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 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
Committee on Energy and Commerce

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