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Before the

Committee on Health, Education, Labor, and Pensions

United States Senate

Washington, DC

April 24, 2008

INTRODUCTION

Mr. Chairman and members of the Committee, I am William K. Hubbard. Before my retirement after 33 years of Federal service, I served for many years with the U.S. Food and Drug Administration, and for my last 14 years was an FDA Associate Commissioner responsible for, among other things, FDA's regulations and policy development. Although I remain retired since my departure from FDA in 2005, I serve as an advisor to The Alliance for a Stronger FDA, a consortium of patient, public interest, and industry organizations whose mission is to urge that FDA's appropriations be increased. The Alliance and its constituent members are greatly concerned that FDA's resource limitations have hampered the agency's ability to ensure the safety of our food and drug supply. Today's hearing is a timely example of one of those concerns—the massive increase in pharmaceuticals being imported into the United States at a time in which FDA's capacity to oversee those foreign producers is in serious doubt. Accordingly, I wish to thank the Committee for inviting me to testify on that subject today.

BACKGROUND

As you know, Congress created the current regulatory structure for assuring the safety of human drugs in 1938, through its enactment of the Food, Drug and Cosmetic Act. That statute recognized that drugs could be a key component of our health care system, but that drugs were also powerful chemicals with the capability to produce great harm if not carefully regulated. Thus, Congress determined it necessary to create a relatively pervasive regulatory system which is comprised of three primary principles:

1) Strictly regulated human testing and thorough FDA review, of drugs before they can be marketed. FDA takes great care that new drugs meet the required standard of safety and effectiveness, and as such has been recognized as the "gold standard" for drug approval. Further, with the resources Congress provided for additional medical staff via the Prescription Drug User Fee Act, FDA now approves new drugs as fast or faster than anywhere in the world, meaning that Americans have first access to new medical breakthroughs while retaining the safety assurances that our citizens expect.

2) Postmarket monitoring of drugs once they are marketed to assure that the approval decision was appropriate. Congress has recognized that more information about a drug's safety will become available through the widespread use that occurs after its approval, and has instructed the agency to affirm that the approval decision was appropriate by tracking each drug's postmarket safety profile. If safety concerns are identified that were not seen in the initial FDA review, the agency can remove a drug from the market, or otherwise intervene to ensure its continued safe use (such as through warnings or restricted distribution).

3) Rigorous oversight of drug manufacturing, to assure that the drug approved by the FDA is the one that is actually manufactured and is of consistently high quality. A drug must be manufactured under specific controls mandated by FDA—known as Good Manufacturing Practices (GMPs). These include requirements that active ingredients of the drug be of a prescribed purity, strength and quality; that the drug be made in well controlled, sanitary conditions; that its labeling and packaging be equally well controlled; and that laboratory tests of the drug be performed routinely using well established

scientific methods and properly calibrated equipment to confirm that the drug is always produced in the form approved by the FDA.

A RECORD OF REMARKABLE SUCCESS

The result of this regime established by Congress and implemented by the FDA has been unsurpassed, and perhaps unequaled, in my opinion, by any American industry. The high standards for drug safety and efficacy that you and the FDA have demanded have led to a cascade of new discoveries across the decades that have placed the U.S. pharmaceutical industry far above foreign competitors in quantity and quality of new therapeutics. Indeed, countries around the world look to the FDA as the "gold standard" for determining if a new drug should be approved and for establishing safe manufacturing controls for marketed drugs. Today, physicians, pharmacists, and their patients have a very, very high confidence that the drugs they prescribe, dispense, and use are well understood, well made, and will perform as expected.

THE GLOBAL SITUATION

The portrait of pharmaceuticals elsewhere around the world is not so positive. Drugs developed and produced in other countries do not always have the same record of therapeutic success as American pharmaceuticals. But perhaps more importantly, unlike the relatively closed U.S. drug market, in most countries these products are subject to normal arbitrage, which means that drugs move about much as do electronics, apparel, auto parts and thousands of other goods. This has meant that drugs are often purchased from suppliers who have little or no oversight by regulatory bodies; that key elements of

safe drug production are ignored—such as quality testing, expiration dating, and labeling controls; and that producers of substandard and counterfeit drugs have a relatively easy access to the marketplace.

