Statement By

William K. Hubbard

Alliance for a Stronger FDA

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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. Today, 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 focused on proposed solutions to the ever increasing numbers of drugs and medical devices being imported into the United States. I will focus my comments on pharmaceuticals, but many of those comments would apply as well to medical devices.

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 has served us well. Under that construct, American patients have access to safe and effective new drugs as fast or faster than anywhere else

in the world, and FDA is widely recognized internationally as the "gold standard" for pharmaceutical regulation. FDA is also tasked with assuring that a drug, once approved for marketing, is actually the same compound that is manufactured and is of consistently high quality. To do that, FDA requires that a drug be manufactured under specific controls mandated by the agency—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. Those controls have resulted in a remarkable record of success for American pharmaceuticals. The U.S. manufacturers of our drugs agree with the need for such strict controls and take great care to implement them faithfully. Accordingly, FDA inspectors generally find adherence to GMPs when they examine a U.S. drug manufacturing facility, and the occurrence of injuries and deaths from improper drug manufacturing in this country is rare.

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, drugs made in other countries – particularly less developed nations -- are often purchased from suppliers who have little or no oversight by regulatory bodies; where key elements of safe

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

In recent years, this Committee has documented numerous reasons for concern about drugs made offshore:

- 80% of our domestic drug supply is now comprised of ingredients produced in other countries, and increasingly those are less developed nations such as China and India.
- FDA has the capability to inspect only a small percentage of foreign drug manufacturing facilities, and inspection rates of drugs arriving at U.S. ports are equally dismal.
- Deaths and injuries from compounds made overseas are seemingly more and more common – from antifreeze substituted for glycerin, melamine in pet food, antibiotics that don't effectively treat bacterial infections, and, of course, most recently, heparin contaminated with chondroitin.
- Counterfeiting of drugs is increasingly common in many countries, and has been steadily growing in the United States. 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 China alleged to be a principle world supplier of such products.

FDA AND IMPORTED DRUGS – NEED FOR A NEW PARADIGM

At a time in which drug safety problems overseas have become more and more prevalent, the FDA has simply not been able to keep up. While it can continue to ensure that drugs made in United States meet our high safety standards, the agency is not positioned and funded to assure the safety of imported drugs. FDA is asked to regulate these products with a law that was enacted 70 years ago – at 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.

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 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 realistic 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.

But the heparin case also demonstrates FDA's inherent weaknesses in its ability to adequately oversee foreign drug production. The facility in China had not been inspected by FDA, the suppliers of raw material to that facility were not registered with the FDA, and the agency's IT systems were not up to the task of identifying and tracking the facilities in China and the movements of their products. In sum, the FDA's poor capabilities, in my view, contributed to the likelihood that a counterfeiter could feel emboldened to substitute the chondroitin with relatively little fear of regulatory action by the United States.

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.

I believe that there are three main principles to be considered in correcting the imbalance between the strong safety oversight of US-produced pharmaceuticals and medical devices and those made overseas:

1) **FDA's statutory construct must be changed to take into account the globalization of drug and devices.** As you know, the current version of the Food, Drug and Cosmetic Act places much of the burden for assuring the safety of imported drugs onto the FDA

and at the point of entry – the border ports. That paradigm is outdated in a world that is far more globalized today, and more of the responsibility needs to be shifted to the source of production – to preventing problems from occurring rather than relying on FDA to find them at the border. FDA also needs to know that imports are equally important in the development of policy and the allocation of resources as domestic programs. Your proposal, if enacted, would make that point in several ways – by requiring the same frequency of inspection for foreign and domestic manufacturing facilities; allocating new resources for foreign inspections; creating a foreign inspectorate dedicated to overseeing manufacturing in exporting countries; giving FDA the information it needs about who is making these products and where they are located; and strengthening inspection of these products when the arrive at our borders with new powers to detain, destroy or recall drugs and devices that are deemed to be dangerous.

