16th Regulatory Conference
PIA-PR

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Information Disclaimer:

The information provided is only intended to be general summary information. It is not intended to take the place of either the written law or regulations.

Opinion Disclaimer:

The comments and opinions expressed are those solely of the presenter. They are not intended to take the place of either the written law or regulations

About FDA

- FDA is responsible for over $2 trillion in medical products, food, cosmetics, dietary supplements and tobacco.
- FDA-regulated products account for about 20 cents of every dollar of annual spending by U.S. consumers.
- The agency has approximately 15,700 full-time employees located around the world.
- FY 2018 budget is $5.1 billion.

Objectives

1. ORA Program Alignment and changes to FDA field
2. FDA ORA OPQO Division 2 Points of Contact
3. Introduction to FDA Concept of Operations
4. New Inspection Protocol Project
5. ORA Inspection Update

FDA

Office of the Commissioner

Office of Foods and Veterinary Medicine

Office of Medical Products & Tobacco

Office of Global Reg. Ops & Policy

Center for **F**ood **S**afety & **A**pplied **N**utrition

Center for **V**eterinary **M**edicine

Center for **D**evices & **R**adiological **H**ealth

Center for **B**iologics **E**valuation & **R**esearch

Center for **D**rug **E**valuation & **R**esearch

Center for **T**obacco **P**roducts

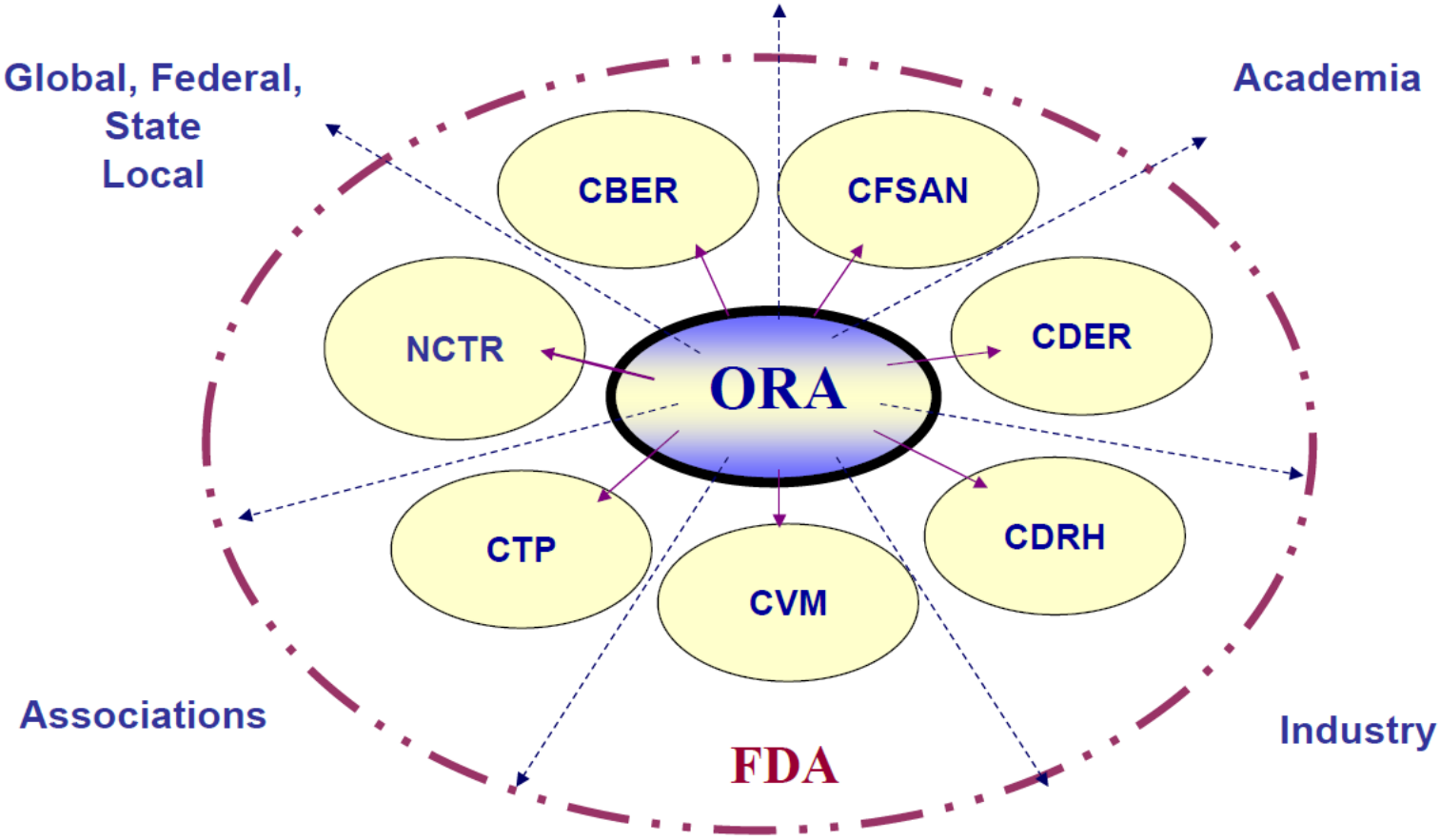
Office of **I**nternational **P**rograms

