October 15, 2020

The Honorable Frank Pallone
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515

Dear Chairman Pallone:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the December 10, 2019, hearing before the Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, entitled "Securing the U.S. Drug Supply Chain: Oversight of FDA's Foreign Inspection Program." This letter is a response for the record to questions posed by the committee.

If you have further questions, please let us know.

Sincerely,

Digitally signed by Andrew M. Tantillo -S
Date: 2020.10.15 14:37:14 -04'00'

Andrew Tantillo
Acting Associate Commissioner for
Legislative Affairs

cc: The Honorable Greg Walden, Ranking Member, Committee on Energy and Commerce

The Honorable Diana DeGette, Chair, Subcommittee on Oversight and Investigations

The Honorable Brett Guthrie, Ranking Member, Subcommittee on Oversight and Investigations

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

Your questions are restated in bold, below, followed by FDA's response.

The Honorable Frank Pallone, Jr. (D-NJ)

1. **A previous report from the Government Accountability Office raised certain concerns about post-inspection processes, such as delays in the Center for Drug Evaluation and Research (CDER) receiving inspection reports and subsequently taking action against firms if necessary. This report also indicated that CDER sometimes did not verify that foreign firms took the corrective actions mandated by the Food and Drug Administration (FDA) after an inspection.**

   a. **When results from an inspection of a foreign firm indicate that corrective action is needed, does FDA always conduct a follow-up inspection to determine whether that firm took those corrective actions? If not, under what circumstances does FDA decide not to conduct a follow-up inspection?**

   b. **What actions other than follow-up inspections does FDA take to confirm whether a foreign firm has instituted necessary corrective actions?**

   Following an inspection in which results indicate that corrective action is needed, firms have an opportunity to provide information to FDA regarding their proposed corrective actions as well as supporting information to demonstrate that the corrective actions are appropriate and sufficient to address the observations. FDA reviews this information when classifying the inspection and determining whether any advisory or enforcement actions may be necessary. Information regarding the inspection observations is also incorporated into a dossier for the facility so that on subsequent inspections investigators can verify implementation of the corrective actions.

   In general, FDA conducts a follow-up inspection to evaluate corrective actions for inspection outcomes classified as "official action indicated;" if classified as "voluntary action indicated," the follow-up verification of corrective actions by inspection usually takes place during the next surveillance inspection. If a firm indicates that they no longer manufacture and distribute product for the U.S. market, FDA will continue to monitor import entries to confirm the firm is no longer exporting, rather than conduct a follow-up inspection. FDA may also list a facility on import alert for appearing to violate applicable statutory or regulatory requirements, for example, for refusing an inspection or not conforming with current good manufacturing practice (CGMP) requirements. The import alerts inform FDA field staff of evidence that the products appear to be violative. Generally, FDA will remove a facility from a CGMP-related import alert after an onsite re-inspection demonstrates that the problems have been remediated and the firm is in compliance with CGMPs. However, if a facility on import alert does not provide any indication that they have remediated problems and are ready for re-inspection, FDA generally will not conduct a follow-up inspection and the facility will remain on import alert.

2. **During the hearing, Ranking Member Guthrie asked you about whether FDA had evaluation criteria to determine the effectiveness of its foreign drug inspection program.**

You indicated that FDA needs to address this issue. Does FDA have plans to create evaluation criteria for its foreign drug inspection program? If so, when does FDA plan to implement such criteria, and what types of factors will be included in these criteria?

FDA works to improve its evaluation of the effectiveness of our inspection programs to ensure that our inspection capacity, procedures, and techniques are suitable in addressing the risks and challenges we face in ensuring drug quality for U.S. consumers.

FDA's Office of Regulatory Affairs (ORA) has an established quality management system (QMS) that aims to provide consistent investigational processes and work products, meet organizational requirements, and enable continual improvement of inspectional operations. The QMS ensures investigators can access procedures and instructions necessary to perform operational activities in a consistent manner, and provides a risk-based approach for capturing, analyzing, and addressing issues. The system includes quality control activities to review work products and quality assurance activities (such as audits and management reviews).

FDA also evaluates the significance of the findings from each inspection to assess the need for further regulatory activity to address non-compliance.

