
February 1, 2004

Making Drugs, Shaping the Rules

By MELODY PETERSEN

THE drug industry has created vast markets for products like Viagra, Celebrex and Vioxx by spending billions of dollars on consumer advertising.

But to sell medicines that treat schizophrenia, the companies focus on a much smaller group of customers: state officials who oversee treatment for many people with serious mental illness. Those patients - in mental hospitals, at mental health clinics and on Medicaid - make states among the largest buyers of antipsychotic drugs.

For Big Pharma, success in the halls of government has required a different set of marketing tactics. Since the mid-1990's, a group of drug companies, led by Johnson & Johnson, has campaigned to convince state officials that a new generation of drugs - with names like Risperdal, Zyprexa and Seroquel - is superior to older and much

cheaper antipsychotics like Haldol. The campaign has led a dozen states to adopt guidelines for treating schizophrenia that make it hard for doctors to prescribe anything but the new drugs. That, in turn, has helped transform the new medicines into blockbusters.

Ten drug companies chipped in to help underwrite the initial effort by Texas state officials to develop the guidelines. Then, to spread the word, Johnson & Johnson, [Pfizer](#) and possibly other companies paid for meetings around the country at which officials from various states were urged to follow the lead of Texas, according to documents and interviews that are part of a lawsuit and an investigation in Pennsylvania.

How did this play out? In May 2001, as Pennsylvania was weighing whether to adopt the Texas guidelines, Janssen Pharmaceutica, a Johnson & Johnson subsidiary that sells Risperdal, paid \$4,000 to fly two state mental health officials to New Orleans, where they dined at an elegant Creole restaurant in the French Quarter, visited the aquarium and met with company executives and Texas officials, according to documents. Janssen also paid two Pennsylvania officials \$2,000 each for giving speeches at company-sponsored educational seminars for doctors and nurses working in the state's prisons.

The payments were discovered a little more than a year ago by Allen L. Jones, an investigator in the inspector general's office in Pennsylvania, who stumbled upon them when he was looking into why state officials had set up a bank account to collect grants from pharmaceutical companies.

With the help of his congressman in Pennsylvania, Mr. Jones, who is 49 and a former parole officer, brought the information to the attention of federal health officials - after, he says, his superiors removed him from the investigation, citing the political influence of the drug industry. The Department of Health and Human Services has asked the health care fraud unit of the Federal Bureau of Investigation to determine whether any laws were broken, according to letters Mr. Jones has received from federal officials.

DETAILS of the drug companies' efforts, recorded in Mr. Jones's investigative files and confirmed in part by drug companies and state officials, offer a glimpse inside the drug industry's behind-the-scenes efforts to promote the new-generation antipsychotics, called atypicals because their action in the body is unlike that of earlier drugs.

There is no proof that drug-industry money changed any state official's opinion about the drugs. And compared with the billions of dollars spent marketing to doctors from their first days as medical students - or the billions spent to underwrite and publish research - the dollar amounts are small.

But questions have multiplied about the many ways that the drug industry tries to influence the medical information that determines its products' success or failure. Last month, for example, some senators sharply criticized the National Institutes of Health for allowing its scientists to accept consulting fees and stock options from drug and biotechnology companies. Officials of the agency said that its top-level scientists

were no longer accepting such compensation.

Sales of the new antipsychotics totaled \$6.5 billion last year, according to an estimate by Richard T. Evans, an analyst at Sanford C. Bernstein & Company. About a third of those sales were to state Medicaid programs, whose costs have ballooned with their adoption of the new medications. Texas, for example, says it spends about \$3,000 a year, on average, for each patient on the new drugs, versus the \$250 it spent on older medications. The escalating costs have prompted a few states to try to limit access to the new antipsychotics - efforts that drug makers have opposed vigorously.

The Texas guidelines advise doctors to choose Risperdal or one of four other new antipsychotics - Zyprexa from Eli Lilly, Seroquel from [AstraZeneca](#), Geodon from Pfizer or Abilify from [Bristol-Myers Squibb](#) - unless they can explain in writing why an older drug would be better. If a patient does poorly on the first medication, doctors at state hospitals and mental health clinics are advised to try another of the new drugs next. Texas officials said such guidelines were simply a road map for doctors, who can explain to the state on written forms why they are not prescribing a recommended drug.

