Remarks of Dara Corrigan
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I. Introduction

It is always a pleasure to be here and to address this audience. Since the last time I was here, I had the opportunity to serve as the Director of FDA's Europe Office. While I was there, a confluence of events triggered the beginning of my work on the Mutual Reliance Initiative. The goal of this initiative was to reach an agreement with the European Union where we would be able to rely on each other's drug manufacturing inspections.

After almost three years of negotiations, we finalized the Mutual Recognition Agreement between the

United States and the European Union in March of this year. I will begin by explaining the value of this agreement and then move to a description of the negotiating process and the agreement itself. I will leave time for questions at the end.

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II. FDA's Pharmaceutical Inspection Regime

While most people who work in or for the drug industry know about the shift of the industry over the last 20 years, I want to focus in particular on the EU, China, and India, and FDA drug inspections in those countries.

This slide shows you the number of drug facilities that were registered with the FDA in 2011.

U.S. facilities dwarf the numbers in the EU and India and China. And, in 2011, the EU had more registered facilities than India and China combined.

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Fast-forward five years and you can see the impact of globalization by looking at the shift in the numbers of drug facilities around the world. Specifically, note the rapid growth – a 66 percent increase - of drug facilities in China and India. This surging growth in overseas drug facilities has made the global supply chain more complex, which has and should have direct ramifications for FDA's approach to overseas inspections.

We are directly addressing this challenge by becoming more strategic about how we allocate

valuable inspection resources to protect public health.

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Now, let's look at where FDA has been allocating its resources around the world. Since 2011 and continuing until today, a vast majority of FDA's foreign inspections are performed in the EU. If we look back to 2011 and move through 2015, FDA on average has performed 43 percent of its inspections in the EU. At the same time, FDA has been able to make significant progress by increasing inspections in India and China by shifting domestic inspection resources to foreign inspections.

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To understand what these inspections reveal in the EU, let's focus on the data. For the EU, FDA inspects almost a third of the region's 1,224 drug facilities -- and 5 percent of these inspections led to a classification of Official Action Indicated, or OAI. As a point of reference, an **OAI** inspection classification occurs when significant objectionable conditions or practices were found and regulatory action is warranted to address the establishment's lack of compliance with statutes or regulations.

By comparison, FDA inspections in the U.S. led to a similar percentage - 5 percent - of OAI classifications.

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For China, in 2016, we inspected 21 percent of the 754 facilities there -- and 22 percent of these inspections led to a classification of OAI. This means that almost one of every five inspections conducted in China in 2016 identified significantly objectionable conditions or practices that could affect public health.

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For India, in 2016, we inspected 23 percent of the 722 facilities there -- and 14 percent of these inspections led to a classification of official action indicated.

The alarming fact in examining this data is that India and China have almost three to four times the

number of inspections classified as OAI as compared to the EU and the United States.

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III. The Pathway to a Mutual Recognition Agreement

Let's turn to the negotiation of the Mutual Recognition Agreement. I will give you a brief timeline, focusing on three critical years.

Nineteen years ago, in 1998, the U.S. and the EU signed the Agreement on Mutual Recognition between the European Community and the United States.

This included a Pharmaceutical Annex providing for recognition of each other's GMP inspections. However, this Annex was never fully implemented.

Five years ago, in 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) gave FDA the tools to recognize other countries when their drug inspectorates are capable of conducting inspections that meet U.S. standards.

Then, beginning three years ago, in May 2014, FDA and EU regulators began a strategic collaboration to once again evaluate whether we could rely on each other's inspectional information. Strengthening our reliance upon each other's expertise and ability to conduct inspections within our respective borders would provide a more practical means to oversee the large number of drug manufacturing sites outside of

the U.S. and EU. Both the FDA and EU had dedicated teams to assess the risk and benefits of entering into a Mutual Recognition Agreement. We had support from both the generic and innovator drug industries on both sides of the Atlantic.

The task of mutual recognition in the EU is complex given that each country has its own drug inspectorate. While EU law provides the overall drug inspection framework, FDA determined that there existed variability between drug inspectorates across the EU. Just two examples: EU regulatory authorities are funded in different ways and the conflict-of-interest provisions vary.

Therefore, FDA developed a standardized process to determine a drug inspectorate's capability – that is, to fulfill the statutory language of FDASIA - of each EU regulatory authority on an individual basis. I'll talk more about this a little later.