3. **During the hearing, you indicated that you would prefer that FDA use a predictive model, as opposed to the site selection model currently used by FDA. Please explain what type of predictive model you envision and why you prefer this type of model to the site selection model currently used by FDA.**

The current site selection model is a risk-based prioritization model. For the future, FDA seeks to implement a predictive risk model to select drug manufacturing establishments for inspection. This statement was in the context of describing the required elements for such a model. Specifically, FDA would likely need manufacturing volume data for each product from each facility and reliable quality indicator data (e.g., quality metrics). Although the current prioritization model is risk-based, it does not predict risk for sites. The predictive risk model would be preferable because its output could be explicit about the level of risk posed by each establishment. However, characterizing risk requires volume information to understand the scale of impact and quality indicator data to describe the state of quality. Although we can describe the locations of API manufacturing facilities, we cannot determine with any precision the volume of APIs that a foreign country is actually producing, or the volume of APIs manufactured in a foreign country that is entering the U.S. market, either directly or indirectly by incorporation into finished dosages.

The Honorable Brett Guthrie (R-KY)

1. **Foreign firms are able to ship over-the-counter drugs and raw materials into the U.S. without FDA registration or inspection. Does FDA see that process as a vulnerability and, if so, what is being done to evaluate that process to make any necessary changes?**

Current mandates for facility inspection prior to import or marketing of a drug in the U.S. are typically in the context of premarket approval requirements. For drugs that are subject to

premarket approval requirements, FDA has an opportunity to evaluate and inspect the manufacturing facilities as part of the application assessment process. However, for drugs that are not subject to premarket approval requirements, manufacturers may not be subject to FDA inspection before such products are shipped to or distributed in the U.S. Notable examples of these types of drugs include active pharmaceutical ingredients (APIs) for compounding, and many over-the-counter (OTC) drugs marketed through conformance with OTC "monograph" regulations (including the APIs used in such OTC drug products). FDA can take action if we become aware of a quality problem with these drugs; however, patients may have already been exposed to the drugs.

Domestic and foreign establishments that manufacture, prepare, propagate, compound, or process drugs in the U.S., or drugs offered for import into the U.S., are required to register with FDA and list such products with FDA. However, some API producers shipping to OTC drug product manufacturers are not known to FDA, particularly where a foreign API producer supplies an API to a manufacturer of a drug product subject to an OTC monograph that is also located outside the U.S. When the API, alone, is not shipped to the U.S., some foreign API producers do not register with FDA and may not know the manufacturer will distribute the product in the United States. The same situation exists for some finished and unfinished drug products that are not directly shipped to the U.S. but are ultimately distributed to U.S. consumers. The Administration's FY2020 Budget Justification[1] included a legislative proposal to address this issue and require more accurate supply chain information.

2. **With regard to the Site Selection Model used to select drug firms by prioritizing those with the highest risk, how has the FDA validated that this model to ensure that FDA is properly scoring the firms with the highest risk?**

In January 2017, the Site Selection Model (SSM) was subjected to an independent external peer review (managed by a contractor) by three experts in risk modeling. The model was evaluated and recommendations for improvement were provided and implemented.

3. **Would adding source information to drug labels to include all information about where the ingredients were manufactured raise consumer awareness and better help put pressure on manufacturers to ensure the purity and safety of their drugs? Has the FDA considered funding studies to determine the usefulness to consumers and physicians of adding sourcing information to drug labels?**

Drug products usually contain multiple ingredients, active and inactive, and often these ingredients are sourced from different suppliers from batch to batch, depending on availability and cost. Reflecting the source of the ingredients in product labeling could potentially result in new labeling for each batch. Additionally, because the status of a facility can change over time, a source that is acceptable today may not be acceptable six months from now, and vice versa. It would be extremely difficult for someone without intimate knowledge of the drug inspection process to make an informed decision on their own as to the acceptability of the source of each of the ingredients.

[1] *https://www.fda.gov/media/121408/download*

Current regulations require drug product manufacturers to test all components (ingredients) before use in manufacturing. FDA is exploring options to modify existing policies with the aim of promoting more mature quality management systems as well as oversight of component/ingredient suppliers. Additionally, FDA is pursuing the generation, collection, and use of specific quality metrics (i.e., quality indicators) that help ensure manufacturers are controlling more critical risks to drug quality.

4. The FDA just added a data field this month to its data system to capture when inspections are announced or unannounced. Does FDA plan to populate that data historically and if so, to what date?

