U.S. FOOD & DRUG ADMINISTRATION

Center for Drug Evaluation and Research - Compliance Central with FDA Center Compliance Directors: Part 1

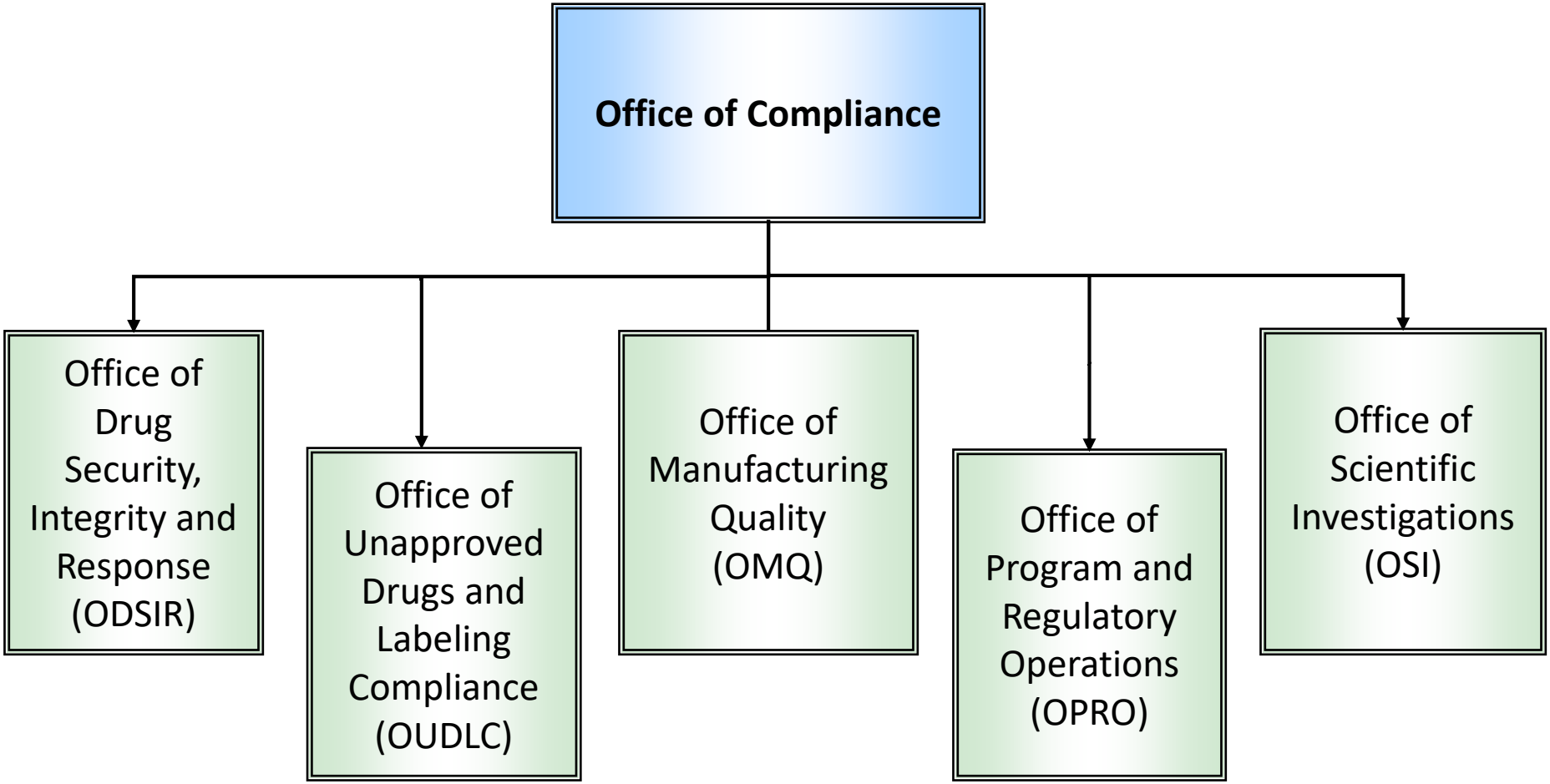
Donald D. Ashley, JD

2017 FDLI Enforcement, Litigation, and Compliance Conference: For the Drug, Device, Food, and Tobacco Industries

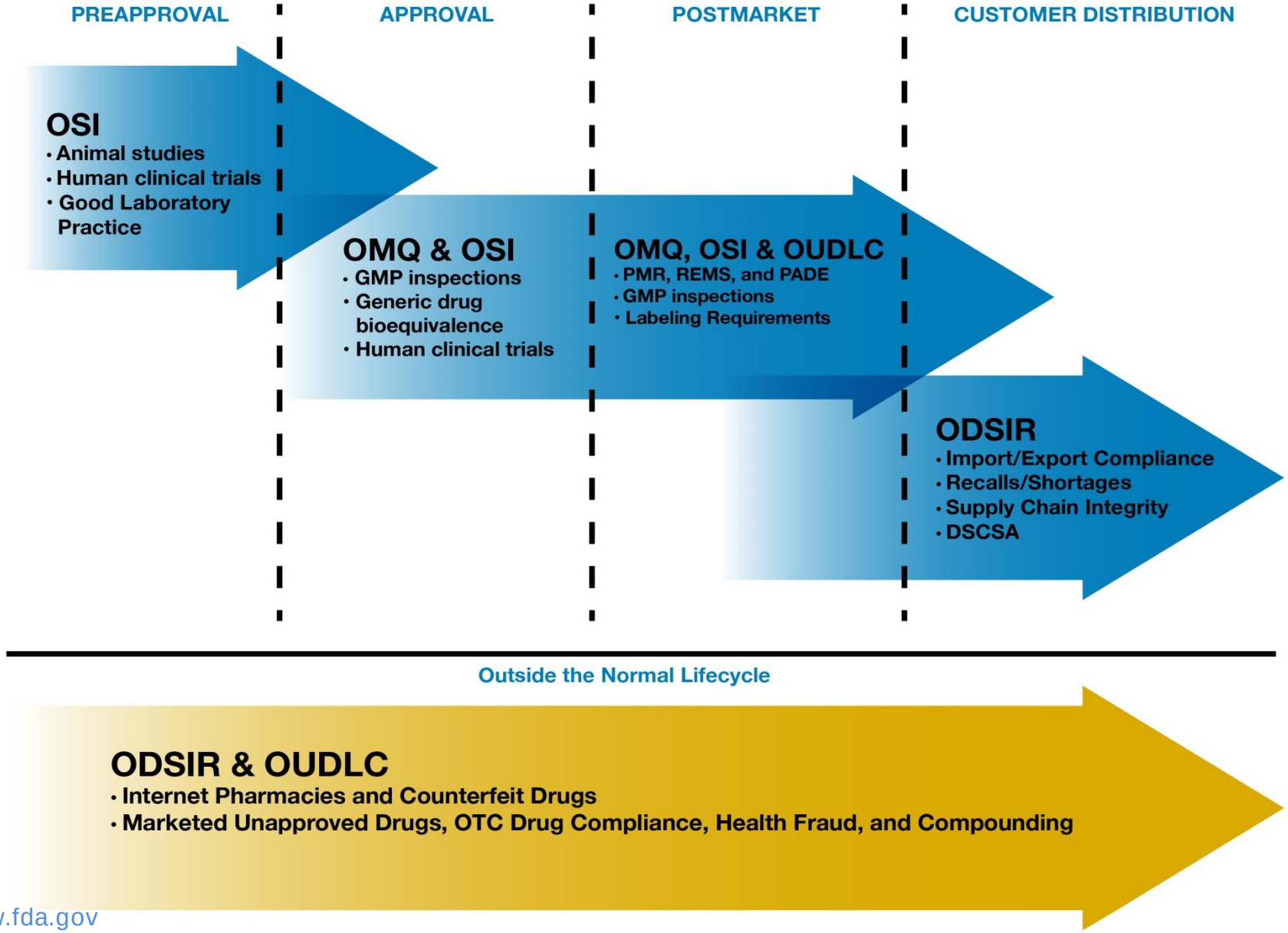
December 6, 2017

CDER Office of Compliance Overview

Office of Compliance Structure

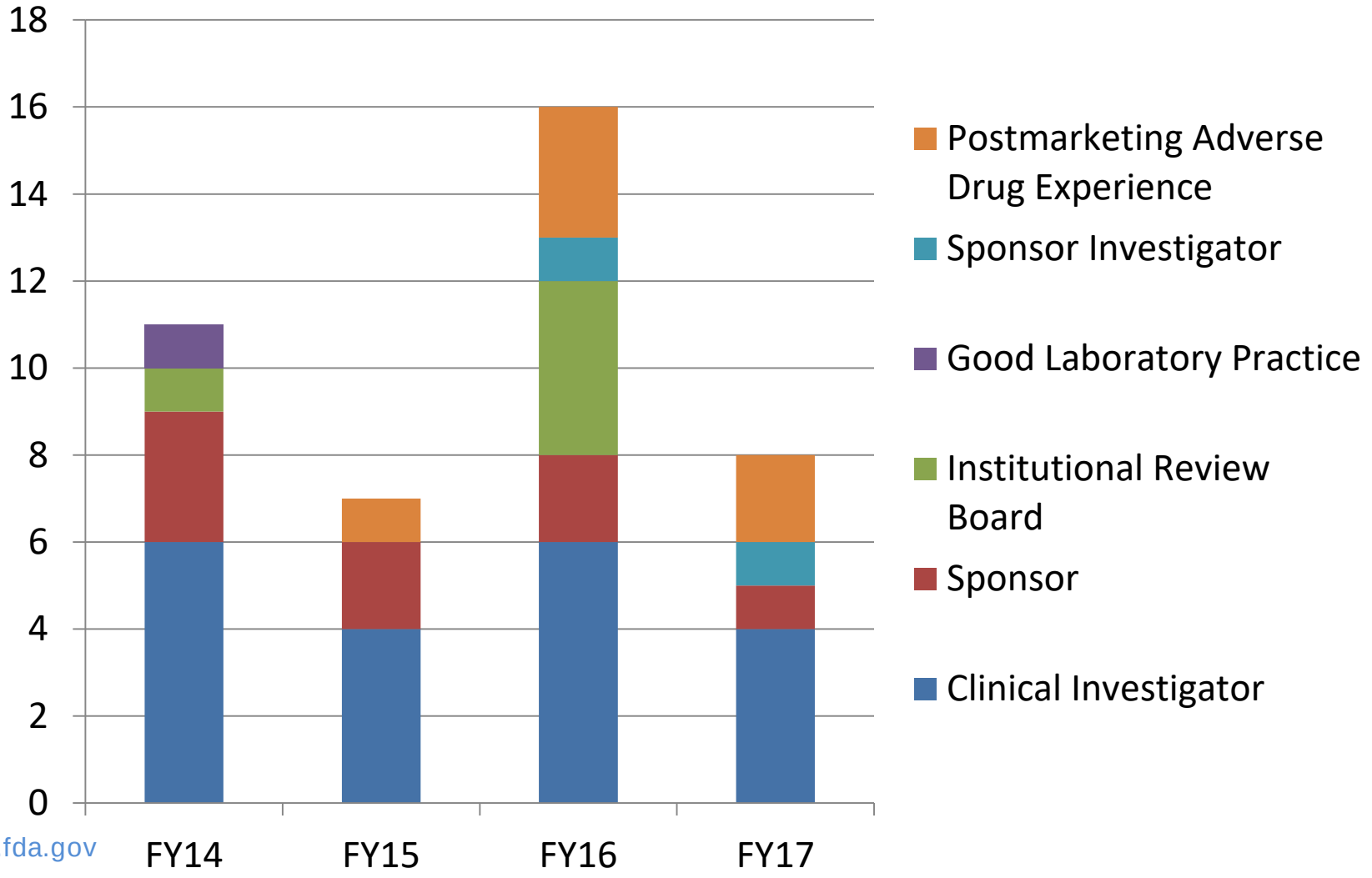


Responsibility Throughout Lifecycle



Office of Scientific Investigations

BIMO Warning Letters issued from FY14-FY17



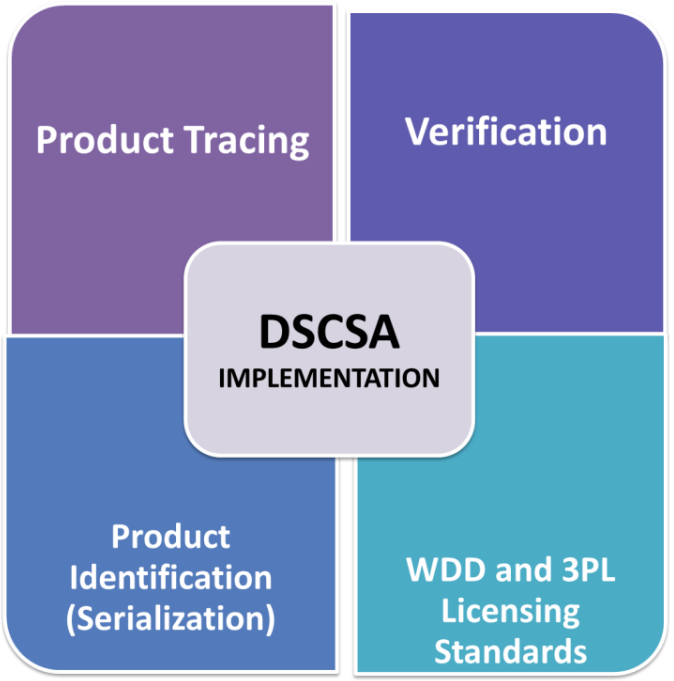