Office of **R**egulatory **A**ffairs

Office of Regulatory Affairs

- Approximately 5,000 employees in 50 states and two territories; 1,810 investigators and 850 lab analysts in 227 field offices and 13 laboratories.
- Field staff performs inspections and investigations at manufacturing sites, farms, warehouses, and ports. Provides leadership on import and enforcement policies.
- Collaborates with state, local, tribal, and territorial regulatory partners, and administers contracts, grants and cooperative agreements to advance integration.
- Maximizes compliance and minimizes risk associated with FDA-regulated products in all areas – food, animal feed, medical products and tobacco.
- Contains the Office of Criminal Investigations (OCI); 282 employees of which 222 are Special Agents.

ORA Partnerships



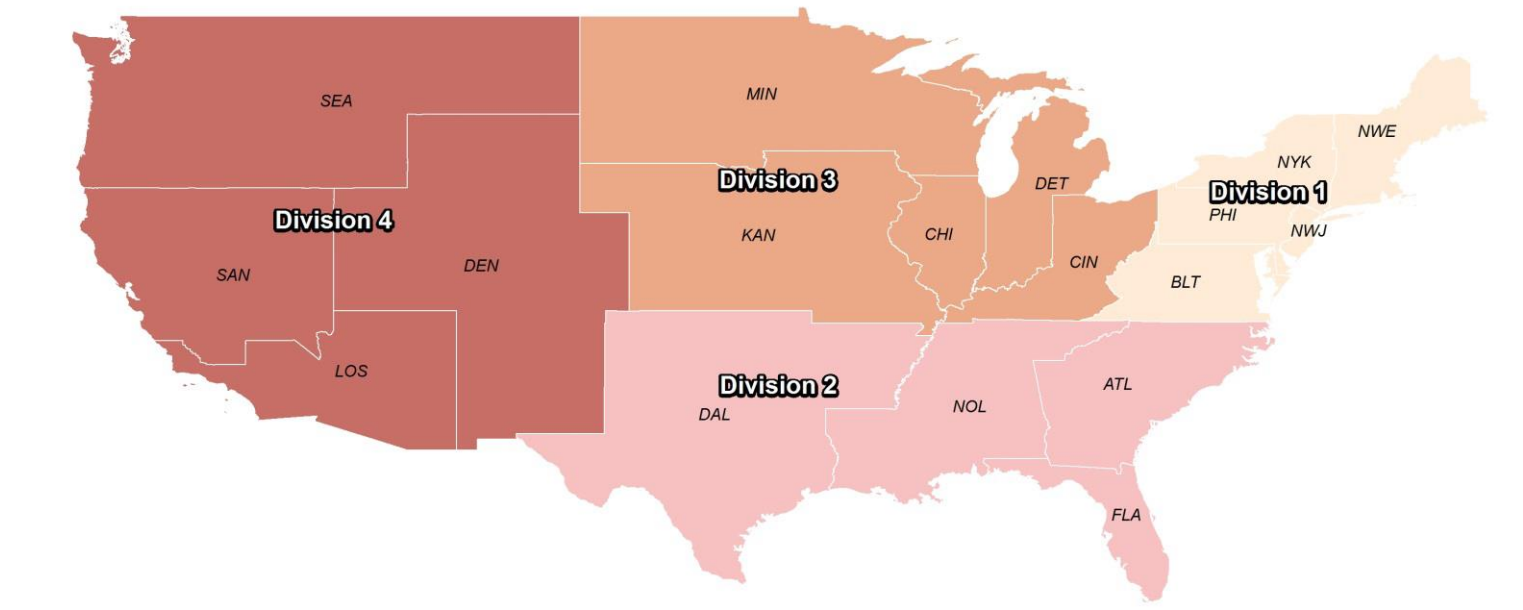
FDA ORA Program Alignment

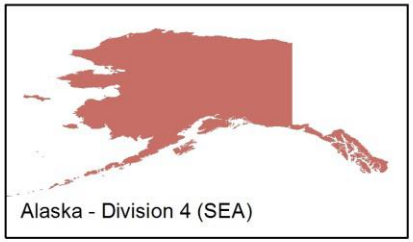
- Implemented on May 15, 2017
- Changed from the historical geographical format to program-based structure.
- Aligned ORA by FDA regulated product.
- Improve public health response and keep pace
- Employees specialize in a particular commodity

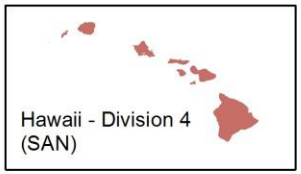
https://www.fda.gov/AboutFDA/CentersOffices/ucm392733.htm

Office of Pharmaceutical Quality Operations (OPQO)

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS







Pharmaceutical Quality Program Divisions

- Division 1 (BLT, NWE, NWJ, NYK, PHI)
- Division 2 (ATL, DAL, FLA, NOL, SJN)
- Division 3 (CIN, CHI, DET, KAN, MIN)
- Division 4 (DEN, LOS, SAN, SEA)
- FDA Current Districts Boundaries

Source: ORA

Prepared by Office of Regulatory Affairs (ORA) Division of Planning, Evaluation & Management (DPEM), Program Evaluation Branch, 2017

