TESTIMONY

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Introduction

Good morning, Chairwoman DeGette, Ranking Member Guthrie, and members of the subcommittee. Thank you for the opportunity to be here today to discuss the Food and Drug Administration's (FDA or the Agency) role in combating our Nation's ongoing crisis of opioid addiction, specifically regarding fentanyl. I am Carol Cave, Director of the Office of Enforcement and Import Operations (OEIO) within FDA's Office of Regulatory Affairs (ORA). OEIO provides direction, assistance, management and oversight of field import operations, including investigational and compliance activities; and serves as the Agency focal point for headquarters/field relationships on all import programs, operations, and problems. OEIO staff monitor more than 43 million import lines[1] in a given year, including medical devices, drugs and biologics, human and animal foods, cosmetics and tobacco products. OEIO coordinates agency import activities with U.S. Customs and Border Protection (CBP), including the development and institution of joint regulations, procedures, policies, and operations; and coordinates activities with other Federal agencies and foreign governments with border responsibilities through interagency agreements, memoranda of understanding, and informal working relationships.

As FDA has stated, and I am sure we all agree, this is one of the most profound public health challenges facing our country. FDA along with our partner government agencies continue to work together, to consider more active and creative steps to make inroads against this crisis. We must continue to be vigilant in our efforts to identify and stop unlawful drugs like illicit fentanyl from entering the United States, and as such, I am pleased to be here today to discuss the work we are doing at our Nation's borders and at the International Mail Facilities (IMF).

How controlled substances are managed at the border

In the commercial environment, CBP is the initial regulatory authority over all imported products and shipments are accompanied by formal entry declarations. For pharmaceutical products, including controlled substances like fentanyl, CBP evaluates these entry declarations and routes entries to the appropriate partner government agency for review. Controlled substances falling directly within the purview of the U.S. Drug Enforcement Administration (DEA) will be processed accordingly by CBP. Controlled substances that are also FDA-regulated drugs (i.e. approved pharmaceuticals or investigational use drugs) will be routed to FDA to determine admissibility: 1) FDA-regulated drugs must come from firms registered with FDA, 2) those firms must include the drugs they intend to market in the U.S. in a list provided to FDA, 3) new drugs must be approved by FDA, and 4) the entry declarations must reflect a supply chain identified in that approval (i.e. the product must be coming from and destined to firms indicated as part of the

[1] An import line is a distinct product within a shipment. A single shipment may include multiple lines.

drug's manufacturing process). If any of these requirements are not met, the drug will be refused admission into the U.S.

In the international mail environment, CBP is the lead interdicting authority for controlled substances, including fentanyl and other opioids. As such, they examine before FDA and generally will act against these types of shipments without forwarding for FDA review. These types of shipments do not fit the business-to-business supply chain pattern that the Agency typically notes for legitimate shipments of drug components.

It is our experience that legitimate commercial shipments of drug products enter the country via conventional means; air, rail, ship, and express consignment can all be part of a legitimate supply chain. However, FDA does not consider informal entry through international mail to be a method that sponsors of legitimate pharmaceutical products commonly use. So far in FY 2019, we have found 99.1% of the drug products entered the U.S. through international mail to be non-compliant.

FDA plays an important role related to the interdiction work that takes place in IMFs and has acted to enhance our operations there. When an illegal controlled substance is identified at an IMF, our partners at CBP will immediately seize it, and it will therefore not come to FDA investigators in these facilities. Instead, FDA is focused on inspecting, and sometimes testing, products that may be FDA-regulated drug products that violate the Food, Drug, and Cosmetic Act; for example, if they appear to be counterfeit or unapproved drug products.

While we examine what initially are believed to be non-opioid drug products, we still identify a large amount of controlled substances, in some cases because they are disguised as other types of drug products. From October 2018 through May 2019, FDA staff at the IMFs processed nearly 17,204 suspicious packages containing 28,356 products that FDA was tasked with inspecting because they were suspected of containing illegal prescription or counterfeit drugs or dietary supplements.

SUPPORT Act and FDA/CBP Letter of Intent

Last year, Congress gave FDA more tools to intercept illicit drugs coming through our Nation's IMFs by enacting the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (the SUPPORT Act). On behalf of FDA, I would like to thank the members of this Committee for your work on these important authorities. It calls for strengthening coordination and capacity between FDA and CBP on activities designed to improve detection and response to illegal controlled substances and drug imports, particularly those imported through the nine IMFs throughout the country. Section 3014 provides that these collaborative activities may be set forth in a memorandum of understanding between FDA and CBP and should include infrastructure and resource enhancements to increase inspection capacity at IMF locations while ensuring employee safety.

