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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

"CHINA'S HEALTHCARE SECTOR, DRUG SAFETY, AND THE U.S.-CHINA TRADE IN MEDICAL PRODUCTS"

BEFORE THE

U.S.-CHINA ECONOMIC AND SECURITY REVIEW COMMISSION

APRIL 3, 2014

FOR RELEASE ONLY UPON DELIVERY

INTRODUCTION

Chairman Shea, Vice Chairman Reinsch, and Members of the Commission, I am Christopher Hickey, Country Director for the People's Republic of China, in the Office of International Programs within the Office of Global Regulatory Operations and Policy at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss FDA's efforts to ensure global product safety and quality and our work related to China.

FDA is responsible for protecting public health by helping to ensure the safety, effectiveness, quality, and security of human and veterinary drugs, vaccines, and other biological products for human use, and medical devices. The Agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, and products that emit electronic radiation; and for regulating tobacco products. Imported products generally must meet the same standards as those produced domestically.

In my testimony today, I will discuss the challenges of an increasingly globalized marketplace, describe FDA's actions to safeguard the global supply chain, and discuss FDA's activities related to China, particularly in connection with medical products.

Challenges of Globalization

Sweeping economic and technological changes have revolutionized international trade over the last several decades and have created a truly global marketplace for goods and services. Products that FDA regulates represent a substantial component of this global economy, and account for about 20 percent of all U.S. consumer spending. Food and medical products, and their ingredients and components—products that directly and profoundly affect the health and welfare of the U.S. public—are increasingly sourced from abroad. Today, FDA-regulated products originate from more than 200 countries and territories and enter our market through more than 300 U.S. ports. The number of FDA-regulated shipments from abroad has more than tripled from 8 million import entry lines per year a decade ago to over 29 million entry lines in Fiscal Year (FY) 2013. In FY 2014, FDA anticipates that entry lines from abroad will reach 31 million.

Please note that FDA tracks import shipments using entry lines. For the Agency, an entry line represents each portion of a shipment that an importer lists as a separate item on an entry document. It is important to highlight the fact that entry lines do not have a direct relationship with the actual number of imported items. Some entry lines may represent one item, while others may represent thousands. This is a known limitation of the data in FDA import systems, because import filers are not required to declare volume per line and there is no standard format for declaring volume. As trade increases and U.S. consumers continue to demand global products, FDA's ability to ensure the safety and quality of these imported products will depend on its execution of a number of key strategies for global engagement.

Americans benefit greatly from global sourcing of medical products. For example, to support the care of patients, health professionals can draw from drugs and medical devices developed anywhere in the world, if they have been approved or cleared by FDA. Approximately 40 percent of finished drugs in the United States come from overseas, as well as more than 50 percent of all medical devices. Approximately 80 percent of the manufacturers of active pharmaceutical ingredients are located outside the United States.

This rapid globalization of commerce poses challenges. For example, drugs and medical device manufacturers have the responsibility for the safety and quality of the drugs and devices they produce. Some countries do not have strong regulatory system oversight to ensure industry is meeting the standards required for safety and quality of these products. Increased numbers of suppliers, more complex products, and intricate multinational supply chains can introduce risks to product safety and quality. Unfortunately, these factors also mean that consumers can more easily be exposed to risks, including those from intentional or unintentional adulteration, as well as those that come from exposure to contaminated products. Below, I will discuss FDA's implementation of its comprehensive strategy to use strong global partnerships to enhance the safety of imported products.

