United States Senate
Committee on Finance

Sen. Chuck Grassley · Iowa
Ranking Member

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Grassley seeks FDA scrutiny of Paxil and suicide risk

WASHINGTON – Senator Chuck Grassley has asked the Food and Drug Administration to carefully scrutinize information it received from drug maker GlaxoSmithKline about the anxiety disorder drug Paxil, based on the contents of a newly available report about the drug's risk for suicide among adults. Grassley also asked the FDA to review findings released earlier this year by the British drug-safety agency which charged that the drug maker has known about suicide risk with pediatric use of Paxil since 1998.

The report cited by Grassley was prepared by Dr. Joseph Glenmullen, a professor of psychiatry at Harvard University. The report asserts that GlaxoSmithKline had to know of Paxil's suicide risk when it sought FDA approval for the drug. The Glenmullen report was recently released from under court seal by a Kansas judge. It is posted with this news release at http://finance.senate.gov.

Grassley asked GlaxoSmithKline about the Glenmullen report last February. Weeks later, the British Medicines and Healthcare products Regulatory Agency released its own report that was four years in the making.

"The British counterpart to our country's FDA found that GlaxoSmithKline withheld important safety data on Paxil," Grassley said. "If the company engaged in this behavior in the U.K., then I want to make sure that the same didn't happen here in the U.S. The FDA should investigate this question thoroughly and be forthcoming about its findings."

Below is the text of Grassley's letter to the FDA, a floor statement he delivered last evening about the matter follows here, and his February letter of inquiry to the drug maker.

June 11, 2008

The Honorable Michael O. Leavitt
Secretary
U.S. Department of Health and Human Services
200 Independence Avenue, S.W.

Washington, DC 20201

The Honorable Andrew C. von Eschenbach M.D.
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Secretary Leavitt and Commissioner von Eschenbach:

As a senior member of the United States Senate and as Ranking Member of the Committee on Finance (Committee), it is my duty under the Constitution to conduct oversight into the actions of the executive branch, including the activities at the Food and Drug Administration (FDA/Agency), a part of the Department of Health and Human Services (HHS).

I have recently received an expert report prepared for litigation by Dr. Joseph Glenmullen, a professor at Harvard University. Based on documents from GlaxoSmithKline (GSK) and the FDA, Dr. Glenmullen concluded that GSK officials knew back in 1989 that Paxil is associated with an increased risk for suicide. I have attached his report for your review and consideration.

Furthermore, I have learned that Britain's Medicine's and Healthcare Regulatory Authority (MHRA) concluded a four year investigation of Paxil. That report found that GSK had been aware since 1998 that Paxil was associated with a higher risk of suicidal behavior in adolescents. However, the British government did not move forward with criminal prosecutions because the laws at the time were not clear enough as to whether GSK should have informed the regulatory agency.

In response to the MHRA report, Britain's public health minister, Dawn Primarolo, told the Guardian newspaper, "Companies that conduct clinical trials should not compromise people's health by withholding information." 1 The Guardian also reported that the British government plans to introduce new legislation later this year to make clear that drug companies should not withhold safety information.

In light of this investigation by the MHRA, I would like you to take a look at the information that agency gathered and determine if the company has withheld safety information here as well. I also request a briefing for my staff on whether or not a review is being conducted by HHS or any of its departments/ agencies regarding whether or not GSK withheld information from FDA.

Should you have any questions please feel free to contact Paul Thacker or Angela Choy of my staff at (202) 224-4515.

Sincerely,

Chuck Grassley

United States Senator
Ranking Member of the Committee on Finance

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1 David Batty et al, "Drug Companies Must Reveal More Data after Seroxat Results Withheld," Guardian, March 6, 2008.

Floor Statement of Senator Chuck Grassley of Iowa
Hidden data on Paxil
Wednesday, June 11, 2008

Mr. President, for the last few years, I have been looking at how drug companies try and influence medical care in America. Companies can do this by, for example, creating studies favorable to their drugs, by hiring doctors to promote their products, and in some cases even intimidating critics of their drugs.

Today, I would like to talk about a different tactic-drug companies hiding data. I don't mean that they actually hide the data. But they make these numbers so difficult to find that they might as well be invisible.

Last February, I asked GlaxoSmithKline to turn over a couple of reports on Paxil, a drug used to treat depression. These reports were written by Dr. Joseph Glenmullen, a professor of psychiatry at Harvard.

Based on the review of documents uncovered in litigation, Dr. Glenmullen concluded that GlaxoSmithKline knew for almost two decades that Paxil is associated with an increased risk of suicide. He submitted these reports as an expert witness in several lawsuits now pending around the country.

So what did GlaxoSmithKline do with these reports? Well, the company tried to hide them. They went to the judge and asked to have Dr. Glenmullen's report and all the confirming documents placed under seal-that means that no member of the public could see them. In fact, Glaxo has been doing everything possible to ensure that this information remains under court seal.

It seems to me that GlaxoSmithKline tried to hide these reports because they seem to demonstrate what the company knew-that Paxil was associated with an increased risk of suicide based on the company's own studies. In fact, Dr. Glenmullen argues that GlaxoSmithKline knew this when they submitted the New Drug Application to the Food and Drug Administration back in 1989.

Essentially, it looks like GlaxoSmithKline bamboozled the FDA.

How did GlaxoSmithKline get away with this? Easy, they just moved around numbers in their studies to make it look like Paxil was safe. Here is how Dr. Glenmullen says they did it.

GlaxoSmithKline ran several studies comparing people on Paxil against people on a placebo, in other words, a sugar pill.

