U.S. FOOD & DRUG ADMINISTRATION

FDA's International Mission and the Global Manufacturing Landscape

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CDER SBIA Webinar: Pharmaceutical Quality for Global Stakeholders

FDA Working Abroad

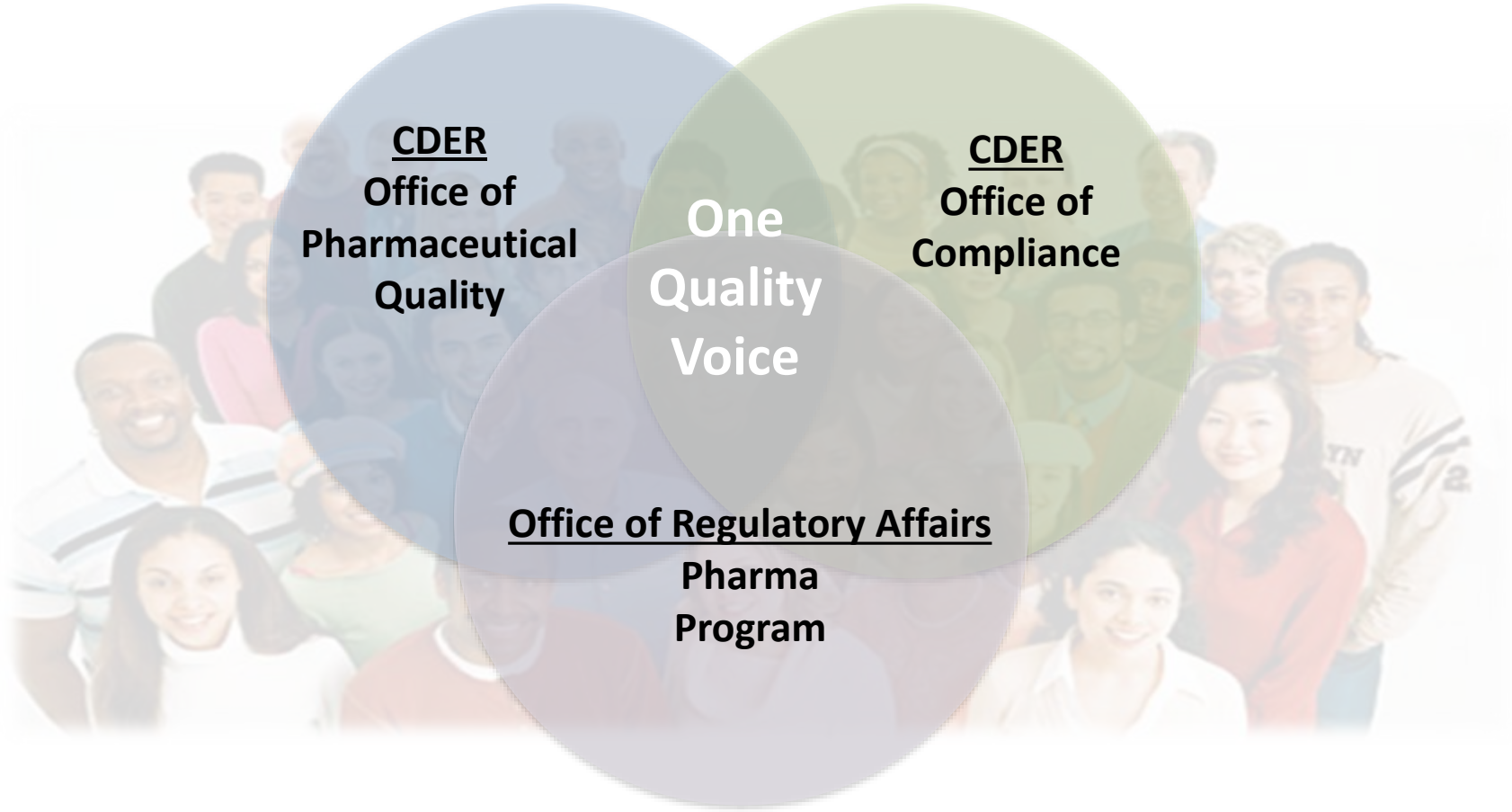
Manages foreign offices in strategic locations around the globe

FDA China Office Mission Statement

"To strengthen the safety, quality, and effectiveness of food and medical products produced in China for export to the U.S."

