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BEFORE THE U.S. SENATE COMMITTEE ON HEALTH, EDUCATION, LABOR AND PENSIONS
HEARING ON "SECURING THE PHARMACEUTICAL SUPPLY CHAIN", SEPTEMBER 14, 2011
TESTIMONY SUMMARY

PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies that are devoted to inventing new, life-saving medicines that help patients live longer, healthier, and more productive lives.

The regulatory system that governs the development, approval, marketing, and surveillance of new drugs and biologics in the United States is the most complex and comprehensive in the world. In addition to the requirement to obtain FDA approval of a New Drug Application (NDA) before a new drug may be sold in the U.S., manufacturers of pharmaceuticals sold legally in the U.S. must also comply with the "gold standard" of quality manufacturing – FDA's current Good Manufacturing Practice (cGMP) regulations. These regulations apply to all new prescription drugs approved for sale in the U.S., wherever they are made, and extend to all components of a finished drug product, including active pharmaceutical ingredients (APIs), without regard to where those ingredients are sourced. In addition, America's prescription drug distribution system is a closed system. Coupled with the comprehensive regulatory requirements and oversight of the FDA, our closed distribution system provides assurance regarding the quality, safety and integrity of the products lawfully sold in the US, and helps minimize the possibility of a consumer receiving a counterfeit drug.

As the Committee considers the issue of securing the pharmaceutical supply chain, we are pleased to provide the following preliminary comments, and look forward to an ongoing dialogue on these important issues.

PhRMA believes that all foreign establishments manufacturing prescription drug products or components destined for import into the U.S. must register with FDA and list their products, to the extent they are not already required to do so under current law.

PhRMA supports granting FDA discretion to set routine inspection intervals for foreign and domestic facilities according to risk. This will enhance the FDA's ability to target its inspection resources efficiently and effectively.

Congress should consider allowing FDA to rely on the inspection results of other foreign regulatory bodies with similarly robust drug regulatory oversight systems or to use accredited third parties to conduct some foreign inspections (such as inspections of facilities considered moderate to low risk, based on appropriate criteria). This will provide FDA with the flexibility to leverage the work of foreign regulatory bodies and maximize its resources, all without foreclosing its ability to inspect any facility.

As we consider whether new authorities are needed to help strengthen our existing prescription drug supply chain, we must also consider the appropriateness of including new burdens on the import of materials for use in preclinical and clinical investigations.

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SEPTEMBER 14, 2011

Mr. Chairman, Ranking Member and Distinguished Members of the Committee:

I am pleased to testify today on the issue of "Securing the Pharmaceutical Supply Chain." My name is Kendra Martello, Assistant General Counsel at the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies that are devoted to inventing new, life-saving medicines that help patients live longer, healthier, and more productive lives. In 2010, America's biopharmaceutical research companies invested more than \$67 billion in the research and development of new medicines.

Biopharmaceutical research and development is a complex, risky and uncertain undertaking. On average, the time to develop a new medicine is 10-15 years, at a cost of over \$1.2 billion. Moreover, our companies provide – directly and indirectly – millions of stable, high-paying jobs for American workers. These jobs can help fuel our nation's economic recovery. Accordingly, FDA's regulation of new medicines should not stifle innovation in the biopharmaceutical sector.

I. FDA Oversight of Prescription Drug Manufacturing

America's patients trust that the medicines they take meet the high standards set by the Food and Drug Administration (FDA) for safety and efficacy and are not substandard or counterfeit, and they rely on our comprehensive drug regulatory system to help ensure that is the case. America's research-based biopharmaceutical companies also depend on a safe, secure prescription drug supply chain.

The regulatory system that governs the development, approval, marketing, and surveillance of new drugs and biologics in the United States is the most complex and comprehensive in the world. FDA regulates virtually every stage in the life of a prescription medicine sold in the U.S., from pre-clinical testing of investigational compounds in animals and human clinical trials before a medicine is sold, to manufacturing, labeling, packaging, and advertising, to monitoring actual experience with the drug after its approval. Further, FDA receives

information about shipments of imported goods into the U.S., and has developed a risk-based information system to help facilitate the targeting of certain shipments for further examination at U.S. ports of entry.¹

In addition to the requirement to obtain FDA approval of a New Drug Application (NDA) or a Biologics License Application (BLA) before a new drug may be sold in the U.S., manufacturers of pharmaceuticals sold legally in the U.S. must also comply with the “gold standard” of quality manufacturing – FDA’s current Good Manufacturing Practice (cGMP) regulations.² These regulations apply to all new prescription drugs approved for sale in the U.S., wherever they are made, and extend to all components of a finished drug product, including active pharmaceutical ingredients (APIs), without regard to where those ingredients are sourced. FDA’s cGMP regulations are based on the fundamental quality assurance principle that quality, safety and effectiveness “cannot be inspected or tested into a finished product,” but instead must be designed and built into a product.³ It is well-established that inspections alone cannot be relied upon to ensure product quality and integrity, but that quality systems are also vital to ensuring the product meets established specifications and requirements.⁴ The quality systems approach to manufacturing drug products is embodied in the cGMP regulations.

