DEPARTMENT OF HEALTH & HUMAN SERVICES

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FOOD AND DRUG ADMINISTRATION
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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"DISCUSSION DRAFT OF THE 'FOOD AND DRUG ADMINISTRATION GLOBALIZATION ACT' LEGISLATION: DRUG SAFETY"

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INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, Food and Drug Administration (FDA or the Agency). Thank you for the opportunity to discuss FDA's progress in responding to the challenges created by drugs for the United States (U.S.) market that are either fully manufactured overseas or that are manufactured in the U.S. but contain foreign components. FDA's mission is to ensure that safe and effective medical products are available to patients in the U.S., regardless of where they are produced. In my testimony today, I will outline activities the Agency is undertaking to accomplish this goal.

ACTION PLAN FOR IMPORT SAFETY

As you know, last year, President Bush issued an Executive Order creating a Cabinet-level Working Group on Import Safety to promote the safety of imported products, and asked Secretary Leavitt to lead the group. The working group, which includes representatives from twelve Federal departments and agencies, including the U.S. Department of Agriculture (USDA), and the Department of Commerce, reviewed the procedures, regulations, and practices for ensuring that imported food, drugs, and other consumer products are safe.

On November 6, Secretary Leavitt presented the "Action Plan for Import Safety" to the President. This Action Plan presents broad recommendations and specific short- and long-term action steps, categorized under the organizing principles of prevention, intervention, and response. Each action item is based on the building blocks identified in the Strategic Framework, released in September 2007. That report concluded that the

U.S. must transition from an outdated "snapshot" approach to import safety, in which decisions are made at the border, to a cost-effective, prevention-focused model that identifies and targets critical points in the import life cycle where the risk of the product is greatest, and then verifies the safety of products at those important phases. In the Action Plan, we identified several new legislative authorities that are needed to do this.

Prevention

To comply with the Food, Drug, and Cosmetic (FD&C) Act, any entity that intends to import drugs into the U.S. must ensure that the drug meets a number of quality and labeling requirements. In the FD&C Act, Congress enacted provisions to create a relatively "closed" distribution system for imported drug products to help ensure the domestic supply is safe and effective. Generally, drugs may be imported into the U.S. only by a manufacturer with an approved application. This manufacturer may receive products or components from its foreign facility or another company's facility that was listed in that particular drug application. All "new drugs," which includes all finished prescription drug products, must be approved by FDA as safe and effective for their intended use. FDA approvals are manufacturer-specific and product-specific, and include many requirements related to the product, such as manufacturing location, formulation, source and specifications of active ingredients, manufacturing controls, the container/closure system, and labeling. Facilities that manufacture drugs for the U.S. market are referenced in an approved application and must meet FDA's current Good Manufacturing Practice (cGMP) requirements.

FDA is seeking to ensure that imported drug products are safe and effective and meet all applicable FDA standards *prior* to reaching U.S. ports-of-entry. FDA is pursuing this goal through the following key efforts.

Maximizing Foreign Medical Product Pre-Approval Inspections. Prior to the approval of a new drug application or abbreviated new drug application, FDA must determine that the manufacturing processes are adequate to produce a safe and effective drug, and ensure its identity, strength, quality and purity. Each year, FDA performs hundreds of foreign pre-approval inspections which assess data in applications and a firm's cGMP compliance. These inspections are designed to evaluate the capability of manufacturing facilities to generate a safe and high-quality product. FDA conducted more foreign inspections in Fiscal Year (FY) 2007 than any other in the Agency's history. For example, in FY 2007, FDA conducted 332 inspections of foreign drug manufacturers, compared to 260 in FY 2004, 266 in FY 2005, and 212 in FY 2006. We plan to conduct 500 in FY 2009. While, inspections are an important component of the Agency's systematic approach to ensuring the safety of imported medical products, they alone cannot fully address these challenges.

