

ONE HUNDRED ELEVENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
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MEMORANDUM

March 5, 2010

To: Members of the Health Subcommittee

Fr: Democratic Committee Staff

Re: Subcommittee Hearing on FDA Update on Drug Safety

On Wednesday, March 10, at 2 p.m., in room 2123 of the Rayburn House Office Building, the Subcommittee on Health will hold a hearing entitled “Drug Safety: An Update from the Food and Drug Administration.” At the hearing, the Food and Drug Administration (FDA) will detail the Agency’s current challenges and successes in the area of drug safety.

I. BACKGROUND

FDA is charged with ensuring the safety, efficacy, and security of human drugs and biological products that are marketed in the United States. Before a drug can enter the marketplace, the company seeking to market that drug must demonstrate to FDA that the drug is safe and effective for its intended use.¹ As part of this pre-approval review, FDA routinely inspects the facility at which each drug will be manufactured, including overseas facilities.²

Since premarket testing of drugs cannot identify all drug risks, FDA also monitors the safety of drugs once they are on the market.³ As part of this post-market oversight, FDA is

¹ Federal Food, Drug, and Cosmetic Act, Section 505 (21 U.S.C. § 355).

² As part of its application, a manufacturer is required to provide FDA with “a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug.” (Federal Food, Drug, and Cosmetic Act, Section 505(b)(1)(D)). In order to verify this information, FDA conducts a pre-approval inspection. *See* FDA Compliance Program Guidance Manual 7346.832.

³ General Accounting Office, *Drug Safety: FDA Has Begun Efforts to Enhance Postmarket Safety, but Additional Actions Are Needed* (November 2009) (GAO-10-68).

required to inspect domestic facilities once every two years.⁴ However, for foreign facilities, FDA's inspection authority is more limited. Specifically, FDA is only authorized "to enter into cooperative agreements with officials of foreign countries to ensure that adequate and effective means are available for purposes of determining" the safety of drugs offered for import into the United States.⁵ FDA does not have the authority to require foreign establishments to open up their facilities for inspection. However, FDA does have the authority to conduct physical examinations of drugs offered for import, and if warranted, prevent the entry of those drugs at the border.⁶

II. RECENT LEGISLATION

In 2006, a series of safety problems with approved drugs, such as Vioxx⁷ and Ketek⁸, prompted the Institute of Medicine (IOM) and the Government Accountability Office (GAO) to thoroughly examine the FDA's post-market surveillance system. IOM and GAO concluded that FDA needed more resources and more legal authority to better protect Americans from unsafe drugs.⁹

In response, Congress passed the Food and Drug Administration Amendments Act of 2007 (FDAAA), to strengthen FDA's post-market drug safety oversight.¹⁰ This legislation gave FDA the ability, for the first time, to require manufacturers to conduct post-market drug safety studies, and to make safety related changes to drug labels.¹¹ Prior to this, FDA could only request that manufacturers take such actions under the threat of withdrawing the drug from the market in the event they failed to comply. Additionally, FDAAA gave the agency the ability to impose a "Risk Evaluation Mitigation Strategy," or "REMS," for drugs and biologics, to ensure that the benefits of a drug or biologic outweigh its risks.¹²

⁴ Federal Food, Drug, and Cosmetic Act, Section 510(h).

⁵ Federal Food, Drug, and Cosmetic Act, Section 510(i)(3).

⁶ Federal Food, Drug, and Cosmetic Act, Section 801(a).

⁷ See, e.g., *F.D.A. Official Admits 'Lapses' on Vioxx*, New York Times (March 2, 2005) (online at: www.nytimes.com/2005/03/02/politics/02fda.html?scp=9&sq=vioxx&st=cse)

⁸ See, e.g., *FDA Warns of Liver Failure After Antibiotic*, New York Times (June 30, 2006) (online at: www.nytimes.com/2006/06/30/health/30fda.html).

⁹ Institute of Medicine, *The Future of Drug Safety: Promoting and Protecting the Health of the Public* (September 22, 2006); Government Accountability Office, *Drug Safety: Improvement Needed in FDA's Postmarket Decision-making and Oversight Process* (March 2006) (GAO-06-402).

¹⁰ P.L. 110-85.

¹¹ Federal Food, Drug, and Cosmetic Act, Section 505(o).

¹² Federal Food, Drug, and Cosmetic Act, Sections 505(p) and 505-1.

FDAAA also provided FDA with certain tools related to drug advertising, such as requiring manufacturers to submit television advertisements to the agency for review prior to launching those ads.¹³

To increase FDA's ability to more quickly detect post-market drug safety problems, FDAAA directed the agency to establish an active post-market drug surveillance infrastructure, in conjunction with external data providers.¹⁴

FDAAA gave the agency enforcement tools, including the authority to impose civil monetary penalties for certain violations of the Federal Food, Drug, and Cosmetic Act with respect to drugs.¹⁵

III. IMPORTED DRUG SAFETY

In recent years, drugs marketed in the U.S. have increasingly been developed and manufactured abroad. In 1998, GAO found that roughly 80 percent of all active pharmaceutical ingredients (API) used by U.S. manufacturers came from abroad.¹⁶ This is a trend that continues today with a significant number of manufacturing sites located in China and India.

Some of the risks associated with an increasingly globalized drug supply were illustrated by the recent Heparin incident.¹⁷ Heparin is a blood thinner used to prevent blood clots; it is critical to heart surgery, dialysis, and many other medical procedures. The active ingredient in heparin is made from pig intestines. Baxter Healthcare Corporation, a major manufacturer of heparin for the U.S. market, bought the active ingredient for its heparin from a company called Changzhou Scientific Protein Laboratories (SPL), located in a Changzhou, China. China is the source of over half of the world's pig supply, and the raw heparin is often produced in small, unregulated family workshops in China.

In late 2007, Baxter began noticing a spike in the number of severe allergic reactions in patients who had been given the company's heparin. In addition, there were reports of patient deaths associated with the drug. In January 2008, Baxter issued a voluntary nationwide recall of its heparin products, even though the company had not yet established a direct link to the adverse

¹³ Federal Food, Drug, and Cosmetic Act, Section 503B.

¹⁴ Federal Food, Drug, and Cosmetic Act, Section 505(k).

¹⁵ Federal Food, Drug, and Cosmetic Act, Section 303(f)(4)(A) and 303(g).

¹⁶ General Accounting Office, *FDA: Improvements Needed in the Foreign Drug Inspection Program* (March 1998) (GAO/HEHS-98-21)

¹⁷ For a complete description of this incident, see House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, *Hearing on The Heparin Disaster: Chinese Counterfeits and American Failures* (online at: energycommerce.house.gov/index.php?option=com_content&view=article&id=627&catid=31&Itemid=58).

events. A total of 81 Americans deaths were linked to the recalled heparin that contained the tainted Chinese API.

FDA later determined that the Baxter's heparin contained a dangerous counterfeit ingredient, oversulfated chondroitin sulfate, which mimicked authentic heparin. In the year prior to this situation, a pig disease had swept through China, forcing heparin producers to seek new sources of the raw material.

A thorough investigation by FDA and this committee revealed that the agency had never inspected the Changzhou SPL facility before allowing the company to supply the active ingredient to Baxter. In addition, the plant was not registered as a drug manufacturing plant in China and therefore had never been inspected by the Chinese authorities.

V. WITNESSES

The following witness is expected to testify:

Joshua M. Sharfstein, M.D.
Principal Deputy Commissioner
Food and Drug Administration