Thus, while FDA inspections are an important part of FDA’s regulatory authority and oversight, and PhRMA member companies are routinely inspected, the cGMPs represent a comprehensive, systems-based approach requiring a company to build quality directly into the entire manufacturing operation, in order to ensure that the process itself is under control and therefore will consistently produce a drug product that meets designated specifications. Further, the word “current” in front of the phrase “good manufacturing practice” in the FDCA recognizes and appreciates that these manufacturing standards are and must be flexible and adaptive to accommodate different types of products and advances in science and manufacturing technologies.

Currently, in addition to the requirement that API must be manufactured in accordance with cGMPs, manufacturers are also required to ensure that representative samples of each shipment of each lot of a drug component are tested or examined “for conformity with all appropriate written specifications for

¹ See Statement of Margaret A. Hamburg, MD, Commissioner of Food and Drugs, Before the Subcommittee on Oversight & Investigations, Committee on Energy & Commerce, “Import Safety: Status of FDA’s Screening Efforts at the Border,” April 13, 2011.

² Under current law, a drug is adulterated if the methods used in, or the facilities or controls used for, manufacturing a drug product do not conform to cGMPs, and FDA regulations and guidance provide additional clarification regarding the expectations of cGMPs in drug product manufacturing. 21 U.S.C. § 351(a)(2)(B).

³ 61 Fed. Reg. 20104, 20105 (May 3, 1996).

⁴ See generally 21 C.F.R. Parts 210 and 211.

purity, strength, and quality.”⁵ Any lot that does not meet such specifications must be rejected by the manufacturer and may not be used.⁶

Finally, the Prescription Drug Marketing Act of 1987 (PDMA) is a critical piece of consumer legislation passed as a result of Congressional investigations into the integrity of the drug distribution system that existed at the time. The PDMA created the closed prescription drug distribution system in place today, meaning that products that have circulated overseas may not lawfully be sold in the United States, unless they have remained under the control of the original manufacturer. Coupled with the comprehensive regulatory requirements and oversight of the FDA, our closed distribution system provides assurance regarding the quality, safety and integrity of the products lawfully sold in the US, and helps minimize the possibility of a consumer receiving a counterfeit drug.

II. Preliminary Ideas to Strengthen Supply Chain Integrity

Even with FDA's comprehensive regulatory system, increasing globalization of pharmaceutical supply chains presents challenges that require biopharmaceutical companies and the FDA to be more adaptive and flexible in the review and oversight of entities located around the world.

FDA should use its powerful existing enforcement authorities to take action against violative products and to promote accountability among regulated entities – enforcement authority that the FDA under the current Administration has made a priority to exercise when warranted. In short, supply chain security is the responsibility of all parties involved in the distribution of medicines to American patients. We appreciate the Committee's long-standing commitment to these issues. As the Committee considers the issue of securing the pharmaceutical supply chain, we are pleased to provide the following preliminary comments, and look forward to an ongoing dialogue on these important issues.

A. Registration of Foreign Facilities

PhRMA believes that all foreign establishments manufacturing prescription drug products or components destined for import into the U.S. must register with FDA and list their products, to the extent they are not already required to do so under current law. By requiring such facilities to register, the FDA will be able to establish a single database that will contain information on all facilities that manufacture products or components of products that are sold in the U.S. Prior Congressional testimony and Government Accountability Office reports suggest that such information appears in several different formats and databases managed by FDA, and, therefore, it is not easily accessible or usable by Agency personnel. A single, standardized database would, among other things, allow the FDA to help ensure that all facilities subject to inspection are identified, that FDA

⁵ 21 C.F.R. § 211.84(d)(2).

⁶ 21 C.F.R. § 211.84(e).

inspections can be prioritized, and that routine inspections occur at appropriate intervals. FDA Commissioner Hamburg has also expressed support for modernizing the Agency's registration and listing function.⁷

B. Enhancements to FDA's Inspection Regime

i. Risk-Based Inspection Intervals

PhRMA supports granting FDA discretion to set routine inspection intervals for foreign and domestic facilities according to risk. The use of risk-based approaches to regulation, and in particular, to cGMP inspections is not a new concept.⁸ We support providing FDA with the flexibility to prioritize inspections of foreign establishments based on the risks they present, and believe relying on set criteria such as compliance history, time since last inspection, and volume and type of products produced, will enhance the FDA's ability to target its inspection resources efficiently and effectively.