The data field has not yet been added to eNSpect (the FDA IT system used to generate inspection reports) but will be implemented in a future release. When it is implemented, we do not plan to populate any historic data.

a. What other data fields were added for collection?

No other data fields have been added at this time; however, as noted above, a data field to track whether an inspection was announced or unannounced will be implemented in a future release of eNSpect.

5. Does FDA think there is a conflict of interest when the firm being inspected provides the translator for FDA's inspection?

During an inspection, FDA investigators should be able to communicate directly with the firm to ensure that the information collected and the messages conveyed are accurate, complete, and fully understood. Language differences can be an impediment to such communication. Therefore, it is important to have translators on hand that can serve as an accurate conduit for our investigatory staff. When possible, FDA uses independent translators. However, that is not always feasible.

6. What resources does FDA have to pay for its own translators? How much of these overall resources are used to support translators in foreign drug inspections?

ORA obligated $2.1M in FY18 and $1.5M in FY19 for translation services. Of the total obligations, approximately three percent are related to drug inspections.

In some cases, FDA can contract, through an Inter-Agency Agreement (IAA) with the State Department, for an interpreter to accompany the investigator on inspection when needed.

In FY18, FDA contracted interpreters to accompany investigators on 89 foreign trips with an average cost of $1,681 per day, with a total average cost of $20,000 per trip. The cost varied across different countries and across languages spoken, but in total the Agency spent over $1.7 million on Agency-contracted interpreters in FY18.

Most of the inspections utilizing the IAA interpreter services in FY18 were in the foods program (79 trips) whereas there were only five drug-related trips that utilized the IAA interpreter services, at a total cost of approximately $100,000.

7. FDA reported to GAO that a primary data source used to calculate the inspection risk model included nearly 1,000 firms that did not actually require FDA inspection. FDA called those firms "washouts." How were the nearly 1,000 "washout" drug manufacturers FDA discovered when the risk model scores were calculated? In your slide presentation, did the baseline data used for the information include "washouts"? If so, please explain washouts. How much greater risk weight in the risk model is given to manufacturers of finished drug products than to manufacturers of APIs?

Some level of 'washout' of assigned inspections is always expected. FDA has been improving its vetting process to minimize the number of washouts. Washouts occur because the establishments are not inspection obligations for FDA due to: a firm going out of business, a firm no longer producing for the U.S. market, data errors, and registration errors. Firms self-register and there is no barrier or fee for registration, so some foreign firms register as a means of self-promotion. It is then incumbent upon FDA to determine if the establishment meets the criteria for an inspection obligation. If it does not, it becomes a washout.

With regard to the number of washouts, please refer to Dr. Janet Woodcock's December 10, 2019, testimony, which states that the number of washouts was 359 out of a total of 965 sites never previously inspected:

> CDER's Catalog showed that as of July 2016, there were 965 foreign manufacturing facilities that had never been inspected by FDA. By the end of FY 2019, FDA had inspected 495 or 51 percent of these previously uninspected facilities (See Figure 4). An additional 359 facilities (37 percent) were removed from the Catalog because they were no longer part of FDA's inspection obligations for a number of reasons: e.g., they had gone out of business, were not serving the U.S. market, or had been registered with FDA erroneously. In addition, 52 or six percent of the facilities had refused inspection; 37 or four percent of the facilities were inaccessible to FDA investigators because they were unable to travel to them (e.g., as a result of travel warnings); and 22 or two percent had no drug shipments.
>
> The SSM does not have different weights, per se, for finished dosage forms (FDF) and API sites. Both are considered "Drug Manufacturers" by the SSM. The model differentiates manufacturers based on the inherent product risk associated with the drugs they make. In general, FDF sites may have higher scores than API sites; but this is because of the higher-risk products (e.g., narrow therapeutic index drugs (i.e., drugs that must be made to tighter assay specification), drugs used in medical emergencies) made at the facility, not because it is an API or FDF facility.

8. The FDA believes that its system for inspecting foreign drug plants – which involves reviewing company-submitted data and conducting pre-announced inspections – is adequate for ensuring quality. Yet that system failed to detect the presence of carcinogens in blood-pressure medicine taken by millions of Americans and potential carcinogens in the diabetes treatment drug Metformin. Should the FDA begin to verify quality, for example by launching a system of chemical testing more imported pharmaceuticals for purity, API amount, and dissolution rate?