Specific examples of dangers in the international drug market abound. Let me list just a few:

- Last year's substitution of ethylene glycol (antifreeze) for pharmaceutical grade glycerin in an elixir that was linked to 46 deaths in Panama, as well as to other deaths in Nigeria, India, South Africa, and Argentina. Those cases were ominously reminiscent of a similar contamination 1996 that was associated with the deaths of 85 children in Haiti. In both cases, the sources of the substitution were reported to be Chinese drug manufacturers, as was the diethylene glycol contamination of toothpaste that was found recently in many countries, including the United States.[1] As the New York Times reported in 2007, the counterfeit glycerin was traced through a pipeline "from the Panamanian port of Colon, back through trading companies in Barcelona, Spain, and Beijing, to its beginning near the Yangtze Delta in a place local people call 'chemical country'."
- In just the past 2 years, seizures of fake drugs in the EU went from 500,000 tablets to almost 3 million. In addition, the UK's version of our

[1] Ironically, and sadly, it was diethylene glycol substitution for glycerin in an elixir that killed over 100 Americans in 1937 and led Congress to enact the Food, Drug and Cosmetic Act, and thus create the drug safety system that the United States relies upon today..

FDA has recently been forced to conduct large scale recalls of counterfeit drugs that have made their way into their health care system.

- A recent “sting” operation by the The Sunday Times of London set up a phony drug wholesaler, who was able to buy large quantities of counterfeit drugs from a Chinese manufacturer, who was reported to make pharmaceutical ingredients for legal sale by day and fake drugs for illicit sale by night. The Times reported that counterfeiters are increasingly turning from fake handbags and currency to drugs, because the drugs are so easy to make and sell on world markets.
- The World Health Organization has reported that in some areas of the world, particularly parts of Africa and Asia, more than one-half of the pharmaceutical supply is counterfeit. Indeed, drug counterfeiting is considered to be endemic around the world, with the United States thus far one of the few exceptions. China is alleged to be a principle world supplier of such products.
- Many of our citizens are lured to purchase prescription drugs directly, via the internet, from suppliers around the world, often masked as Canadian or European pharmacies, but in reality providing counterfeit and substandard drugs from some of the darkest corners of the globe.
- Within China itself, deaths from counterfeit and substandard drugs have often been described; some reports place them as high as 200,000 to 300,000 annually.

I could go on with numerous other examples, many of which would include a frequent reference to China. But I do not intend to suggest that "Made in China" should become a synonym for danger. That country's enormous economic development in recent years has made it the source around the world of increasing percentages of many nations' consumer goods. Here in the United States, it is estimated that 40% of all consumer products we purchase originate in China. Most are assuredly safe and an attractive bargain for Americans seeking to stretch their income as far as possible.

But drugs are not socks or running shoes. They are special, and Congress recognized their unique importance to health—and their potential risk—when it gave FDA the authority so many years ago to create a comprehensive regulatory system over pharmaceuticals. I believe FDA did its part, and did it well—by bringing to bear the best scientific knowledge of drug development and production to create rules and procedures for assuring that our drugs are safely manufactured. However, I believe that we may now be at a turning point at which our future actions will determine whether we will go the way of other countries or stay on the path that has served us so well.

FDA AND IMPORTED DRUGS

At a time in which drug safety problems overseas have become more and more prevalent, the United States has seen a massive change in sourcing of its pharmaceuticals. Today,

the vast majority of our drugs have foreign components, either as so-called "finished dosage form" -- the pill we get from the pharmacy; or Active Pharmaceutical Ingredient -- the active ingredient that is shipped to the United States for production of the final pill form. Yet in the face of this flood of drugs and drug ingredients from overseas, what are we doing to assure that they are as safe as drugs produced in this country?