Many of the challenges associated with globalization manifest themselves in China; however, challenges we see in China mirror challenges we see in other countries with developing regulatory systems. In recent years, FDA has faced several public health threats related to imports from China. The members of this Commission will recall the threats to the safety of the country's heparin supply in 2007 and 2008, which emerged when Chinese suppliers of heparin (a

critical drug that helps to prevent blood clots) substituted a lower-cost, adulterated raw ingredient in their shipments to U.S. drug makers. This substitution caused numerous deaths, as well as severe allergic reactions. In 2007, FDA found shipments of toothpaste from China that contained poisonous levels of diethylene glycol, a product used in antifreeze. And in China's domestic supply chain in 2012, numerous companies used industrial-grade gelatin to make pharmaceutical-grade gelatin capsules for drugs and dietary foods. This industrial-grade gelatin contained more chromium than the edible gelatin that firms should have used.

FDA's success in protecting the American public depends increasingly on the Agency's ability to reach beyond U.S. borders and engage with its regulatory counterparts in other countries. This collaboration encourages the implementation of science-based standards to ensure the quality and safety of FDA-regulated products manufactured overseas and imported into the United States. It is equally important for FDA to partner with industry, and with regional and international organizations to accomplish this goal. FDA works with numerous partners to enhance responsibility and oversight for safety and quality throughout the supply chain.

Safeguarding the Global Supply Chain

To address the challenges described above and strengthen protections for American consumers, FDA engages in several different ways and collaborates with numerous stakeholders. Our efforts are in line with the 2012 U.S. *National Strategy for Global Supply Chain Security*,[1] which emphasizes the importance of taking a layered, risk-based approach to building global supply chain systems that are secure, efficient, and resilient. In 2011, FDA released its report, *Pathway*

[1] *http://www.whitehouse.gov/sites/default/files/national_strategy_for_global_supply_chain_security.pdf*

to Global Product Safety and Quality (the *Pathway* report),[2] which outlined the Agency's strategy to transform itself from a predominantly domestically focused Agency to one that is equipped to engage in today's complex, globalized regulatory environment. I would like to discuss just a few of the activities we are pursuing as part of this strategy.

International Offices and Foreign Posts

FDA's international offices and foreign posts help to build strong partnerships with our foreign counterparts by providing enhanced opportunities for cooperation and capacity building. They also expand our knowledge base, and provide a local platform for inspection of foreign facilities, particularly in emergency situations, when the ability to deploy in-country investigators is most vital. We now have a permanent FDA presence overseas in 11 foreign posts in eight countries. Our overseas officials are posted in China, India, Latin America, Europe, and South Africa.

Risk-based Monitoring of Imported Products

The Agency electronically screens all imports using an automated risk-based system to determine if shipments meet identified criteria for physical examination or other review. To enhance our ability to target high-risk products, FDA developed the Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting application, or PREDICT. This is a sophisticated screening application that uses information from many sources—such as intrinsic product risks, past inspection results, intelligence data, and even information about threats such as extreme weather that could spoil a shipment—to provide FDA entry reviewers with risk scores on every import line. PREDICT utilizes information sources that include data from FDA and the U.S. Customs and Border Protection (CBP), as well as data collected from our foreign

[2] *http://www.fda.gov/downloads/AboutFDA/CentersOffices/OC/GlobalProductPathway/UCM259845.pdf*

offices, foreign regulatory counterparts, other Federal agencies, and our state counterparts. It also utilizes risk analyses we receive from academic institutions and international organizations. As we continue to increase data sharing with state, Federal, and foreign government partners, as well as private partners, we will continue to incorporate more information into PREDICT. This application allows FDA to focus its resources on imports that are most likely to pose a danger, while simultaneously facilitating entry of low-risk products. FDA, the U.S. Department of Agriculture (USDA), and the U.S. Department of Homeland Security have also developed improved systems for monitoring for the potential of economically motivated adulteration, which uses CBP and trade data.

Technical Cooperation and Capacity Building

FDA recognizes the need to engage in effective regulatory cooperation with our global partners. It is important, where possible, for FDA to provide strategic support for counterpart regulators: governments are uniquely positioned to provide regulatory oversight of products, which today move fluidly through complex global supply chains. FDA is working strategically with key regulatory agencies to provide information, tools, training, and exchange programs that contribute to strengthening overall capacity, which can help to undergird our global safety net. Later in my testimony, I will describe some of our collaborative efforts with the Chinese Government.

