US-EU Mutual Recognition Agreement

Alonza Cruse, Director, Office of Pharmaceutical Quality Operations

121st AFDO Educational Conference

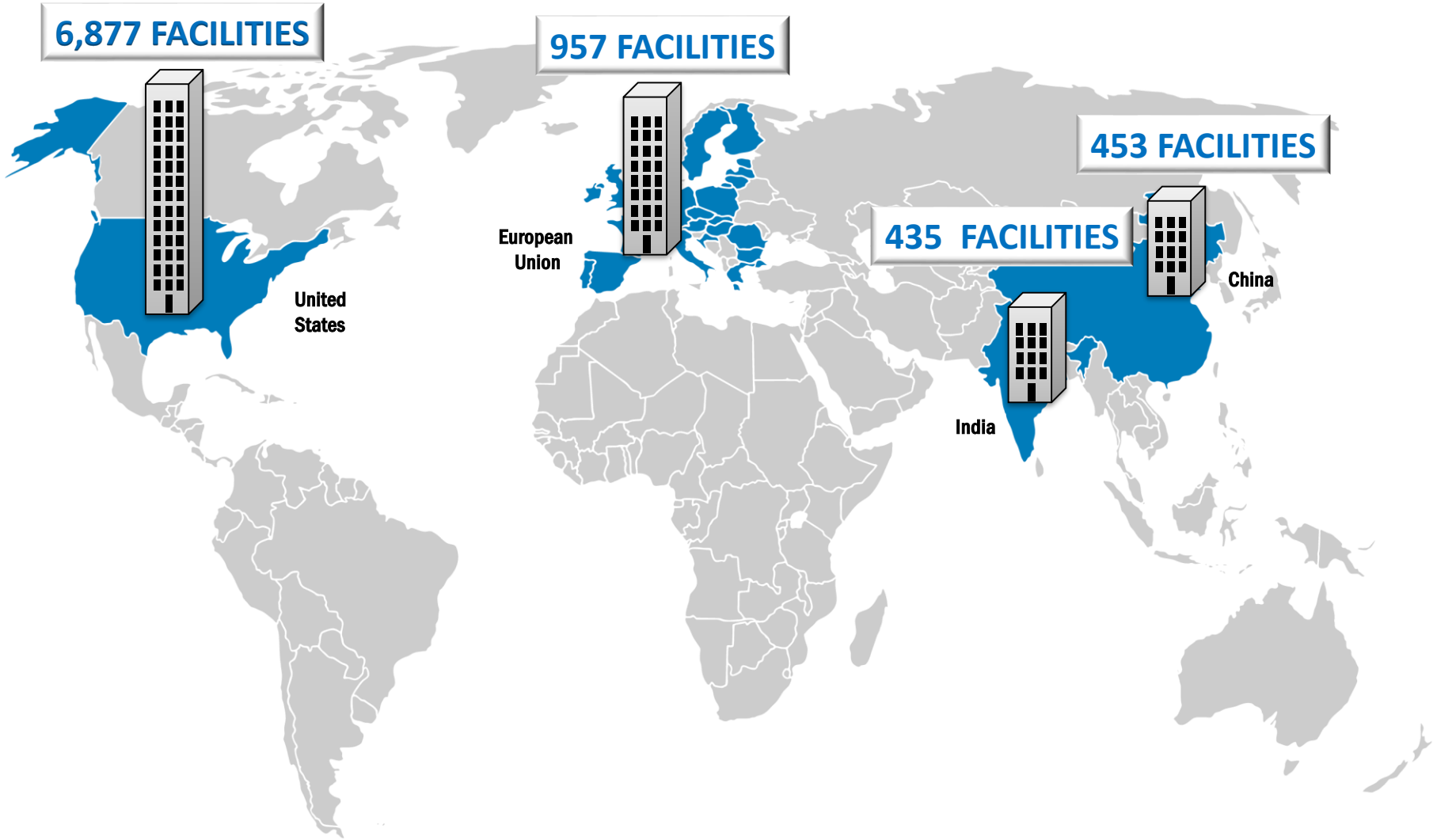
June 20, 2017

Benefits of Mutual Recognition

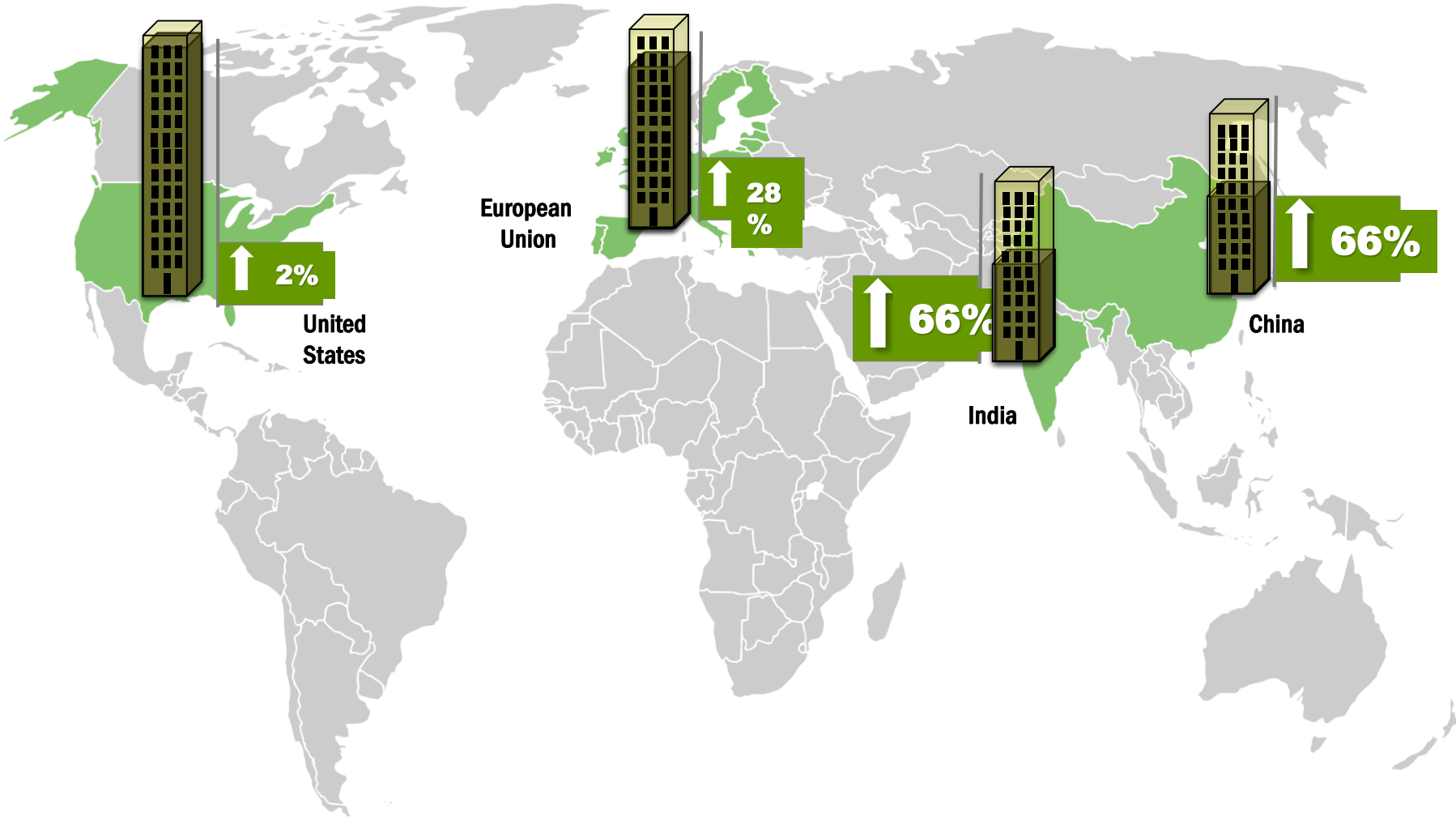
The EU and member state authorities and FDA relying upon each other's data and information from Good Manufacturing Practice (GMP) inspections.

GOAL: To reallocate scarce resources to areas of higher risk by recognizing inspections performed by capable foreign regulatory authorities.