Much of the recent concern about the quality of imported drugs focuses on whether FDA is capably regulating those products. I think not, but the reason for their failure is a critical piece in our understanding of how to correct the problems. We must recognize that FDA is asked to regulate these products with a law whose 70th anniversary is this year – a time in which there were few drugs being made anywhere in the world, and none being imported into the United States. The system created in 1938, with origins dating all the way to the turn of the last century, authorized FDA to examine imported drugs at the border and refuse entry to any drug that "appeared" to be unsatisfactory. Thus, the law placed the responsibility on the FDA to catch a problem and stop the drug's entry into our country, as opposed to asking the foreign manufacturer to demonstrate that they were taking care to follow established standards for drug production. So, while domestic drug manufacturers are held to a high standard of drug safety, with regular GMP inspections, foreign producers often need worry only about the remote possibility that an FDA inspector at a border crossing will find a problem and stop the drug's entry. Moreover, a domestic drug manufacturer using foreign ingredients can adhere to strict

quality control procedures, yet be victimized by a contaminated ingredient that was unsuspected. [2]

More specifically, we have failed to provide FDA with the appropriations and other tools it needs to carry out the mission we have assigned to them, such as:

- Staff to conduct regular inspections in foreign facilities as are now done for domestic manufacturing plants. The Food, Drug and Cosmetic Act dictates that each U.S. drug manufacturer be inspected at least every two years, but the current rate of foreign inspections is infrequent at best. Thus, we are buying ever larger percentages of our drug ingredients from producers in developing countries who receive virtually no FDA inspection, despite a Congressional determination that domestic manufacturers be inspected regularly.
- Modern IT systems that would allow FDA to effectively track and monitor the production and movement of imports. The import data system is so old and communicates so poorly with other FDA information systems that it is difficult for FDA officials to use risk as a predominant driver of their compliance;
- Registration procedures for foreign drug manufacturing that would allow us to know who is making drugs for our market, where they are located, and what they are manufacturing; and
- Port inspectors to examine the almost 20 million annual shipments of foods, drugs, and other products that FDA is expected to regulation. For over 400

[2] There is a long history of illegal additions and substitutions to our foods and drugs from foreign sources, ranging from illegal antibiotics in seafood, to the aforementioned antifreeze for glycerin, to the polysaccharide inulin in apple juice, to melamine in pet food, and most recently chondroitin to heparin.

ports of entry, FDA has only 450 inspectors, meaning that most ports aren't staffed at all and many can be staffed only part time.

THE HEPARIN EXAMPLE

We are, of course, especially mindful today of the recent deaths from contaminated heparin. It is, sadly, a good example of the problem FDA faces in assuring the safety of imported drugs. Indeed, I believe one could use the well worn cliché of a "perfect storm" in describing the conditions upon which the heparin incident unfolded -- initial extraction of heparin on pig farms that have been described as "primitive," no regulation by authorities in the producing country, no FDA inspection of the heparin exporter's manufacturing facility, and violative conditions found by FDA in the manufacturing facility when subsequently inspected. When you add to that the technical capability of chemists to modify and substitute chondroitin for heparin, the resulting profit margin by using cheaper ingredients, the low risk of being caught substituting another ingredient, and the even more remote likelihood of being punished by U.S. authorities, one could accurately conclude that there was highly fertile ground upon which this could occur.

I cannot overemphasize the disparity between such conditions and those in the United States. While certainly FDA has at times found U.S. manufacturing facilities in violation of GMPs, the circumstances here are far different. U.S. drug manufacturers accept the need for high standards in drug development and manufacturing and generally adopt those standards faithfully. Indeed, drugs manufactured in the United States are subject to a long list of stringent regulatory requirements, and failure of any of those requirements

will render the drug "adulterated" and thus illegal in this country. Moreover, drugs made in the United States under FDA's rigorous quality control standards have an extraordinarily good safety record, as measured by the paucity of manufacturing defects and deaths and illnesses related to manufacturing deficiencies.

