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## F.D.A. Issues Strictest Warning on Diabetes Drugs

By [GARDINER HARRIS](#)

WASHINGTON, June 6 — The [Food and Drug Administration](#) has called for the toughest safety warning on two [diabetes](#) drugs, Avandia and Actos, whose health risks have become a focus of Congressional concern.

That decision, disclosed on Wednesday by the F.D.A. commissioner at a packed House hearing, comes more than a year after the agency's safety reviewers strongly recommended just such a step. And it occurs amid a Congressional investigation into why the agency delayed its warnings about Avandia for years.

In a written statement, the commissioner, Andrew C. von Eschenbach, said the agency has asked the makers of Actos and Avandia to carry the more prominent warning, a so-called black box warning, of its heart risks because "despite existing warnings, these drugs were being prescribed to patients with significant heart failure."

The statement said the agency requested the label changes on May 23, which was two days after a medical journal article and editorial about Avandia's potential heart risks set off the current controversy. Word of the label changes, however, had not been made public before Wednesday's hearing.

Dr. Rosemary Johann-Liang, a drug safety supervisor for the agency, had said in an interview this week that she was reprimanded last year for advocating the very label change that Dr. von Eschenbach said the agency was now asking the drug companies to make. Avandia, a Type 2 diabetes treatment made by [GlaxoSmithKline](#), has been the focus of most of the recent safety concerns, based on evidence that it can potentially cause heart attacks or other cardiovascular problems. But its closest competitor, Actos, a drug from Takeda Pharmaceuticals and [Eli Lilly & Company](#), has also been seen as carrying some risk of problems, including heart failure.

The makers of both drugs said that they were discussing the new warnings about heart failure with the drug agency. "This is generally a process that takes weeks to months," said Dr. Robert Spanheimer, a senior medical director at Takeda.

Democrats on the House panel voiced harsh criticism of the drug agency and Dr. von Eschenbach, whom the Bush administration named commissioner in September 2005.

Representative [Henry A. Waxman](#), a California Democrat who is chairman of the panel, the House Committee on Oversight and Government Reform, said the agency had "dropped the ball" in its oversight of Avandia's safety. The agency should have insisted years ago that Glaxo test whether Avandia increased the risks of heart attacks, Mr. Waxman said.

"Avandia is a case study of the need for reform of our drug safety laws," Mr. Waxman said. "F.D.A. needs the will, the resources and the authority to be a more effective watchdog of drug safety."

Democrats asked Dr. von Eschenbach if he believed his agency needed more authority from Congress to require drug makers to perform safety studies or correct drug advertisements. Dr. von Eschenbach said his agency required more money, not authority. And he characterized as “more destructive than constructive” proposals by some of the agency’s Congressional critics to separate the F.D.A.’s drug approval and drug safety functions.

Some Republican members of the committee criticized Democrats on the panel for making too much of uncertain information about Avandia, a popular diabetes pill that has been taken by an estimated seven million people worldwide.

Representative Virginia Foxx, Republican of North Carolina, said she was concerned that those studying the drug had spoken to Democrats on the committee but not to anyone at the drug agency.

“I’d like members of the press to investigate what members of Congress knew about this” and whether those members joined some F.D.A. staff members and others “to create maximum embarrassment to the agency,” Ms. Foxx said.

Representative Darrell Issa, Republican of California, said the committee was coming dangerously close to “politicizing science.” And he closely questioned Dr. Steven E. Nissen, a cardiologist at the Cleveland Clinic whose May 21 article in [The New England Journal of Medicine](#) questioned the safety of Avandia.

“This does look like in fact that this was a political concoction to anecdotally go after a company, and I object to it,” Mr. Issa said.

As with most hearings involving the F.D.A., members of Congress sometimes seemed bewildered by some of the technical answers given by witnesses on Wednesday, and several lawmakers stumbled over medical terms at the heart of the debate.

The agency officials themselves appeared confused when Representative Stephen F. Lynch, Democrat of Massachusetts, asked the three agency witnesses to look at Avandia’s drug label and find its warning about heart attacks.

“Have you found it yet?” Mr. Lynch kept asking.

Dr. von Eschenbach deferred to Dr. John K. Jenkins, head of the F.D.A.’s office of new drugs. Dr. Jenkins eventually referred to a small table in the labeling information.

“That’s it?” Mr. Lynch asked. “You’re not seriously telling me that that’s it.”

Dr. von Eschenbach said that the agency was in the process of improving the readability of all drug labels.

Representative Diane E. Watson, Democrat of California, said she had diabetes and had been taking Avandia until her doctor told her that she had developed a heart murmur.

“My doctor said, ‘Get off of Avandia — there are other options out there,’ ” Ms. Watson said.

She told Dr. von Eschenbach that warnings about such heart problems should be prominently displayed on the drug’s label.

“You ought to have heart attack on the label, and I believe I was heading toward just that when I went to my physician,” Ms. Watson said.

Dr. von Eschenbach said the F.D.A. was studying the data to decide whether to do that.

Dr. John B. Buse, an endocrinologist at the [University of North Carolina](#) School of Medicine and the incoming president of the American Diabetes Association, said that when he spoke publicly in 1999 about his fears that Avandia might increase heart risks, he was threatened in phone calls from the drug’s maker.

“During those calls, it was mentioned on two occasions that there were some in the company who felt that my actions were scurrilous enough to attempt to hold me liable for a loss in market capitalization” of \$4 billion, Dr. Buse said.

“I was characterized as a liar,” Dr. Buse said. “I was characterized as being for sale.”

Dr. Moncef Slaoui, chairman of research and development for GlaxoSmithKline, said in his own statement that he was “extremely disappointed” by editorials published Tuesday in The New England Journal of Medicine questioning Avandia’s safety. Dr. Slaoui said he and the company “strongly believe that the overall safety of Avandia is comparable to other available oral anti-diabetes medicines.”

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