OPQO Office Structure

OFFICE OF MEDICAL PRODUCTS AND TOBACCO OPERATIONS
OFFICE OF PHARMACEUTICAL QUALITY OPERATIONS

Alonza Cruse
Director, Office of Pharmaceutical Quality Operations

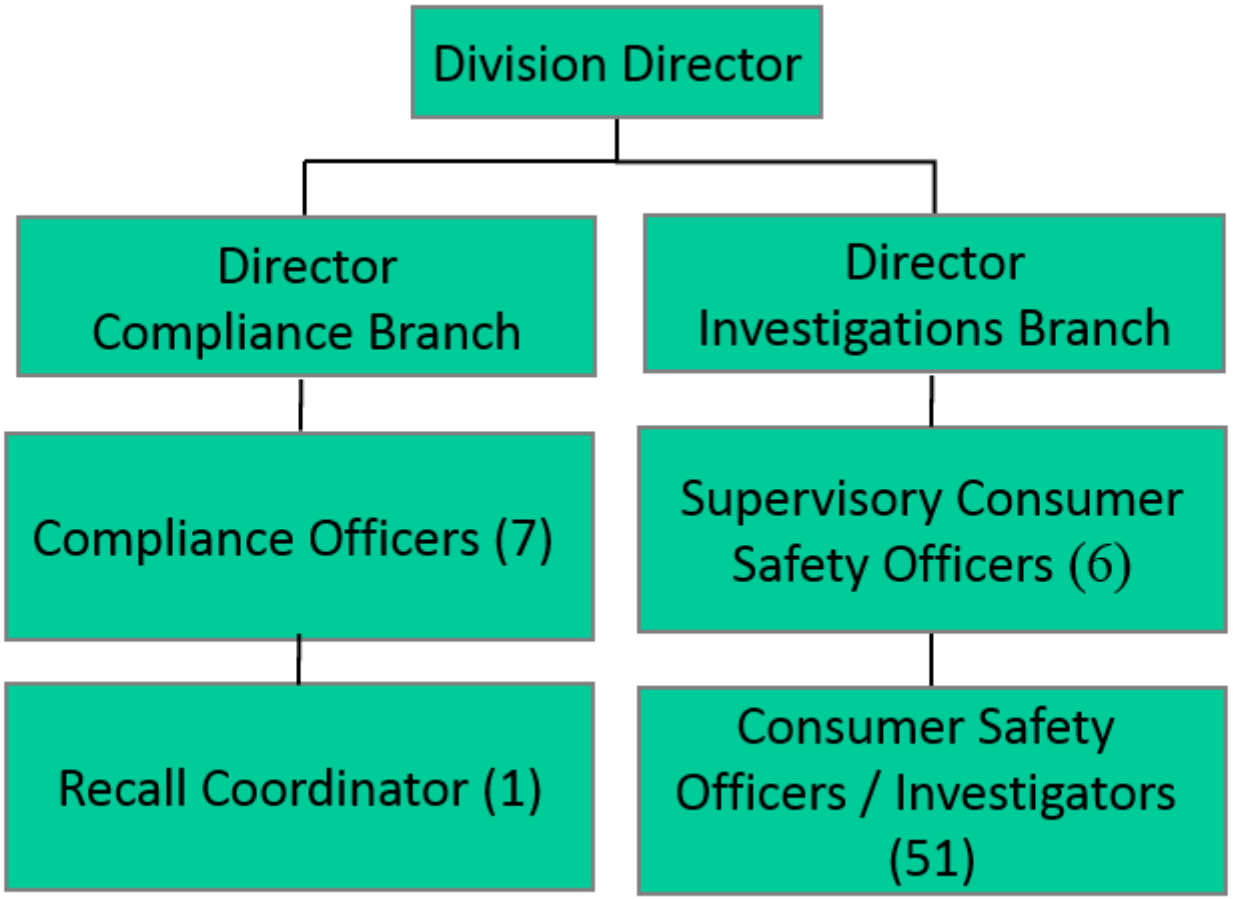
- DIVISION OF PHARMACEUTICAL QUALITY OPERATIONS I
- DIVISION OF PHARMACEUTICAL QUALITY OPERATIONS II
- DIVISION OF PHARMACEUTICAL QUALITY OPERATIONS III
- DIVISION OF PHARMACEUTICAL QUALITY OPERATIONS IV
- DIVISION OF PHARMACEUTICAL QUALITY PROGRAMS
- DIVISION OF FOREIGN PHARMACEUTICAL QUALITY INSPECTIONS

About the Office of Pharmaceutical Quality Operations

A specialized office to help protect and promote the safety and quality of human and animal drug products.

- A program within ORA's Office of Medical Products and Tobacco Operations
- 200+ investigators conduct foreign and domestic inspections of drug products for humans and animals
- 25 compliance officers and a mission support staff are assigned to the OPQO
- 7 Pharma Labs: DET, NRL, PHI, PSW, SJN, FCC, WEAC
- Advise and counsel agency leaders on pharmaceutical product field operations and emergency response activities
- Collaborates with CDER and CVM on all FDA-regulated pharmaceutical and biopharmaceutical products, and implementation of legislative mandates
- Provides technical assistance on investigational operations

Division II Organizational Chart



Division II – Points of Contact

- Program Division Director – Ms. Monica R. Maxwell (Dallas)
  - Monica.Maxwell@fda.hhs.gov (214) 253-4915
- Director, Investigations Branch – Ms. Tamala Magee
  - Tamala.magee@fda.hhs.gov (310) 647-2920 (will be changing)
- Director, Compliance Branch – LCDR John W. Diehl (Dallas)
  - John.Diehl@fda.hhs.gov (214) 253-5288
- Recalls – Ms. Kenitra Hewitt (Fort Worth Resident Post)
  - orapharm2recalls@fda.hhs.gov and Kenitra.Hewitt@fda.hhs.gov
  - (817) 334-5218 x 1104
- FDA 483 Responses and Other Correspondence – Email preferred
  - ORAPHARM2_RESPONSES@fda.hhs.gov