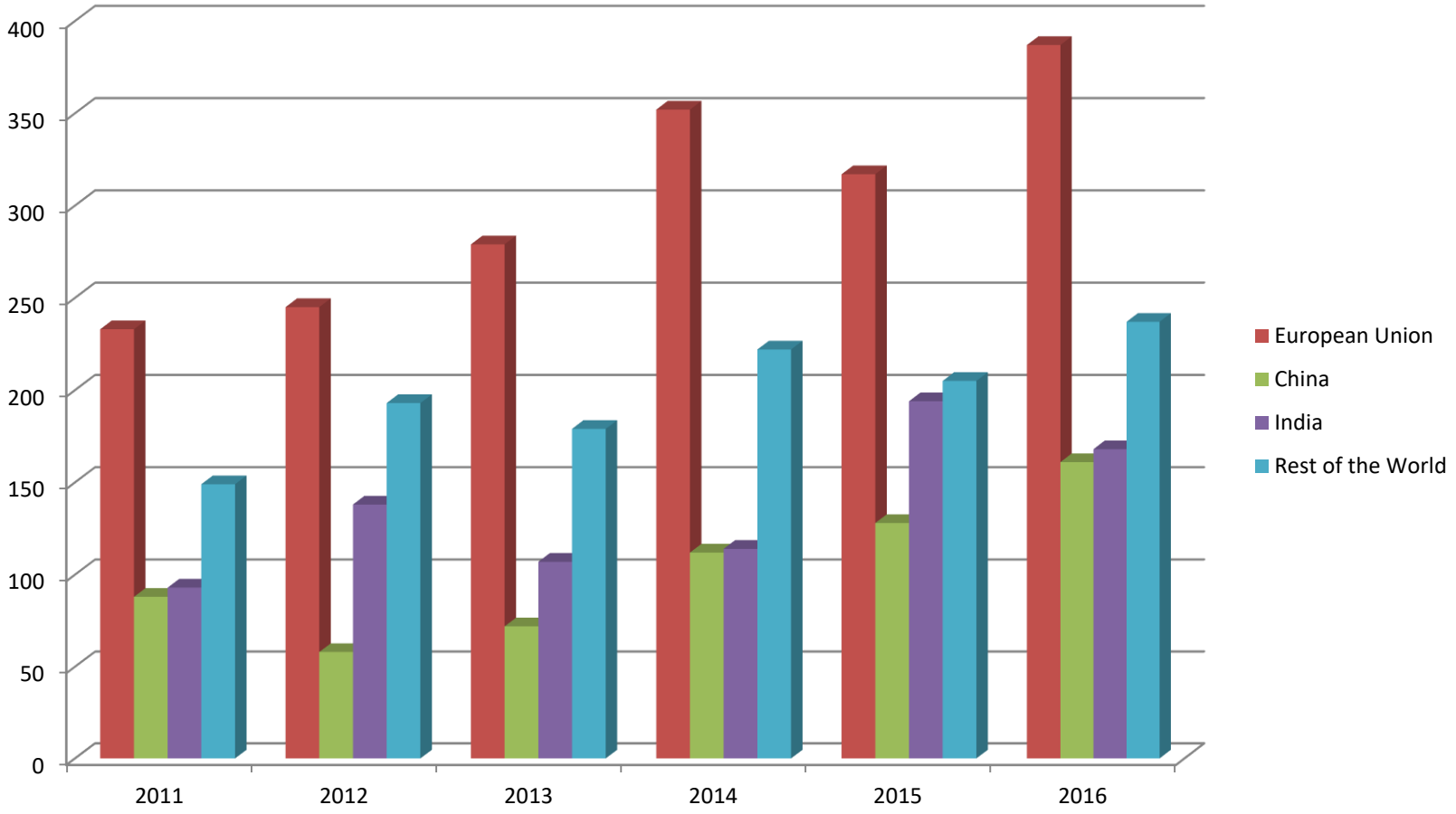
FDA Registered Drug Facilities 2011



FDA Registered Drug Facilities 2016

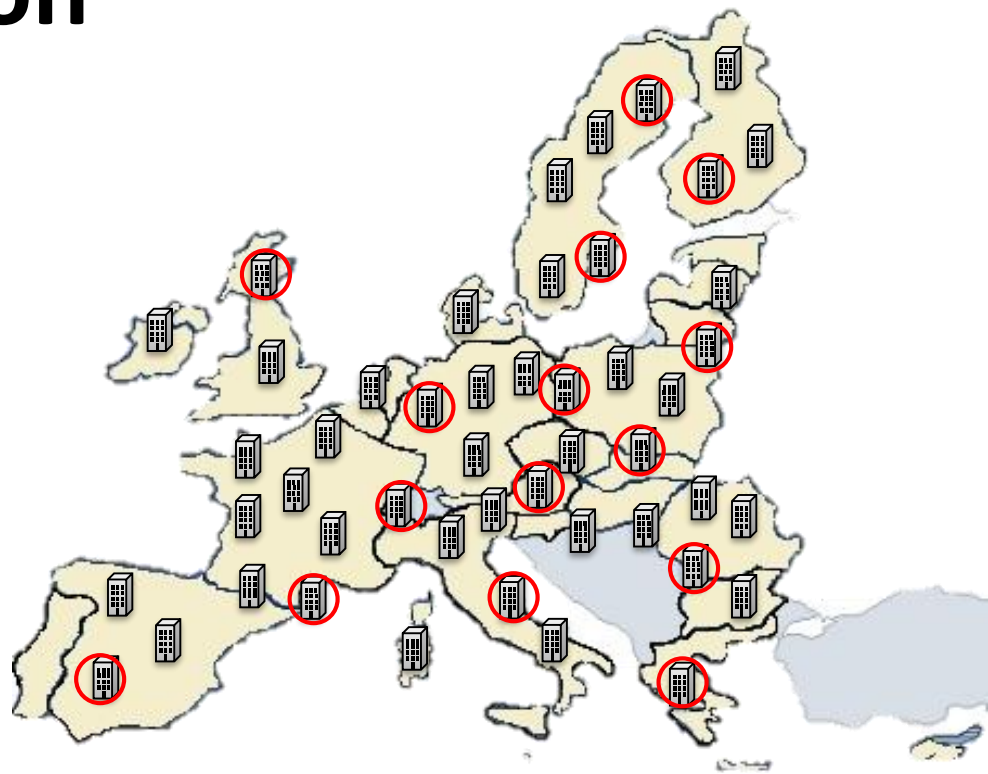


FDA Inspections Throughout the World



FDA Inspections In The European Union

- In 2016, there were 1224 drug facilities in EU
- FDA inspected 32% of the drug facilities in EU
- 5% of inspected facilities in
  EU led to an Official Action Indicated classification



KEY

= ~ 25 Drug Facilities

= Facilities inspected in 2016

FDA Inspections In China

- In 2016, there were 754 drug facilities in China
- FDA inspected 21% of the drug facilities in China
- 22% of inspected facilities in China led to an Official Action Indicated classification