- Conducting establishment inspections
- Collaboration with Chinese Regulatory Authorities
- Outreach and Education to industry
- Monitoring China landscape that could impact product safety in the U.S.

Interactions with the Centers

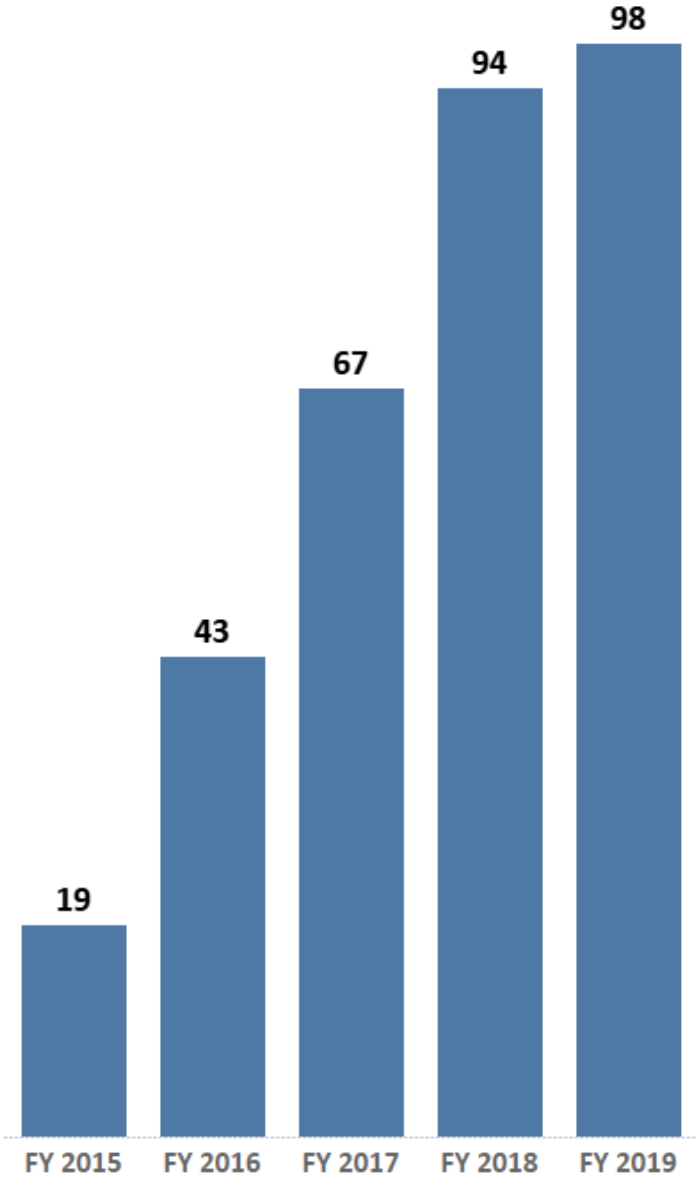


OMQ Warning Letters FY15-19

Warning Letters by Region

State	FY 2015	FY 2016	FY 2017	FY 2018	FY 2019
United States	2	7	15	19	54
China	2	14	19	24	14
India	9	11	14	15	17
Europe	3	5	8	8	2
South Korea			2	9	5
Canada	1		3	7	1
Japan		1	3	3	
Taiwan		3		2	1
Australia				3	
Mexico				3	
Brazil		2	1		
Singapore			1		1
New Zealand	1				
Thailand	1				
Philippines			1		
Dominican Republic				1	
Costa Rica					1
Malaysia					1
Turkey					1
Grand Total	19	43	67	94	98

Compounding Warning Letters not included.