Beyond Our Borders Initiative. The FDA Beyond Our Borders Initiative is a multi-pronged approach to promote and verify compliance of imported food, cosmetics, and medical products with FDA requirements. This Initiative includes increased FDA presence in China, increased FDA inspections, greater sharing and use of foreign competent authority inspection reports and other information, use of third party

certification, and increased capacity building with countries that have less developed regulatory systems to ensure product safety.

Foreign Presence. China is one of the largest exporters of drug products for the U.S. market. Recently, FDA and HHS leadership, the Department of State, and the U.S. Ambassador to China committed to establishing an FDA office in China this year**.** On March 8, 2008, the Department of State approved FDA to place 13 total staff in China (eight FDA personnel and five Foreign Nationals). This staff will be responsible for building closer working relationships with our Chinese counterparts, carrying out inspections, and working with Chinese inspectors to provide training. FDA is in the process of making the necessary arrangements and preparing to hire staff. This effort builds on two recently-signed Memoranda of Agreements (MOA) with two Chinese FDA counterpart agencies that facilitate broader access to Chinese production facilities on an expedited basis. This is a significant step toward ensuring the safety and efficacy of medical products produced for the U.S. market. FDA's efforts will build stronger cooperative relationships with counterpart agencies in China, enhance technical cooperation with these agencies, and foster the flow of information between regulatory systems. Having an overseas presence in China will improve our ability to inspect facilities in China and, very importantly, foster greater interactions between FDA staff and Chinese manufacturers to help ensure that products shipped to the U.S. meet FDA standards for safety and manufacturing quality. In addition, FDA is working to establish beneficial collaborations with India, another large exporter of drug products to the U.S.

Ramping Up The Field & International Staff. To meet the challenges posed by the increase in the globalization of U.S. drug development, FDA must significantly strengthen its field and international inspection operations. Goals for FY 2009 include increasing foreign and domestic inspections and sampling, improving our laboratory infrastructures, continuing to develop tools for rapid analysis, and, as previously mentioned, establishing an in-country presence in China.

Sharing Foreign Inspection Reports. FDA currently has in place more than 70 cooperative arrangements with foreign counterparts. As previously mentioned, Secretary Leavitt signed a MOA with the State Food and Drug Administration of the People's Republic of China to enhance the safety of drugs and medical devices imported into the U.S. from China. In addition, FDA now has over 30 confidentiality arrangements with trusted foreign counterparts, many of which provide mechanisms for sharing inspection reports. FDA intends to increase the use of these arrangements to obtain useful information that can help the Agency make more informed judgments about the acceptability of foreign-sourced products, in prioritizing our foreign inspection activities, and on detaining unsafe products.

Providing for Certification by Third Parties. Another component of the Agency's Beyond Our Borders Initiative leverages private sector resources. As recommended in the President's Action Plan for Import Safety, FDA is pursuing the use of third party certification to verify compliance with FDA requirements. These third parties may include foreign government agencies and independent entities who have been accredited by FDA or accreditation organizations recognized by FDA. With proper structuring to

stimulate the use of third party certification, this certification would complement, but not supplant, FDA inspectional and other regulatory activities.

Providing Technical Assistance. Another essential element of the Agency Beyond Our Borders initiative focuses on helping foreign regulators understand FDA standards, laws and regulations by providing technical assistance to counterpart foreign regulators and outreach assistance to foreign industries that engage in trade with the U.S.

Intervention

FDA recognizes the importance of a strong and effective intervention capacity to identify problems as they occur.

Information Technology (IT). FDA has several plans to enhance its IT systems in ways that will enable the Agency to better utilize risk-based information from the entire life-cycle of imported products. These projects will improve databases, enhance interoperability of systems within the Agency and among other regulatory agencies, and provide better analytical function to assess and control risk. We expect these improvements will help to target our intervention efforts related to foreign firms. For example, FDA plans to improve its listing and registration systems to allow the Agency to more accurately identify who is manufacturing medical products and what is being commercially distributed in the U.S.

