

Study Sees a Slant in Articles on Drug

By Nicholas Bakalar

A new analysis of reviews and articles about the controversial diabetes drug Avandia has found that experts who were paid by its manufacturer have been significantly more likely than others to draw positive conclusions about the drug's safety and efficacy.

Since 2007, scientists have published hundreds of studies, reviews and opinion articles about Avandia in scientific journals and elsewhere, arriving at a range of conclusions, some sharply opposed to one another.

Avandia, or rosiglitazone, is prescribed, along with diet and exercise, to help control blood glucose levels in people with Type 2 diabetes. In 2007, *The New England Journal of Medicine* published a review of studies and concluded that its use was associated with a significant increase in the risk for heart attack.

After a Congressional investigation, the Food and Drug Administration imposed a "black box" safety warning on the medicine. In February, *The New York Times* described confidential F.D.A. reports recommending that Avandia be removed from the market.

To explore possible links between authors' financial interests and opinions, researchers reviewed 202 articles by 180 authors who wrote about Avandia and the risk of heart attack. Then they had independent reviewers with no conflicts of interest grade each article as favorable, neutral or unfavorable, based on the authors' positions on an association between Avandia and heart attacks and on their recommendations for continuing or ending its use. The study was published online on March 18 in the journal *BMJ*.

Often, authors with favorable opinions of the drug were paid both by Avandia's maker, GlaxoSmithKline, and by its competitors. Of those who offered favorable views, 87 percent had potential conflicts with Glaxo. Among authors who had unfavorable opinions, only 20 percent had received money from Glaxo.

Mary Anne Rhyne, a spokeswoman for Glaxo, said in an e-mail message: "Of the 202 articles, only 10 were original scientific research. Many of the articles reviewed were opinion pieces — editorials, commentaries or letters. It is important to note that the authors' conclusions do not impugn the validity of the scientific data."

interviews last week, Dr. Rudy Bilous and Dr. Mark W. Stolar, two of the scientists who reported favorable findings on Avandia, said drug company financing could create an appearance of bias.

"We can't have it both ways," said Dr. Bilous, an endocrinologist at James Cook University Hospital in Middlesbrough, England. "If people want drugs, the only people in the current environment doing the work and funding the research are the pharmaceutical industry, and their concern is for licensing, not necessarily the science."

Dr. Stolar, a professor of clinical medicine at Northwestern, had a similar view. "There is no broad enough funding on the national level for significant research," he said. "The problem is that the interpretation of the findings gets skewed because of that. There are very few people in whom I don't detect bias based on where their conflicts lie."

The *BMJ* review found that 90 of the 202 articles were by people with potential conflicts,

but only 69 of them had a statement disclosing the fact. They uncovered the 21 remaining conflicts by searching the Internet and other publications by the same authors.

The study's authors acknowledged that their work was observational and that they were unable to assign a monetary value to any of the relationships they found.

Dr. Amy T. Wang, the lead author and a resident in internal medicine at the Mayo Clinic, emphasized that the study drew no conclusions about the safety or efficacy of Avandia.

Ms. Rhyne said GlaxoSmithKline "will disclose research payments made to health care professionals and their institutions" beginning in 2011, with the disclosures covering research studies that began on or after Jan. 1, 2010.

An article on Tuesday about financing of research into the diabetes drug Avandia misstated a researcher's relationship with the drug industry. The scientist, Dr. Mark W. Stolar, an associate professor of medicine at Northwestern, who reported findings favorable to Avandia, has received payments from Takeda Pharmaceuticals, which makes diabetes drugs, but not from GlaxoSmithKline, which makes Avandia.