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Doctor Says Drug Maker Tried to Quash His Criticism of Avandia

By [STEPHANIE SAUL](#)

When a Congressional committee holds a hearing next Wednesday, the subject will be the safety of the [diabetes](#) drug Avandia and whether federal drug regulators have paid close enough attention to its potential risks.

But for one witness who is scheduled to appear, Dr. John B. Buse, a nationally noted diabetes specialist, the hearing will take a different turn, focusing on whether he was the target of an effort by the drug's maker, [GlaxoSmithKline](#), to silence his criticism of the drug.

In a statement last night, Dr. Buse said his full story would be told at the hearing, including the account of how he was intimidated by Glaxo. But he said the company apologized and he later reported his concerns about the drug to the [Food and Drug Administration](#).

"It was upsetting, but it was not life-altering," Dr. Buse's statement said. "I hold no ill will toward Glaxo or any of its employees."

Congressional investigators have been looking into what they have called "very serious" claims that Avandia's maker "silenced one or more medical professionals who attempted to speak out about the potential for cardiovascular problems with Avandia," according to a letter to Glaxo last week from the Senate Finance Committee.

Glaxo denied yesterday that it made any effort to stifle a scientific discussion of its drug, used for Type 2 diabetes. Avandia is the company's second-largest product with more than \$3 billion in sales last year.

Dr. Buse has declined to discuss any details of his story, saying he wanted them to come out during sworn testimony. But one of his friends, a [University of Michigan](#) diabetes expert, Dr. Charles F. Burant, said that Dr. Buse had been troubled by the pressure he had received from Glaxo.

Dr. Burant said he was not familiar with specifics, but that the pressure had included Glaxo's contacting the [University of North Carolina](#) medical school, where Dr. Buse was then on the faculty and is now the head of endocrinology.

Although Glaxo is based in London, it has major operations in Research Triangle Park, N.C., and the company's foundation has donated millions of dollars to the University of North Carolina.

Dr. Buse, who is about to become the president of the American Diabetes Association, was an early and frequent critic of Avandia after it reached the market in 1999. In a March 2000 letter to the F.D.A., he said Avandia might raise patients' risk of heart attacks, and he criticized the company's marketing, saying it

employed “blatant selective manipulation of data” to overstate the drug’s benefits and understate its risks.

The following year, after demanding that Glaxo strengthen the language on Avandia’s label describing its potential heart risks, the F.D.A. sent Glaxo a letter reprimanding the company for playing down those risks in discussions between sales representatives and undercover investigators at a medical conference.

Dr. Buse, meanwhile, had also raised his concerns about Avandia in speeches to other doctors. Avandia, an oral medication, is used for a patient population already at increased risk for [heart disease](#).

More recent questions about Avandia’s potential risks, as outlined in a [New England Journal of Medicine](#) article last week, have prompted the Congressional hearing. The author of that article, Dr. Steven E. Nissen, a heart specialist at the Cleveland Clinic, has also been called to testify.

In an interview this week, Glaxo’s president of United States operations, Chris Viehbacher, acknowledged that the company was looking for any records that would shed light on the accusations that it tried to suppress Dr. Buse’s criticisms. Mr. Viehbacher said that the events occurred years ago and that the employee who was thought to have been involved had left the company.

In that interview, Mr. Viehbacher repeated Glaxo’s ’s contention that Avandia’s risks were in line with those of other diabetes medications.

Yesterday, in a written statement issued by a spokeswoman, Mary Anne Rhyne, the company said: “Discussions occurred with Dr. John Buse in 1999 and 2000 regarding his views on Avandia, and we had a scientific disagreement that was later resolved. We regret if, at any time, Dr. Buse felt the conduct of any GSK employee was contrary to the spirit of open, scientific debate regarding his views on Avandia.” The statement also said that the company “does not condone any efforts by GSK’s staff to limit an individual’s ability to discuss or publish adverse events related to Avandia.”

Dr. Buse’s friend, Dr. Burant, said in a telephone interview, “I never wrote a prescription for Avandia because of the heavy-handed way Glaxo treated John Buse.”

When Glaxo sales representatives have asked him why he was not prescribing Avandia, “I was very straight with them,” Dr. Burant recalled.

“When they were giving John a hard time, I just told them that if this is the way you’re going to treat people who are doing their usual scientific review of the product, it’s not the kind of company I’m going to support,” Dr. Burant said. “I just told them flat-out.”

When Dr. Buse addressed his concerns about Avandia to the F.D.A. in early 2000, he was one of several physicians who had been outspoken supporters of Rezulin, a diabetes drug that was taken off the market that year after being linked to liver disease. After viewing early data on Avandia, he said, he concluded that it might be just as hazardous as Rezulin, if for different reasons.

Dr. Buse has served as a consultant to Parke-Davis, the maker of Rezulin, as well as Takeda Pharmaceutical and [Eli Lilly](#), which make a competing oral diabetes medication called Actos. In the past, however, he had also been a consultant for SmithKline Beecham, which merged with Glaxo Wellcome in 2000 to become GlaxoSmithKline.

In a recent interview, Dr. Buse identified himself as a member of a “gang of three” — a group of endocrinologists who raised early questions about Avandia after evidence that the drug had negative effects on fats in the blood and the emergence of signals that it increased the risk of heart attack.

Another member of the “gang,” according to Dr. Buse, was Dr. Anne L. Peters, a diabetes expert who runs a clinic for Los Angeles County and is affiliated with the Keck School of Medicine at the [University of Southern California](#).

In a recent interview, Dr. Peters said that she had previously received money from Glaxo as a speaker on behalf of Avandia, but had resigned because she was worried about the drug’s risks.

About five years ago, she said, she helped change the formulary — or list of preferred drugs — for Los Angeles County so that patients in her clinic would get prescriptions for Actos rather than Avandia.

“The Avandia people, it was just so surprising, they asked me what I wanted to keep Avandia on the formulary,” Dr. Peters said, recounting events that occurred sometime in the 2000-to-2002 period. “They asked me, ‘What can we give you that will have you keep it on the formulary?’ ”

Dr. Peters said that she asked the company to establish a database at the clinic that would track the outcomes of patients on both drugs.

When she asked for the database, which would have cost several thousand dollars, she said, a company representative replied: “That’s all you want? Other doctors ask to go to the Caribbean.”

Dr. Peters said that Glaxo representatives first asked her to write a proposal, then asked her to go to Philadelphia to meet with company officials before the database could be approved. She decided to purchase it herself.

“They wanted to give me everything but approve my request,” said Dr. Peters, who has served as an adviser or consultant to Takeda and Eli Lilly. During a recent interview, Dr. Buse said that although he was outspoken in criticism of Avandia in the early days, he now argues that the drug should remain on the market until Glaxo completes a large clinical trial, which the company says will answer questions about Avandia’s cardiovascular risk.

“A few times I was over the top, I just got carried away,” he said of his early warnings about Avandia. “The truth of the matter is, it was pretty much a statement of the facts with a little bit of imploring to not stick your head in the sand.”

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