DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

AUG 2 8 2008

The Honorable Bart Stupak
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-2201

Dear Mr. Chairman:

Thank you for your letter of July 22, 2008, cosigned by Chairman John D. Dingell, Committee on Energy and Commerce, requesting information and documents regarding the activities of the Food and Drug Administration (FDA or the Agency) related to Ranbaxy Laboratories Limited (Ranbaxy).

Information contained in the enclosures may include information that is trade secret, commercial confidential, or other information protected from disclosure to the public under the Freedom of Information Act (Title 5, *United States Code* [U.S.C.] 552), the Trade Secrets Act (18 U.S.C. 1905), the Privacy Act (5 U.S.C. 552a), or FDA regulations. The Committee should not publish or otherwise make public any such information. We would be glad to discuss with the Committee staff the protected status of any specific information. Some documents have been redacted for personal privacy information such as patient identifiers. We have not provided documents that are part of any open regulatory matters or criminal investigations.

In your letter, you questioned whether FDA acted appropriately to protect the public health in the face of information that Ranbaxy may have engaged in unlawful conduct under the Federal Food, Drug, and Cosmetic (FD&C) Act. You refer to a Motion to Enforce Subpoenas and Points and Authorities filed in the U.S. District Court for the District of Maryland (Southern Division) on July 3, 2008, by the U.S. Attorney for the District of Maryland, and express concern about the continued distribution of Ranbaxy's products in the United States.

The fact that Ranbaxy products remain on the market does not mean that the Agency has ignored the relevant circumstances for Ranbaxy products and failed to take action to protect the public health. The enclosed documents establish that, in August 2005, FDA immediately initiated steps to investigate and take appropriate action when the Agency became aware of information that Ranbaxy—a major supplier of generic drugs based in India— may have failed to comply with U.S. regulations regarding manufacturing and laboratory practices and may have engaged in fraud. These efforts were driven by FDA's fundamental, and critical, mission to help ensure the safety and effectiveness of drugs on the American market.

In August 2005, FDA's Center for Drug Evaluation and Research (CDER) became aware of information that Ranbaxy may have engaged in fraud and that the firm's manufacturing and laboratory operations in Dewas, India, and in Paonta Sahib, India, were not in compliance with FDA's current Good Manufacturing Practice (cGMP) regulations. CDER evaluated the information, decided to inspect Ranbaxy facilities in Paonta Sahib and Dewas, and shared the information with FDA's Office of Criminal Investigations. FDA also decided to inspect a related facility that supplied active pharmaceutical ingredient (API) to the Paonta Sahib operation. The three manufacturing sites were inspected in early 2006.

In February 2006, FDA inspected the Paonta Sahib site and documented deviations from cGMP in the manufacture of human drug products, including the failure to retain complete drug testing data, insufficient documentation to demonstrate that stability tests were valid, and the lack of sufficient laboratory personnel and instrumentation in Ranbaxy's Quality Control Unit to conduct drug stability testing.[1] FDA's field investigators classified this inspection as "Voluntary Action Indicated," the middle level in the Agency's three-level inspection classification system.

Between February and May 2006, FDA took the additional step of testing many of Ranbaxy's products manufactured either at the firm's Paonta Sahib or Dewas facility in an effort to determine whether laboratory tests would reveal problems with the products. FDA field staff collected samples of selected Ranbaxy products manufactured at Paonta Sahib and Dewas for marketing in the U.S. or in association with the President's Emergency Plan for AIDS Relief (PEPFAR) program. Through contacts with its sister agency, the Centers for Disease Control and Prevention, FDA also obtained samples of Ranbaxy drugs distributed in Africa through PEPFAR. Generally, FDA does not sample and analyze the products of firms not operating in compliance with cGMP. FDA did so in this case, however, because of the specific nature of the information about Ranbaxy's practices. This sampling and testing were done to give FDA assurance that Ranbaxy's products met their specifications. FDA determined from this sampling and testing that the products met applicable specifications.