This Commission asked FDA to articulate its views on Rx360. Rx360 is a nonprofit organization led by volunteers from the pharmaceutical and biotech industries. Both manufacturers and suppliers participate in Rx360's efforts to enhance the security of drugs by ensuring the quality and authenticity of products as they move through the supply chain. FDA

has been invited to participate in some Rx360 meetings, including Rx360's Supply Chain Steering Committee, as an observer. Rx360—especially its Supply Chain Steering Committee—has been a valuable resource for FDA. This Steering Committee has frequently solicited FDA's input so that Rx360 can, where appropriate, more closely align with FDA goals. In this context, Rx360 has often provided useful information to FDA in connection with supply chain security issues. Rx360's valuable work is exemplified by a recent campaign entitled "Protect Your Patients -- Know Your Supplier," which aims to educate the public about the following:

- The current global context in which counterfeiting and diversion occur.
- The challenges of unapproved drugs sourced from outside of the United States, especially when these products are pitched to health care providers as cost-saving measures.
- Risks associated with purchasing unapproved medication, such as threatened patient safety and criminal and civil liability for purchasers.
- How to determine if a product is legitimate.
- Tips for purchasing medication and verifying legitimacy.

We have found this campaign as well as other Rx360 collaborative efforts with FDA to be productive, and we look forward to continued partnership in the years to come.

Implementing Major New Laws

In addition to these activities, FDA is helping ensure the safety of imported medical products with the significant new authorities provided to it by Congress.

- The Food and Drug Administration Safety and Innovation Act (FDASIA)

  With the passage of FDASIA in 2012, Congress granted FDA important new authorities, reauthorized FDA's ability to collect user fees for its reviews of applications to market human drugs and medical devices, and similarly, authorized FDA, for the first time, to collect user fees for reviews of generic human drugs and biosimilar biologics. These authorities and fees will help to promote and protect public health in a number of key areas. They will help the Agency to continue to strengthen a predictable and efficient review process for medical products. These authorities and fees will also help FDA to combat drug shortages and enhance our efforts to ensure that American consumers have more timely access to safe, high-quality, affordable medicines. Finally, FDASIA will help to create incentives for industry to develop new antibacterial and antifungal drugs.

  Title VII of FDASIA focuses on improving the safety and integrity of the drug supply chain and drugs imported into the United States. Title VII's new authorities increase FDA's ability to act in several key areas. First, Title VII enhances FDA's ability to collect and analyze data to support risk-informed decision-making. Second, it gives FDA more tools to make accurate evaluations of facilities on the basis of risk. Third, it gives FDA greater authority to partner with foreign regulatory authorities to leverage resources through information-sharing and recognition of regulatory counterparts' inspections, when FDA deems such recognition appropriate. Finally, at the broadest level, it gives the Agency greater authority to mandate that firms meet more stringent requirements for safety and quality throughout the supply chain. For example, the law requires foreign and domestic companies to provide complete information on threats to the security of the drug supply chain and improves current

registration and listing information, which will help to ensure that FDA has accurate and up-to-date information about foreign and domestic manufacturers.

The new authorities that FDASIA provides align with the strategies outlined in the *Pathway* report. FDASIA promotes collaboration with global regulatory partners, use of data systems to facilitate information-sharing, and the key role of risk analytics. FDA is making significant strides in its implementation of this important new law.

