United States Senate
COMMITTEE ON FINANCE
WASHINGTON, DC 20510–6200

April 28, 2008

**Via Electronic Transmission**

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

Dear Commissioner von Eschenbach:

As Ranking Member of the Committee on Finance (Committee), I have a responsibility to the more than 80 million Americans who receive health care coverage under the Medicare and Medicaid programs to oversee the proper administration of these programs and ensure that taxpayer and beneficiary dollars are appropriately spent on safe and effective drugs and devices.

An increasing amount of the drugs and active pharmaceutical ingredients (API) Americans use are being manufactured in foreign countries. Yet, as reported by the Government Accountability Office (GAO) in November 2007, the Food and Drug Administration (FDA or Agency) does not know how many foreign establishments are subject to inspection and the Agency conducts relatively few inspections each year. As I am sure you will agree, it is critical that sufficient standards be in place to ensure accountability and the quality of the drug products we import into this country. To do otherwise can have devastating results, as the heparin situation so aptly demonstrates. This blood-thinning drug is a life-saving and life-sustaining medication. It is my understanding that there is only one company that has developed a traceable distribution system that provided sufficient assurances to the FDA so that the company can continue providing heparin to the American public and many throughout the world. It is with this in mind that I am writing to you today.

The FDA's investigation of the contamination of the U.S. heparin supply highlighted significant weaknesses in oversight of the production and supply chain. While one manufacturer, Baxter, conducted audits and inspections of its heparin API supplier, Changzhou SPL, there were no mechanisms ensuring that the upstream providers—the consolidators, the crude heparin processors, and the slaughterhouses—were providing a quality product to Changzhou SPL. Prior to the recall of its heparin products, Baxter manufactured about 50 percent of the heparin sodium used in the United States.

Last week, my staff was briefed on a traceable distribution system, which tracks the production of its heparin sodium from the pig through manufacture of the final product. The company using this system has its own facility in China to purify the crude

heparin and informed my staff that it had already been testing its heparin using one of the two methods that FDA subsequently required of all heparin manufacturers to screen for the contaminant in their API. It is my understanding that this company developed its traceable distribution system in 2003 to ensure that the extraction and purification of crude heparin was conducted under strict controls. In 2005 this same company obtained the FDA's approval to use this system for its heparin production. It appears that because of the system this company has in place, it was able to avoid contamination of its heparin API. As I understand it, no other heparin manufacturer employs a similar tracking system.

Accordingly, please respond to the following questions by no later than May 19, 2008:

1. In your opinion, if other manufacturers had a traceable distribution system like the one described in this letter, would the contamination of our heparin supply been avoided or at least significantly limited? Could this system reasonably be put in place by other manufacturers? If not why not?

2. During last week's telebriefing, the FDA stated that the heparin events demonstrated a need for more well-developed testing and screening methods as well as an enhanced scrutiny of the supply chain. What steps is FDA taking to ensure greater oversight of the supply chain?

3. I understand that the FDA is working with U.S. Pharmacopeia to revise and update the current testing methods for detecting contaminants in heparin. Has the FDA sought input from all stakeholders or experts on developing methods and standards that will ensure the quality of our heparin supply? Please identify any other stakeholders or experts being consulted.

4. Is it your understanding that, prior to this year's contamination, there was only one heparin manufacturer employing a system to track and trace the manufacture of heparin at all stages of production?

Thank you for your attention to this important matter. If you have any questions, please do not hesitate to contact Emilia DiSanto or Angela Choy at (202) 224-4515. All formal correspondence should be sent electronically in PDF format to Brian_Downey@finance-rep.senate.gov or via facsimile to (202) 228-2131.

Sincerely,

Charles E. Grassley
Ranking Member