Office of Unapproved Drugs and Labeling Compliance: FY17 Compounding Activities

- Conducted 141 compounding inspections
- 62 warning letters have been issued to compounders
- Brought 2 injunctions against compounders
- Oversaw 41 recall events
- Held 2 Pharmacy Compounding Advisory Committee meetings
- Issued 6 guidance documents
- Issued 3 rules

Office of Drug Security, Integrity and Response

Drug Supply Chain Security Act Goals

- Develop an electronic, interoperable system by **2023** to identify and trace certain prescription drugs as they move through the U.S. supply chain to:
  - Facilitate the exchange of information by trading partners at the individual package level
  - Improve efficiency of recalls
  - Enable prompt response to suspect and illegitimate products when found
  - Create transparency and accountability in the drug supply chain
- Establish national standards for licensure for wholesale distributors and third-party logistics providers



Office of Manufacturing Quality Concept of Operations ("Con Ops")

- The Program Alignment initiative created a program-based management structure that aligns staff by FDA-regulated product. CDER and ORA developed a Con Ops that outlines how OMQ, Office of Pharmaceutical Quality and ORA will work within this programmatically-aligned environment, and applies to the following types of human drug facility inspections:
  - Pre- and post-approval inspections
  - For-cause inspections
  - Surveillance inspections
- Con Ops supports GDUFA II FY19 commitment to communicate final inspection classifications that do not negatively impact approvability of any pending application within 90 days of the end of the inspection
  - Creates 90-day decisional letters for surveillance inspection outcome
- 6 month goal date for issuing Warning Letters
- CDER and ORA have begun to operationalize Con Ops
  - Internal policies and procedural documents will be updated as needed

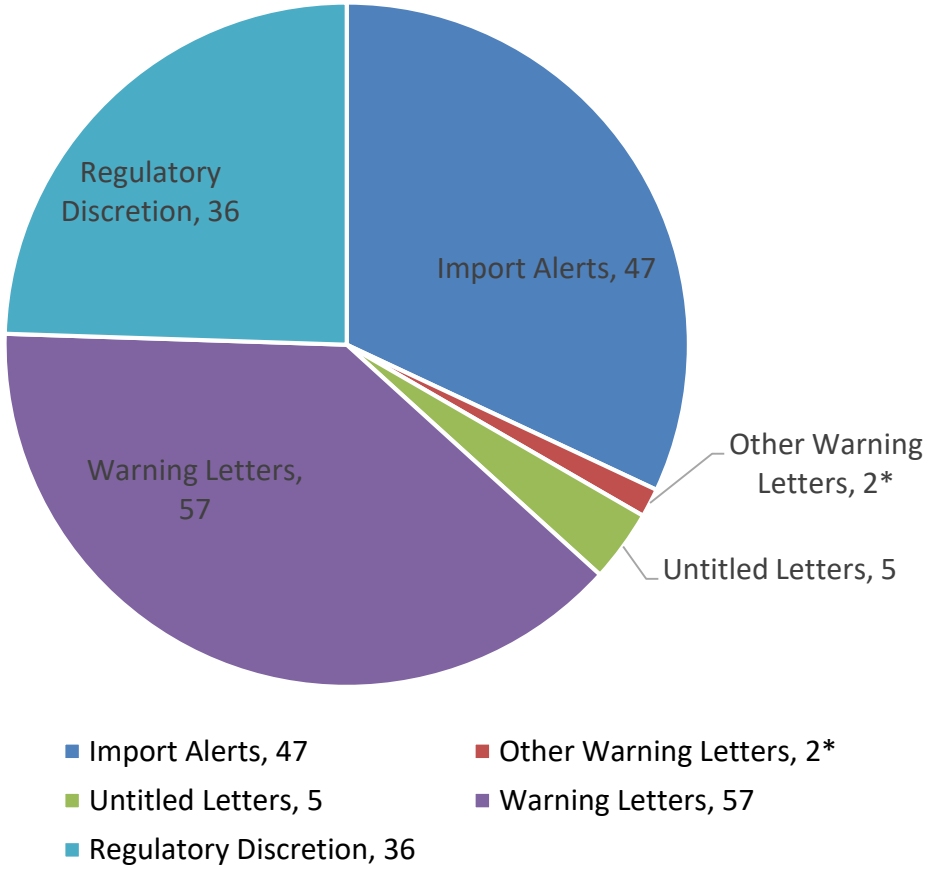
Concept of Operations ("ConOps")

