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OF**

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**BEFORE THE  
COMMITTEE ON HEALTH, EDUCATION, LABOR AND PENSIONS**

**UNITED STATES SENATE**

**“SECURING THE PHARMACEUTICAL SUPPLY CHAIN”**

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## **INTRODUCTION**

Good morning, Chairman Harkin and Members of the Committee. I am Deborah Autor, Deputy Commissioner for Global Regulatory Operations and Policy at the Food and Drug Administration (FDA or the Agency) in the Department of Health and Human Services (HHS). Thank you for the opportunity to discuss the safety of the American drug supply.

When President Franklin Delano Roosevelt established the modern FDA in 1938, the percentage of medical products imported into the United States was minimal. Today the landscape is reversed. Nearly 40 percent of the drugs Americans take are made elsewhere, and about 80 percent of active pharmaceutical ingredients (APIs) used in drugs manufactured in the United States come from outside our borders—from more than 150 countries, many with less sophisticated manufacturing and regulatory systems than our own. In addition to the sheer volume of imports and foreign facilities, there has been an increase in the variety of sources, shippers, methods of transportation and supply chain complexity of imported products, and our current authorities have not kept pace with the challenges of the current global marketplace. Combined, these factors create great challenges to FDA and industry in ensuring that all drugs are high quality and travel safely throughout their complex supply chains. These factors also provide opportunities for criminals to adulterate drugs for economic or other malevolent reasons.

When we refer to the drug supply chain, we are talking about the increasingly complex path that medical products travel, from raw source materials to finished products for consumers. At every stage in this process, opportunities arise for the product to be contaminated, diverted, counterfeited, or otherwise adulterated. The Internet presents an additional layer of complexity by introducing more players into the system and more opportunities for criminals to reach

consumers. Our efforts to secure the supply chain both in the United States and abroad include minimizing risks that arise anywhere along the supply chain continuum, from sourcing a product's raw material, ingredients, and components through the product's manufacture, storage, transit, sale and distribution. A breach at any point in this continuum could lead to dangerous and even deadly outcomes for consumers. Supply chain safety threats also impact manufacturers' bottom lines due to costs associated with both recalls and decreased public confidence.

As Members of this Committee well know, this threat is not purely hypothetical. Recent incidents of adulteration, counterfeiting, and cargo theft have posed serious threats to public health. The consequences, throughout the world, have been tragic. In recent years, glycerin in fever medicine, cough syrup, and teething products was adulterated with the highly toxic solvent, diethylene glycol (DEG), resulting in the deaths of adults and children in Panama, and children in Haiti and Nigeria. Over the last 20 years, drug products containing glycerin contaminated with DEG have caused an estimated 570 deaths worldwide. Also in 2007, pet food adulterated with the industrial chemical melamine and cyanuric acid sickened several thousand pets in our country. The same contaminant was added to infant formula in China, fatally poisoning six babies and making 300,000 others gravely ill. And Members of this Committee are well aware of the 2008 heparin contamination crisis that resulted in several deaths and cases of serious illness.

Counterfeit drugs raise significant public health concerns, because their safety and effectiveness is unknown. A counterfeited drug could be made up of a substance that is toxic to patients. But even a non-toxic counterfeit drug with a substitute or no active ingredient could prove harmful to patients who take it, thinking that they are taking a lifesaving or life-sustaining medication. In

2003, over \$20 million in illegally imported and counterfeit Lipitor, a popular cholesterol-lowering drug, was distributed throughout the United States. The source and manufacturing methods of the product were unknown and had the potential to endanger patients.