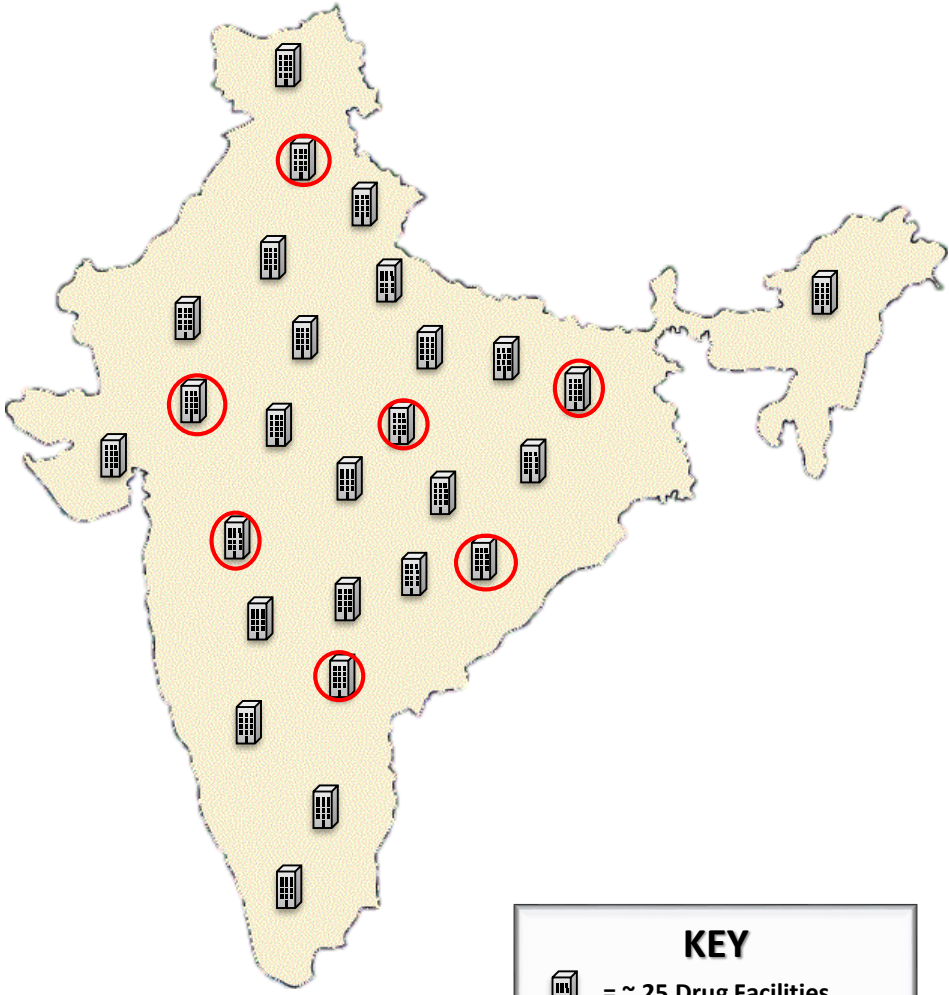
KEY

= ~ 25 Drug Facilities

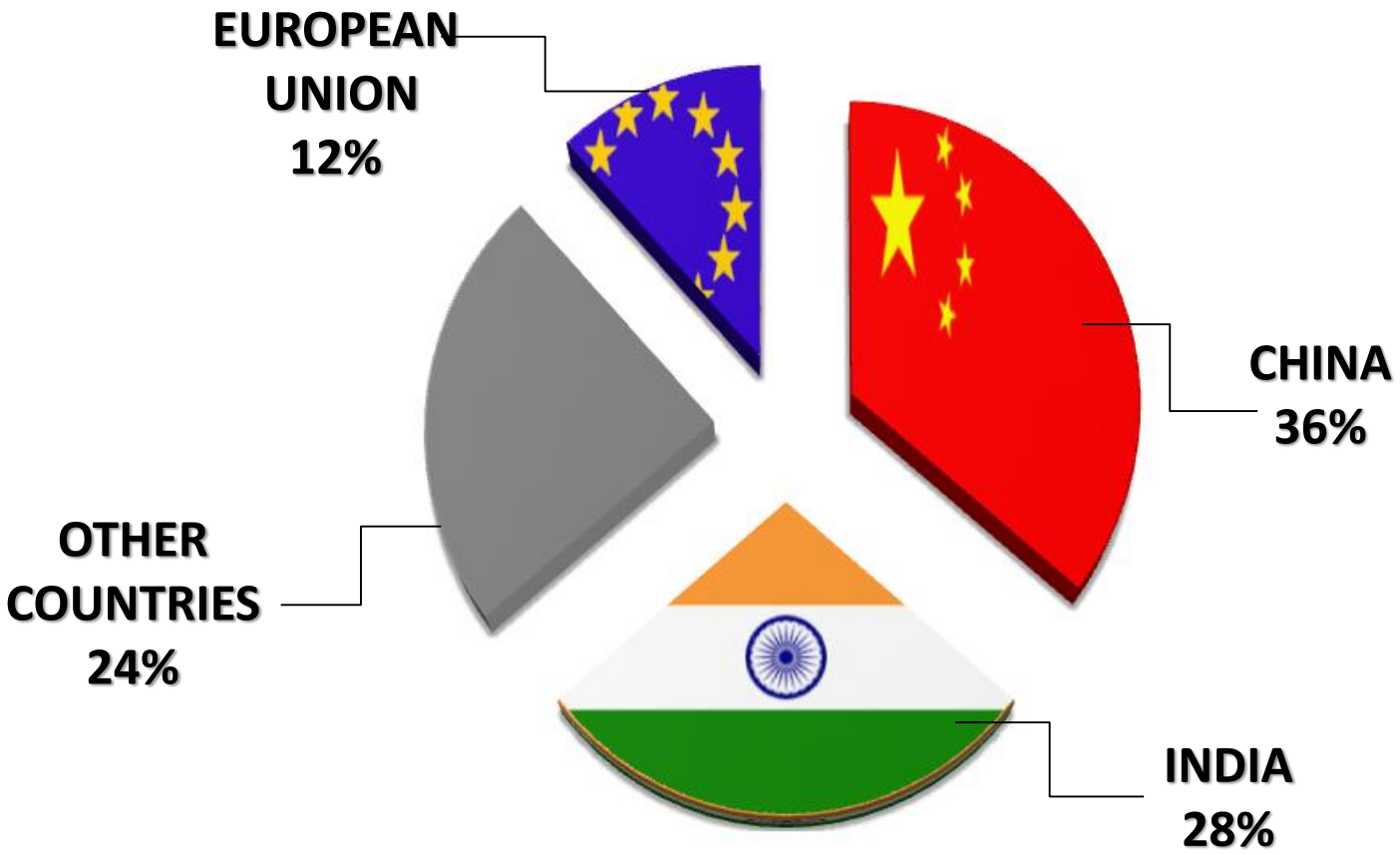
= Facilities inspected in 2016

FDA Inspections In India

- In 2016, there were 722 drug facilities in India
- FDA inspected 23% of the drug facilities in India
- 14% of inspected facilities in India led to an Official Action Indicated classification



FDA's Inspection Outcomes: Import Alerts Issued



Negotiation of the U.S. – EU Mutual Recognition Agreement

- **Exchanged and analyzed ideas**

In the beginning...

