Avandia controversy highlights broken pharmaceutical regulatory system

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An FDA administrative hearing was held this week about cardiovascular risks relating to diabetes medication Avandia. While the hearing did not suggest a recall or discontinuance of Avandia, the ultimate decision lies with the agency's commissioners, who will likely release their decision soon. Agency scientists and medical experts were largely divided on what should be done about the popular diabetes drug.

The case of Avandia is instructive, as it follows the well-worn path of so many drugs, hailed as miracles at their inception, advertised widely and reaping huge revenues, before their dangerous, poorly understood characteristics are exposed, leaving many shattered lives in their wake. The case of Avandia shows how big business is more than willing to deal with lawsuits filed by victims' families as a cost of doing business. It is one more example of how the parasitic, privately owned drug companies come between scientific and medical professionals and their patients.

Avandia, or Rosiglitazone, belongs to a family of anti-diabetes drugs called thiazolidinediones, which have, at best, a mixed history in regard to safety. These drugs manipulate gene expression in peripheral tissues to increase sensitivity to insulin, which results in lower blood glucose levels. Others of this group have been associated with liver and kidney damage. Only a handful have been approved for use by the FDA.

The FDA approved Avandia in 1999 for general treatment of Type 2 diabetes. Almost 9 percent of the US population has this form of the disease, also called adult onset diabetes. It is marked by a reduced receptivity of relevant tissue/cells to insulin, the hormone that regulates the amount of blood glucose. In some cases, Type 2 diabetes is the result of the body's decreased capacity for insulin production. Type 1 diabetes, in contrast, is the complete inability to produce insulin and is sometimes called juvenile diabetes.

Avandia came under scrutiny in 2007, following publication of a study by Dr. Steven E. Nissen that concluded that the drug increased the risk of death from cardiovascular disease, including a 43 percent increase in the risk of heart attacks. The study recommended that patients and providers should take into account the potential for serious adverse cardiovascular effects of treatment with rosiglitazone (Avandia) for Type 2 diabetes, given the high correlation between the disease and cardiovascular problems. The authors note that more than 65 percent of deaths in patients with diabetes are from cardiovascular causes. The precise mechanism by which Avandia increases risk of cardiovascular disease is not fully understood.

Largely as a result of this study, in 2007 the FDA reevaluated Avandia. The advisory committee found by a large majority that Avandia increased the risk of cardiovascular diseases like heart attack and stroke. The committee ultimately decided, by a 22-1 vote, against removing it from the market. Meanwhile, Avandia manufacturer GlaxoSmithKline saw a two-thirds decline in the drug's sales following the 2007 publication of the study in the New England Journal of Medicine. Another factor in this $2 billion loss for Britain's largest drug maker was the rise of new diabetes medicines manufactured by its rivals, including Merck, Eli Lilly and others.

More recently, additional clinical studies about the effects of Avandia have substantiated the 2007 article by Dr. Nissen, finding increased risk of stroke, heart failure and mortality generally. One study by the Institute for Safe Medical Practices linked Avandia to 1,354 deaths in 2009 alone. Just last week, GlaxoSmithKline settled with over 10,000 plaintiffs

(out of 13,000) for $460 million in lawsuits arising from Avandia's ill effects.

Avandia's reputation has also been harmed by repeated claims that GlaxoSmithKline has hidden evidence from regulators and lawmakers and even failed to disclose entire studies that implicate the drug in cardiovascular deaths. Documents made available to a Senate Finance Committee investigation last week reveal that the company actively promoted Avandia while covering up evidence of its dangers as far back as 2000.

The split among the FDA's own experts as well as in government circles generally is largely of a tactical nature. One section reflects concern within the ruling elite that the regulatory system too openly favors drug manufacturers and runs the risk of generating skepticism about private ownership of the industry in general. The other group articulates more openly the interests of the drug companies and the corporate elite as a whole, favoring a loose regulatory environment. From the perspective of the drug companies' bottom line, any scrutiny of a profitable drug constitutes an inexcusable encroachment on company profits. The simpler the process from research and development to consumer product, the lower are the costs of drug production, resulting in higher profits.

Senators Max Baucus (D., Mont.) and Chuck Grassley (R., Iowa) led the Finance Committee's probe, and assured the media in essence that, while the status quo will remain, it needs a facelift.

Grassley had the following to say on the matter: "What's happened with this drug further makes the case about the need to strengthen the office within the FDA that monitors drug safety after a drug is on the market and being sold to patients… A lack of accountability damages public confidence and hope in new drugs. Trust can be rebuilt through the work of a more independent FDA."

Not to be outdone, Baucus feigned concern for patients and medical practitioners: "Patients and doctors have a right to know the risks of the medicines they use and prescribe, and drug companies have a responsibility to release data regarding safety concerns about their products." He added, "We will continue working with the FDA on Avandia to ensure patients and doctors have the information they need to make safe, informed decisions about their medications."

The operative word in Baucus' statement is "continue," as in continuing his efforts at bolstering undeserved confidence in the private ownership of the entire healthcare industry. The Senators' indignation is entirely fraudulent.

A statement by Representative Rosa DeLauro (D., Connecticut), who heads the House subcommittee in charge of the FDA's budget, also reflected concern with the image of the federal agency. "If the FDA is to be a force for change and for returning to the gold standard for safety for which it was once known, then its upcoming decision on whether to pull Avandia from the market will be the defining moment for the agency under the Obama administration," said DeLauro.

At the other end of the political spectrum, the more brazen representatives of the financial elite have complained of a witch-hunt that threatens corporate profits. This was the theme of an opinion piece in the *Wall Street Journal* last week entitled "Avandia on Trial" on Friday.

As this headline suggests, the piece takes the posture that Avandia faces sacrifice on the altar of political expediency. The article attacks Dr. Nissen, author of the 2007 New England Journal of Medicine Study on Avandia as well as an important figure in exposing the risks associated with Vioxx, as a "pharma scourge." The *Wall Street Journal* article reflects the view of those who have no time for any criticism of the pharmaceutical firms. About the latest development it warns, "With a final regulatory decision imminent, the episode is a useful lesson in the complexities and uncertainties of modern medicine. Not to mention, ahem, the inability of the political class to behave responsibly when it is looking for corporate villains."