- Ensures consistency, efficiency and transparency
- Advances strategic alignment by creating clear roles and responsibilities
- Improves operational capacity by enhancing collaboration
- Meets User Fee commitments
- Improves timeline for actions

Enforcement and Advisory Tools

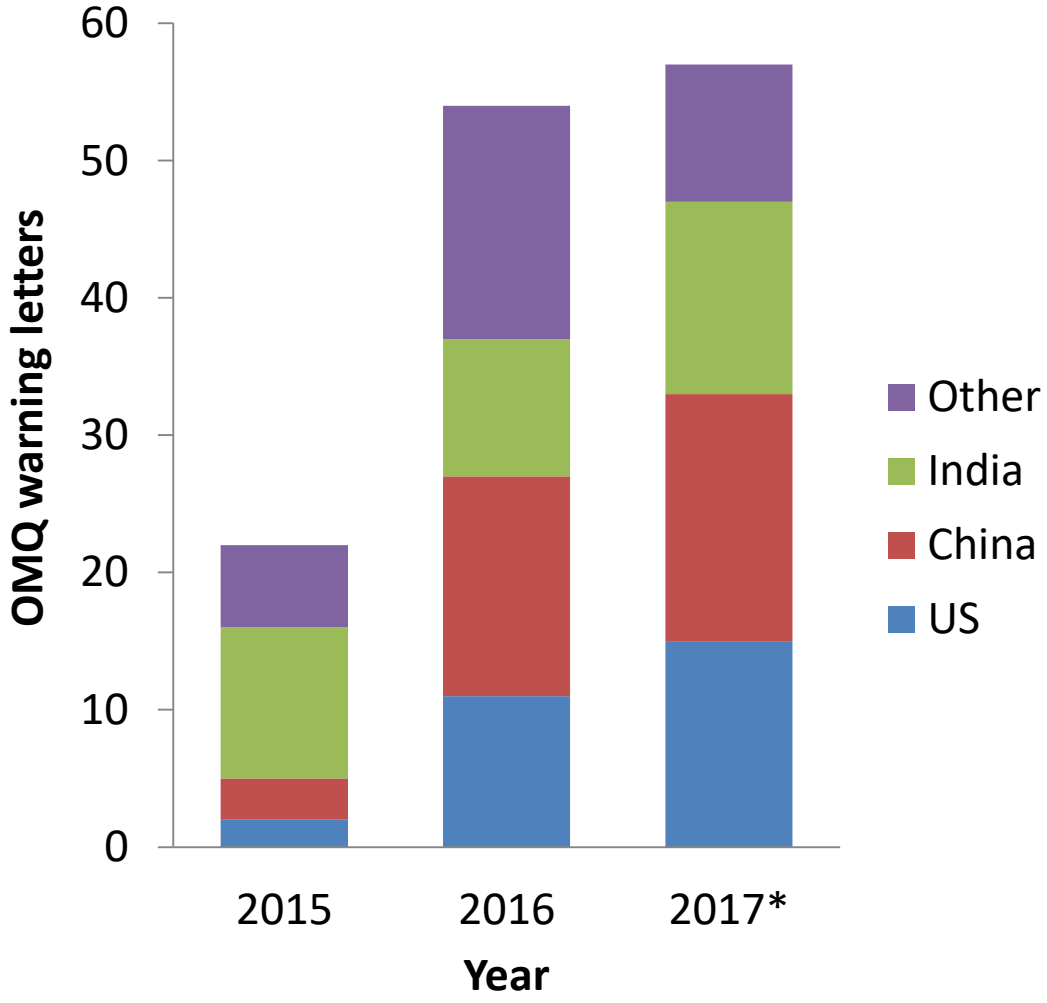
- Regulatory Meetings
- Injunctions
- Consent Decrees
- Import Alerts
- Seizures
- Warning Letters
- Untitled Letters
- Others