EU's legal and regulatory framework for GMP oversight

EU's Conflict of Interest policy for drug investigators

Jobs

EU's management of its inventory

28 member states

Competence and Comparison of Inspectorates

Fear

Change

Global Risk

Resources

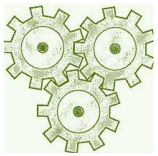
Negotiation of the U.S. – EU Mutual Recognition Agreement

- Exchanged and analyzed ideas
- Developed Capability Assessment Process

Joint Audit Programme (JAP)

Purpose

- Ensure consistency of GMP standards and a harmonized approach



Process

- EU auditors from two different EU countries go into a third EU country

Tools

- PIC/S Evaluation Guide
- EU auditor's inspectional expertise and experience

Capability Assessments

Negotiation of the U.S. – EU Mutual Recognition Agreement

- Exchanged and analyzed ideas
- Developed Capability Assessment Process
- Amended 1998 Agreement

2017 Revision to Pharmaceutical Annex to the 1998 U.S./EU MRA

Decision No 1/2017

of the Joint Committee established under Article 14 of the Agreement on Mutual Recognition between the European Community and the United States of America, amending the Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs)

THE JOINT COMMITTEE,

Having regard to the Agreement on Mutual Recognition between the European Community and the United States of America (the "Agreement") done in 1998, and in particular its Article 14 and Article 21; and

Whereas the Joint Committee is to take a decision to amend the Sectoral Annex on GMPs pursuant to Article 21(2) of the Agreement;

HAS DECIDED AS FOLLOWS:

1. Attachment A to this Decision is the United States – European Union Amended Sectoral Annex for Pharmaceutical Good Manufacturing Practices ("Amended Sectoral Annex") which amends the Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs) done in 1998 and replaces it with a consolidated version.

2. Attachment A has been agreed by the Parties.

This Decision, done in duplicate, shall be signed by representatives of the Joint Committee who, pursuant to Article 21(2) of the Agreement are authorized to act on behalf of the Parties for purposes of amending the Annexes. This Decision shall be effective from the date of the later of these signatures.

