

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

September 28, 2010

To: Members of the Subcommittee on Health

Fr: Subcommittee on Health Democratic Staff

Re: Hearing on Discussion Draft of Drug Safety Legislation

On Thursday, September 30, 2010 at 10:00 a.m. in room 2123 of the Rayburn House Office Building, the Subcommittee on Health will hold a hearing on the recently released discussion draft of drug safety legislation by Representatives Waxman, Dingell, Pallone and Stupak.

I. BACKGROUND

The Food and Drug Administration (FDA) is charged with ensuring the safety, efficacy, and security of human drugs and biological products that are marketed in the United States market. 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 preapproval review, FDA routinely conducts inspections of the facility at which each drug will be manufactured, including facilities located abroad.²

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.

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 drug safety oversight, FDA is required to conduct inspections of domestic facilities once every two years.⁴ FDA's inspectional authority is more limited with respect to foreign facilities. More 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, to prevent the entry of those drugs at the border.⁶

II. IMPORTED DRUG SAFETY

In recent years, drugs marketed in the U.S. have increasingly been developed and manufactured abroad. A 1998 General Accountability Office (GAO) study found that roughly 80 percent of all active pharmaceutical ingredients (API) used by U.S. manufacturers came from abroad.⁷ 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 starkly illustrated by the 2007 heparin incident.⁸ Heparin is a blood thinner used to prevent blood clots; it is a critical component to heart surgery, dialysis, and many other medical procedures and conditions. The active ingredient in heparin is made from pig intestines. Baxter Healthcare Corporation, a major manufacturer of heparin sold in the U.S., bought the active ingredient for its heparin supply from Changzhou Scientific Protein Laboratories (SPL), a company located in Changzhou, China. China is the source of over half of the world's pig supply; 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

³ GAO, *Drug Safety: FDA Has Begun Efforts to Enhance Postmarket Safety, but Additional Actions are Needed*, at 4 (November 2009).

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 GAO, *FDA: Improvements Needed in the Foreign Drug Inspection Program* (March 1998).

⁸ 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: http://energycommerce.house.gov/index.php?option=com_content&view=article&id=627&catid=31&Itemid=58).

deaths associated with the drug. Beginning 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 events. In total, 81 Americans deaths were linked to the recalled heparin which contained the tainted Chinese API.

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

After a thorough investigation by the FDA and this Committee, it was revealed that FDA had never inspected the Changzhou SPL facility before allowing the company to supply 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.

III. THE DRUG SAFETY DISCUSSION DRAFT

On September 20, 2010, Rep. John D. Dingell, Chairman Emeritus of the Committee on Energy and Commerce, Rep. Henry A. Waxman, Chairman of the Committee on Energy and Commerce, Rep. Frank Pallone, Chairman of the Subcommittee on Health, and Rep. Bart Stupak, Chairman of the Subcommittee on Oversight and Investigations, released a discussion draft of legislation designed to equip the FDA with the authorities and funding it needs to regulate what is now a global marketplace for drugs.

The discussion draft builds on H.R. 759, the Food and Drug Globalization Act, which was introduced by Reps. Dingell, Pallone and Stupak last year. The discussion draft reflects FDA's priorities and recommendations in an effort to enhance the safety of our drug supply.

In brief, the discussion draft would do the following:

Drug Safety Discussion Draft

- **Creates an up-to-date registry of all drug facilities serving American consumers:** Requires all domestic drug facilities and foreign facilities exporting to the U.S. to register with the FDA annually and pay a registration fee.
- **Generates funding for increased Good Manufacturing Practices (GMP) inspections for brand and generic drugs:** Registration fees would fund increased inspections by the FDA and to improve information systems. Funding would supplement, not supplant existing appropriations. Failure to register or pay the fee would be a cause for denying entry of the facility's product into the U.S.
- **Increases pre-approval inspections:** To address the concern that the FDA is failing to conduct pre-approval inspections of foreign drug facilities with very questionable safety records, pre-approval inspections would be required to be conducted unless FDA makes a

determination that, based on the inspectional history of the facility, an inspection isn't needed to ensure compliance with GMPs, to verify the data in the application or to otherwise ensure the safety of the product.

