DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUN - 2 2008

The Honorable Bart Stupak
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

Dear Mr. Chairman:

On April 29, 2008, the Food and Drug Administration (FDA) held a hearing entitled "The Heparin Disaster: Chinese counterfeits and American Failures." During that hearing you requested a list of the Chinese companies known to FDA to have been in the supply chain for heparin found to be contaminated (the list is enclosed). Please note that we do not know which of these firms, if any, are the cause of the contamination. It is not clear whether the contamination occurred before, while, or after the products were in the firms' possession. In addition, the fact that a firm is on the list does not mean heparin products from the firm are being shipped, or have been shipped, to the United States (U.S.). Some of the companies on this chart have never shipped heparin to the U.S.

Please be advised that the enclosure includes information received from foreign government counterparts with whom FDA has confidentiality arrangements to not further disclose the information. 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.

We note that the Subcommittee has raised concerns about FDA's ability to protect the American people from contaminated heparin. In fact, FDA has taken comprehensive steps to prevent contaminated heparin from entering the domestic drug market.

Shortly after discovering an increase in adverse reactions to certain heparin sodium products, FDA designed test methods that identified the contaminant (oversulfated chondroitin sulfate or OSCS) and then established and posted on the internet test methods for analyzing heparin for this impurity, *http://www.fda.gov/cder/drug/infopage/heparin/default.htm#screening.* FDA also quickly began on-site inspections and investigations to evaluate the nature and extent of the contamination. FDA inspected both domestic finished dosage form facilities and international active pharmaceutical ingredient (API) suppliers to determine the presence and cause of the contamination, to map the supply route of contaminated products, and to gauge the inspected firms' compliance with current good manufacturing practices (CGMPs).

The API made by one firm, Changzhou-SPL, was associated with a signal of increased adverse events in the U.S. An FDA inspection found significant violations of current good manufacturing practices (CGMP), FDA issued the firm a warning letter, and FDA added the firm to an import alert for firms that have not met CGMPs.

Soon after determining that certain heparin had been contaminated, and even before it had identified the specific contaminant, FDA instituted measures to effectively prevent contaminated heparin from entering the U.S. drug supply. On March 14, 2008, FDA issued a sampling assignment to provide instructions to FDA staff about sampling imported heparin. Under the sampling assignment, all shipments of heparin sodium API are sampled and tested using the methods posted on FDA's website. Some of the testing is conducted by U.S. manufacturers receiving imported heparin products, many of which have made written commitments to FDA that each lot of heparin will be tested for the OSCS. Under the testing commitments, the U.S. firms use FDA's published screening methods and forward their test results within three days to FDA, where the results undergo a two-tiered review. FDA responds with comments and requests for additional information, as appropriate. Under the sampling assignment, if there is not a written testing commitment from a domestic manufacturer FDA tests the heparin API that has been offered for import for OSCS. In addition to sampling and testing, all shipments of heparin sodium API are physically examined upon entry by FDA to verify the security and integrity of the shipment, the nature of the imported product, and the various declarations accompanying the entry (manufacturer, shipper, product description, etc.).

For heparin products other than heparin sodium API, the sampling assignment instructs FDA staff to conduct the reconciliation exam and instructs import reviewers to consult with the appropriate FDA Center, through FDA's Division of Import Operations and Policy, about whether to sample and test the shipment. FDA has ordered sampling and testing of every shipment of crude heparin that has arrived in the U.S. since March 14. FDA's strategy has assured that every declared shipment of heparin sodium API and crude heparin imported since mid-March has been tested for contamination.

Thus, while some of the firms listed may have shipped heparin to the U.S. at some time, FDA has not put any of them on an import alert relating to contaminated heparin. This step is unnecessary because heparin is being effectively stopped at the U.S. border and testing of it for OSCS is being assured. Even if on import alert, the importer would have the opportunity to show the product is compliant, such as by testing for contamination.

FDA believes that, under the circumstances, it has implemented the best approach to protect the public health by having testing conducted by FDA or by a finished dosage form manufacturer that has committed to conduct the testing under circumstances where FDA has sufficient confidence that the firm can appropriately do so. Nonetheless, FDA continues to aggressively gather more information and to monitor the situation to determine whether it should take any different or additional measures to protect the public health.

Beyond testing products upon entry, FDA has inspected and will continue to inspect the firms that supply heparin to the U.S. FDA prioritizes its inspections based on, among other considerations, the need to assure the continued supply of heparin, the participation of U.S. firms in the voluntary testing program, and testing results.

Through all of these actions, FDA has been carefully and diligently taking measures to preserve the availability of medically necessary heparin to U.S. patients and to ensure that the heparin is not contaminated.

Thank you for your interest in this very important matter. We hope that you find the enclosed information useful. If you have any further questions, please let us know.

Sincerely,

Stephen R. Mason
Acting Assistant Commissioner
for Legislation

Enclosure

*Chinese Firms Known To FDA To Have Been In The Supply Chain For Heparin Found To Be Contaminated**		
Firm Name	**City**	**Province**
1. Changzhou SPL Co Ltd.	Changzhou	Jiangsu
2. Changzhou Techpool Pharmaceutical	Changzhou	Jiangsu
3. Changsha KEFA New Products Experimental Co., Ltd	Hangzhou	Zhejiang
4. Chongqing Imperial Bio-chem Co., Ltd.	Chongqing	Sichuan
5. Changzhou Qianhong Bio-Pharma Co., Ltd.	Shanghai	
6. Hangzhou Ruihua Biochemical Product	Hangzhou	Zhejiang
7. Nanjing King Friend Biochemical Pharmaceutical Co., Ltd.	Nanjing	Jiangsu
8. Newsmart Chem-Spec Ind. (Trading Firm)	Nantong	Jiangsu
9. Shanghai No.1 Biochemical and Pharmaceutical Co., Ltd.	Shanghai	
10. Shenzhen Hepalink Pharmaceutical Co.	Shenzhen	Guangdong
11. Sichuan Longxin Trading Co., Ltd.	Chengdu	Sichuan
12. Yantai Dongcheng Biochemical Co., Ltd.	Yantai	Shangdong
* Includes shipments from the firms to anywhere in the world. Includes information supplied by foreign governments with whom FDA has confidentiality arrangements to not further disclose the information.		