 12-fold. He became chief executive officer in 2006. In Pfizer's [ethics guide](#), he says stories about misbehaving companies and executives abound.

"Pfizer truly stands apart," he says. "I am proud of our record." On Oct. 1, Kindler was elected to the board of the [Federal Reserve Bank of New York](#). Kindler declined to comment.

Peapack, New Jersey-based [Pharmacia & Upjohn Inc.](#) developed Bextra, which was approved by the FDA only for the treatment of arthritis and menstrual discomfort in 2001.

Sales Manager Pleads Guilty

P&U and Pfizer had by then already crafted a joint marketing agreement to sell the drug. In November 2001, Mary Holloway, a Pfizer regional manager for the Northeastern U.S., began illegally training and directing her sales team to market Bextra for the relief of acute pain, Holloway admitted in a March 2009 guilty plea.

On Dec. 4, 2001, Pfizer executives sent Holloway a copy of a nonpublic letter from the FDA to the

company. The agency had denied Pfizer's application to market Bextra for acute pain. Clinical trials had shown Bextra could cause heart damage and death.

Pfizer bought Pharmacia & Upjohn in April 2003. From 2001 to the end of 2003, P&U, first as an independent company and then as a unit of Pfizer, paid physicians more than \$5 million in cash to lure them to resorts, where salespeople illegally pitched off-label uses for Bextra, P&U admitted in its Sept. 2 guilty plea.

'Golf, Massages'

"Pharmacia paid targeted physicians both airfare and two to three days' accommodations at lavish resorts in the Bahamas, Virgin Islands and across the United States and further entertained these physicians with golf, massages and other recreation activities," according to prosecutors' findings.

In her guilty plea, Holloway said her team had solicited hospitals to create protocols to buy Bextra for the unapproved purpose of acute pain relief. Her representatives didn't mention the increased risk of heart attacks in their marketing.

They told doctors that side effects were no worse than those of a sugar pill, Holloway admitted in her guilty plea.

In 2003, Holloway reported her unit's off-label promotions of Bextra up the corporate ladder at Pfizer, according to a pre-sentencing memo to the judge written by **Robert Ullmann**, Holloway's attorney. Top managers didn't attempt to halt the illegal conduct, the memo said.

"Corporate tracked this information, and at no time did it inform Ms. Holloway that any of the reported protocols were inappropriate," he wrote. "Instead, the instruction was to get more protocols."

Blockbuster Status

By the end of 2004, Bextra reached blockbuster status, with annual sales of \$1.29 billion. Holloway promoted Bextra until the FDA asked Pfizer in April 2005 to **pull it from the market** for all uses, evidence in her case shows.

The agency concluded that the drug increased the risk of heart attacks, chest infections and strokes in cardiac surgery patients. In June 2009, Holloway, 47, was **sentenced** to two years on probation and fined \$75,000. She didn't return phone calls seeking comment.

Ronald Rainero, a Pfizer district sales manager and employee for more than 20 years, says he was responsible for promoting Bextra in New York from 2001 to 2005. In September 2007, Rainero, 47, began cooperating with federal prosecutors on the Bextra case.

Hotel Meetings

He says he met monthly with his fellow managers at a Hilton hotel in Staten Island, New York, to discuss sales methods of promoting Bextra off-label. As a whistle-blower, Rainero was awarded \$9.3 million as part of the September settlement.

In the same time period that Pfizer was marketing Bextra off-label, the company's sales force was promoting another drug, Zyvox, improperly, Pfizer admitted at the time of its September plea agreement.

Zyvox was approved in 2000 by the FDA for treating MRSA-caused pneumonia and skin infections. Rainero told federal prosecutors that Pfizer began the Zyvox campaign in 2001. The company admitted to falsely claiming that the drug was better than other medications for treating MRSA pneumonia.

Pfizer told doctors to use Zyvox rather than vancomycin, a generic antibiotic that cost \$18 a day. Pfizer sold Zyvox for about \$150 a day. A table on page 30 of a 35-page **fact book** produced by Pfizer for Zyvox says the drug is less effective than vancomycin for MRSA pneumonia.

'Misleading Promotion'

On July 20, 2005, the FDA sent a **letter** to **Hank McKinnell**, then Pfizer's CEO, saying, "Your

misleading promotion of Zyvox, and in particular your unsubstantiated implied claims regarding its superiority to vancomycin, poses serious health and safety concerns.”