Initially, the negotiation of the U.S.-EU MRA was part of the Transatlantic Trade and Investment Partnership, or TTIP. However, it quickly became a regulatory conversation and the EU and FDA agreed to a singular focus: analyzing the terms of the 1998 Agreement and revising it in a way that would lead to successful implementation.

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IV. The 2017 Revision to the 1998 Mutual Recognition Agreement

The culmination of this detailed, intensive years-long collaboration took place just two months ago. On March 2, the U.S. and EU completed an exchange of letters to amend the Pharmaceutical Annex to the 1998 U.S.-EU Mutual Recognition Agreement. Now, for the first time ever, the FDA will be able to utilize the GMPs of pharmaceutical manufacturing facilities of capable EU inspectorates. This is the realization of the goal implicit in FDASIA; conduct rigorous analysis that can lead to mutual recognition, reallocate limited inspectional resources, and increase public health protection.

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V. The Scope of MRA

The scope of the MRA is broad, including most but not all drugs. Products such as vaccines and veterinary products are more challenging and will be reevaluated during the next few years for possible inclusion.

Vaccine manufacturers in the U.S. and the EU provide safe, quality vaccines to patients who need them. However, because having adequate supplies of safe vaccines is critical, it is important for the US and the EU to manage the available supply. That is why a step-by-step approach makes sense here. As we learn from our implementation of this agreement, which covers the vast majority of drugs, we will find the right path for vaccines over the next few years.

For veterinary products, a separate capability assessment process needs to be conducted by both the FDA and EU because often the authority for veterinary drugs resides in a different agency within an EU country. Both Parties have committed to exchanging views on how to assess respective authorities by the end of the year, and develop a plan for inclusion of veterinary products in the next couple years.

The scope of the agreement includes both post-approval – that is, surveillance - and under certain conditions, pre-approval inspections.

As most of you probably know, drugs that have already been approved undergo periodic surveillance inspections to ensure that the drug's manufacturer at a specific facility continues to produce high quality drugs.

Pre-approval inspections are conducted when a drug company submits an application for a drug. Unlike surveillance inspections, pre-approval inspections must be tailored to the underlying application and there are mandatory time limitations for conducting pre-approval inspections in the U.S. When possible, the FDA will request and use pre-approval inspections from the EU.

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VI. The Deliverables

Some of the provisions of the agreement became effective upon the exchange of letters on March 2, 2017. Some upcoming dates of interest defined in the agreement include July 2017, when the EU has committed to completing its own capability assessment of the FDA, and November 2017, when the FDA has committed to completing capability assessments of regulatory authorities from eight EU countries.

As I previously mentioned, the FDA has developed a standardized process for determining the capability of EU regulatory authorities. The assessment is comprehensive and requires the collaboration of numerous Centers and Offices within the FDA.

The assessment includes FDA experts traveling to the EU to observe their internal audits of their own countries' regulatory authorities, and a review of the country's conflict-of-interest policies, specific legislation related to good manufacturing practices, samples of inspection reports, inspector training records, inventory of drug manufacturing facilities, surveillance programs, and numerous standard operating procedures.

We expect to complete the FDA capability assessments of all EU countries' regulatory authorities by July of 2019 and at that point and beyond, determine the inclusion of other products within the parameters of the MRA.

In November of this year, FDA will recognize inspections from those EU regulatory authorities that FDA has determined to be "capable." FDA will utilize inspection reports and other relevant inspectional information and data from capable EU regulatory authorities. We will have the added benefit of utilizing the data from EU inspection reports for the first time and we will be able to reallocate our resources to areas of greatest risk.

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VII. The Future State

Now, let's think hypothetically for a moment. Think back to the earlier slides in which we examined FDA inspection numbers in China and India – 21 percent and 23 percent respectively of all FDA-registered facilities in each nation.

On this slide, each building unit in this schematic represents approximately 25 facilities. The red circles represent the facilities that were inspected by the FDA in 2016. The blue circles represent the theoretical coverage FDA alone could have had in China and India if we did not inspect in the EU and instead, relied on the EU to oversee the firms located within its countries.

Now imagine this: If the Pharmaceutical Annex to the 1998 US/EU MRA had been fully implemented in 2016, we could have taken these resources and reallocated them to India and China.

This would have allowed FDA alone to almost double the total number of inspections conducted in India and China.

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VIII. Conclusion

What is the hope in the next few years?

One goal would be a truly collaborative inspectorate, containing investigators and inspectors from the FDA and from across the EU.

We at the FDA understand that we must engage with our global partners. And I say with confidence, the Mutual Recognition Agreement is a bold and significant step in that direction.

Thank you.

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