On April 4, 2019, FDA and CBP leaders signed a Letter of Intent that addresses the areas of cooperation outlined in Section 3014, including information sharing, operational coordination for better targeting of higher risk parcels, and collaborative strategies more specific to each agency's respective regulatory enforcement requirements. FDA and CBP have been actively working to expand the scientific presence at IMFs where most appropriate and to explore ways to enhance collaboration and increase efficiency of operations by sharing existing, limited space.

Section 3022(d) of the SUPPORT Act gives FDA new authority to treat imported articles as drugs when they meet certain requirements, even in the absence of certain evidence of intended use. This authority, codified as section 801(u) of the Federal Food, Drug, and Cosmetic Act, applies to articles that are "ingredients that present significant public health concern," and that are, or contain, either 1) active pharmaceutical ingredients (APIs) in a drug or biologic approved or licensed for marketing or for investigational use; or 2) an analog of that API. Furthermore, the article must not be accompanied by an electronic import entry submitted using an authorized electronic data interchange system and not be designated in such system as an article that is FDA-regulated (in other words, the import entry is not a commercial entry that is filed in the Automated Commercial Environment (ACE)). This means any imported product entering the U.S. via international mail that meets the requirements of section 801(u) is considered a drug under FDA jurisdiction. This allows FDA to apply its existing authorities to appropriately detain, refuse, and/or administratively destroy these subject articles.

Between March 4, 2019, when 801(u) implementation began, and the end of May 2019, FDA staff in the IMFs processed 7,011 parcels containing 11,295 products. Of those 11,295 products, we have applied our new 801(u) authority to 4,017 drug products (35.6% of the overall products encountered; and 39.8% of the drug products encountered). Of the 4,017 drug products on which we have used our 801(u) authority, 2,639 have been refused admission into the U.S. and will be destroyed; another 1,176 have been detained and identified for destruction, if refused. As of the end of June, an additional 185 drug products are still going through our admissibility process. For those drug products without a final admissibility decision, a final decision will be made based on additional review and follow-up.

The implementation of 801(u) is an unquestioned success: in FY2018 we destroyed approximately 5% of refused drug products; in FY2019 pre-801(u) implementation that number was about 16%. Since 801(u) implementation (through May 2019), we have raised our overall destruction rate to 35%; for 801(u) products specifically, our destruction rate is roughly 99%. FDA continues to identify additional APIs amenable to 801(u).

Office of Criminal Investigations

My office works closely with ORA's Office of Criminal Investigations (OCI). OCI's Special Agents work with other federal law enforcement agencies in a combined effort to disrupt and dismantle criminal organizations that threaten public health through the manufacture and sale of unlawful FDA-regulated products, including drug products containing illicit fentanyl. OCI

focuses their investigative efforts involving imported fentanyl specifically to drug counterfeiting operations to ensure case work is not duplicated and resources are properly managed. Many of OCI's investigations concerning fentanyl involve raw materials or tooling originally manufactured in other countries, such as China, and shipped to the United States via internet sales.

FDA's intelligence obtained through criminal investigations, data from import and regulatory inspections, and open source information shows that many Chinese-based manufacturing operations not only lack sufficient controls for drug products, but also produce and export a variety of synthetic opioids. Some of these manufacturers also synthesize new substances that produce effects similar to opioids with pre-market analytical reference names, such as Am-2201, Jwh-018, and U-47700. In addition, many counterfeit drugs sold online that appear to be FDA-approved medications, such as Oxycontin (oxycodone), Xanax (alprazolam), Vicodin (hydrocodone), or Percocet (oxycodone), may contain fentanyl or fentanyl analogs. OCI has investigated several such cases.

FDA continues to work with foreign authorities to combat the illicit manufacture of drugs. When actionable criminal information or intelligence is obtained, OCI works jointly with foreign and domestic law enforcement partners to identify and dismantle the source of supply. OCI has developed relationships with our law enforcement partners in India and the United Kingdom, for example, to work joint operations targeting illicit FDA-regulated products, including those that have been adulterated to contain fentanyl, intended for distribution in the United States.

OCI's Import Operations Program Special Agents are assigned to IMFs and directly coordinate investigative leads generated by the inspectional activities of FDA. These agents work closely with other Federal partners such as DEA, CBP, U.S. Immigration and Customs Enforcement, and the U.S. Postal Inspection Service to investigate the source and destination of parcels found to contain illegal FDA-regulated products as well as share valuable intelligence with our domestic and foreign law enforcement partners.

Facility, equipment and information technology improvements

Improvements and upgrades to facilities and resource enhancements to strengthen coordination and increase inspection capacity at IMFs are ongoing and have been accomplished to varying degrees across the nine IMFs throughout the country. As set forth in the Letter of Intent, FDA and CBP will be working through FY 2019 to improve the effectiveness and efficiency of their operations in the IMFs by continuing to share existing space and have submitted to the General Services Administration (GSA) space requests cooperatively, looking for co-location opportunities that meet each agencies' requirements.

