ONE HUNDRED TENTH CONGRESS

U.S. House of Representatives
Committee on Energy and Commerce
Washington, DC 20515–6115

February 11, 2008

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

Dear Dr. von Eschenbach:

Under Rules X and XI of the Rules of the U.S. House of Representatives, the Committee on Energy and Commerce and its Subcommittee on Oversight and Investigations are investigating the drug Vytorin (ezetimibe/simvastatin) and the ENHANCE (Effect of Combination Ezetimibe and High-Dose Simvastatin vs. Simvastatin Alone on the Atherosclerotic Process in Subjects With Heterozygous Familial Hypercholesterolemia) trial, ClinicalTrials.gov Identifier NCT00552097. We are most concerned about the delay in releasing the study results, as well as Merck and Schering-Plough's attempt to change the study's endpoints.

On Friday, January 25, 2008, the Food and Drug Administration (FDA) held an Early Communication briefing on Vytorin and Zetia (ezetimibe). In that briefing, FDA indicated that it approved the original protocol for the ENHANCE trial, as well as the statistical analysis plan (SAP) for the study. FDA appears, however, to have been uninformed of Merck and Schering-Plough's plans to change the study's endpoints or of their interim "Vanguard" pilot study designed to assess the quality of their data by altering the study's protocol to allow for unmasked, synchronous ultrasound readings.

Therefore, we ask that FDA provide the following:

1. All records relating to all protocols for the ENHANCE trial, including but not limited to, the initial ENHANCE trial protocol provided to FDA by Merck/Schering-Plough, as well as the final protocol agreed to by FDA;

2. All records relating to any and all amendments to any ENHANCE protocol;

3. All records relating to all SAPs for the ENHANCE trial, including but not limited to, the initial SAP provided to FDA by Merck/Schering-Plough, as well as the final SAP agreed to by FDA;

4. All records relating to any and all amendments to the ENHANCE SAP;

5. All records relating to all Operator Manuals and Reader Manuals for the ENHANCE trial, including but not limited to, the initial Manuals provided to FDA by Merck/Schering-Plough, as well as the final Manuals agreed to by FDA;

6. All records relating to any and all amendments to the ENHANCE Operator Manuals and Reader Manuals;

7. All records relating to the analysis, assessment, and approval of the ENHANCE protocol, SAP, Operator Manuals, and Reader Manuals, by FDA officials;

8. All communications between FDA officials, Merck/Schering-Plough officials, and other ENHANCE study officials (e.g., Dr. John Kastelein, the ENHANCE principal investigator) related to the ENHANCE trial protocol;

9. All Adverse Event Reports related to either Vytorin or Zetia; and

10. All records relating to the Early Communication briefing on January 25, 2008.

Please deliver copies of the requested records to the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce, Room 316, Ford House Office Building, no later than two weeks from the date of this letter. Please note that for the purpose of responding to this request, the terms "record" and "relating" should be interpreted in accordance with the attachment to this letter. After review of the records, we may require additional records and/or staff interviews with FDA officials.

Thank you for your prompt attention to this matter. If you have any questions related to this request, please contact us or have your staff contact John F. Sopko or Paul Jung with the Committee on Energy and Commerce staff at (202) 226-2424.

Sincerely,

John D. Dingell
Chairman

Bart Stupak
Chairman
Subcommittee on Oversight and Investigations

Attachment

cc: The Honorable Joe Barton, Ranking Member
Committee on Energy and Commerce

The Honorable John Shimkus, Ranking Member
Subcommittee on Oversight and Investigations

ATTACHMENT

1. The term "records" is to be construed in the broadest sense and shall mean any written or graphic material, however produced or reproduced, of any kind or description, consisting of the original and any non-identical copy (whether different from the original because of notes made on or attached to such copy or otherwise) and drafts and both sides thereof, whether printed or recorded electronically or magnetically or stored in any type of data bank, including, but not limited to, the following: correspondence, memoranda, records, summaries of personal conversations or interviews, minutes or records of meetings or conferences, opinions or reports of consultants, projections, statistical statements, drafts, contracts, agreements, purchase orders, invoices, confirmations, telegraphs, telexes, agendas, books, notes, pamphlets, periodicals, reports, studies, evaluations, opinions, logs, diaries, desk calendars, appointment books, tape recordings, video recordings, e-mails, voice mails, computer tapes, or other computer stored matter, magnetic tapes, microfilm, microfiche, punch cards, all other records kept by electronic, photographic, or mechanical means, charts, photographs, notebooks, drawings, plans, inter-office communications, intra-office and intra-departmental communications, transcripts, checks and canceled checks, bank statements, ledgers, books, records or statements of accounts, and papers and things similar to any of the foregoing, however denominated.

2. The terms "relating," or "relate" as to any given subject means anything that constitutes, contains, embodies, identifies, deals with, or is in any manner whatsoever pertinent to that subject, including but not limited to records concerning the preparation of other records.