ConOps Agreement

- Covers Pre- and Post-Approval, Surveillance, and For-Cause Inspections at domestic and international drug facilities
- Does not cover compounding, bioresearch monitoring, and pre-approval inspections for biotech products
- For ORA and CDER staff involved in these inspections, outlines
  - workflow
  - roles and responsibilities


U.S. FOOD & DRUG ADMINISTRATION

Integration of the Facility Evaluation and Inspection Program for Human Drugs –A New Operating Model

INTEGRATION OF FDA FACILITY EVALUATION AND INSPECTION PROGRAM FOR HUMAN DRUGS: A CONCEPT OF OPERATIONS

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF REGULATORY AFFAIRS

DATED JUNE 6, 2017

Why Concept of Operations?

Needs

- Better oversight of increasingly complex and global manufacturing of drugs
- Improved efficiency in line with the ORA Program Alignment into vertically integrated, program aligned areas
- Enhanced IQA approach – alignment/integration between field professionals and review staff
- New commitments and improved coordination and efficiency of work performed under generic drug program as per GDUFA II

Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations

Jointly developed operating model to advance the pharmaceutical quality program.

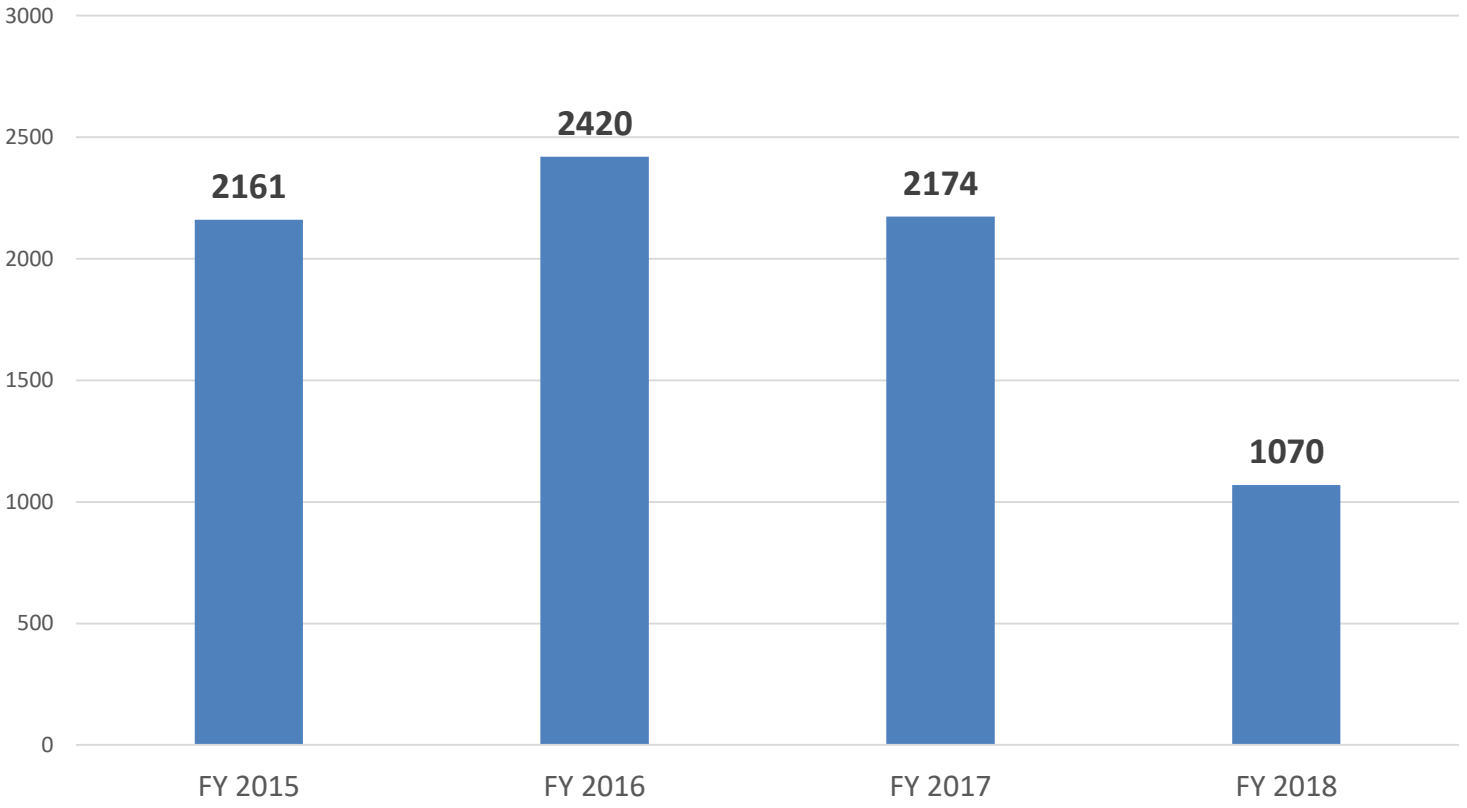
- Improve consistency, transparency and collaboration in our respective operations to promote one quality voice;
- Reduce uncertainty for industry by providing timely and expected communication of our inspectional findings and facility assessments;
- Reduce the time to issue advisory and enforcement actions;
- Eliminate redundant reviews in the classifications of inspections and achieves parity of domestic and international facilities;
- Clarify roles and responsibilities and increases access to facility and decisional information.