FDA has an active program for sampling and testing drugs to verify they meet required quality attributes and specifications. FDA also collaborates with foreign partners by sharing data, especially about critical issues of safety and efficacy. For additional information, please see Dr. Janet Woodcock's statement on December 5, 2019.[2]

Generally during CGMP inspections, we review the records that manufacturers must maintain regarding required testing, including testing for the expected and controlled impurities and degradation compounds. No single test can detect all potential impurities. Tests are selected based on assessments of what impurities may develop as a result of the manufacturing process. In other words, it generally needs to be recognized that there's a risk of an impurity occurring as a result of a manufacturing process to know the impurity that should be tested for. Before we undertook this analysis, neither regulators nor industry fully understood how nitrosamines could form during these manufacturing processes.

Some have raised the question of why we do not test every drug product before it enters the United States. FDA performs thousands of tests on drug products each year pre- and post-market. Only a small percentage (about one percent) of drugs that are tested fail to meet the established quality specifications. Testing by FDA or third parties of each batch of drug product in U.S. commerce, which amounts to millions of batches and trillions of individual tablets, capsules, and other dosage forms, before they enter the U.S. market would not be feasible at a practical level. For example, in 2018 there were almost 186 trillion tablets and capsules on the U.S. market. The current approach is effective and efficient.

9. After September 11, 2001, then-HHS Secretary Tommy Thompson asked Congress to add 600 more inspectors and laboratory personnel,[3] increasing the total FDA field staff to about 4,000 in 2002. In 2007, the *New York Times* reported that the FDA budget did not keep up with inflation and the field staff decreased 13% to 3,488, even fewer than the 3,500 original staff totals in 2002 before the hiring increase.[4] The 2012 enactment of the Generic Drug User Fee Act added resources for FDA to support the hiring of more drug inspectors, and yet in the last few years there has been a sharp decrease in the number of drug inspectors down from 245 inspectors to 188 since 2016. FDA historically has struggled to hire more inspectors, even with user fees. Given this

---

[2] *https://www.fda.gov/news-events/press-announcements/statement-janet-woodcock-md-director-fdas-center-drug-evaluation-and-research-impurities-found*.

[3] Government Accountability Office, *Food Safety: FDA's Imported Seafood Safety Program Shows Some Progress, but Further Improvements Are Needed* (Jan. 2004) (GAO-04-246).

[4] *Food Imports Often Escape Scrutiny*, The New York Times (May 1, 2007).

problem over almost 20 years, why did the FDA wait until 2019 to request direct-hire authority for inspectors?

In May 2008, FDA was granted direct hire authority for the consumer safety officer position (0696), and approximately 800 FTEs were hired as a result of this effort agency-wide.

In April 2016, our Office of Regulatory Affairs (ORA) submitted a request for additional direct hire authority for the consumer safety officer position (0696). That request was returned with comments. We revised the direct hire request in July 2016 and September 2019 to address concerns and submitted it forward for consideration. We received direct hire authority on October 16, 2019. We are currently executing and expect hiring selection to begin in the next few weeks.

a. The hiring and retention of FDA inspectors has been a longstanding problem. Does FDA plan to commission an outside consultant to study the problem and recommend solutions and if so, when will that occur and what is the anticipated date of completion?

We have no plans to hire an outside consultant at this time.

10. Earlier this year, the Committee sent FDA a bipartisan letter asking, in part, about the FDA's India pilot program and why the program was not extended. In response, FDA told the Committee that the FDA's drug inspection initiative in India was not extended "based on a lack of protocols and evaluation criteria. No formal report or evaluation was completed." Republican Committee staff subsequently asked that FDA provide information about the evaluation criteria for its foreign drug inspection program. To date, FDA has not provided this information. Does FDA have evaluation criteria for the effectiveness of its foreign drug inspection program? What are they?

FDA evaluates each inspection report prepared following each inspection regardless of program purpose to ensure that each inspection was conducted appropriately and acted on in accordance with FDA policies and procedures.

Chapter 5 of FDA's Investigations Operations Manual (IOM) includes evaluation criteria for the format and review of foreign inspection reports.[5] FDA also operates under established timeframes associated with timely completion of foreign inspection reports and issuance of any follow up decisional letters after each inspection. Additionally, the Dedicated Foreign Inspection Cadre and the GDUFA Investigators are evaluated each year to ensure that they meet either the required number of inspections conducted and/or complete the necessary weeks of foreign travel per year.