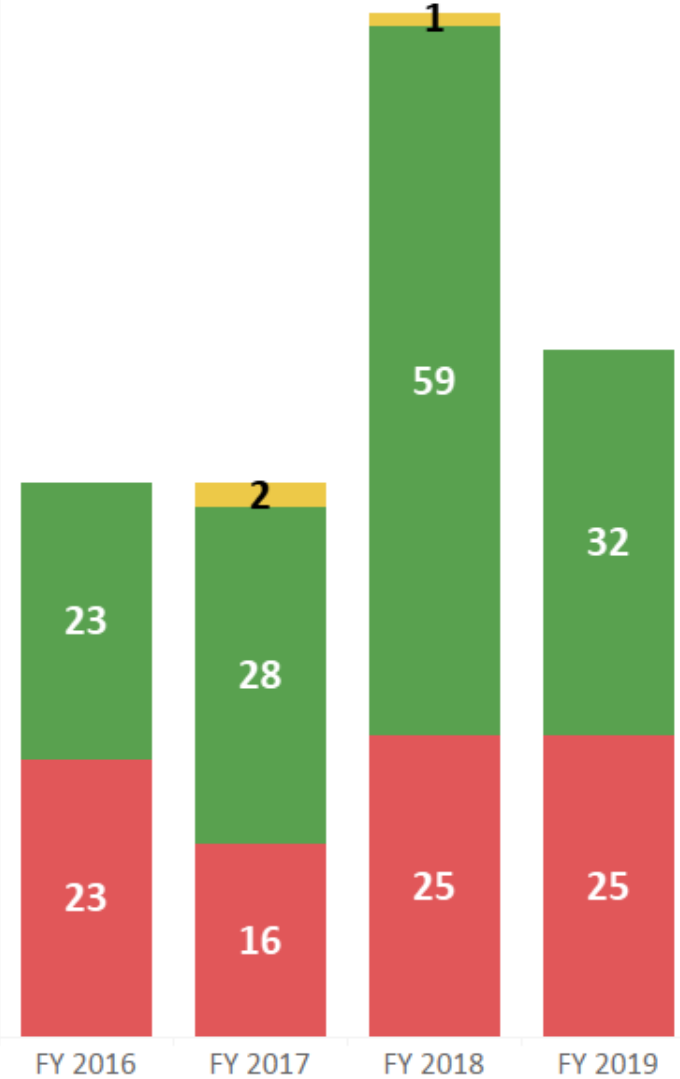
OMQ Warning Letters by Region FY15 to FY19

Compounding Warning Letters not included.

Total Import Alerts by Country (FY16-FY19)

55-05
66-40
99-32

Total Import Alerts by FY



A Brief History Lesson

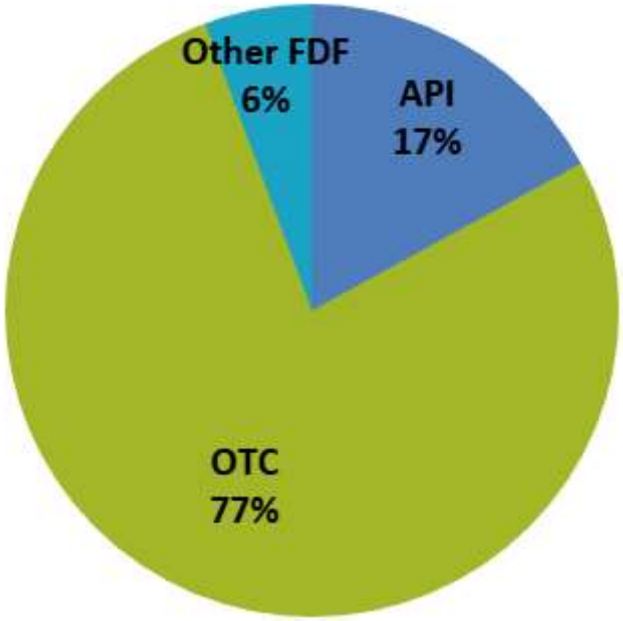
- Before 2012, the FD&C Act required inspections of domestic drug manufacturers every 2 years.
  - But the law was silent on foreign sites …
- At the same time, globalization of drug manufacturing occurs.
  - Resulted in a large imbalance in which facilities were inspected.

