

# United States Senate

COMMITTEE ON FINANCE

WASHINGTON, DC 20510-6200

October 26, 2009

## Via Electronic Transmission

Francis Collins, MD, PhD  
Director  
National Institutes of Health  
9000 Rockville Pike  
Bethesda, MD 20892

Dear Director Collins:

First, let me congratulate you on your new position as Director at the National Institutes of Health (NIH/Agency). Over the last several years, I have been examining conflicts of interest at your Agency, and I am sure that we will enjoy working together on this important issue.

As a senior member of the United States Senate and the Ranking Member of the Committee on Finance (Committee), I have a duty under the Constitution to conduct oversight into the actions of executive branch agencies, including the activities of the NIH. In this capacity, I must ensure that NIH properly fulfills its mission to advance the public's welfare and makes responsible use of the public funding provided for, among other things, biomedical studies. This research often forms the basis for action taken by the Medicare and Medicaid programs.

I was troubled by a front page article in today's *The Chronicle of Higher Education* discussing several NIH grantees with conflicts of interest regarding their research. I was drawn to one passage noting that Dr. Christie M. Ballantyne of Baylor College of Medicine received over \$34,000 for consulting with Merck regarding the cardiovascular drug Vytorin. At the same time, Dr. Ballantyne is on several NIH grants that concern cardiovascular studies. According to current NIH regulations, Baylor should have reported to NIH that Dr. Ballantyne had received more than \$10,000 from a company. However, the article states explicitly that Baylor was "confident that its rules guard against any financial conflict of interest, saw no need to tell the NIH of payments by Merck to [Dr. Ballantyne]."

Accordingly, I request that NIH brief my staff on this issue and explain how they plan on handling these allegations. I have attached a copy of the article to this letter, for ease of review. I thank you again for your continued cooperation. If you have any questions please contact my Committee staff, Paul Thacker at (202) 224-4515. All formal correspondence should be sent electronically in PDF searchable format to [Brian\\_Downey@finance-rep.senate.gov](mailto:Brian_Downey@finance-rep.senate.gov) by no later than November 16, 2009.

Sincerely,



Charles E. Grassley  
Ranking Member

Attachment

October 25, 2009

## University Doctors Got Paid in Drug's Sales Campaign

Money for speeches highlights murky area for conflicts of interest



*Getty Images*

*By Paul Basken*

Fourteen university-affiliated physicians collected more than \$400,000 from the makers of the anti-cholesterol drug Vytorin as part of a campaign to encourage the use of the medication. The 2008 campaign went on after an internal company study showed that the drug, with several billion dollars in sales, had little or no overall value for most patients.

The physicians, many of them prominent in the field of cardiovascular disease, accepted the money from the manufacturers Merck & Company and the Schering-Plough Corporation for delivering speeches to health practitioners and attending advisory meetings. Sergio Fazio, a professor of medicine at Vanderbilt University, was paid \$82,260, for example. Michael H. Davidson, a professor of medicine at the University of Chicago, was paid \$71,150, and Antonio M. Gotto Jr., dean of the Weill Cornell Medical College, collected \$27,146.

The payments were revealed recently to *The Chronicle* by U.S. Senate investigators pursuing complaints about drug marketing. They suggest that many institutions are struggling to set ground rules for relationships between researchers and industry that eliminate financial conflicts of interest while still allowing interactions that enhance the science.

"It becomes very complicated," said Harlan M. Krumholz, a professor of internal medicine at Yale University who has criticized such payments. In March 2008, Dr. Krumholz, director of the Clinical Scholars Program at Yale, gave a stark assessment of the internal Vytorin study that helped persuade the American College of Cardiology to recommend that doctors sharply cut their use of the drug. Vytorin consumers and insurers followed with lawsuits, and 35 state governments opened investigations, later settled by the manufacturers, alleging that most patients could have used much cheaper, and possibly more beneficial, alternatives.

Several of the doctors who received the money said the payments did not influence their evaluations of Vytorin but were legitimate compensation for their time and expertise. "The jury with regard to Vytorin is still out," said Ishwarlal Jialal, a professor of internal medicine at the University of California at Davis, who collected more than \$25,000 from the companies, noting that lower cholesterol levels have "been repeatedly shown to help people."

Dr. Krumholz said many doctors who serve as paid advisers to drug companies end up becoming too dependent on their benefactors to objectively assess the effectiveness of the companies' medicines. Yet he acknowledged that it is not so easy to adjudicate cause and effect. "We can't say all these guys did the wrong thing," he said of the physicians.

### **A One-Two Combination**

Vytorin is a combination of two other prescription drugs: Zocor, by Merck, and Zetia, by Schering-Plough. (The companies have agreed to merge.) Zocor is a statin, which is a class of drugs found to prevent the liver from making cholesterol. Zetia acts by decreasing cholesterol absorption in the intestine. Statins are widely recognized as effective, and Zocor was one of the most popular, with U.S. sales reaching \$4.6-billion in 2004, according to IMS Health, which tracks industry data.