11. Your written testimony states that to help ensure that safe and effective drugs are sold in the United States, the FDA tests selected drugs in state-of-the-art FDA laboratories. What state-of-the-art FDA laboratories do this testing?

[5] *www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/investigations-operations-manual*

FDA has laboratories throughout the U.S. CDER's laboratories are located in St. Louis, Missouri, and at the main FDA campus in Silver Spring, Maryland. ORA has medical product laboratories in Atlanta, Georgia; Cincinnati, Ohio; Detroit, Michigan; Irvine, California; Jamaica, New York; Philadelphia, Pennsylvania; and San Juan, Puerto Rico.

a. What kinds of testing are conducted?

FDA's laboratories are capable of a wide variety of testing, both chemical and microbiological. The testing we conduct on any given sample is determined on a case-by-case basis. Some types of testing are:

- Identity – is it the right drug as indicated on the label?
- Assay – how much drug is there and is it consistent with the labeled amount?
- Impurities – are there process impurities or degradation impurities?
- Dissolution – does the active ingredient dissolve out of the dosage unit so that the drug is available for the body to absorb?

b. How the drugs selected for testing?

We select hundreds of samples each year based on certain criteria.

- Some testing decisions are event-driven. For example, we might test product samples after receiving a pattern of complaints about reduced effectiveness. These reports come to FDA via FDA's MedWatch Safety Information and Adverse Event Reporting program.

- We also rely on the experience of internal and external experts to alert us to emerging safety, effectiveness, or quality issues with currently marketed drug products. For example, results from independent research may require FDA testing and investigation.

Sometimes, manufacturing or facility concerns may trigger additional FDA monitoring and testing. For instance, FDA may sample products with difficult manufacturing processes or drug products with complex dosage forms such as patches, drugs designed to target a specific area, and drugs that release the active ingredient in a controlled manner. FDA may also sample drugs produced by manufacturing processes that require additional controls to assure each dosage unit will perform as expected, such as delivering a precise amount of active ingredient within a narrower range, because even slight deviations could cause quality issues.

We use a risk-based approach to quality testing. This means that in cases where there is a known or likely safety, effectiveness, or quality issue with a product, FDA scientists perform tests specifically for this vulnerability. For example, if an active pharmaceutical ingredient is likely to become contaminated with a harmful impurity during the manufacturing process, FDA tests for that specific impurity, rather than testing for all potential impurities.

12. Has FDA management interviewed FDA drug inspectors to get their perspectives on relying on translators provided by the firm being inspected?

No, there have not been any formal documented interviews with drug investigators to get their perspectives on relying on translators provided by the firm being inspected.

13. FDA has recently entered into mutual reliance agreements with the European Union. How will these agreements help provide more staffing and resources for FDA to focus more on higher risk foreign drug inspections?

.

The Mutual Recognition Agreement (MRA) between FDA and EU member states allows drug inspectors to rely on each other's factual findings from their good manufacturing practice inspections of drug facilities. The MRA reduces duplicate inspections of the same facilities and yields greater efficiencies that allow us to reallocate our resources to inspect other high-risk facilities. Developing the MRA took time and resources. Beginning in 2014, FDA experts were sent to Europe to observe EU officials audit each of the 28 EU member state (EUMS) inspectorates as part of a larger program to ensure that they could conduct inspections at a standard similar to a U.S. inspection. The FDA completed this work for the most common type of drug manufacturing inspections in July 2019.

a. How long will it take until FDA realizes these kinds of benefit from the mutual reliance agreements?

FDA and the EU have been collecting data on the operational impact of the MRA ever since the first countries were found capable on November 1, 2017, and the numbers are quite promising. With respect to CDER-regulated products, as of November 2019, the EU has conducted 29 inspections at FDA's request and FDA has conducted 14 inspections at the EU's request. Moreover, FDA has deferred 157 inspections in the EU after review of the inspectional information provided by our trusted partners. We anticipate seeing an even greater impact now that the MRA has been implemented in all 28 EU countries for human drug products.

b. How can the FDA work with friendly foreign regulatory counterparts to help improve oversight of higher risk foreign drug facilities?