To Address the Imbalance

- Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 changed the requirement for FDA to inspect domestic and foreign drug establishments **"in accordance with a risk-based schedule."**

Regulatory and Enforcement Actions for "Never Inspected" Sites

Warning Letter by Drug Type



Warning Letter Data from October 1, 2014 to September 30, 2019

- Increase in OAI classification causes an increase in regulatory and enforcement actions
- Majority are OTC sites
- Topical treatments, Toothpastes, Acne Treatments, Cleaning/Cleansing Wipes, Sunscreens

Non-compliance Trends for OTCs

1. Data integrity
2. Facility and/or equipment concerns
3. Lack of raw material and finished drug testing
4. Concerns with glycerin
5. Contract manufacturers

1978 Preamble to the Drug GMPs

- It has been FDA's experience that "small" manufacturers can attain the same degree of quality of their drug products as large manufacturers.

- **There cannot be different standards of quality of drug products for large and small manufacturers, nor can there be different standards of quality for OTC and prescription drug products.**

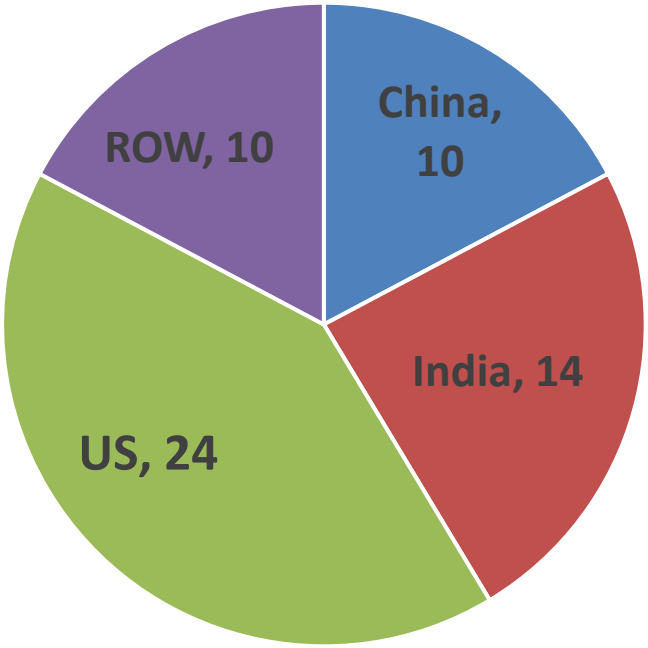
  Link: https://www.fda.gov/media/78493/download