Cargo thefts of prescription drugs also pose a significant public health risk. In 2009 alone, an estimated 46 drug cargo thefts occurred, valued at a total of \$184 million. These incidents are concerning to companies and consumers alike. Cargo thefts can cost drug manufacturers millions of dollars. They can also put consumers at risk because the stolen drugs may not have been stored or handled properly or may have been tampered with while outside of the legitimate supply chain. In March of 2010, thieves broke into a warehouse and stole \$75 million worth of prescription drug products, including chemotherapy, antidepressants, and blood-thinners. These products have not yet been recovered, and we fear they could be distributed, in spite of public warning. In 2009, stolen insulin was reintroduced into the drug supply and caused adverse events in patients. The stolen insulin, which requires refrigeration, lost its potency and did not provide the needed glucose control.

In our increasingly complex and globalized world, additional authorities could be important tools to help support FDA's efforts to protect the safety of imports and the health of our citizens. New regulatory authorities may also help ensure that industry takes principal responsibility for the security and integrity of their supply chains and the quality control systems they use to produce medical products for the American people. FDA's efforts are also critical to ensuring product integrity. As such, we intend to further transform FDA over the next decade from a predominantly domestically focused Agency, operating in a globalized world, to an Agency fully prepared for a regulatory environment in which product safety and quality know no borders.

In June, FDA published a special report, “Pathway to Global Product Safety and Quality,” our global strategy and action plan that will allow us to more effectively oversee the quality, safety, and efficacy of all products that reach U.S. consumers in the future. The Agency is developing a new, more global operating model that relies on strengthened collaboration, improved information sharing and gathering, data-driven risk analytics, and the smart allocation of resources, leveraging the combined efforts of government, industry, and public- and private-sector third parties. Toward this goal, FDA Commissioner Margaret Hamburg created a directorate focused on grappling with the truly global nature of today’s world—food and medical product production and supply, as well as the science that undergirds the products we regulate—so that FDA can move from being a regulator of domestic products to one overseeing worldwide enterprises. She appointed me as Deputy Commissioner for Global Regulatory Operations and Policy to provide broad direction and support to FDA’s Office of Regulatory Affairs and Office of International Programs, with a responsibility to address the challenges of globalization and import safety a top priority in the years to come and to ensure that we fully integrate our domestic and international programs to best promote and protect the health of the public. I appreciate the opportunity to testify before you in my new role and look forward to working together to address the challenges we face in protecting our nation’s health in this increasingly globalized world.

#### Steps to Secure Our Nation’s Drug Supply Chain

FDA has undertaken a wide range of activities aimed at addressing the challenges and opportunities of globalization, including efforts to harmonize scientifically rigorous standards internationally, to share scientific and technical expertise with our fellow regulators, to provide training around the world in crucial regulatory disciplines, to strengthen detection, surveillance and assessment systems, and to design innovative risk-modeling systems.

We now have permanent FDA overseas posts in Beijing, Shanghai, and Guangzhou, China; New Delhi and Mumbai, India; San Jose, Costa Rica; Mexico City, Mexico; Santiago, Chile; Brussels, Belgium; London, England; and Parma, Italy. This year, we have opened posts in Amman, Jordan and Pretoria, South Africa. These offices enable us to have a regional presence around the world and serve as important hubs for improved coordination with regulatory authorities and industry in other nations. They also conduct and facilitate inspections and other on-the-ground activities in foreign sites. We have more than 30 agreements with foreign counterpart agencies to share inspection reports and other non-public information that can help us make better decisions about the quality and safety of foreign products.

When governments collaborate to strengthen safety standards, the results are safer, higher-quality products and enhanced economic development through a productive industry and a strong, reliable export market. The arrangement is mutually beneficial. To a large extent, our success or failure in this effort will be contingent on the relationships we establish with our foreign partners. That is why we are working closely with our sister regulatory authorities, international and national organizations, and industry to leverage resources to accomplish FDA's mission. Especially in the area of good manufacturing practices for drugs, we already have agreed with major foreign counterparts on some harmonized international standards. By using the results of their inspections to assure us that their manufacturing plants are adhering to our agreed standard, we free up our inspectional resources to help ensure that such manufacturing practices are being followed in other, higher-risk parts of the world. This also lessens the regulatory burden on industry, by allowing companies to manufacture to a common standard and to undergo fewer inspections by multiple authorities.