In addition to FDA's collaboration with the EU member state inspectorates, we support other countries in their development of regulatory systems that are as capable as FDA's own system. We do that by collaborating in the development of inspectional policies and competency as a member of the Pharmaceutical Inspection Cooperation Scheme (or PIC/S), a non-binding, informal co-operative arrangement between regulatory authorities in the field of Good Manufacturing Practice (GMP) of medicinal products for human or veterinary use. PIC/S aims to harmonize inspection procedures worldwide by creating common standards in the field of GMPs and by providing training opportunities to inspectors. FDA has collaborated with our counterpart members to leverage inspection information, such as notifications of compliance problems and product recalls. Additionally, FDA also collaborates with industry and other regulators in establishing

harmonized guidance covering quality, safety, efficacy, and marketing application submissions. These activities and other collaborations with trusted foreign counterparts (e.g., mutual reliance on testing for the presence of nitrosamine contamination) have been helpful in supporting FDA's public health protection responsibilities.

The Honorable H. Morgan Griffith (R-VA)

1. **Has FDA considered issuing public statements to encourage drug producers to inquire about whether the API that they purchase is sourced from a manufacturer that has been inspected by FDA or another regulatory agency recognized under a Mutual Recognition Agreement? And to purchase API from facilities that have been recently been inspected?**

FDA posts inspection information on its public website that includes the name of the site inspected, date of inspection, inspection type, and the final inspection classification (indicating the severity of any objectionable inspection findings). FDA has publicly discussed the availability of this information and, in fulfillment of a GDUFA-2 commitment, updates the information every month. This data includes inspections performed by a trusted counterpart, such as EU inspectorates. FDA's regulations at 21 CFR part 211 (subpart E) require drug product manufacturers to evaluate the quality of components (i.e., active and inactive ingredients) before use in drug product manufacturing. FDA's guidance for industry, *Contract Manufacturing Arrangements for Drugs: Quality Agreements*, recommends that drug product manufacturers take additional efforts to evaluate their suppliers before they purchase ingredients for use in drug manufacturing, which also includes evaluating past regulator inspections.

2. **Has FDA considered publishing the investigator's establishment inspection report and any Form FDA-483 issued or regulatory action taken for foreign API manufacturers that the Agency has inspected so that API repackers and drug producers can make informed decisions about whether to purchase from those entities?**

FDA posts final FDA 483s on its website along with warning letters and untitled letters, and also announces import alert, seizure, and injunction actions. As noted in the previous response, drug product manufacturers have existing requirements to evaluate the quality of components before use in drug product manufacturing.

3. **Besides banning imports to the United States, how can FDA protect the supply chain when a foreign facility refuses an FDA inspection? When an importation ban is placed on a manufacturer, what does FDA do about API it has already introduced into the United States?**

There are a variety of advisory and enforcement actions that FDA may take when a foreign facility refuses an inspection. Import alerts allow FDA to act quickly to inform field staff of evidence that products appear to be violative, as compared to pursuing enforcement actions such as injunctions or seizures. There are steps that can be taken to strengthen the ability to use import alerts. For example, currently there are facilities that may not be subject to FDA inspection before they ship drugs to the United States. There are some firms that supply APIs that are

incorporated into products marketed in accordance with OTC monographs (and other non-application drugs), but that do not register with FDA because they do not ship directly to the U.S. As a result, some firms that produce APIs for such products are not known to FDA. Addressing these gaps in our awareness would improve our ability to use import alerts to protect the public health. FDA can request recalls for drugs manufactured in foreign or domestic facilities; however, the regulatory intervention and risk mitigation may be slow because most drug recalls are voluntary. Currently, FDA does not have the legal authority to order a mandatory drug recall other than for controlled substances when it find a reasonable probability that the controlled substance would cause serious adverse health consequences, and we only recently obtained that authority in the SUPPORT Act.

Facilities located outside the U.S. that refuse an FDA inspection may be placed on Import Alert 99-32, "Detention Without Physical Examination of Products from Firms Refusing FDA Foreign Establishment Inspection." All products exported to the U.S. by a facility on the import alert are subject to Detention Without Physical Examination (DWPE) and not released into U.S. commerce until FDA is able to inspect the facility.

FDA's application of DWPE is effective as of the date of inspection refusal. FDA does not retroactively apply the DWPE but can request recalls for drugs in the U.S. market that were previously imported and are now subject to an import alert.