On behalf of the United States of America

Signed in Washington DC, on January 19, 2017

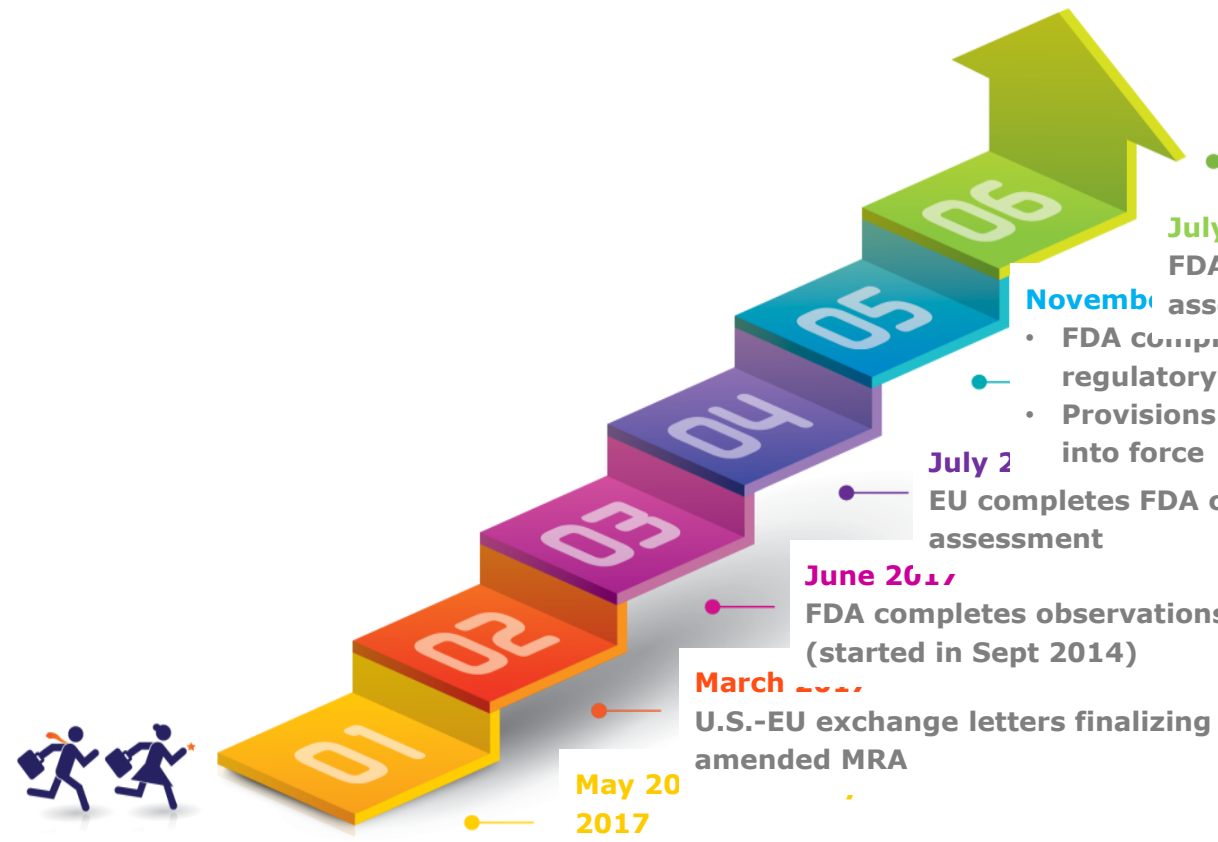
On behalf of the European Union

Signed in Brussels, on March 1st 2017

Scope

- Includes a vast majority of drugs
- Certain products will be reevaluated in the future, such as vaccines and veterinary products
- Surveillance and, under certain conditions, pre-approval inspections of marketed human drug facilities located within the U.S. and EU

Major Deliverables



MAY 2014
Start...
FDA and EU exchange and analyze ideas

May 20
2017
Negotiations to amend MRA

March
U.S.-EU exchange letters finalizing amended MRA

June 20
FDA completes observations of all scheduled internal EU audits (started in Sept 2014)

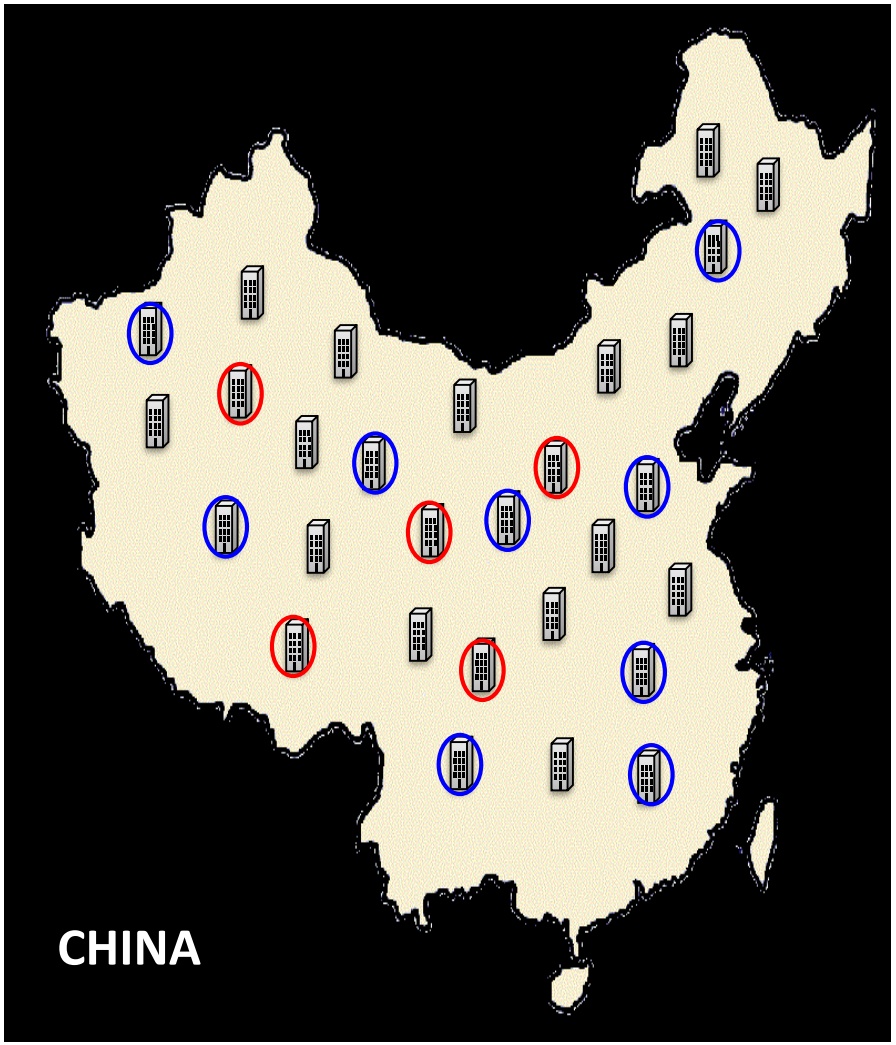
July 2
EU completes FDA capability assessment