The drug companies deny doing anything untoward. They say it was appropriate for them to help pay for the development of guidelines aimed at giving patients the best care. The ones for schizophrenia, they say, were written by medical experts and Texas officials without industry interference.

"Janssen did not participate in nor

influence the content or the development of the guidelines," said Doug Arbesfeld, a spokesman for Janssen Pharmaceutica. Officials in some states asked the company for financial grants so that they could learn about the guidelines, he said.

Dr. Steven P. Shon, who as medical director of the Texas mental health department led the work on the guidelines, said the effort was not the drug companies' idea. Rather, he said, state officials decided that guidelines were needed because of the wide variations in prescriptions being written for patients.

Dr. Shon said that the condition of many patients had improved when their care followed the guidelines. Even without them, he added, doctors in Texas would have prescribed the new drugs. "Everyone wants to use the new thing," he said.

WHEN work on the Texas guidelines began in 1995, only two of the new-generation drugs were approved for sale: Risperdal and Clozaril, a medicine from [Novartis](#) that doctors were uncomfortable prescribing because of its known potential to cause a life-threatening blood disorder.

At the time, Janssen had little research on which to base its claims that Risperdal represented a medical advance. In fact, when federal regulators approved the drug, they forbade the company from claiming in marketing materials that it was better than the older drugs.

Now, doctors widely prefer the new medications, saying that the older drugs cause a higher incidence of side effects

like stiffness, trembling and uncontrollable jerks that can stigmatize patients and prompt them to stop taking the drugs.

But some recent studies have complicated the picture for doctors by showing that the new medicines have potentially serious side effects, too, including the development of diabetes in some patients. On Tuesday, four medical groups, including the American Psychiatric Association, warned that the new drugs could increase a patient's risk of obesity, diabetes and high cholesterol - which can all lead to heart disease. Some leading experts on schizophrenia, after reviewing the accumulated scientific evidence, have developed a set of guidelines that clash with the Texas policy. These recommendations, produced entirely with federal government financing, say that physicians should not consistently choose the new drugs over the older medications.

"You choose the one that seems the best for the patient," said Dr. Anthony F. Lehman, the chairman of the psychiatry department at the University of Maryland School of Medicine. Dr. Lehman was the leader of the panel, called the Patient Outcomes Research Team, that put together the alternate guidelines under a grant from the National Institute of Mental Health. The guidelines are expected to be published this spring.

As early as 1999, physicians were raising questions about the drug industry's financing of the Texas guidelines. In an article that year in *The Journal of Practical Psychiatry and Behavioral Health*, Dr. Peter J. Weiden and Dr. Lisa Dixon argued that corporate financing

created a potential conflict of interest that could hurt the project's credibility.

Dr. Weiden, professor of psychiatry at the State University of New York Downstate Medical Center in Brooklyn, said in an interview last month that he believes the new drugs have benefits over the older ones. But he continues to worry, he said, that the industry controls too much of what doctors learn in psychiatry. For example, Dr. Weiden said, industry-sponsored educational events focus on medications, while subjects like how to talk to patients to motivate them to get better fall through the cracks.

"The industry drives education right now," Dr. Weiden said. "Across the board, there has been a shifting of education toward psychopharma," meaning drug treatment.

Mr. Arbesfeld, the Janssen spokesman, said that the company disagreed with the recommendations of Dr. Lehman's panel. A growing body of evidence, Mr. Arbesfeld said, shows the benefits of the new drugs. He pointed to a 2002 study that found that patients treated with Risperdal had a lower risk of relapse than those treated with Haldol. He also noted that the National Institute for Clinical Excellence, part of the National Health Service of the British government, recommends the new drugs as a first-choice treatment for schizophrenia.

Other companies say it is important that they help educate doctors about the intricacies of their drugs. "There is no one who knows more about our products than we do," said Mariann Caprino, a spokeswoman for Pfizer. The company, like many others, gives financial grants for educational events but says that it is

not involved in writing the instruction materials.