- *Reiterated in 2012 FDASIA legislation: OTC and prescription*

Diving into Water Systems

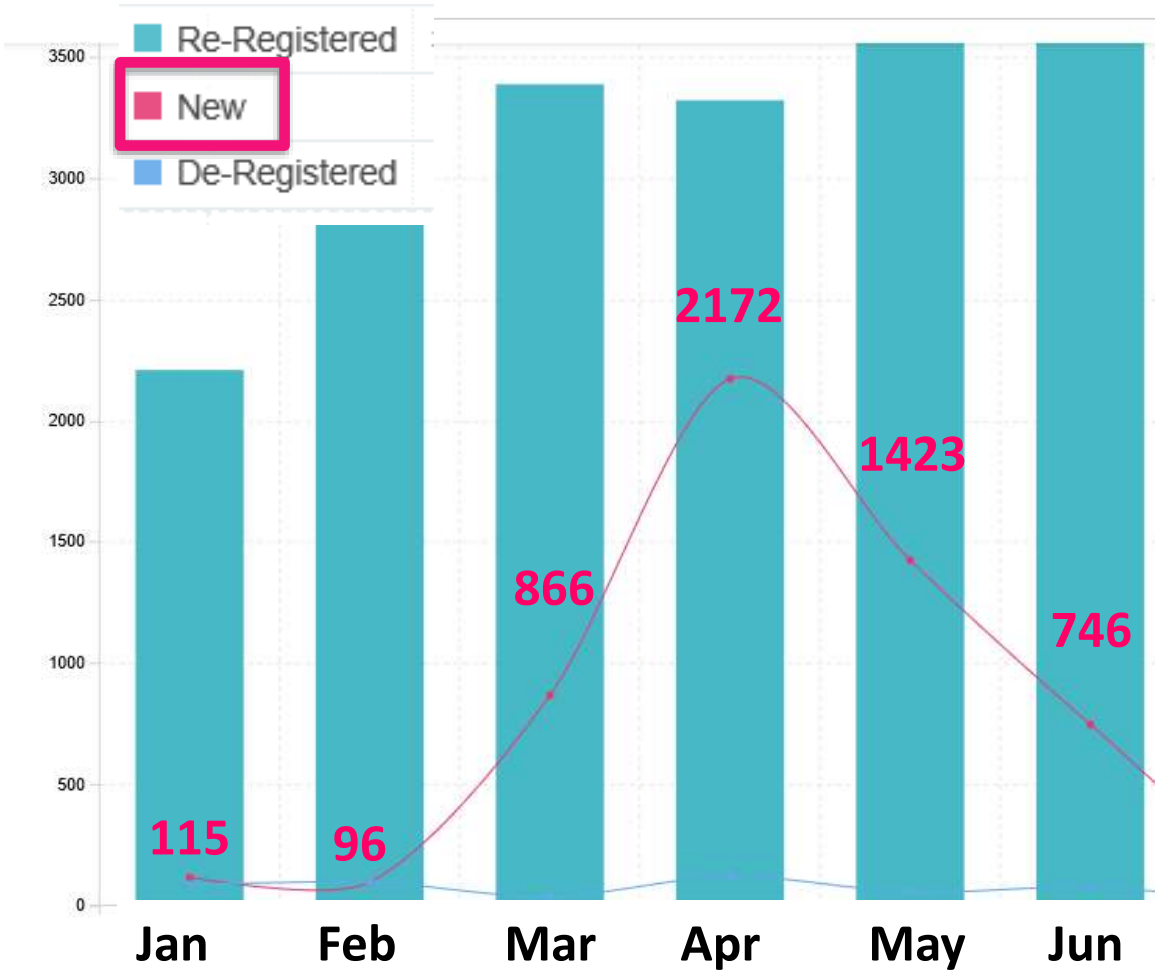
- Majority of cases were OTC, purified water systems
- ~16% included water system violations
- Examples of Violations:
  - Improper storage conditions
  - Inadequate design and maintenance
  - Lack of validation
  - Lack of appropriate testing including microbiological and chemical attributes
  - Data integrity

WLs Citing Water System Issues



Data taken from WLs issued from 12/23/2015 to 4/23/20

CY 2020 Facility Registrations



- Globally over 5000+ new registrations since March
- Inventory has doubled for firms registered in China
- Driver of this increase in registrations is for hand sanitizers and cleansing wipes

FDA warns against using 5 more hand sanitizers found to contain methanol

By Allen Kim, CNN
Updated 2:17 PM ET, Tue July 7, 2020

Link:
www.cnn.com/2020/07/07/us/fda-hand-sanitizer-trnd/index.html

The FDA has discovered additional hand sanitizers with methanol.

- **July 2, 2020 News Release: FDA Takes Action to Warn, Protect Consumers from Dangerous Alcohol-Based Hand Sanitizers Containing Methanol.** Includes a full list of FDA-tested and recalled hand sanitizers
- **Import Alert 66-78:** "Detention without Physical Examination of Drugs, Based Upon Analytic Test Results"
- **Hand Sanitizers: Guidance for Industry and Consumers**

Useful References

- On September 5, 2018, FDA published its internal policy on how manufacturing facilities are prioritized and scheduled for surveillance inspections.
  https://www.fda.gov/media/116004/download
- On August 25, 2017, FDA published its internal policy on requesting records in advance or in lieu of drug inspection.
  https://www.fda.gov/media/124338/download
- Published November 2016, Guidance for Industry - Contracting Arrangements for Drugs: Quality Agreements
  https://www.fda.gov/media/86193/download

Summary

- FDA's foreign offices are committed to effectively advance globally FDA's mission to protect and promote the public health of Americans through working with our regulatory counterparts, industry and academia.
- All drug manufacturers (including OTCs), are subject to recurring FDA inspections and oversight based on risk and are expected to adhere to the same CGMP standards.
- FDA remains transparent on requirements, vigilant on safety concerns and will continue to take action when significant quality issues arise.

谢谢大家!!!

Send inquires to:

US-FDA-CNO@FDA.HHS.Gov