Following the February 2006 inspection at Paonta Sahib, CDER was actively engaged with Ranbaxy in an effort to resolve the manufacturing and other deficiencies at the Paonta Sahib facility through the exchange of correspondence; however, the firm's explanations and submissions failed to resolve all issues completely. Given Ranbaxy's inadequate response and the global nature of at least one deficiency at Paonta Sahib, CDER reclassified the inspection "Official Action Indicated," the highest level of concern of FDA's three-level classification system. Thereafter, in June 2006, FDA concluded that issuing a Warning Letter to Ranbaxy was the appropriate regulatory action based on the information obtained in the regulatory investigation at the time. The Warning Letter discussed the cGMP deviations in detail and stated that drugs manufactured at the Paonta Sahib facility were adulterated under the FD&C Act, 21 U.S.C. 351(a)(2)(B). The Warning Letter also notified Ranbaxy that until these

---

[1] Among other things, stability testing ensures that a drug will continue to deliver an adequate level of the active drug ingredient to patients during the product's shelf life.

deficiencies were corrected, FDA would withhold approval of new applications (Abbreviated New Drug Applications and New Drug Applications) for finished drug products manufactured at Paonta Sahib. Absent approval, Ranbaxy drugs covered by the pending applications would be barred from the U.S. market.

Since the Warning Letter was issued in June 2006, FDA has worked with Ranbaxy to facilitate correction by the company of the violations cited in the Warning Letter. This has included several meetings between FDA and the company, as well as the exchange of numerous letters regarding the regulatory issues presented. FDA is currently monitoring the Paonta Sahib facility, continues to consider additional regulatory measures, and has an open criminal investigation[2] pertaining to Ranbaxy. As noted above, while there have been important concerns about the company's compliance with FDA regulations, FDA's analysis of Ranbaxy's product samples has not produced evidence to suggest that Ranbaxy's marketed products fail to meet their specifications.

Although FDA's Office of Generic Drugs has continued to *process* approval applications sponsored by Ranbaxy during this period of investigation, FDA has not issued a final approval for any Ranbaxy application for drugs to be manufactured at the Paonta Sahib facility since October 2005. The Agency will continue to assess this matter, consistent with our mission to protect the public health by helping to ensure safe and effective drugs are available to the public.

Also, on July 28, 2008, by telephone, David Nelson of your staff requested a list of all Ranbaxy facilities listed in approved applications from January 1, 2005, to July 22, 2008. This information is enclosed at Tab A.

We have repeated your requests below in bold, followed by our response.

1. All documents that convey preapproval inspection assignments.

Documents responsive to this request are enclosed at Tab B.

2. All documents that describe the tasks undertaken and all findings by the investigators during the preapproval inspections, including but not limited to any 483s or Establishment Inspection Reports (EIRS).

Documents responsive to this request are enclosed at Tab C.

3. All documents relating to any "for cause" inspection of Ranbaxy or its active pharmaceutical ingredient (API) suppliers.

Documents responsive to this request are enclosed at Tab D.

---

[2] It is FDA's policy not to confirm or deny the existence of an open criminal investigation; however, in this matter the existence of such an investigation has been made public by the Department of Justice.

4. A list of all API suppliers and any 483s, EIRs, or other documents that describe the tasks undertaken and the findings resulting from inspections of those suppliers.

Documents responsive to this request are enclosed at Tab E.

5. A list of all laboratories performing bioequivalence studies, noting which Ranbaxy drug substances were tested, when they were tested, and the test results.

Documents responsive to this request are enclosed at Tab F.

6. Any 483, EIR, or comparable document that would describe inspections (if any) of the laboratories that performed bioequivalence testing for Ranbaxy.

Documents responsive to this request are enclosed at Tab G.

7. A list of FDA personnel that conducted and/or reviewed each inspection listed above.

Documents responsive to this request are enclosed at Tab H.

Thank you again for your interest in this matter. If you have any further questions, please let us know. A similar letter with the enclosures is being sent to Chairman Dingell.

Sincerely,

Stephen R. Mason
Acting Assistant Commissioner
for Legislation