The agency ordered the company to stop the promotion. In response, Pfizer told the FDA it would stop saying Zyvox was more effective against MRSA pneumonia than vancomycin.

Despite its 2005 pledge to the FDA, Pfizer continued to tell hospitals and doctors that Zyvox would save more lives than vancomycin, **the company admitted** in the September settlement.

By 2007, the criminal and civil cases against Pfizer, its employees and its subsidiaries had started to mount. The tally of drugs cited by federal prosecutors for off-label promotion reached six by 2009. In April 2007, P&U pleaded guilty to a felony charge of offering a **\$12 million kickback** to a pharmacy benefit manager.

\$2.2 Billion in Penalties

Pfizer paid a criminal fine of \$19.7 million. Thomas Farina, a Pfizer district sales manager, was **convicted** in federal court in March 2009 for destroying records during the Bextra investigation. Farina, 42, was sentenced to three years on probation, including six months of home confinement. He didn't return calls seeking comment.

Pfizer itself was called to account on Sept. 2, when it agreed to pay the \$2.2 billion in fines and penalties. P&U pleaded guilty to a felony charge of misbranding Bextra with the intent to defraud. After the settlement, Pfizer general counsel **Amy Schulman** said the company had learned its lesson.

“We regret certain actions we’ve taken in the past,” she said. “Corporate integrity is an absolute priority for Pfizer.”

One reason drug companies keep breaking the law may be because prosecutors and judges have been unwilling to use the ultimate sanction -- a felony conviction that would render a company's drugs **ineligible for reimbursement** by state health programs and federal Medicare.

“It's potentially a death sentence for a drug company,” prosecutor Sullivan says.

Fig Leaf

A legal fig leaf allows a parent company to continue to participate in government programs even after its subsidiary has pleaded guilty.

Pfizer maintains its good standing with such agencies because its subsidiaries, Warner-Lambert and P&U, and not the corporation itself, entered the guilty pleas to felony charges.

A felony conviction of a pharmaceutical giant could lead to disaster for shareholders, Loucks says, adding that's a step that may have to be taken for repeat offenders.

“I think it's something the trigger will get pulled on,” he says from his ninth-floor office in the **federal courthouse**, with a sweeping view of Boston Harbor. “It's just a question of when.”

At Pfizer's Pharmacia sentencing on Oct. 16., U.S. District Court Judge **Douglas Woodlock** said companies don't appear to take the law seriously.

“It has become something of a cost of doing business for some of these corporations, to shed their skin like certain animals and leave the skin and move on,” he said.

Eli Lilly

Lilly's rap sheet goes back to 1985. That's when the company pleaded guilty to **25 federal misdemeanor charges** related to its misbranding of Orflex, an arthritis drug.

Lilly stopped selling the drug four months after U.S. sales began in 1982, following the company's failure to tell the FDA about illnesses and deaths tied to the medication. Lilly paid a \$25,000 fine.

Twenty years later, in 2005, Lilly paid \$36 million in a guilty plea to **one federal misdemeanor** for off-label marketing of Evista, a drug the FDA had approved for bone strengthening.

In 1997, the agency had rejected Lilly's application to market the drug to reduce the risk of breast cancer. Yet beginning the next year, Lilly adopted an Evista marketing plan that included a seminar with doctors designed to appeal to women's breast cancer concerns, Lilly admitted in its 2005 guilty plea.

In 2007, the FDA approved Evista for preventing breast cancer in **two limited groups**.

Back in Court

In January 2009, Lilly was back in **federal court**. Prosecutors in Philadelphia accused the company of earning hundreds of millions of dollars by illegally promoting its schizophrenia drug Zyprexa for the unapproved treatment of dementia from 1999 to at least 2003.

In 2001, Lilly's senior management decided not to seek FDA approval for Zyprexa to treat dementia because of what they viewed as mixed results in clinical trials and safety risks, according to admissions by Lilly in its 2009 guilty **plea**. In its marketing, Lilly promoted the drug as effective.

Zyprexa has been Lilly's best-selling drug for the past decade.

"Eli Lilly undertook this illegal off-label promotion for its own financial gain despite the potential risk to patients' health and lives," prosecutors wrote in their sentencing **memo**.

Lilly Chairman and CEO **John Lechleiter** said after the settlement that the company was devoted to acting responsibly.