FDA has assigned additional dedicated staff to coordinate space requirements and formal GSA space requests and has submitted these requests for seven of the nine IMFs. In many cases, onsite space is very limited and difficult to secure, and alternatives, such as the use of nearby sites and placement of office trailers and mobile laboratories on a temporary basis are being considered. Facility "build out" plans to improve capacity and efficiency of existing facilities are being developed while FDA and CBP await a final national GSA/U.S. Postal Service (USPS) common lease agreement. FDA is working collaboratively with GSA and USPS leadership towards reaching an agreement. The common lease agreement will dictate terms of GSA leases with USPS at the IMFs.

As FDA is able to increase the amount of space allocated to its activities in the IMFs, FDA can further add staff, enabling the Agency to expand its admissibility review of drugs shipped into the U.S. in international mail parcels.

FDA is committed to adding dedicated personnel to support increasing IMF workloads, particularly to help stop illegal opioids and other controlled substances from coming into the U.S., and to increase overall inspection capacity. As of July 1, 2019, ORA has hired more than half of the 125 full-time equivalents (FTEs) allocated to this purpose. This includes import review Consumer Safety Officers, OCI Special Agents, laboratory personnel, and support staff. ORA has developed a strategic hiring plan to maximize the ability to recruit and hire additional FTEs, and expects to have the remaining FTEs hired by December 2019.

The Letter of Intent also addresses FDA's and CBP's commitment to establish an expanded scientific presence at IMFs considered most at risk of receiving opioids and other illegal or dangerous drugs entering the United States. FDA and CBP are looking at ways to develop and refine laboratory-based methods to identify unapproved, counterfeit, and other unlawful controlled substances.

ORA's Forensic Chemistry Center (FCC) is a rapid-response laboratory that performs laboratory research and analyses on a day-to-day basis, regularly providing expert technical support for OCI. The laboratory also provides forensic analyses for high profile samples collected within the rest of ORA and other Federal and State agencies. The FCC has evaluated field-deployable instruments in the IMFs, resulting in recommendations regarding toolkits for screening of counterfeit or unknown substances. The FCC continues to evaluate new field-deployable devices to assess applicability for use to detect additional substances. Efforts to develop laboratory-based methods to identify and quantify fentanyl, fentanyl analogs, and other natural, semi-synthetic, and synthetic opioids continues at the FCC. In addition, FDA/ORA Medical Products Laboratories are also standing up capabilities to identify and quantify selected opioids as well as other illegal/unapproved drugs in preparation for confirmation of field-based findings in pharmaceutical products.

FDA is currently expanding its use of field-deployable instruments to detect illegal drugs in mail parcels. Laboratory personnel hired in support of this work are expected to provide permanent scientific and technical coverage at selected IMFs, but finding space that would allow laboratory

analysts to work alongside FDA import review staff and OCI's Special Agents remains a challenge. Plans are underway that will provide permanent space for analytical equipment and laboratory analysts to conduct testing.

While plans for larger and more permanent space to detect and test for illegal drugs by FDA laboratory personnel are being developed, discussions with CBP to identify space at selected IMFs to place temporary or mobile laboratories are ongoing. Provided space agreements between GSA and USPS can be reached, the intention is to have these temporary labs in place and operational by the end of FY19. In addition, we are developing plans for the FCC building renovation to include expansion within its current facility. Additional FCC laboratory space is needed to house personnel and analytical tools required to support FDA's commitments at the IMFs and Ports of Entry.

ORA import managers have met several times with their counterparts at CBP and USPS to discuss each agency's operational processes and look at their respective data systems to assess how they can be utilized to share data and information on actions taken by the agencies on individual parcels and commodities. All three agencies are considering the most appropriate and efficient means of using existing data streams to share IMF-specific data and investigational outcomes. For years, agencies have been working to align with ACE, as this may be the most efficient way to provide access to agencies that need it.

FDA is also improving IT infrastructure within the IMFs to increase overall connectivity and speed. Historically, connectivity to FDA systems from within the IMFs has been limited; we are currently assessing several approaches to determine effectiveness in enhancing connectivity within the IMFs.

ORA's Office of Regulatory Science continues to work with the CBP Director of Laboratory and Scientific Services to plan for laboratory personnel from both agencies to have a greater presence and complementary tools to share real time data at IMFs. The agencies will share historical data to improve consistency in their decision making. This will include sharing analytical reference library information developed by each organization related to this work.

Conclusion

We remain committed to using our regulatory authority to the fullest extent to address the opioid crisis, including using new authorities granted to FDA by the SUPPORT Act, and building on the important work I have outlined to change the trajectory of this crisis. As the committee continues to address this crisis, FDA looks to support where we can. Thank you for the opportunity to testify today, and I look forward to answering your questions.