If a patient attempted suicide before a study began before the study began that person was automatically put into the placebo group. That means the company was comparing Paxil users against patients who were already prone to suicide. So when you compared the placebo numbers to the Paxil numbers, it looked like Paxil was the same as the placebo.

But, when Dr. Glenmullen re-analyzed the data, he found that Paxil WAS associated with a risk for suicide. And it looks like this is what GlaxoSmithKline was trying to hide from the American public.

Thankfully, a judge in Kansas made one of Dr. Glenmullen's reports public.

Finally, I would like to address GlaxoSmithKline's responses to my questions about whether it hid data on Paxil. I am unhappy to say that Glaxo's answers were a little more than word games. I don't wish to use the word "lie" but let me say this: their answers were less than candid.

Let me give you one example. In a letter to GlaxoSmithKline, I asked them when they learned that Paxil was associated with suicide risk. They wrote back that they "detected no signal of any possible association between Paxil and suicidality in adult patients until late February 2006…."

So GSK claims to a United States Senator they knew nothing about suicidality in adults until February 2006. But in the United Kingdom, government investigators found that the company had the data back in 1998.

Two weeks after I received the letter from GSK, England's Medicines and Healthcare products Regulatory Agency released a report on Paxil.

The report concluded that data from GlaxoSmithKline's own clinical trials confirmed that patients under 18 had a higher risk of suicidal behavior. This report involved four years of investigation by this agency which is England's counterpart to our FDA. It was the largest most thorough report in the history of that agency.

According to the Medicines and Healthcare products Regulatory Agency, the only reason that criminal charges were not filed in the UK is because "the legislation in force at the time was not sufficiently strong enough…." So the company didn't get off because it didn't do anything wrong. It got off because the laws in UK did not address such situations.

Today, I am asking the FDA to take a look at the same information that was examined in the UK. And I am asking the FDA if we need to change any laws here in the United States.

We cannot live in a nation where drug companies are less than candid, hide information and attempt to mislead the FDA and the public. These companies are selling drugs that we put in

our bodies, not sneakers. When they manipulate or withhold data to hide or minimize findings about safety and/or efficacy, they put patient safety at risk. And with drugs like Paxil, the risks are too great.

The CEO of GlaxoSmithKline, Jean-Pierre Garnier, is resigning. I hope that the company's new leadership will do right by the public and be more open about side effects of their products.

What happened with Paxil, as well as, in my investigations involving the painkiller Vioxx and the antibiotic Ketek are only a few examples of why it is important that bad actors be held accountable when they withhold data, submit questionable or fraudulent data, or attempt to mislead the FDA, the medical community, and the public.

That's why I am also working on legislation that would require that companies certify to the FDA that they gave the FDA complete and accurate data related to the safety and efficacy of their products and that the information is not false or misleading. If a company knowingly violates those certifications, it could be subject to civil and possibly criminal penalties. I yield the floor.

February 6, 2008

Mr. Christopher Viehbacher
President
U.S. Pharmaceuticals
GlaxoSmithKline
5 Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Mr. Viehbacher:

As the Ranking Member of the United States Senate Committee on Finance (Committee), I have an obligation to the more than 80 million Americans who receive health care coverage under Medicare and Medicaid to ensure that taxpayer and beneficiary dollars are appropriately spent on safe and effective drugs and devices. This includes the responsibility to conduct oversight of the medical and pharmaceutical industries that provide products and services to Medicare and Medicaid beneficiaries.

As reported today in New Scientist, several documents were unsealed on January 18, 2008, in the case of O'Neal v. SmithKline Beecham d/b/a GlaxoSmithKline. Several of these documents and transcripts suggest that GSK knew as far back as 1989 that Paxil is associated with an increased risk of suicide. However, the American public was never adequately informed of this risk until May 2006 in a "Dear Healthcare Professional" letter that reported a "higher frequency of suicidal behavior" associated with Paxil as compared to placebo.

Specifically, Dr. Joseph Glenmullen, a Clinical Instructor in Psychiatry at Harvard

Medical School, prepared an expert report based on a review of internal GSK documents. Dr. Glenmullen's report suggests that GSK ensured that suicides and suicidal attempts were systematically included in the placebo arm of GSK's study, which had the effect of making it more difficult to detect suicide risks associated with Paxil. This information was then submitted to the FDA.

Dr. Glenmullen concluded in his report:

Analyses of GlaxoSmithKline's data demonstrate a causal link between the antidepressant and suicidal behavior. This has been true since 1989 although the "bad" Paxil numbers obscured the risk for a decade-and-a-half.

It is my understanding that 9 pages of Dr. Glenmullen's report are not available publicly. Accordingly, please respond to the following questions and request for information. Please repeat each enumerated question and follow it with your response.

1. When did GSK first learn that Paxil was associated with an increased suicide risk?
2. When did GSK first report to FDA that Paxil was associated with an increased suicide risk?
3. When did GSK first notify patients and doctors that Paxil was associated with an increased suicide risk? Please provide all pertinent documents and communications.
4. Please provide the Committee with the complete, unredacted version of Dr. Glenmullen's report. Along with that report, please provide the appendix and all documents that are referred to in the report, in the order that they are referenced.
5. Please provide the Committee with the accompanying children and adolescents report. Along with this report, please provide the appendix and all documents that are noted in the report, in the order that they are referenced.

Thank you again for your continued assistance in this matter. Because I understand that these documents are already available in electronic format, I would appreciate receiving the documents and information requested by no later than February 14, 2008.

Sincerely,

Charles E. Grassley
Ranking Member