'Deeply Regret'

"We deeply regret the past actions covered by the misdemeanor plea," he said. "Doing the right thing is nonnegotiable at Lilly."

In a written response to questions from Bloomberg News, Lilly said, "Lilly entered into a very narrow guilty plea. Even though the company disagrees with and does not admit to the allegations, Lilly agreed to settle the dispute."

Lilly paid \$1.42 billion for a fine and penalties in the January settlement with federal and state governments. That included the largest criminal fine in U.S. history -- until Pfizer pleaded guilty in September.

The Justice Department could have charged Lilly with a felony. Prosecutors decided that it wouldn't be fair to innocent Lilly employees, shareholders and pensioners to potentially shut down the company, according to the **sentencing** memo.

'All the Factors'

"The government considered all the factors in its decision," prosecutors wrote. "Those factors included other persons not proven personally culpable."

Federal regulators have detected a similar pattern of dishonesty by other pharmaceutical firms. **Schering-Plough Corp.** drug salesmen pitched off-label uses of a cancer drug called **Temodar** at the **American Society of Clinical Oncology's** annual conference in San Francisco in May 2001.

Schering-Plough representatives said Temodar compared favorably to a placebo in clinical trials for the off-label uses and was approved by the FDA for first-line use in treating brain tumors.

An FDA employee attending the conference took note. The next month, the FDA accused Schering of lying.

There had been no such clinical trials and the agency had not approved Temodar as the salespeople had claimed, the FDA said in a **June 28, 2001, letter** to Mary Jane Nehring, Schering's senior director of marketed products. The agency ordered the company to immediately cease illegal promotion of Temodar.

Kenilworth, New Jersey-based Schering-Plough was quick to respond. On July 12, 2001, it wrote back to the FDA, assuring regulators that the San Francisco activity was an isolated incident.

'Certainly Inconsistent'

"It was certainly inconsistent with the direction provided by the home office," the drug company wrote, according to prosecutor's records.

The FDA told Schering-Plough three weeks later that it had closed its investigation.

Schering-Plough didn't stop pitching the drug for unapproved uses. At the direction of top management, Schering ordered widespread off-label marketing of Temodar and Intron A, another cancer drug, until December 2003, the company admitted in an August 2006 guilty plea.

Schering, which agreed in March to be acquired by Merck & Co., earned a pre-tax profit of \$124.2 million from the illegal sales after promising the FDA in 2001 it would stop marketing for off-label uses, the company admitted.

Schering-Plough **pleaded guilty in August 2006** to conspiring to make false statements to the FDA. The company agreed to pay \$435 million to settle the case.

'Upsetting to Me'

U.S. District Court Judge **Patti Saris**, who had presided over the Neurontin whistle-blower case before the Pfizer probe, accepted Schering's plea in her Boston courtroom in January 2007. She expressed dismay with the drug industry.

"It's been upsetting to me how many of the big pharmaceutical companies have engaged in what I view as clearly illegal behavior in terms of off-label marketing," she said. "It almost seems as if the pharmaceutical companies said 'Yeah, yeah, yeah' to the FDA and then went and did it anyway."

Brent Saunders, a Schering-Plough senior vice president, said after the settlement that his company had made great progress in putting integrity at the center of its work.

"With this agreement, we are putting issues from the past behind us," he said. Schering declined to comment further.

As prosecutors continue to uncover patterns of deceit in off-label marketing by pharmaceutical companies, millions of patients across the nation remain in the dark. Doctors often choose the medications based on dishonest marketing by drug company salesmen.

'A Morass'

"It's a morass of undifferentiated information out there," Public Citizen's Lurie says. "And the doctors, let alone patients, aren't able to distinguish the good from the bad."

One thing all people should do, Lurie says, is ask whether their prescriptions are for FDA-approved uses, and if not, whether strong evidence supports using the drug, particularly if it can be dangerous.

Loucks says that putting an end to the criminal off-label schemes by the pharmaceutical industry is more difficult. As drugmakers repeatedly plead guilty, they've shown they're willing to pay hundreds of millions of dollars in fines as a cost of generating billions in revenue.

The best hope, Loucks says, is that drug companies actually honor the promises they keep making -- and keep breaking -- to obey the law of the land.

To contact the reporter on this story: **David Evans** in Los Angeles at davidevans@bloomberg.net

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