But Merck's patent on Zocor expired in 2006, allowing competitors to produce lower-cost generic versions. Merck moved to protect its share of that lucrative market by strategies that included the development of the combined drug, Vytorin. The sales pitch included a \$200-million-a-year campaign of television ads telling consumers that Vytorin worked against "the two sources of cholesterol," food and family inheritance.

After persistent pressure from Congress, however, Merck released study data in January 2008 evaluating the effects of combining Zocor with Zetia. The study, which had been completed two years earlier but not publicized, showed that a \$100-a-month Vytorin prescription did better than Zocor

alone in lowering cholesterol levels but didn't lead to any better results in preventing the buildup of plaque in the arteries, which leads to heart attack and stroke.

Combined sales of Vytorin and Zetia, which had reached \$5-billion in 2007, dropped 23 percent in the first five months of 2008 as the study results circulated.

The physicians paid by Merck and Schering-Plough helped the company fight back by emphasizing the lower cholesterol levels. In the specific case of Vytorin, however, lower cholesterol levels don't mean reduced atherosclerosis, Dr. Krumholz told the American College of Cardiology in March 2008. Zetia may be "just an expensive placebo," he said.

The money for university-affiliated doctors was only part of the companies' effort to fight such criticisms in the scientific arena. Merck documents provided to Senate investigators also described expenditures of \$60-million over four years for "continuing medical education" classes to help doctors learn the latest practices and treatment options for heart disease.

Such practices are widespread in the industry. The Accreditation Council for Continuing Medical Education reported that drug and device companies provided \$1-billion in educational grants last year, although that is down 14 percent from 2007.

And Merck, in the first of what the company said would be a quarterly reporting of such payments, issued a statement last week showing it paid about \$3.7-million over three months this summer to more than 1,000 physicians and other health professionals who gave speeches to colleagues about its products and related subjects.

Merck and other drug companies have begun the disclosures under pressure from Congress, which is considering legislation that would require the public identification of physicians who receive \$100 or more a year from pharmaceutical companies and device manufacturers. Several states already have new laws requiring companies to disclose payments to physicians, and Massachusetts and Vermont have put outright limits on such payments.

### **'No Impropriety'**

Several dozen universities have also recently adopted new disclosure rules. Harvard University, home to three of the 14 doctors paid by Merck and Schering-Plough as part of the Vytorin sales effort, is in the middle of a yearlong review of its conflict-of-interest policies.

Yet officials at several other universities with doctors on the Merck payment list expressed comfort with their institutions' behavior.

Dr. Fazio, whose publications included an April 2008 article in the *Journal of the American College of Cardiology* encouraging the use of Vytorin with niacin, a known cholesterol-reducing agent, acknowledged his payments from Merck to Vanderbilt's Conflict of Interest Committee. "The committee found there is no indication of impropriety," said John Howser, a spokesman for Vanderbilt's Medical Center. The details of that finding are confidential, he said.

The National Institutes of Health financed work by Dr. Fazio and four others on the Merck list, but its rules don't even require disclosure of the drug-company money. The NIH asks the university only to certify that any conflict is being "managed, reduced, or eliminated."

The Baylor College of Medicine, confident that its rules guard against any financial conflict of interest, saw no need to tell the NIH of payments by Merck to Christie M. Ballantyne, a professor of medicine, said Lori E. Williams, a Baylor spokeswoman. Dr. Ballantyne collected more than \$34,000 from the companies for speeches and other services while receiving an NIH grant to study therapies to reduce cholesterol.

In a March 2006 news release from Merck and Schering-Plough, he is quoted as saying Vytorin was "significantly better than Lipitor," a statin drug made by Pfizer, while acknowledging the need for further studies "to confirm these findings." Dr. Ballantyne said he always pointed out in company-financed speeches that the benefits of adding Zetia to Zocor are unknown.

"I have no interest in helping a company to increase market demand," he said, "and this did not ever appear to be the purpose of our advisory meetings."

Dr. Fazio said his Merck-paid speeches involved discussions with other physicians about treatment options. "I certainly hope that my lectures are not considered advertising," he said.

He also said he opposed any direct-to-consumer marketing of pharmaceuticals, and said it was reasonable for a patient to question whether a doctor paid by a drug company might not be an objective source of information on its products. Such questions "are fair," he said.

That points out the problem, said Steven E. Nissen, chairman of cardiovascular medicine at the Cleveland Clinic and past president of the American College of Cardiology. Even if the doctors paid by Merck were giving unbiased assessments of Vytorin, the payments leave patients wary, he said.

"If patients don't believe that their physicians are acting independently and in the patients' best interests," Dr. Nissen said, "we lose everything."

Apparently, however, many physicians do not believe there is a money-trust trade-off. After Merck announced that it would begin disclosing names of physicians in its speakers program, the company says that about 99 percent of them agreed to stay in it.