FDA U.S. FOOD & DRUG ADMINISTRATION

February 12, 2020

The Honorable Charles E. Grassley
Chairman
Committee on Finance
United States Senate
Washington, DC 20510

Dear Chairman Grassley:

Thank you for your letter regarding the Safe Importation Action Plan (Action Plan) and your interest in how the U.S. Food and Drug Administration (FDA or the Agency) will ensure the safety and efficacy of drugs imported under the Action Plan. We appreciate hearing from you on this important issue.

As you are aware, in July 2019, the Department of Health and Human Services (HHS) and FDA released the Action Plan to describe steps HHS and FDA will take to allow the safe importation of certain drugs originally intended for foreign markets.[1] The Action Plan describes two pathways to provide safe and effective drugs to consumers in the United States at a lower cost. On December 23, 2019, FDA published the Notice of Proposed Rulemaking (NPRM) and the Notice of Availability for the Draft Guidance associated with each respective pathway.

Pathway 1 involves an NPRM that would implement an importation program under section 804 of the Federal Food, Drug, and Cosmetic Act. The rule, if finalized, would allow importation of certain prescription drugs from Canada under programs sponsored by states or certain other non-federal governmental entities and authorized by FDA. The NPRM includes requirements to ensure that the importation poses no additional risk to the public's health and safety and that the program will achieve significant cost savings to the American consumer.

Pathway 2 involves a guidance which would provide recommendations to manufacturers for importing FDA-approved drug products they manufactured, and originally intended to sell, in foreign countries. To use this pathway, the manufacturer, or person authorized by the manufacturer, would establish with FDA that the foreign version is the FDA-approved product (e.g., it is manufactured in accordance with the specifications in the FDA-approved application). FDA would then allow the drug to be imported and labeled for sale in the United States. Manufacturers could acquire and use a new National Drug Code for those products, potentially permitting them to offer a lower price compared to what their current distribution contracts require.

[1] See: https://www.fda.gov/about-fda/reports/fda-safe-importation-action-plan

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Toward the goal of lowering prescription drug prices in the United States, we will be working hard to review comments made to the *Federal Register* dockets for the NPRM and draft guidance and to finalize these documents on an expedited basis.

Your letter also encouraged the use of unannounced inspections and stated that it was unclear how track-and-trace would apply to products under the Action Plan. HHS and FDA understand the vital importance of preserving the drug supply chain's security for continued patient access to safe and effective medicines. Under both proposed pathways outlined in the Action Plan, FDA could take action to protect patients when the Agency finds violations of applicable requirements, including those that pose a significant risk to public health.

The U.S. drug supply chain is among the safest in the world. FDA prioritizes domestic and foreign inspections based on the facilities and medicines that have the potential to be the most problematic. The Agency inspects drug manufacturing facilities around the world, and 80 to 90 percent of them – regardless of location – are substantially compliant with good manufacturing practice requirements. When FDA identifies manufacturing issues, regardless of whether the facility is located in the United States or elsewhere in the world, we quickly take action to address such issues.

Drug manufacturing has become increasingly complex and global, requiring FDA to remodel its oversight of these tasks to improve the Agency's efficiency and reach. In June 2017, the Center for Drug Evaluation and Research (CDER) and the Office of Regulatory Affairs (ORA) entered into an unprecedented concept of operations (ConOps) agreement to integrate FDA's facility evaluations and inspections for human drugs.[2] The agreement, *Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations*, outlines the responsibilities and the workflow for pre-approval, post-approval, surveillance, and for-cause inspections at domestic and international facilities. ConOps enables CDER and ORA to effectively manage the growing complexity of the pharmaceutical landscape.

Despite FDA's efforts, there may still be "bad actors" that fail to meet the good manufacturing practice obligations. Over the past 4 years, CDER's Office of Compliance has substantially increased the number of warning letters issued to human drug manufacturers regulated by FDA. For example, in fiscal year (FY) 2018, the Agency issued nearly five times as many warning letters to human drug manufacturers as in FY 2015. FDA does not believe that the increased number of warning letters reflects a growing problem in drug quality but instead reflects the Agency's ability to better utilize resources to target problem areas. The Agency uses "risk-based" targeting to prevent, uncover, and combat data and manufacturing problems.[3]

FDA conducts both domestic and foreign inspections with comparable depth and rigor. For both inspections, the Agency uses the same highly trained investigators who conduct each inspection

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[2] For more information on the ConOps agreement, visit https://www.fda.gov/drugs/pharmaceutical-quality-resources/integration-fda-facility-evaluation-and-inspection-program-human-drugs-concept-operations and https://www.fda.gov/media/107225/download.

[3] The Office of Pharmaceutical Quality's Manual of Policies and Procedures (MAPP) 5014.1, *Understanding CDER's Risk-Based Site Selection Model*, outlines the policies and procedures for the Site Selection Model used by CDER staff to prioritize manufacturing sites for routine quality-related (current good manufacturing practice) surveillance inspections. This MAPP is available at https://www.fda.gov/media/116004/download.

in accordance with the same compliance programs. In many cases, FDA must announce its intention to conduct a foreign inspection in advance to be sure the firm is operational and to avoid wasting inspection resources. However, when the Agency determines the need to do an unannounced inspection, FDA can and does conduct such operations. For example, over the past several years, FDA investigators have conducted unannounced inspections at foreign manufacturing facilities in India and China when needed. When significant issues are uncovered at a foreign manufacturing facility, regardless of whether the inspection was announced in advance, the Agency acts expeditiously to protect patients by placing the facility on an import alert to block its medicines from reaching U.S. patients.

Although it takes only one bad actor to create a health issue for patients, it is important to note that most facilities and companies pass FDA's inspections and are manufacturing safe, effective, and high-quality medicines. FDA's laboratory testing for drug quality, using testing standards set by the United States Pharmacopeia or submitted in marketing applications, has consistently shown that medicines manufactured in foreign countries meet U.S. market quality standards.

Thank you again for your interest in this important matter. The Agency looks forward to working with you as it executes this plan.

Sincerely,

Hahn

Stephen M. Hahn, M.D.
Commissioner of Food and Drugs