New Inspection Protocol Project

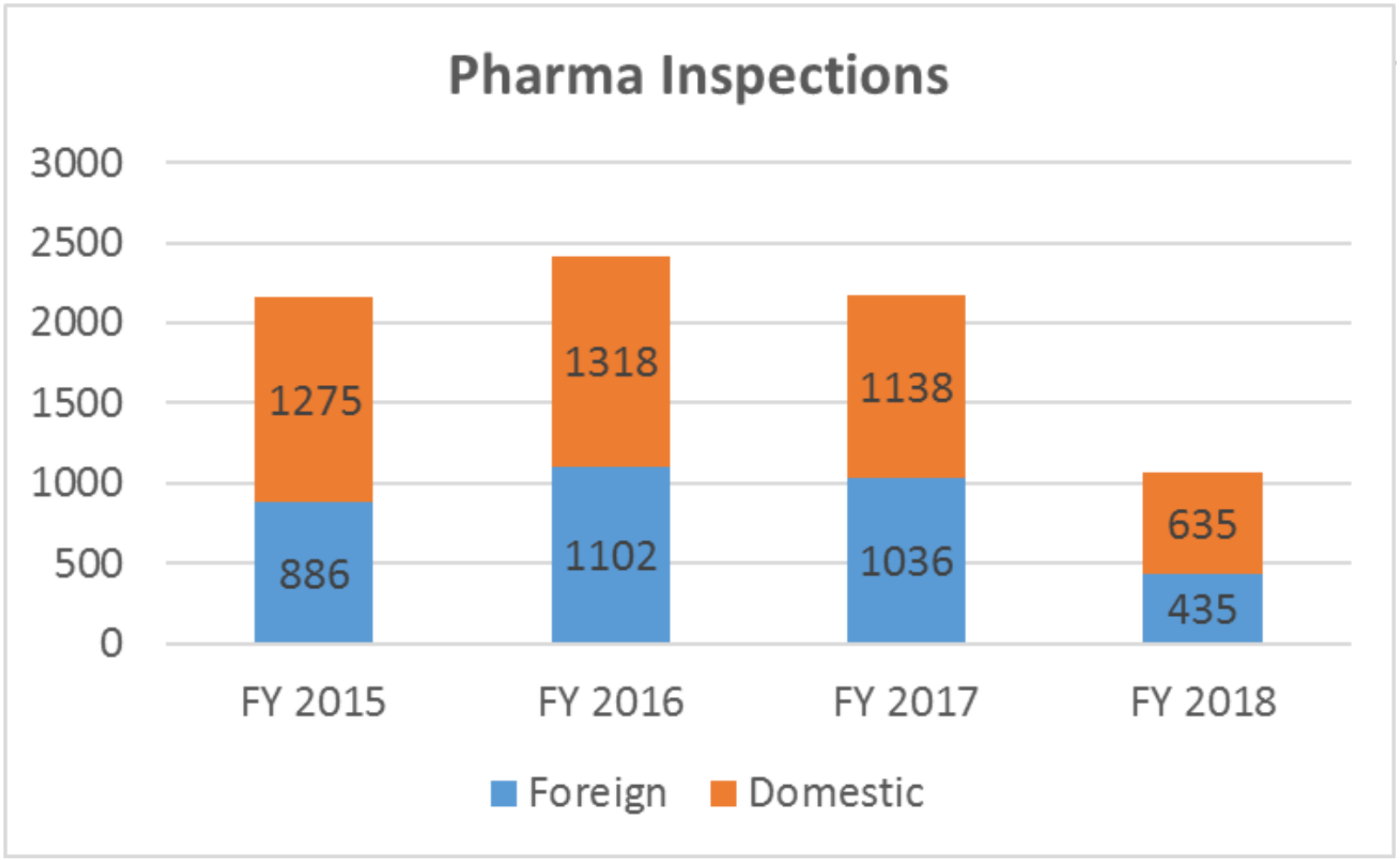
- Consistent inspections for high risk areas
- Efficient report writing
- Involves questions of focus
- Protocols on handheld tablets
- Used in domestic and international inspections