## After Heparin

The 2008 heparin contamination crisis is a case study in the vulnerabilities of the global supply chain. Heparin is a widely used injectable anticoagulant, derived from the mucosal tissue of pigs. In early 2008, contaminated heparin from China was associated with an increase in deaths in the United States. Whatever was contaminating this imported heparin could not be identified by the tests used at the time. After launching a far-ranging investigation, FDA scientists, working closely with academia and industry, developed a test methodology that identified a previously unknown contaminant in Chinese-manufactured heparin. The contaminated heparin contained oversulfated chondroitin sulfate (OSCS), an intentionally added adulterant. An outbreak of blue ear pig disease had killed off a large portion of China's pig population, creating an incentive for criminals to seek an alternative that mimicked the chemical makeup of heparin but, tragically, proved dangerous to consumers.

FDA publicly referred to the heparin contamination crisis as a "wake-up call." It was an alert not only for FDA, but also for U.S. citizens, industry, and lawmakers about our dependence on a globalized drug supply and the key vulnerabilities in our drug supply chain. FDA has taken a number of significant steps to safeguard the U.S. supply of this medically necessary drug. The Agency invested considerable resources to inspect heparin manufacturing and testing facilities related to the supply of heparin in the United States. Additionally, the United States Pharmacopoeia, a standards-setting organization upon which FDA relies, now calls for the testing of heparin to detect the presence of OSCS, the contaminant that sickened patients in 2008. FDA has also implemented heparin-specific import surveillance including an import alert and multiple warning letters to ensure that adulterated heparin does not enter our borders.

But our efforts have not stopped there. The heparin crisis was a crime of opportunity, and we need to minimize these opportunities. We are committed to putting preventive measures in place that will protect American consumers from adulteration of all imported drugs. We combine risk-based approaches with sound scientific evidence to protect the public from adulterated and unsafe drugs. The Agency takes several factors into account in determining whether a particular drug ingredient may be at risk for adulteration. For example, when a drug ingredient depends on raw materials that are particularly expensive, criminals may have extra incentive to find a cheaper alternative to the expensive ingredient. If the cheaper alternative can mimic the chemical activity of the product and thereby go undetected by standard testing, as was the case in the heparin and melamine incidents, the risk of adulteration is higher. To date, FDA has systematically ranked more than 1,000 APIs in order of their respective risk of adulteration, based on a multi-factorial, risk-based model we developed. A subset of these higher-risk ingredients is targeted for additional sampling and special testing at the border. In addition, FDA is working to reduce the risk that counterfeit or adulterated drug products reach consumers in the U.S. market by developing standards for a track-and-trace system that would enable the identification of these products and facilitate efforts to recall them.

Through the creation of my position and other activities at the Agency, we have made addressing the challenges of globalization a top priority. To support this effort, FDA can benefit from new legislative authorities that are, at a minimum, commensurate with those of its major global counterparts.

#### Drug Safety Authorities

In general, new regulatory authorities may help ensure that industry takes principal responsibility for the security and integrity of its supply chains and the quality control systems it uses to



produce drugs for the American people. In an era of globalization, new authorities can help to level the playing field between domestic and foreign manufacturers, ensure product safety and provide FDA with the information it needs to protect consumers. Those authorities may include:

### *Leveling the Playing Field*

- Refusal of product admission to the United States if inspection of the manufacturing facility is delayed, limited, or denied – this authority is critical to providing a strong incentive for foreign facilities to allow FDA to perform inspections and to permit FDA to exclude from domestic commerce products whose foreign manufacturers or facilities try to avoid subjecting themselves to the same requirements as domestic manufacturers and facilities. This authority is not currently explicit in FDA’s law for any product other than foods.
- Require information upon importation – the Agency can refuse entry of an import that appears from examination of samples or otherwise to be adulterated or misbranded, but FDA lacks authority to require certification or other assurance of compliance with applicable standards or requirements as a condition of importation, consistent with FDA’s standards and requirements for the domestic drug supply. This is the opposite of the approach taken by many other countries, which place the burden on the importer or product owner to prove that its drug is compliant with country requirements.
- Quality management systems – FDA currently works with industry to ensure that individual companies have effective quality management systems in place; however, additional statutory authority could place greater responsibility on manufacturers to account for the quality and provenance of the materials that go into their products. This would level the playing field between the companies that work diligently on their quality management systems to provide high quality products, and those that do not.