While inspections are not the only solution to these problems, they are an absolutely necessary piece. It is particularly important that we place a focus on drugs and devices made in countries without a history of safe manufacturing and internal regulation. Without GMP inspections in less developed nations, 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.

Your proposed creation of a dedicated foreign inspectorate will go far in ensuring that the inspection requirement can be successful. 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

2) **Build upon the best practices many U.S. firms already use in securing their supply chain.** Supply chain integrity is increasingly a watch word among leading pharmaceutical manufacturers. The most advanced firms today have contractual arrangements with suppliers that require strict conformance to quality control procedures, and insistence that every party to their supply chain be known to them and of sufficient technical competence. And those firms regularly inspect and monitor the performance of their suppliers, as well as test ingredients for purity, stability and other necessary qualities. I believe that your bill will reinforce the commitment of those firms already utilizing such practices and should encourage others to join in them. For example, the bill would ease entry into the United States of drugs and drug ingredients that can document compliance with applicable FDA drug safety requirements. Further, it will provide for additional contaminant testing which, in the light of the heparin injuries, will be a necessary part of a strengthened system of import controls.

3) **Send a message to foreign manufacturers and their nations' governments that the focus of regulation will shift from FDA's border inspection of drugs to the conditions in the overseas manufacturing facilities.** In the past, there have been relatively few incentives for foreign manufacturers to be assertive in protecting exported drugs and devices from contamination or other violations of FDA drug safety standards. Indeed, some contend that the current system – of placing most of the burden for catching unsafe drugs onto the FDA – has comprised a disincentive, thus indirectly encouraging ingredient substitution and other cost saving "short cuts." Your bill will start an important shift toward expecting exporters to take greater care in manufacturing drugs for our market – by requiring all foreign producers to declare their identity and location, by permitting FDA to suspend a facility's registration if it impedes an FDA inspector's ability to carry out his duties, by ensuring parity among U.S. and foreign drug inspections, by encouraging certification and other evidence of quality controls on the part of foreign drug facilities, by requiring foreign drug manufacturers to pay facility registration fees that mostly been limited in the past to American facilities, by ensuring that violative drug imports are more likely in the future to be either detained or destroyed if found at U.S. ports, and by requiring contaminant testing of drug ingredients before they leave the exporting country.

ADDITIONAL CONSIDERATIONS

While I believe that your bill contains most of the elements that FDA's scientists would like to have instituted for a safer drug import system, there are two additional considerations that I would urge you to include:

- Appropriated funds to strengthen the FDA. Your bill includes user fees to pay for more FDA oversight. Such fees are reasonable for facility registration, as domestic manufacturers must now pay such a fee, and bringing foreign facilities on par would be a logical addition. Plus, fees could have the complementary effect of driving from pharmaceutical manufacturing business some inadequate foreign facilities for which registration would trigger an eventual inspection. However, I am skeptical that user fees are the solution to FDA's funding problems, as budget officials have tended in recent years to shift agency funding from appropriated dollars to user fees, leaving the agency with little or no net gain. Indeed, some programs, such as food safety and FDA's inspection corps, have absorbed large staff cuts over the past decade, and I believe those cuts are largely attributable to the fact that other parts of FDA were receiving new funding from user fees (for drug and device application review). We, as American taxpayers, today spend only 1 and ½ cents per day on the FDA. I believe the vast majority of our citizens would gladly pay 2 or 3 cents a day for an effective FDA that can vigorously protect our food and drug supply.

- A commitment to information technology improvements. As your Oversight and Investigations Subcommittee, the GAO, and FDA's Science Board have all documented, FDA's inadequate IT systems are a fundamental lag on the agency's ability to improve its import program. I urge you to make IT enhancements a key goal of your legislation, even if that is achieved merely by a sense of the Congress statement about your expectations for IT 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.

In conclusion, 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. 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 for inviting me to give my views on this subject.