- Drug Quality and Security Act (DQSA)

  The recently enacted DQSA outlines critical steps to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States.[3] Drug manufacturers, wholesale drug distributors, repackagers, and many dispensers (primarily pharmacies) will be called on to work in cooperation with FDA to develop this new system over the next decade. Within 10 years of enactment of this law, this new system will facilitate the exchange of information about where a drug has been in the supply chain, even down to the level of individual packages. The new system will enable FDA to verify the legitimacy of drug product identifiers down to the package level; enhance detection and notification of illegitimate products in the drug supply chain; and facilitate more efficient recalls of drug products.[4] Manufacturers, wholesale distributors, repackagers, and pharmacies must immediately quarantine and promptly investigate drug products deemed suspect or illegitimate. This could include suspected counterfeits, unapproved drugs, or

[3] In the *Administration's White Paper on Intellectual Property Enforcement Legislative Recommendations*, March 2011, at p. 2 ("White Paper"), the Administration recommended legislation to adopt a track-and-trace system for pharmaceuticals and related products. See *http://www.whitehouse.gov/sites/default/files/ip_white_paper.pdf*.

[4] Under current law, recalls for drug products are voluntary, as FDA does not have the authority to issue mandatory recalls of drug products.

dangerous goods, such as a recalled drug product. The relevant stakeholders noted above will be responsible for alerting FDA about such findings. This new system will improve detection and removal of potentially dangerous drugs from the drug supply chain to protect U.S. consumers.

FDA Activities Related to China

Nowhere is the shift toward a global marketplace more evident than in U.S. trade with China. China is the source of a large and growing volume of imported foods, medical products, and ingredients. Establishments that are involved in the production and distribution of medical products intended for use in the United States generally are required to register annually with FDA. Most of these establishments are also required to list the products that are made there. For example, in FY 2008 (the first year that data was collected in accordance with current standards), there were about 2,700 registered Chinese establishments; in FY 2013, there were almost 4,000. In FY 2008, there were about 10,500 device listings associated with Chinese establishments, while in FY 2013, there were more than 17,000 device listings, the vast majority of which were for Class I (low-to-moderate risk) and Class II (moderate-to-high risk) medical devices. As I mentioned earlier, FDA tracks import shipments by entry lines—the portion of a shipment listed as a separate item on an import entry document. In the years spanning FY 2007 and FY 2013, the total number of shipments of FDA-regulated products from China increased from approximately 1.3 million entry lines to 5.16 million lines. Of the 5.16 million lines arriving from China in FY 2013, almost 25,000 lines were drugs and biologics and 3.4 million lines were medical devices—again, the majority of these (96 percent) were Class I or Class II medical

devices, including surgical drapes and gowns, syringes and tubing, graduated medication containers, and gloves.

As the number of medical products coming from China has increased, so have the challenges. There are currently a number of active FDA Import Alerts that include medical products from firms located in China. These alerts signal FDA investigators at the U.S. border to pay special attention to a particular product, or a range of products from a particular country, manufacturer, shipper, or importer. Under these Import Alerts, products may be detained at the border and may be refused admission into U.S. commerce, unless the importer is able to demonstrate that the products are in compliance with relevant laws and regulations. The Import Alert process is a dynamic one, with firms and countries being added and removed on a regular basis. Product recalls are another challenge. Recalls of Chinese medical devices have been on the rise since 2011, from 11 in 2011 to 32 in 2013. FDA has issued most of these recalls because of design-related issues.

Drug inspections in China also have been increasing. In 2010, FDA conducted 46 drug inspections in China; in 2011, that number increased to 88; in 2012, FDA conducted 58 drug inspections; and in 2013, the Agency conducted 84 such inspections. The majority of the drug inspections FDA conducts in China focus on manufacturers of active pharmaceutical ingredients intended for use in generic drugs and on sites that produce over-the-counter drugs.