ii. Increase Foreign cGMP Inspections

We also recognize that while FDA has broad authority to conduct inspections of domestic and foreign facilities, it currently conducts limited numbers of cGMP inspections of foreign facilities, including API manufacturers. Therefore, we recommend that FDA generally increase its cGMP inspections of foreign facilities, including API manufacturers, to help ensure that cGMPs are being followed. The targeting of these increased foreign inspections should be accomplished by utilizing the risk-based approach described above.

iii. Foreign Inspection Reports/Accredited Third Parties

In recognition of the fact that the Agency does not have unlimited resources and in order to help ensure that foreign inspections occur on a more regular basis, Congress should consider allowing FDA to rely on the inspection results of other foreign regulatory bodies with similarly robust drug regulatory oversight systems or to use accredited third parties to conduct some foreign inspections (such as inspections of facilities considered moderate to low risk, based on appropriate criteria). These inspections would not take the place of FDA inspections, which are a necessary and important part of the Agency's mandate; however, they would provide FDA with the flexibility to leverage the work of foreign regulatory bodies and maximize its resources, all without foreclosing its ability to inspect any facility. FDA recently acknowledged and embraced the concept of relying on "public and private third parties to conduct

⁷ See Statement of Margaret A. Hamburg, MD, Commissioner of Food and Drugs, Before the Subcommittee on Oversight & Investigations, Committee on Energy & Commerce, "Import Safety: Status of FDA's Screening Efforts at the Border," April 13, 2011.

⁸ See e.g., "FDA Guidance: Risk-Based Method for Prioritizing GMP Inspections of Pharmaceutical Manufacturing Sites – A Pilot Risk Ranking Model," (Sept. 2004).

audits and other oversight activities on behalf of FDA.”⁹ FDA intends to quickly “establish the framework and approach for capturing this opportunity.”¹⁰

iv. Exemption for Materials Intended for Research Use

As we consider whether new authorities are needed to help strengthen our existing prescription drug supply chain, we must also consider the appropriateness of including new burdens on the import of materials for use in preclinical and clinical investigations. The continued, uninterrupted access to clinical trial materials, including APIs, is essential to ensure that vital research into innovative, life-saving and life-enhancing new treatments is not hindered in any way. Materials and articles used in pre-clinical research and development activities are never consumed by humans, but instead are used in laboratory testing as scientists try to understand how the test article works and its safety profile. The FDA requires reports of non-clinical laboratory testing and the submission of detailed information in a range of areas in order to justify the study of a candidate drug in humans, and materials used in the pre-clinical research and development process are not studied in humans. Further, investigational drugs and drug components imported for use under an Investigational New Drug (IND) application are subject to strict FDA regulation and oversight at all times and must be manufactured according to cGMPs, including appropriate standards for testing and quality control.

Thus, we strongly encourage the inclusion of an exemption for drugs, API, and other materials intended for use in clinical trials that comply with other FDA requirements relating to the proper use of investigational material, including labeling and import of investigational products and materials for use in U.S.-based clinical trials under an IND application filed with the FDA into any new provisions related to securing our pharmaceutical supply chain. Including these investigational products and materials in any new provisions could potentially be duplicative of existing requirements. Additionally, exempting investigational materials, drugs, and drug components used for pre-clinical and clinical research from any new provision could help ensure that the development of new medicines is not delayed or hindered and that clinical trials and research and development continue to occur in the U.S. – thus helping ensure that related jobs stay in the U.S. as well.

III. Conclusion

We commend the Committee for its focus on and commitment to the issue of securing the pharmaceutical supply chain. We recognize the importance of

⁹ “Pathway to Global Product Safety and Quality: Special Report,” Food and Drug Administration, (July 7, 2011), at 31, available at: <http://www.fda.gov/AboutFDA/CentersOffices/OC/GlobalProductPathway/default.htm>.

¹⁰ Id.

ensuring that the regulatory system in place today for prescription drugs continues to remain the best and the safest in the world. We cannot underemphasize the potential that exists for unsafe and potentially dangerous counterfeit drugs to enter the U.S. should Congress act to open our borders to more expansive prescription drug importation proposals. These proposals would allow non-U.S. approved drug products to be sold on U.S. pharmacy shelves next to FDA-approved drug products that have undergone our rigorous testing, review and approval process and put American patients at risk, and the FDA agrees.¹¹

Our system of prescription drug supply chain security today is very, very good, but even good systems can be improved upon. We look forward to continuing to work with the Committee, FDA, and other stakeholders on these important issues. Thank you for the opportunity to testify today and I welcome any questions you may have.

¹¹ See e.g. FDA Home Page: "Importing Prescription Drugs," <<http://www.fda.gov/Drugs/DrugSafety/ucm170594.htm>>.