- While FDA does not seek to interfere with regulatory authorities outside the United States, having express authority to address threats to U.S. consumers, whenever and wherever they may arise, is critical.

### *Increasing Drug Safety*

- Mandatory recall authority – while in most instances firms eventually agree to voluntarily recall drugs that FDA believes pose a risk, FDA lacks the authority to compel such recalls and critical time can be lost in negotiations between FDA and a firm, leaving the public exposed to potentially serious health risks. The Agency currently has mandatory recall authority for medical devices, infant formula, and now many other foods, but not for drugs.
- Administrative destruction at the border – absent this streamlined authority, FDA is often forced to return violative products to their senders because the current process for destruction requires a hearing, which is time-consuming and costly. Foreign drugs can then find their way back to U.S. ports of entry several times, posing a potential threat to consumers and wasting critical resources that could be better spent identifying new threats. This authority would level the playing field for those who produce compliant products, whether located in the United States or abroad.
- Administrative detention – while FDA has the authority to administratively detain illegal foods and medical devices in U.S. commerce, it does not have a similar authority for drugs. Currently, we cannot immediately detain dangerous drug products when we find them. Absent this immediate tool, consumers can be exposed to unnecessary risks.
- Enhanced criminal and civil penalties for foreign and domestic suppliers – statutory changes could help to deter would-be criminals from targeting drug products, and bring FDA’s penalties in line with those for other serious federal health and safety violations.

### *Increasing Information*

- Modernization of drug registration and listing – revising these statutory provisions may improve the timeliness, completeness, and accuracy of FDA’s current registration and listing information, making sure FDA has accurate and up-to-date information about foreign and domestic parties involved in medical product manufacture.
- Notification to FDA – this authority would permit FDA to require foreign and domestic companies to provide complete information on threats such as counterfeiting, theft, non-compliance with regulatory standards, mislabeling or misbranding, or other threats to the security of the drug supply chain. Among other things, this would allow FDA to better spot emerging risks and trends across companies and then inform industry or take other proactive, preventive steps.
- Unique facility identifier – the absence of a system of unique drug facility identifiers, such as a D-U-N-S number, submitted to FDA both as a condition of registration and import, makes it difficult for FDA to properly follow threats up the supply chain and makes it more difficult to get different systems, including at different agencies, to properly cross-reference.
- Authority to share certain non-public information with other regulatory agencies and foreign governments – this authority would allow FDA to share certain information that could lead to timely identification, prevention, and resolution of emerging threats. Our ability to form global coalitions of regulators will be hampered if we cannot share critical information with our trusted partners.
- Track and trace – requiring a cost-effective track-and-trace system for all drug products throughout the supply chain would improve the security and integrity of the drug supply

and ensure transparency and accountability of product manufacturing and distribution, whether the product is manufactured domestically or internationally.

In our increasingly complex and globalized world, these additional authorities represent important tools to help support efforts to protect the safety of imports and the health of our citizens.

## **CONCLUSION**

Given the challenges and threats posed by an increasingly globalized marketplace, we must modernize our approach to drug safety. We appreciate the comments of Chairman Harkin and Ranking Member Enzi in July in support of including legislation in the reauthorization of the Prescription Drug User Fee Act (PDUFA) to address the challenges of globalization. We look forward to continuing to work together to achieve our shared goal of protecting American consumers. I would be happy to answer any questions.