Industry financing of the Texas guidelines began in 1996, when Janssen agreed to help pay for a survey of dozens of experts about the best way to treat schizophrenia, according to the article by Dr. Weiden and Dr. Dixon.

Texas officials relied on the experts' conclusions to help them write the guidelines, which were first applied to patients in 1997. The initial ones called for doctors to use either Risperdal or one of the earlier generation of antipsychotics. Three years later, Janssen and five other companies helped underwrite an update of the consensus; Texas, in turn, used it in updating the guidelines. The 1999 version established a preference for the new drugs.

Dr. Shon said 11 drug companies had given Texas a total of \$285,000 for the project. The effort produced guidelines for treating schizophrenia as well as for treating bipolar disorder and major depressive disorder in adults, and attention deficit hyperactivity disorder and major depression in children.

In all, Texas has spent about \$6 million on the guidelines and on educating doctors about how to use them, Dr. Shon said. In addition to the drug industry support, the state has received help from the federal government, universities and nonprofit foundations. The largest grant, \$2.4 million, came from the Robert Wood Johnson Foundation, a leading backer of health care research, which was established by the estate of a longtime chief executive of Johnson & Johnson.

David J. Morse, a vice president of the foundation, said that it made the grant because one of its goals is to help find the best possible medical treatments. The foundation has about 50 percent of its financial assets invested in Johnson & Johnson stock, he said, and has former company executives on its board. But it is "completely independent" of Johnson & Johnson, Mr. Morse said.

IN May 2002, a manager in Pennsylvania's public health department reported to state investigators that mental health officials had created a bank account to collect grants from drug companies.

Mr. Jones said the inspector general's office soon dispatched him to look into the report. Pennsylvania's ethics law covering state workers bars them from accepting honorariums and gifts if they are made to influence officials' decisions; ethics officials say the ban can also extend to accepting reimbursements for travel in some cases. Violators can be punished by fines and criminal penalties.

Mr. Jones said he began to believe that drug companies were trying to buy the loyalty of state officials. "The more research I did, the more alarmed I became," he said in an interview.

As he reconstructed the flow of deposits into the account, he interviewed drug company executives and state officials. Pennsylvania mental health officials, he determined, were beginning to express interest in the Texas guidelines by October 2000. Janssen paid twice for Dr. Shon to fly to Pennsylvania, according to notes from an interview Mr. Jones conducted with Janssen executives in

September 2002. Janssen made the grant covering Dr. Shon's travel expenses "to expand atypical usage," according to a company document that was given to Mr. Jones.

On April 17, 2002, Janssen paid for an educational seminar on the guidelines for doctors and nurses working in Pennsylvania's prisons. Each of the speakers - including Steven J. Fiorello, the top pharmacist in Pennsylvania's mental health office, and Dr. Frederick R. Maue, clinical services director of the state's Department of Corrections - was paid \$2,000, according to Mr. Jones's interviews and documents he obtained. Comprehensive NeuroScience, a marketing company in White Plains working for Janssen, provided Mr. Fiorello with slides to use as a model for his talk, according to an e-mail message that Comprehensive NeuroScience sent to Mr. Fiorello. In the message, Comprehensive NeuroScience asked him to personalize the slides and then send them back for Janssen's review.

Sandra Forquer, vice president for educational services at Comprehensive NeuroScience, said in an interview that Mr. Fiorello had written his own speech. She also said that Mr. Fiorello had requested that his \$2,000 payment be given to charity, but that her company sent it to him directly by mistake. According to Mr. Jones's interview notes, Mr. Fiorello described several instances in which drug companies gave him honorariums but said he was unsure about which ones he had kept and which ones he had given to charity.

Stephanie Suran, a spokeswoman for the Department of Public Welfare in

Pennsylvania, said Mr. Fiorello was not available for comment. She said that she could not comment on Mr. Jones's findings because of a continuing investigation.