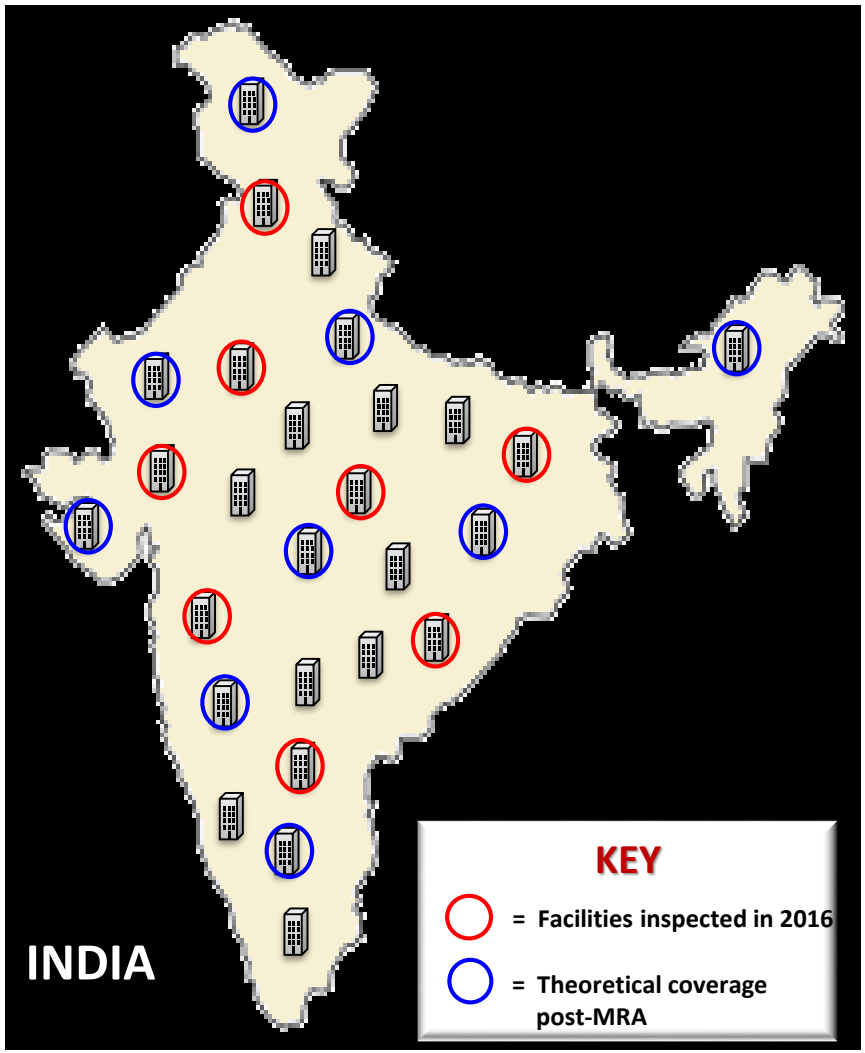
Novemb
- FDA c
- regulatory authorities
- Provisions operationalizing amended MRA enter into force

July
FDA completes all capability assessments

2019 and beyond
Continued collaboration to include other products

Potential FDA Inspection Coverage





Pharmaceutical Annex to the 1998 U.S.-EU MRA

MRA

Cements the FDA and EU's collaboration by taking concrete steps to rely upon each other to benefit public health.

Enables the FDA and EU to avoid the duplication of drug inspections and devote those resources to other parts of the world, where there may be greater risk.

A New World for Pharmaceutical Inspections

The Mutual Recognition Agreement

http://www.fda.gov/go

Questions? FDA-MRA@fda.hhs.gov