ORA Inspection Update

Total Pharma Inspections



Data as of 5/25/18; does not include BIMO.



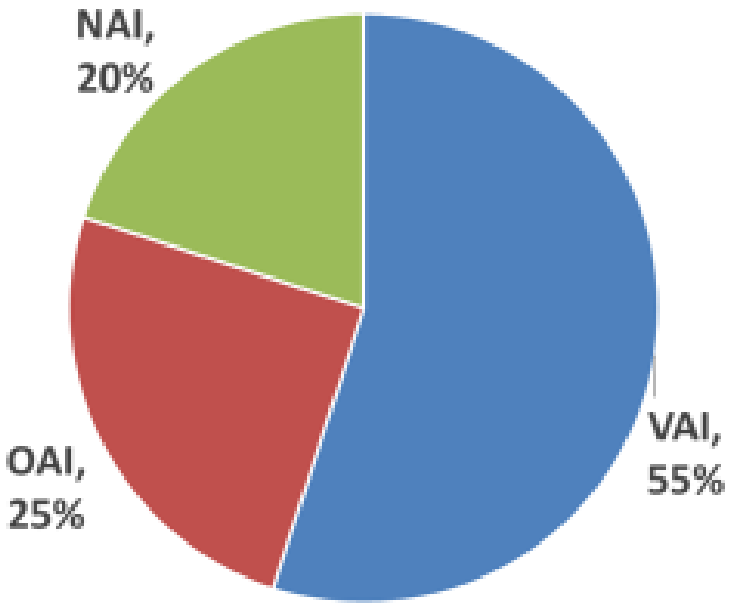
Data as of 5/25/18; does not include BIMO.

Never Inspected Firms

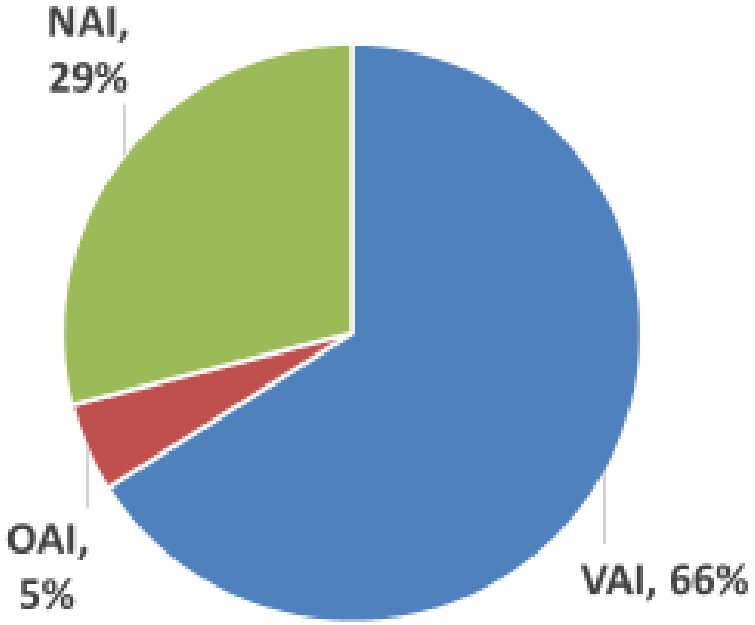
- Beginning in FY17, goal to inspect entire inventory with in 3 years
- Will likely complete in FY18
- Increasing global oversight by inspecting all foreign drug firms
- Significant risk in never inspected firms