Mr. Jones's interview notes show that Ms. Forquer also told him that Janssen, through Comprehensive NeuroScience, paid Dr. Maue \$2,000 for each of two other speeches, in Orlando, Fla., and Sacramento. A spokeswoman for Dr. Maue said that he had turned over any honorariums he received to the state; state officials confirmed that he had sent the money to the state's general fund.

But Mr. Jones learned that Janssen nurtured other ties to state officials. It named Dr. Steven J. Karp, medical director of Pennsylvania's mental health office, to the advisory board of a newsletter, Mental Health Issues Today, that a marketing firm created for Janssen. Janssen paid to fly Dr. Karp, as well as top officials from other states, to advisory board meetings in Seattle, Washington, D.C., and Tampa, Fla.

ACCORDING to Mr. Jones's interview notes, Dr. Karp said he eventually became uncomfortable about attending the meetings because a Janssen executive was always present. Ms. Suran, the spokeswoman for the Department of Public Welfare, said that Dr. Karp was not available for comment.

The records that Mr. Jones compiled in his investigation are now part of a lawsuit he filed against his supervisors in the Pennsylvania inspector general's office after they removed him from the inquiry. Mr. Jones said he did not know if the inspector general's office had investigated

the matter further.

Mr. Jones contends in the lawsuit, which has been transferred to the United States District Court in Scranton, Pa., that his bosses violated his rights by trying to hide the evidence he found.

"I was told that drug companies write checks to politicians on both sides of the aisle," said Mr. Jones, who still works as an investigator in the inspector general's office.

W. Scott Foster, a spokesman for the inspector general's office, said that the office did not comment on lawsuits or its investigations. In court, lawyers for the state health officials have argued that the officials did nothing wrong and did not violate the rights of Mr. Jones.

Pennsylvania officials believe that the schizophrenia guidelines, adopted by the state in 2001, are saving money, Ms. Suran said. In the past, many doctors prescribed more than one drug for schizophrenia patients, the mental health office found. The guidelines, however, rarely allow multiple prescriptions. Preliminary data also show that the mental health of some patients has improved, Ms. Suran said.

Before he was pulled off the investigation, Mr. Jones said, he learned that Janssen was not the only drug company that had made payments to Pennsylvania officials involved in adopting the guidelines. According to Mr. Jones's interview notes, Mr. Fiorello said that Pfizer had paid twice for him to travel to its Manhattan headquarters from Harrisburg for meetings of "an elite group of pharmacists," put him up at one of the

Millennium hotels in Manhattan and paid him an honorarium of less than \$1,300 for each meeting.

According to the notes, Mr. Fiorello also told Mr. Jones that Pfizer had paid for him to travel with a Pfizer sales representative to Maryland to meet with a mental health official from that state and discuss Pennsylvania's use of the guidelines. Pfizer paid him an honorarium, he said, but he could not remember how much.

Ms. Caprino, the Pfizer spokeswoman, said the company finances development of treatment guidelines to ensure that patients get the best possible medications. The company, she said, plays no role in writing the guidelines. In addition, Ms. Caprino said, Pfizer often hires medical professionals as consultants and pays them for their time.

Pfizer cooperated with Pennsylvania officials as they investigated the payments, she said, and the officials later told the company that it had not acted inappropriately.

SOME payments went to patient groups instead of directly to state officials. In 2002, Janssen gave the Olympia, Wash., chapter of the National Alliance for the Mentally Ill a grant of \$15,000 to fly Dr. Shon and other Texans to speak to Washington state legislators about the guidelines, according to Bill Pilkey, the chapter's former treasurer. Each speaker, he said, was paid \$1,500.

Dr. Shon said that he gave the \$1,500 to the Texas mental health department. In all, he said, he has traveled to more than a dozen states to talk about the

guidelines, with most of the trips paid for by grants from either the Robert Wood Johnson Foundation or the federal government.

When he asked the drug industry to cover various expenses, Dr. Shon said, it was because of a lack of state money. "It was the only source of funding to complete or do all the things we wanted to do," he said.

Dr. Shon said he was working with three more states -Alabama, Hawaii and Wyoming - to help them adopt the guidelines.

Referring to the effort to draw up state guidelines that began in 1995, he said, "None of us ever imagined it would grow into what it has become."