Expanding Laboratory Capacity & Development of Rapid Test Methods. FDA must be agile and scientifically sophisticated, with the ability to develop rapid test methods for detection of pathogens and other contaminants in drugs, and to ensure that these test

methods are available at ports-of-entry to assist in determining whether a product should be admitted into the U.S. FDA research laboratories develop and validate methods, such as the test FDA developed to determine the contaminant in heparin ingredients imported from China. This novel testing method is now accepted and used worldwide to detect the presence of hypersulfated chondroitin sulfate in heparin.

Increasing Surveillance Inspections. In addition to pre-approval inspections mentioned previously, FDA conducts surveillance inspections of domestic and foreign manufacturers and uses a risk-based priority model to determine which facilities may pose a risk to the American consumer. FDA staff must consider a number of elements in making a risk-based priority determination. In part, these elements include: the dosage form coming to the U.S. from the foreign country, the date the facility was last inspected, the compliance history of the firm, the firm's shipping volume and history, and information from the local regulatory authorities regarding the manufacturing quality and regulatory status of the establishment.

Holding U.S. Manufacturers Accountable. The President's Action Plan for Import Safety outlines several action steps intended to help ensure that domestic companies importing foreign source material meet their responsibility to import safe and effective medical products. These manufacturers have a responsibility to ensure the safety of foreign-manufactured components and ingredients used in their finished products. FDA inspects all facilities listed in a drug application, both foreign and domestic, to determine if they meet the Agency's quality standards. During these inspections, FDA routinely evaluates the domestic drug manufacturer's testing and controls of ingredients (domestic

and foreign-sourced) and supplies. If deficiencies are discovered, the Agency may take enforcement action.

Response

When a health threat emerges with any FDA-regulated product, whether manufactured domestically or abroad, FDA must be ready to take immediate action.

Making the Border an Integrated Checkpoint. FDA works with Customs and Border Protection (CBP) at the border to refuse admission of products that appear to violate the FD&C Act. When we have sufficient information to refuse future shipments of a product, FDA can issue an Import Alert for Detention Without Physical Examination. This means FDA can detain regulated articles based on information that the articles appear to violate the FD&C Act, rather than on the results of actual sample examination. The Action Plan for Import Safety calls for increased FDA and CBP cooperation, including the development of interdepartmental procedures for clearing and controlling shipments at ports-of-entry, co-locating FDA and CBP at locations to improve coordination and efficient use of resources, and greater import information sharing between FDA and CBP through new technology applications.

Rapid Deployment of "For Cause" Inspections. When FDA has information that raises doubts about the safety of a regulated product, it will rapidly conduct domestic or foreign "for cause" inspections. In such cases, the Agency targets a particular firm or product as an inspection priority based on this information and rapidly deploys an inspection team.

Expanded Use of Track-and-Trace Technologies. FDA is working to facilitate the adoption of track-and-trace technologies to identify and track a product along the product life-cycle. These technologies will facilitate the timely recovery of the violative product and reduce the opportunity for harm, as well as secure the integrity of the supply chain by providing an "e-pedigree," an electronic record documenting that the drug was manufactured and distributed under secure conditions**.** The use of track-and-trace technologies will give FDA the ability to connect the dots and link important life-cycle information back to the point-of-origin. Under the Food and Drug Administration Amendments Act of 2007, FDA is working to develop or recognize electronic standards and validation for track and trace technologies.