Jan. 1 – Nov. 1, 2017



Excludes compounding-related actions
* Warning letters from another office within CDER
Compliance with OMQ CGMP violations

Office of Manufacturing Quality Warning Letters by Calendar Years



*Through November 1, 2017. Does not include compounding warning letters or warning letters from another office within CDER Compliance with OMQ CGMP violations.

Office of Manufacturing Quality
FY17 Activities

EpiPen Warning Letter (September 2017)

- First combination product WL that includes charges from CDER and CDRH
- CDER considered compliance with all drug CGMP violations and FDA's Center for Devices and Radiological Health (CDRH) considered compliance with specified provisions under 21 CFR part 4
- Facility was considered violative separately by each FDA center under the applicable regulations
  - Firm was not appropriately investigating failures and complaints
  - Firm did not reopen and broaden the investigation, or recall products until FDA inspection

Office of Manufacturing Quality
FY17 Activities

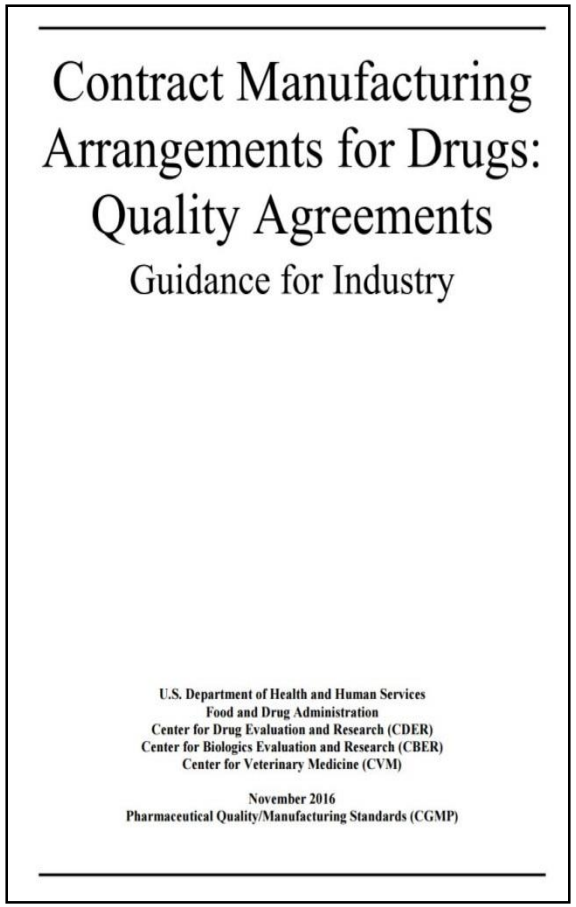
Contract Manufacturing: From Bad to Worse

"Drugs Made for You by Firm B

You have engaged Firm B to manufacture Firm A Perox-A-Mint, **(b)(4)**. These products […]are adulterated as enumerated in the preceding violations. **They are also adulterated for the reasons set forth in Warning Letter 515029, issued by FDA to Firm B on June 29, 2017**. Among other things, *Firm B manufactured your oral solution drugs using the same equipment in which Firm B manufactured toxic industrial-grade* car washes and waxes. **You are responsible for ensuring that all of your products are manufactured in accordance with CGMP, including oversight of the manufacturing operations conducted by your contractor, Firm B, on your behalf**. Contractors are extensions of the manufacturer, and you are required to ensure that your drugs are made in accordance with section 501(a)(2)(B) of the FD&C Act to ensure safety, identity, strength, quality, and purity…"

-WL July 2017

Office of Manufacturing Quality FY17 Activities


Contract Manufacturing Arrangements for Drugs: Quality Agreements

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

November 2016
Pharmaceutical Quality/Manufacturing Standards (CGMP)

Final Guidance on Quality Agreements: Quality agreements can be used to define expectations and responsibilities in a contract manufacturing arrangement up front.

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM353925.pdf

THANK YOU