WHAT MUST BE FIXED

We must find a way forward to ensure that drugs made with foreign ingredients meet the same high standards as those of fully domestic origin, by assuring the enforcement of the rules that govern drug production and the promulgation of needed new rules. It does no good to have rules if they are not obeyed, no good to set high standards if they are not used, and no good to develop advanced scientific skills if they are not employed. That some less developed countries have a record of serious problems in drug manufacturing is indisputable. And the disparity in drug inspections – in which FDA inspects U.S. facilities regularly and those in China and India almost never -- is indefensible.

Some would say that we should not be buying products such as drugs from developing nations, but that flies in the face of the reality of global free trade. Others would rely upon agreements negotiated with foreign countries, under which those nations would assure the safety of drugs exported to the United States. I believe that a developing country without a strong counterpart to the FDA is incapable of effectively implementing such an agreement, and that such a course of action is a prescription for frustration. In the end, I believe we must rely upon what we know has worked in the past to protect our

drug supply – rigorous control of pharmaceuticals within a system closed to unregulated and unscrupulous suppliers and overseen by a strong FDA.

More precisely, I urge you to consider the following ideas:

1) **An immediate infusion of new appropriations for FDA's drug oversight activities.** As FDA's Science Board recently concluded, the agency is massively underfunded, and the paucity of resources for overseeing imported drugs is particularly glaring. Indeed, despite the fact that such a large proportion of our drug supply is of foreign origin, FDA's funding for regulating imported drugs is less than 2% of the agency's budget.

2) **A requirement for GMP inspections of foreign drug manufacturing facilities, with an immediate focus on drugs made in countries without a history of safe drug production and internal regulation.** Without such inspections, we essentially have no oversight of those manufacturers. A GMP inspection is far more than just a snapshot of that facility the day the inspector arrives. It is a detailed survey of how that plant has been operating for months, which allows a realistic conclusion about whether that facility can and does follow accepted drug production procedures. Relying on testing by the FDA or the U.S. drug company that receives the foreign ingredients is not a substitute for examining the source of production.

3) **Creation of a Foreign Inspectorate for the FDA that is dedicated to inspecting foreign manufacturing facilities.** Currently, FDA must utilize its domestic inspection force to travel overseas to conduct inspections. That practice is expensive and often a hardship on inspectors. The agency needs to recruit an inspection force that is hired and

trained to do foreign inspections, and many will need to be housed in the countries with the greatest number of manufacturing facilities.

4) **A requirement that all foreign drug producers register annually with the FDA.** As the GAO has noted, FDA does not even have an accurate listing of drug manufacturers overseas. We need to know who is making our drugs, what compounds they are sending to our country, and where they are located.

5) **Appropriations and a specific Congressional mandate to improve FDA's IT systems.** If we don't even have a system for capturing who's making these products, where they are, what's coming into our country, and related critical information needs, we can't hope to begin the process of improving our coverage of imports. The IT systems should be configured in a way that allows the agency to use a myriad of risk factors, including potential impact on the public health, to direct its inspectional and import efforts. The Science Board recommends increased appropriations of $800 million for FDA's overall IT needs, so there is a long way to go if FDA is to have state-of-the-art information systems, but we could at least start with funding an effective import information system.

6) **A vigorous mechanism for testing drugs for ingredients or contaminants that are not approved for that compound**. History has shown that processors, especially in less developed countries, can be adept at adding substances to increase the value of the product or decrease costs of production. But the danger of doing so is well established, and poses an enormous hole in the safety net we are trying to maintain.

7) **Clear authority for FDA to inspect in foreign countries.** This is a very simple proposition - if a nation sending pharmaceutical ingredients to our country is unwilling to

allow FDA inspectors to examine facilities in their country for adherence to our safety standards, then those ingredients should not be allowed into the United States.

I believe FDA's scientists and regulatory officials are nothing short of terrific. They are well trained, intensely dedicated to the public health, and a true bargain for the American taxpayer. But they have been handed a task -- an expectation -- that they realistically cannot fulfill with their current resources. But history has shown that when FDA is given the resources and tools it needs to be effective, it will perform well and in doing so protect the health of those who depend every day on this critical agency.

Thank you again for inviting me to give my views on this subject.