ONE HUNDRED TENTH CONGRESS

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

JOHN D. DINGELL, MICHIGAN
CHAIRMAN



February 21, 2008

The Honorable Michael O. Leavitt
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Leavitt:

We have attached our letter to Food and Drug Commissioner von Eschenbach regarding an alleged policy change that may place Americans in the same grave danger currently faced by consumers of Baxter's blood-thinning drug Heparin. In addition to the letter's request for policy clarification and staff interviews, the Committee on Energy and Commerce needs additional information to determine if emergency legislation is needed to protect Americans from prescription medications that have been insufficiently investigated prior to approval.

As the Administration's official responsible for both the Food and Drug Administration (FDA) and the Office of General Counsel (OGC), we request that you supply the Committee with all records in your possession or control relating to FDA's preapproval inspection policy. These records should include, but are not limited to, any and all legal memoranda, training manuals, policy statements, budget justification documents, and briefing materials. The terms "records" and "relating to" are defined in the attachment to this letter.

In addition, we request that you explain to the Committee your interpretation of the legal status of drugs shipped into United States commerce by a drug company that knew or should have known that FDA had not performed a preapproval inspection, as is alleged in the Heparin case.

Please provide the requested information by no later the close of business on Friday, February 22, 2008, as the Committee needs reasonable time to prepare for your upcoming testimony. Should you have any questions regarding this request, please contact David Nelson or Chris Knauer of the Committee 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.

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February 21, 2008

The Honorable Andrew C. von Eschenbach, M.D.
Commissioner
Food and Drug Administration
5600 Fisher Lane, Room 1555
Rockville, MD 20857

Dear Dr. von Eschenbach:

We are seeking clarification of what appears to be a change in the Food and Drug Administration's (FDA) drug approval policy regarding pre-approval inspections. On February 15, 2008, the Committee on Energy and Commerce staff interviewed your staff regarding the ongoing concerns with Baxter International's manufactured blood-thinning drug Heparin. Your staff confirmed that the Chinese plant that provides the active pharmaceutical ingredient for Heparin had never been inspected by FDA, despite the policy of pre-approval inspections that has been followed by Administrations for nearly two decades.

In addition, FDA staff acknowledged that there is no statutory requirement for a pre-approval inspection before a firm begins shipping drug product to the United States, but rather it is FDA policy to conduct such an inspection. We were further informed that FDA is under no obligation to withhold approval or otherwise bar shipment until such an inspection is completed. Most importantly, your staff advised that selling a drug product from a plant that has never undergone a pre-approval inspection does not constitute the distribution of an unapproved drug.

If FDA has abandoned, either formally or informally, its vital pre-approval inspection policy for the U.S. drug supply, this represents a troubling development that puts consumers at risk. For a drug to be eligible for approval by FDA, it has been the understanding of Congress that the agency must approve each step of drug manufacturing, including all ingredient sources. We understood that a pre-approval inspection was accomplished through a formal physical visit of the facility to ensure it meets current Good Manufacturing Practices. This understanding is shared by the Government Accountability Office, who recently testified at a hearing before the Subcommittee that:

> "Preapproval inspections of domestic and foreign establishments are conducted before FDA will approve a new drug to be marketed in the United States. These inspections occur following FDA's receipt of an NDA or ANDA and focus on the manufacture of a specific drug product. Preapproval inspections are designed to verify the accuracy and authenticity of the data contained in these applications and ensures that the manufacturer of the finished drug product, as well as each manufacturer supplying a bulk drug substance used in the finished product, manufactures, processes, and packs the drug adequately to preserve its identity, strength, quality, and purity."

The need for such inspections was highlighted more than 20 years ago after this Committee exposed similar problems with the generic drug industry. Preapproval inspections were designed to assure that drug manufacturers would never again be able to gain FDA approval by asserting that drugs would be produced pursuant to a valid manufacturing process and with qualified suppliers of ingredients when the facility was incapable of manufacturing the drugs as specified. Apparently, FDA has deliberately failed to apply this inspection policy to drug manufacturers in China.

Accordingly, we request that you provide to us a written clarification of FDA's current policy for preapproval inspections. Further, we ask that you make available Dr. Janet Woodcock, Margaret Glavin, and those reviewers responsible for the approval of the active ingredient supplier for the Heparin now under scrutiny by your agency, for briefings with Committee staff.

We ask that you please respond to this letter and assure that the requested briefings are concluded prior to Friday, February 22, 2008. If you have any questions, please have your staff contact David Nelson or Chris Knauer 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

cc: The Honorable Joe Barton, Ranking Member
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