- **Requires parity between foreign and domestic inspections:** Requires the FDA to inspect foreign and domestic drug facilities every two years. Allows the FDA to modify an individual facility's inspection schedule only if the FDA determines that sufficient information exists about that facility's inspection history and compliance record to justify less frequent inspections.
- **Prohibits entry of drugs coming from domestic and foreign facilities that limit, delay or deny FDA inspections.**
- **Prohibits the entry of drugs into the U.S. lacking documentation of safety:** Rather than solely relying on the FDA to determine if a drug shipment appears to be dangerous based on the limited information currently provided at the border, the HHS Secretary would have authority to require certain documentation or safety information for drugs imported or offered for import into the United States.
- **Requires manufacturers to know their supply chain:** To aid in preventing and investigating incidents such as the heparin crisis, requires manufacturers to maintain and provide to the HHS Secretary, upon request, documentation of their complete supply chain (beginning with the raw materials) and to document measures taken to secure their supply chain.
- **Requires manufacturers to identify and mitigate risk throughout their supply chain:** Requires finished dose and active ingredient manufacturers to have in place written plans to identify and control risks specific to the drug being produced. Requires manufacturers to conduct on-site audits of ingredient suppliers.
- **Country of origin labeling:** Requires drug manufacturers to list on their website the country of origin for all active drug ingredients and for the finished product.
- **Creates an up-to-date registry of importers:** Requires all importers of drugs to register with the FDA and pay an annual registration fee.
- **Requires unique identification numbers for drug establishments and importers:** To improve the accuracy of data and the ability of the FDA to more quickly identify parties involved in a crisis situation requires the creation of unique identification numbers for all drug establishments, importers, and custom brokers.
- **Creates a dedicated foreign inspectorate:** Increases the capacity of the FDA to monitor foreign facilities producing drugs for American consumers.

- **Prohibits false or misleading reporting to the FDA:** Extends the current prohibition against making false or misleading reports related to devices to include drugs.
- **Provides protection for whistleblowers that bring attention to important safety information:** Prohibits entities regulated by the FDA from discriminating against an employee in retaliation for assisting in any investigation regarding any conduct which the employee reasonably believes constitutes a violation of federal law.
- **Provides strong new enforcement tools:**
 - **Destruction:** Allows the FDA to destroy counterfeit or adulterated imports if they pose a risk of injury or death.
 - **Civil monetary penalties:** Creates new authority to impose fines for any violation of the Food, Drug and Cosmetic Act related to drugs.
 - **Criminal penalties:** Increases penalties related to counterfeit drugs to 10 years from one year.
 - **Mandatory recall:** Authorizes new FDA authority to mandate recalls of unsafe drugs.
 - **Administrative detention:** Authorizes new FDA authority to detain unsafe drugs.
 - **Subpoena:** Authorizes new FDA authority to subpoena records related to possible violations.

IV. WITNESSES

The following witnesses have been invited to testify:

Panel I

Janet Woodcock, M.D.

Director, Center for Drug Evaluation and Research
Food and Drug Administration (FDA)

Panel II

Allan Coukell

Director, Medical Safety Portfolio
The Pew Charitable Trusts | Pew Health Group

William Vaughan

Health Policy Analyst
Consumers Union

William Hubbard

Alliance for a Stronger FDA

Kendra A. Martello

Assistant General Counsel

Pharmaceutical Research and Manufacturers of America (PhRMA)

Andrew Emmett

Managing Director

Biotechnology Industry Organization (BIO)

Gordon Johnston, R.Ph, M.S.

Vice President of Regulatory Sciences

Generic Pharmaceutical Association (GPhA)