FDA is addressing the challenges outlined above in several different ways. We currently have 13 staff in China, posted in Beijing, Shanghai, and Guangzhou. This includes eight U.S. civil servants and five Chinese staff. Using funding Congress provided in 2013, FDA is currently

working to increase to 27 the number of U.S. officers it posts in China. The mission of FDA's China Office is to strengthen the safety, quality, and effectiveness of FDA-regulated products produced in China for export to the United States. FDA's China Office works to fulfill this mission through:

- Collaborating, capacity-building, and confidence-building with Chinese regulatory counterparts at central, provincial, and municipal levels;
- Conducting outreach to regulated Chinese firms that wish to export their products to the United States to enhance understanding of—and compliance with— FDA requirements;
- Monitoring and reporting on conditions, trends, and events that could affect the safety and effectiveness of FDA-regulated products exported to the United States;
- Conducting inspections at facilities that manufacture FDA-regulated goods; and
- Working closely with other key government and non-government stakeholders who work to strengthen the safety of FDA-regulated products manufactured in China.

In addition to other budget requests that focus on imports from China, the Agency's FY 2015 budget has requested $10 million in funding specifically for continuing the China Initiative. These new resources will strengthen the protection of American patients in the following ways:

- Strengthening FDA's inspectional and analytical capabilities by adding nine drug inspectors to FDA's China Office. The United States and China were able to address problems associated with visas for these staff during the visit of Vice President Biden to Beijing in December 2013, and FDA anticipates posting these new staff in country in

Fiscal Years 2014 and 2015. This will allow more rapid access to Chinese facilities and will help to increase the number of FDA inspectors who have in-depth knowledge and expertise about current challenges that Chinese industry faces.

- Broadening the range of inspections FDA performs in China. In addition to inspecting Chinese facilities that manufacture food and medical products for export to the United States, FDA will increase the number of sites it inspects that conduct clinical trials pursuant to investigational new drug (IND) applications, and will also perform follow-up inspections to ensure that firms continue to produce and manufacture food and medical products under safe conditions.

- Increasing opportunities for engagement with Chinese regulatory counterparts. Direct observation of FDA inspections can bolster Chinese regulators' understanding of FDA's requirements and processes and strengthen China's inspectional capacity.

- Enhancing Chinese regulators' knowledge of U.S. safety standards through participation in workshops and seminars, such as the International Conference on Harmonisation and the International Pharmaceutical Regulators Forum. These opportunities help facilitate dialogue and encourage scientific exchange on the critical role inspections play in improving the safety and quality of food and medical products.

- Strengthening FDA's ability to use informatics tools, such as trend analysis, predictive modeling, and geospatial mapping. These tools will help to sharpen FDA's understanding of potential public-health risks. Increased use of data will help FDA strengthen its systems in several key areas, including the implementation of science-based, harmonized standards. The ultimate goal is to detect and address risks through preventive, risk-based approaches before those risks result in harm to U.S. consumers.

China's Food and Drug Administration

China's Food and Drug Administration (CFDA) is responsible for regulation of food, drugs, and devices for domestic distribution in China, and for regulation of certain exported food, drugs, and devices. In March 2013, as part of attempts to reform China's food safety system, Chinese central authorities created CFDA as the inheritor of the role formerly played by the State Food and Drug Administration (SFDA). Even with this reform, which is still in process, CFDA remains an agency with several key remaining challenges. In 2011, SFDA published new requirements for good manufacturing practices for drug manufacturing—standards that were widely viewed as a significant step forward. By the end of 2013, CFDA had made numerous strides in implementing these requirements, but significant work remains. Like many Chinese Government ministries, CFDA also faces significant challenges as it works to balance the role of central and provincial authorities. CFDA will continue to work for some time to develop sufficient technical and scientific depth to address China's current challenges.

FDA, through efforts led by its China Office, has established a strong working relationship with CFDA. Since 2008, we have conducted formal monthly meetings with CFDA to discuss strategic regulatory issues, collaboration and joint capacity building, and emerging issues of bilateral concern. Collaborative discussions on the staff level occur on a weekly, or even daily, basis. And each year since the signing of our 2007 Agreement with SFDA on the safety of medical products, we have convened a high-level bilateral meeting between senior U.S. and Chinese regulatory authorities.

