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ONE HUNDRED ELEVENTH CONGRESS

# Congress of the United States

## House of Representatives

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July 29, 2010

The Honorable Margaret A. Hamburg, M.D.  
Commissioner  
The Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20903

Dear Dr. Hamburg:

We write to follow up on our July 22, 2010, letter to you regarding the unsolved case of heparin contamination and to convey information to you in support of your upcoming visit to China. The heparin matter, the largest and longest case of contamination of the global drug supply we are aware of, is of some urgency. All evidence points in the direction of a man-made contaminant that was introduced in China. The contamination of the heparin supply was a crime. You are going to the source country of that crime, and your trip represents the best hope of a breakthrough in solving this case.

As you noted in your June 22, 2010, speech at the Woodrow Wilson International Center for Scholars, one of your top priorities is the Food and Drug Administration (FDA) response to globalization, "especially the urgent issue of import safety." You noted specifically that the recent problem "with contaminated heparin . . . and the growing prevalence of counterfeit drugs make clear that we must bring our oversight in line with the reality of the global economy." You further noted that "[t]he new global reality requires new global partnerships." We hope this means you will seek a new global partnership to help solve the heparin contamination case.

In preparation for your visit to China and meeting with Chinese government officials next month, we wish to assist you by providing the following information that details why solving the heparin contamination matter is a top priority for protecting U.S. public health and ensuring confidence in imported drug products from China.

China is an important source of heparin and other pharmaceuticals for the U.S. As noted in an April 2010 research report, "Potential Health & Safety Impacts from Pharmaceuticals and Supplements Containing Chinese-Sourced Raw Ingredients," prepared by NSD Bio Group at the request of the U.S.-China Economic and Security Review Commission, China exported a total of 30 tons of heparin sodium (about 27, 215 kg) in the first quarter of 2009. From prior research, this report notes that it was estimated that in the U.S. alone, during 2006-2008 two tons of heparin per month were required, 70% sourced from China. Minority Committee staff has also obtained non-public 2009 data indicating that more than 80%

of U.S. unfractionated heparin was sourced from China. The NSD Bio Group report further notes that China is America's Number One pharmaceutical trade partner, as reflected by China's 16.24% share of U.S. imports of pharmaceutical ingredients (as of data for 2008). The report concludes that the trend toward increased outsourcing of heparin to China is expected to continue.

Even though the FDA has taken steps to prevent Oversulfated Chondroitin Sulfate (OSCS) contamination in heparin entering the U.S. drug market, significant risks to the safety of heparin in the U.S. remain because of the inherent vulnerabilities in Chinese heparin supply chains, the problems posed by the unsolved case of heparin contamination, and the lack of Chinese government oversight over critical parts of the supply chain. According to non-public industry information dates 2010 obtained by Minority Committee staff, the three main risks to the Chinese crude heparin supply chain are: unauthorized sources and/or unapproved suppliers; crude heparin contaminated with non-porcine animal material; and crude heparin contaminated with chemical material. Although the heparin industry has mitigation strategies to address these risks, the ability of industry and regulators to deal with the risk of economically-motivated adulteration of crude heparin with chemicals is highly reliant on market intelligence and investigation.

Our investigation has revealed that the Chinese government presented barriers to the U.S. investigation and to gaining market intelligence on who was involved in OSCS contamination and how the contamination was perpetrated. The affected U.S. actions include FDA's criminal investigation, where the Chinese government reportedly denied a visa to FDA's criminal investigator. Because the case is unsolved, the bad actors who caused the contamination are still at large and perhaps operating in the Chinese heparin industry, and could find new ways to adulterate heparin that pose a threat to U.S. public health. Furthermore, a recent report in the Korean news media on heparin market conditions indicates that foot-and-mouth disease may be killing pigs in China, causing a shortage in heparin and an increase in prices. This could potentially result in market conditions similar to the ones in 2006 and 2007 and new attempts to contaminate the heparin supply with a possibly dangerous adulterant other than OSCS.

With respect to Chinese government oversight of the crude heparin supply chain, it is our understanding that, while slaughterhouses are highly regulated by the Chinese government, there is no Chinese government regulation of casing workshops, crude heparin workshops, and crude heparin consolidators. This lack of oversight compounds the problem of tracing back contaminated heparin to identify who introduced the contaminant.

As we noted in our July 22, 2010, letter, the Chinese government informed a U.S. government official on June 18, 2008, that investigation of the heparin matter would not be pursued as either a criminal or administrative case. However, we have been advised that companies responsible for producing adulterated drugs can be charged in China with violating Chapter 3, Section 1, Article 140 of the Chinese Criminal Law, which governs adulterated products such as adding OSCS to heparin; or Chapter 3, Section 1, Article 141 of the Chinese Criminal Law, which governs the production and sale of counterfeit medicine. While exporting adulterated drugs is considered general illegal activity which is not a crime, it is still considered an administrative violation.

Further, we question whether China's State Food and Drug Administration (SFDA) still believes that OSCS does not cause adverse events, the main ruling reportedly preventing investigation. As we mentioned in our July 22 letter, FDA and others have found more evidence since June 2008 that strengthens the case of OSCS causing allergic-type serious adverse events. Moreover, it has been reported to the Minority Committee staff that some Chinese government officials have been working cooperatively with the U.S. with respect to preventing OSCS contamination. In 2009, Professor Jin Shaohong, who works at the National Institute of Biological Standardization and Control (NIBSC) in the SFDA, was a member of U.S. Pharmacopeia's Reference Standards Expert Committee, which helped

USP revise and update the USP monograph to deal with potential OSCS contamination. We have also learned of a report that the Chinese Pharmacopeia and a Chinese institute were revising their heparin monograph(s), adding assay methods to identify potential OSCS contamination, and that this new monograph would be published in the 2010 edition of the Chinese Pharmacopeia. In addition, it is our understanding that SFDA mandated that all heparin manufacturers register with the SFDA and test each batch of products and raw materials for OSCS regardless of destination of sales. Such actions by SFDA suggest that the Chinese government views it in its self-interest to protect its domestic heparin supply and to maintain the confidence of its export markets in Chinese heparin, and perhaps even more broadly, in Chinese pharmaceutical exports. The SFDA's actions also appear to be in contradiction to the June 2008 ruling, and justify our requesting that you ask the Chinese government to reopen the heparin contamination investigation.

In light of the concerns we have outlined, we request that you provide a briefing to both of us and the Minority Committee staff about your meetings with the Chinese government on the heparin matter as promptly as possible upon your return, no later than September 22, 2010.


Your prompt attention to this request is appreciated. If you have any questions, please contact Minority Committee staff at (202) 225-3641.

Sincerely,



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Joe Barton  
Ranking Member



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Michael C. Burgess  
Ranking Member  
Subcommittee on Oversight and Investigations

cc: The Honorable Henry A. Waxman, Chairman

The Honorable Bart Stupak, Chairman  
Subcommittee on Oversight and Investigations