NEW AUTHORITIES REQUIRED

The Action Plan for Import Safety called for providing a number of new authorities in order to enhance the safety of imported products. It requests authority to establish both voluntary and mandatory import certification programs -- using accredited third parties (which could include federal departments, foreign governments, or private entities) -- to verify compliance of foreign products with U.S. safety and security standards. As appropriate, import certification would include periodic on-site inspections, random testing and certification renewal based on product risk. Product certification could be mandatory for certain high-risk products coming from countries with which the U.S. has entered into agreements. Under the agreements, the countries or accredited third-parties would certify products as meeting U.S. standards prior to their export to the U.S. Such a procedure would be limited to high-risk products that have been shown to pose a threat to

public health. Additionally, the plan recommends authorizing FDA to refuse admission of a foreign manufacturer's product when FDA encounters undue delay, limits, or denials of access to the foreign manufacturing sites where the product was produced. At present, foreign firms can deny inspectors access to their facilities without any adverse consequence. The plan also requests authority to expedite destruction of refused medical products, which will prevent unsafe medical products for personal use from entering the U.S. market. Finally, amending the FD&C Act to include asset forfeiture remedies for certain criminal offenses involving fraudulent or counterfeit products would allow the forfeiture of all vessels, vehicles, aircraft and other equipment used to aid in the importing, exporting, transporting, selling, receiving, acquiring and purchasing of violative products by those who knowingly and willingly violate the Act.

The lack of explicit jurisdiction for the FD&C Act offenses can hamper FDA's ability to investigate the overseas offenders that violate the FD&C Act, but whose conduct occurs entirely outside the territorial jurisdiction of the U.S. For example, foreign firms can often deny U.S. officials access to their facilities without any adverse consequences. Amending the FD&C Act to provide for explicit extraterritorial jurisdiction for conduct that occurs outside the U.S. where products subject to the FD&C Act are intended to be imported into the U.S. would be consistent with principles of due process. Such an amendment would better enable FDA to address criminal conduct that occurs entirely outside of the U.S. and threatens the health and safety of consumers within the U.S.

FDA GLOBALIZATION ACT OF 2008

We commend the Members of this Subcommittee and their staffs for developing the discussion draft entitled, the "Food and Drug Administration Globalization Act of 2008." We recognize and appreciate the Committee's efforts to include new authorities requested by the Administration in support of the Action Plan for Import Safety.

We are in the process of reviewing the discussion draft in detail and we look forward to working with you on this legislation. At this time we can, however, make some general principles that guided the development of the Action Plan for Import Safety which we believe should also guide the development of product safety legislation.

- Any legislation should allow FDA to set requirements and priorities based on a strong scientific FDA risk assessment.
- Given the breadth and scope of drug products imported into the U.S., as well as those produced domestically, FDA cannot rely on inspection as its primary means of ensuring product safety. Any legislation should build on the framework in the Action Plan for Import Safety, i.e., building in safety measures to address risks throughout a product's life cycle and focus efforts on preventing problems first, and then using risk-based interventions to ensure preventive approaches are effective, coupled with a rapid response as soon as a problem is detected.
- While the Administration is supportive of user fee programs in which regulated industry provides funding for additional performance and efforts or programs designed to recoup the costs of regulatory actions resulting from findings of violations (such as reinspections), the Administration will carefully review any

proposed user fee program to ensure that it is being assessed against identifiable recipients of special benefits derived from Federal activities beyond those received by the general public.

- Any legislation should be carefully designed to avoid creating real or perceived trade barriers, and several provisions of the bill may need to be reviewed in light of U.S. trade agreement obligations. We are reaching out to the U.S. Trade Representative for further insight on these.
- Any legislation should empower robust voluntary private sector efforts already underway.

With these in mind, we believe the proposed legislation should be more closely targeted and prioritized according to risk. Several of the legislative sections appear not to be sufficiently focused on high-risk products. Some of these requirements would divert resources, which could detract from important drug safety and security priorities. In addition, the legislation should more explicitly incorporate the Administration's strategy of leveraging third party certification and efforts by foreign nations already underway.

CONCLUSION

As you can see, efforts are underway at FDA to ensure the safety and efficacy of human drugs, regardless of where they are manufactured. We share your interest in enhancing the safety of imported products and look forward to continuing to work with Members and staff on the Committee and Subcommittee. We also look forward to working with you on the Action Plan for Import Safety. Thank you for the opportunity to testify today, and I am happy to respond to any questions you may have.