We have made key strides with CFDA. In 2009 and 2010, as SFDA worked to reform its GMP regulations for drugs, it sought out FDA's input into its draft regulations. The FDA China Office, working with experts in FDA's Center for Drug Evaluation and Research, provided feedback on these draft provisions and saw significant elements of FDA's suggestions incorporated into SFDA's new standards, which were published in 2011. When CFDA went to implement these standards, an expert from FDA's China Office conducted training for over one thousand Chinese inspectors on how to conduct inspections against such standards.

In the area of clinical trials, we have made substantive efforts, as well. Over the course of three years, from 2010 through 2012, an FDA expert conducted multiple workshops with SFDA to create a self-sustaining system to train Chinese inspectors on how to assess the quality and reliability of data from sites that conduct clinical trials.

In the area of medical devices, experts from FDA's Center for Devices and Radiological Health now meet regularly with their counterparts from CFDA under the auspices of the International Medical Devices Regulatory Forum, as China has recently joined this key Forum. FDA's China Office helped to encourage CFDA's participation in this important multilateral venue.

In the area of inspections and enforcement, FDA has made significant progress with CFDA, as well. CFDA inspectors now regularly observe FDA inspections in China. And since 2012, FDA's Office of Criminal Investigations has worked closely with CFDA to enhance U.S.-China collaboration in the fight against Internet-based, illegal distribution of adulterated drugs. In recent years, CFDA has taken initial steps to learn about the requirements to join the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme

(PIC/S), an international organization consisting of 44 member regulatory agencies (including FDA) and partner organizations, such as the World Health Organization and the United Nations Children's Fund, which oversee the manufacture of pharmaceutical drugs imported into their regions. FDA has met with CFDA on several occasions to explain the PIC/S accession process and what is needed to apply and become a member. PIC/S' Secretariat has also encouraged CFDA to participate in PIC/S' international training programs.

Finally, FDA has seen significant strides in cross-cutting areas as well. Following a high-level agreement during the visit of FDA Commissioner Margaret Hamburg to China in August 2012, FDA and SFDA created a working group on economically motivated adulteration (EMA). EMA—the fraudulent substitution of a substance in a product to increase value or reduce production costs for the purposes of economic gain—has played a key role in a number of recent product safety crises in China, including the series of adverse events associated with adulterated heparin in 2008, and the 2012 use of so-called "gutter oil" in antibiotics manufactured in China.[5] EMA continues to be a key factor in understanding product safety issues in China today. The U.S.-China working group on EMA in medical products now meets on a regular basis, linking Washington-based experts with CFDA's key decision-makers. Through its engagement in this working group, FDA aims to expand the thinking of Chinese regulators about EMA and to create a common platform to work to address the underlying incentives that prompt some perpetrators to adulterate products to make a quick profit.

[5] "Gutter oil" can be defined as spent cooking oil that is normally discarded (into the street) and that might contain toxic products from thermal degradation.

CONCLUSION

Thank you for giving FDA the opportunity to describe the Agency's efforts to address the challenges of our globalized marketplace and to discuss our work in China. FDA is implementing a comprehensive strategy to enhance the safety of imported products and to establish an effective global safety net.

Our priorities in China are consistent with our priorities everywhere. The best way to ensure the integrity of medical products is to make sure firms consistently follow appropriate processes for safeguarding safety and quality in production. Manufacturers are best situated to ensure these processes, and regulatory bodies should hold companies accountable for lapses in the production process and not simply rely on testing after the fact to detect flaws. Inspections and testing play an important role in that process, but they need to be used as part of a larger system that emphasizes a systematic, proactive, preventive approach to the production of safe, effective, high-quality medical products. And in our globalized world, it is increasingly important that regulatory partners work together to ensure the safety of products as they move across borders. While many future challenges remain as we engage Chinese regulators and industry on these key issues, we will continue to expand on successes we have seen in recent years.

I am happy to answer any questions you may have.