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May 6, 2009

Dr. Joshua Sharfstein
Acting Commissioner
The Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903

Dear Dr. Sharfstein:

The management of the heparin issue by the Food and Drug Administration (FDA) continues to be of great interest to us and others on the Committee on Energy and Commerce. We are writing to you to follow up on previous letters regarding heparin.

With respect to the FDA's investigation into the contamination of heparin, we have reason to believe that FDA has databases of (i) heparin test results from FDA's own testing and/or all heparin companies, including reports of the existence of overly-sulfated chondroitin sulfate (OSCS), as well as information about the samples of the contaminated lots that were tested; and (ii) the clinical adverse events linked to the percentages of OSCS contamination. Beginning in March 14, 2008, pursuant to a sampling assignment to the FDA field to ensure safety of heparin products in the United States, FDA asked manufacturers of heparin-containing products to test the heparin active pharmaceutical ingredient (API) used in these products with the two screening methods posted to FDA's website: capillary electrophoresis (CE) and proton nuclear magnetic resonance (H-NMR). FDA required companies to provide monthly updates of test results and to notify FDA of any positive results within 3 days of the testing. Beginning on or around March 3, 2009, FDA no longer required monthly updates on heparin test results. We also are aware of a 2008 published article on contaminated heparin associated with adverse clinical events, which reported contamination levels in lot samples of heparin procured by FDA.

In light of the continuing interest in the heparin matter, please provide the following information and responses to questions within two weeks from the date of this letter:

1. A list and description of all FDA databases related to heparin contamination and/or adverse events related to heparin (covering a time period starting on January 1, 2006, or a time period starting on January 1, 2005, as applicable to each firm).

2. Copies of all monthly updates of heparin test results and OSCS-positive test results submitted to the FDA. These should include all Heparin Analytical Result Reports. It appears from the Excel worksheet format of these Reports that the levels of OSCS contamination were not required to be reported. Is that correct, and if so, why not? Did FDA receive reports of OSCS contamination levels in final product? If so, please include those reports. Did FDA receive information on OSCS contamination from firms in which the level of OSCS contamination could be calculated? If so, please include the reports containing this information.

3. All heparin test results from FDA laboratories or other laboratories doing testing of heparin samples obtained by FDA, including levels of OSCS contamination (in either API or final product) and the corresponding lot number and manufacturer information. Please note the date of the test, the laboratory that conducted the test, the contamination test results, and the testing methods used.

4. All FDA summaries and analyses of the heparin test results and OSCS-positive test results and/or the clinical adverse events linked to the percentages of OSCS contamination. Was there any analysis provided by the FDA's Office of New Drug Quality Assessment (ONDQA) specifying any chemical linkage of the clinical adverse events and abnormal deaths? If so, please provide. If not, why was there no analysis by ONDQA? Under what circumstances, if any, would FDA require that ONDQA chemists re-analyze data and prepare review documents based on data analysis?

5. What FDA offices collected samples pursuant to the sampling assignment to the field? What are FDA's requirements for sample collection and chain-of-custody? Were there any deviations during the conduct of the sampling assignment from such requirements by FDA in sample collection? If so, why? Would it affect the integrity of the test results?

6. For FDA work on heparin, what was the methodology for determining OSCS contamination levels and was this methodology validated using FDA standards?

7. Did FDA conduct an investigation tracing back the origins and timing of OSCS contamination? If so, what is the status of this investigation and has the FDA sought assistance from the Chinese government in this investigation? If not, why not? Does FDA have reason to believe that the Chinese government is taking any action(s) related to heparin contamination? If so, what are the actions, and what is the basis for the belief?

8. Will FDA make any information from the database related to heparin contamination publicly available? If so, when? If not, why not?

We would respectfully request, if the Department withholds any documents or information in response to this letter, that a Vaughan Index or log of the withheld items be attached to the response. The index should list the applicable question number, a description of the withheld item (including date of the item), the nature of the privilege or legal basis for the withholding, and a legal citation for the withholding claim.

Your consideration and response is greatly appreciated.

Sincerely,

Joe Barton
Ranking Member

Greg Walden
Ranking Member
Subcommittee on Oversight and Investigations

cc: The Honorable Henry Waxman, Chairman
The Honorable Bart Stupak, Chairman
Subcommittee on Oversight and Investigations