FY17 Inspection Classifications

Never Inspected (foreign)



Routinely Inspected (foreign)

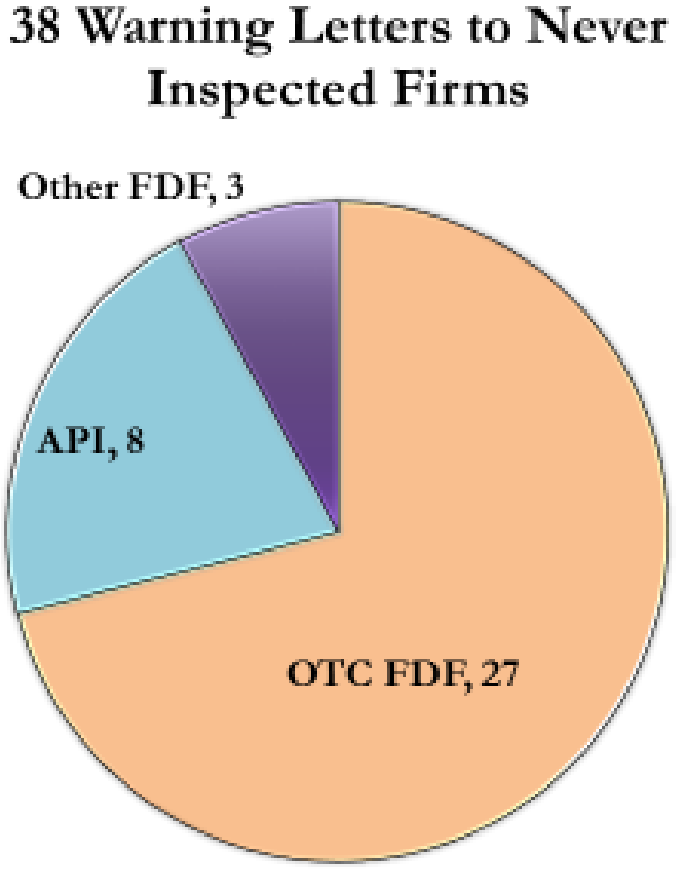


Data is as of December 19, 2017, and includes final classification if available, initial classification if not. NAI = No Action Indicated; VAI= Voluntary Action Indicated; OAI = Official Action Indicated

Advisory Actions Against Firms on the "Never Inspected" List

- 38 Warning Letters issued
- 68 firms* added to Import Alerts
  - 41 on to 66-40 (CGMP)
  - 30 on to 99-32 (refusal)

*three firms were added to both 99-32 and 66-40



Data from 06/21/2016 to 01/09/2018. API = Active Pharmaceutical Ingredient; FDF = Finished Dosage Form; OTC = Over the Counter

Top Warning Letter Charges for OTC and Other FDF Manufacturers from the "Never Inspected" List

- 211.165(a) - Testing and release for distribution.
- 211.22(a) - Responsibilities of quality unit.
- 211.84(d) - Testing and approval or rejection of components, drug product containers, and closures.
- 211.100(a) - Written procedures; deviations.

Total WL's in FY2017 and FY2018

- https://datadashboard.fda.gov/ora/cd/complianceactions.htm
- Search by "Drugs" and "FY2017 and 2018"
- Total Warning Letters = 254 (includes compounding warning letters, unapproved drug warning letters, finished drug manufacturer, etc).
- Does not break down by CFR Cite
- Provides Recall Data (1172 recalls in FY17 and FY18)

Areas of Emphasis

- Data Integrity (211.68, 100, 180, etc)
  - Observed Data Integrity CGMP violations
  - Important component of ensuring safety, efficacy and quality of drugs
  - Evaluate, Assess Risk, Remediate
- Quality Control Unit (21 CFR 211.22)
  - Product meets specification prior to distributing
  - Investigate and determine cause of failures
  - Need management support

Thank You

Questions and Discussion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