ONE HUNDRED TENTH CONGRESS

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

JOHN D. DINGELL, MICHIGAN
CHAIRMAN

October 2, 2007

The Honorable Andrew C. von Eschenbach, M.D.
Commissioner
U. S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-0001

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 ability of the Food and Drug Administration (FDA) to protect the American public from excessive risks associated with imported prescription drugs and the ingredients that are used in their manufacture. As part of this investigation, Committee staff recently accompanied FDA staff on several foreign inspections in both China and India, which are major manufacturers and exporters of pharmaceutical products. We appreciate the cooperation we received from your agency to ensure that our staff could observe these inspections as well as your staff's assistance with our overall investigation.

The Committee examined the FDA's foreign drug inspection program nearly 10 years ago and identified a number of deficiencies. Unfortunately, many of these deficiencies appear to continue to plague the program today, and in some cases appear to be worse. For example, databases and computer systems used by FDA to track drug firms exporting to the U.S. still seem incapable of providing meaningful, real-time data regarding which firms are actively shipping products to the U.S. and when they were last inspected. Moreover, the amount of time between surveillance inspections appears inconsistent and, in some cases inspections are quite overdue. Finally, constraints on general resources appear to be having a direct effect on a several aspects of the program. This includes the ability to hire and use language interpreters so that FDA staff are not forced to use an interpreter provided by the drug firm being inspected; the length of time they can stay at a particular firm for an inspection; and the ability to do rapid follow-up inspections once problems are identified.

Given the limitation on these resources and the effect it is having on the program, coupled with the increasing growth in overseas drug manufacturers seeking to export products to U.S. markets, the Committee remains concerned about the overall capability of the FDA's foreign drug inspection program and its ability to keep up with a changing global marketplace. As the U.S. increasingly relies upon drug products from foreign manufacturers, it is critical that FDA have a robust capability to oversee foreign drug manufacturing facilities, which will clearly require significant re-tooling of this program. We believe your office should give this matter increased and immediate attention.

To date, Committee staff has attempted to both obtain basic data on FDA's foreign drug inspection program and its present workload obligations. This has included several meetings and conference calls with FDA officials responsible for managing this program. Perhaps because of the limitations and configurations of current FDA databases that provide information on drug imports, FDA has apparently experienced considerable difficulty in providing basic information to the Committee. These limitations include the inability to provide: (1) number of firms currently exporting to the U.S.; (2) when they were last inspected; (3) where they are located, and (4) projections of new firms seeking to export drug products to the United States. On August 23, 2007, Committee staff conducted a conference call with members of your staff to obtain a basic outline of data regarding FDA inspections of foreign drug product manufacturers. From that discussion, Committee staff understood your employees to represent the following information regarding FDA's present knowledge about foreign drug manufacturers that ship product to the U.S. (and other related inspection activities). Based on this, we request that your office confirm whether the following information is accurate, and that you supply additional information as requested:

1. As of August 23, 2007, there were 2,967 pharmaceutical product-manufacturing firms registered with the U.S. that are likely shipping to the U.S. and would be subject to: (a) pre-approval inspection; and (b) ongoing surveillance inspections.

2. Of these nearly 3,000 firms, they break down as follows: (a) 183 are making both dosage/active pharmaceutical ingredients (API) products; (b) 1,146 are making API only; (c) 1,036 are making dosage only; and (d) 600 firms are making products "unknown to the FDA." Please provide a description of what is meant by "unknown to FDA."

3. FDA has conducted approximately 1,379 foreign inspections since Fiscal Year 2002—1,196 were both pre-approval and current good manufacturing practice (CGMP) inspections, 107 were pre-approval inspections only, and 76 were CGMP inspections only.

4. Each year, FDA defines and identifies through its risk model approximately 100 "high risk" firms for CGMP surveillance inspection, but can only undertake about 25 such inspections annually due to resource constraints. Please provide the risk scores for the top 150 firms assessed by FDA's risk model for 2006 inspections.

5. FDA does not know the exact number of firms that currently manufacture and export over-the-counter (OTC) products to the U.S. or whether those firms have been inspected.

6. FDA databases do not provide full accounts of what is entering the U.S. at any given time and what is the present inspection workload. FDA is, however, working to update and "coordinate" these databases.

7. FDA is currently unable to easily distinguish between firms which are "registered" to ship to the U.S. and firms which are actually "shipping" to the United States.

Finally, we request additional information on the following questions:

1. Please provide a comprehensive list of all foreign companies that manufacture drug products, including OTC drugs, prescription drugs, and APIs, and the specific products each firm exports to the United States.

2. For each firm on this list, please provide: (a) where the company is located; (b) how long the firm has been exporting to the U.S.; and (c) when FDA last inspected the firm. Also, please identify which firms have undergone a New Drug Application or Abbreviated New Drug Application inspection (referred hereafter as a "pre-approval" inspection). Please further identify which of these firms have received a CGMP inspection and with what frequency.

3. Please provide a detailed description of the risk management model FDA currently uses to determine which foreign inspections to undertake.

4. How many foreign firms manufacture drug products for export to the U.S. but have never received an FDA inspection of any kind?

5. Pursuant to 21 USC 360(h), it is required that every *domestic* "establishment engaged in the manufacture, propagation, compounding, or processing of a drug" be inspected by the FDA at least once every two years. Does FDA inspect domestic firms once every two years? If not, which firms subject to the requirement are not inspected once every two years? If a subset of firms is identified in this category, please explain why they are not subject to an inspection once every two years.

6. What are the average differences in the frequency of inspections between foreign and domestic firms? Are there any difficulties for FDA in obtaining these data?

7. What statutory or regulatory requirements exist for FDA to inspect foreign drug manufacturing firms at a particular frequency?

8. In its 1998 report entitled "FDA: Improvements Needed in the Foreign Drug Inspection Program," the Government Accountability Office (GAO) found that FDA lacked a comprehensive, automated system for managing its foreign inspection program. At the

time, GAO observed that 15 different computer systems—very few of which were integrated—were used to manage FDA's foreign drug inspection program. Almost 10 years later, FDA officials have told staff that they still have considerable difficulty with the computer databases used to track and manage foreign inspections for those firms exporting drug products to the United States. What are the current limitations on FDA's ability to track drug exports sent to the U.S., and what limitations do the present systems have on managing foreign inspections? What action is FDA taking to strengthen this information technology?

9. Please provide a detailed description of the personnel structure for foreign inspections. How do foreign inspectors fit within FDA's Division of Field Investigations (DFI)? Who performs foreign inspections, and how many of these inspectors are there? How are inspections assigned? What are the requirements for inspectors to prepare for foreign inspections? Do they specialize in certain regions of the world?

10. Does FDA assess and work with foreign inspectorates to maximize the effectiveness of its foreign inspection program? Describe how FDA's DFI works with the Department of State to ensure an adequate level of in-country knowledge and support (e.g., for translations and logistics) for foreign inspections?

We appreciate your attention to this matter and look forward to working with you to address this important public health matter. We are requesting that you provide answers to these questions on a rolling basis, but no later than three weeks from the date of this letter. If you have any questions about this request, please contact us or have your staff contact Chris Knauer or Joanne Royce with the Committee Majority staff at (202) 226-2424 or Peter Spencer with the Committee Minority staff at (202) 225-3641.

Sincerely,

John D. Dingell
Chairman

Joe Barton
Ranking Member

Bart Stupak
Chairman
Subcommittee on Oversight and Investigations

Ed Whitfield
Ranking Member
Subcommittee on Oversight and Investigations