United States Senate
Committee on Finance

Sen. Chuck Grassley · Iowa
Ranking Member

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M E M O R A N D U M

TO: Reporters and Editors
FR: Jill Kozeny, 202/224-1308
for U.S. Senator Chuck Grassley of Iowa
RE: Questions about statements regarding drug trial
DA: Tuesday, February 12, 2008

Senator Grassley is continuing his inquiries related to Schering-Plough's drug Vytorin and has asked for documents and a list of all company statisticians who had access to the ENHANCE trial data. The ENHANCE trial was an attempt to determine if Vytorin, a combination pill of Zetia and a statin, performed better than a generic statin alone. Senator Grassley has expressed concern that individuals who had early access to this data could have learned that Vytorin did not offer more value than an inexpensive statin. The ENHANCE trial ended in April 2006, but the results were not released until almost two years later on January 14, 2008.

Here is the text of his February 11 letter to the Schering-Plough Corporation.

February 11, 2008

Via Electronic Transmission

Mr. Fred Hassan
Chairman of the Board, Chief Executive Officer
Schering-Plough Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Mr. Hassan:

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 spent in a fiscally sound manner. This also includes the responsibility to conduct oversight of the medical

and pharmaceutical industries to ensure that Medicare and Medicaid dollars are spent appropriately on safe and effective drugs and devices.

I am following up on my prior letter to you regarding the delayed release of the ENHANCE trial by Schering-Plough and Merck.[1] This study examines whether Vytorin provides better health benefits than generic simvastatin. Vytorin is a pill that combines the statin, simvastatin, with a drug called ezetimibe that decreases absorption of cholesterol by the digestive tract.

It has come to my attention that Schering Plough and Merck would not need to unblind the data to understand that Vytorin performed no better than generic simvastatin. The ENHANCE trial is a non-inferiority study. These studies try to detect a statistically significant difference between treatment groups on the primary endpoint. Once the results are recorded, the study is then unblinded to determine which drug is the better performer. However, if the drugs performed the same, meaning there is no statistically significant difference in the treatments, then this information is apparent before the study has been unblinded.

According to your own press release on the ENHANCE results, "There was no statistically significant difference between treatment groups on the primary endpoint."[2] My concern is that anyone who had access to the blinded data could have run simulations and learned that Vytorin performed just the same as simvastatin.

My Committee investigators have learned that the ENHANCE trial data were routed from all of the trial centers to Dr. John J.P. Kastelein of the University of the Netherlands. Dr. Kastelein then transmitted the data to the Schering-Plough Research Institute in Kenilworth, New Jersey.

Accordingly, please respond to the following questions and request for documents. For each response, first repeat the enumerated question followed by the appropriate answer.

1. Please explain how the ENHANCE carotid ultrasound data was transferred from the core laboratory to the Schering-Plough Research Institute.

2. Please name all Schering-Plough employees who had access to the ENHANCE data during or after completion of the trial. For each individual, please provide
a. Name;
b. Title;
c. Technical expertise (lawyer, statistician, medical doctor, etc.)

3. Please provide the names of all statisticians at the Schering-Plough Institute. Please indicate which of these employees were involved in any analysis of the ENHANCE trial analysis.

4. Please provide all emails, documents and communications discussing the results of the ENHANCE trial, including any simulations regarding the results. The scope of this request covers employees at the Schering-Plough Institute or elsewhere within the company, from the

period of July 2005 to the present.

5. Please provide any and all e-mails and communications between Dr. John Kastelein and Schering-Plough employees from July 2005 until the present.

In cooperating with the Committee's review, no documents, records, data, or other information related to these matters, either directly or indirectly, shall be destroyed, modified, removed, or otherwise made inaccessible to the Committee.

I look forward to hearing from you by no later than February 22, 2008.

Sincerely,

Chuck Grassley
United States Senator
Ranking Member, Committee on Finance

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[1] Alex Berenson, "Cardiologists Question Delay of Data on 2 Drugs," The New York Times, November 21, 2007.
[2] Schering-Plough News Release, "Merck/Schering-Plough Pharmaceuticals Provides Results of EHANCE Trial," released on company Website on January 14, 2008.