

Enforcement Trends

New England Chapter PDA

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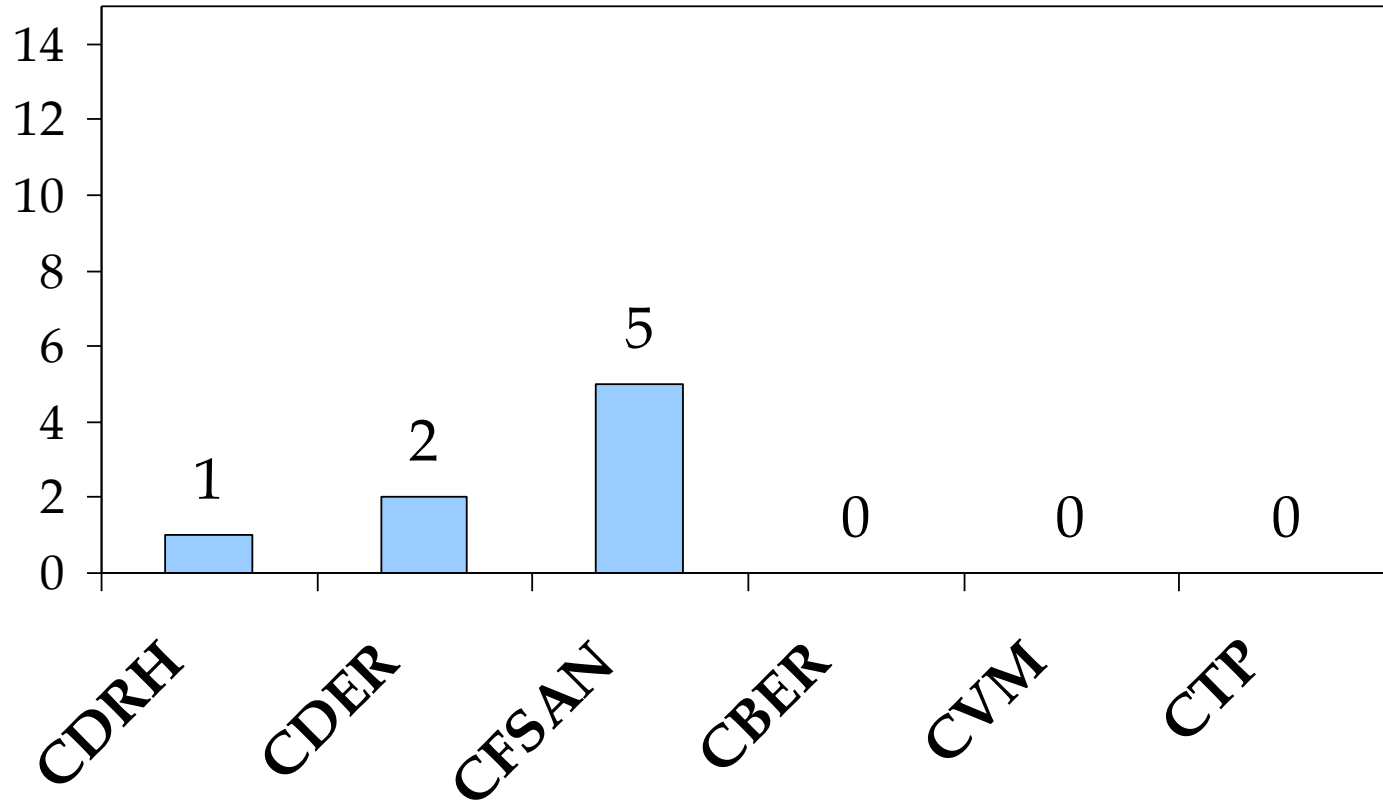
FDA Enforcement Statistics

Summary

Fiscal Year 2012

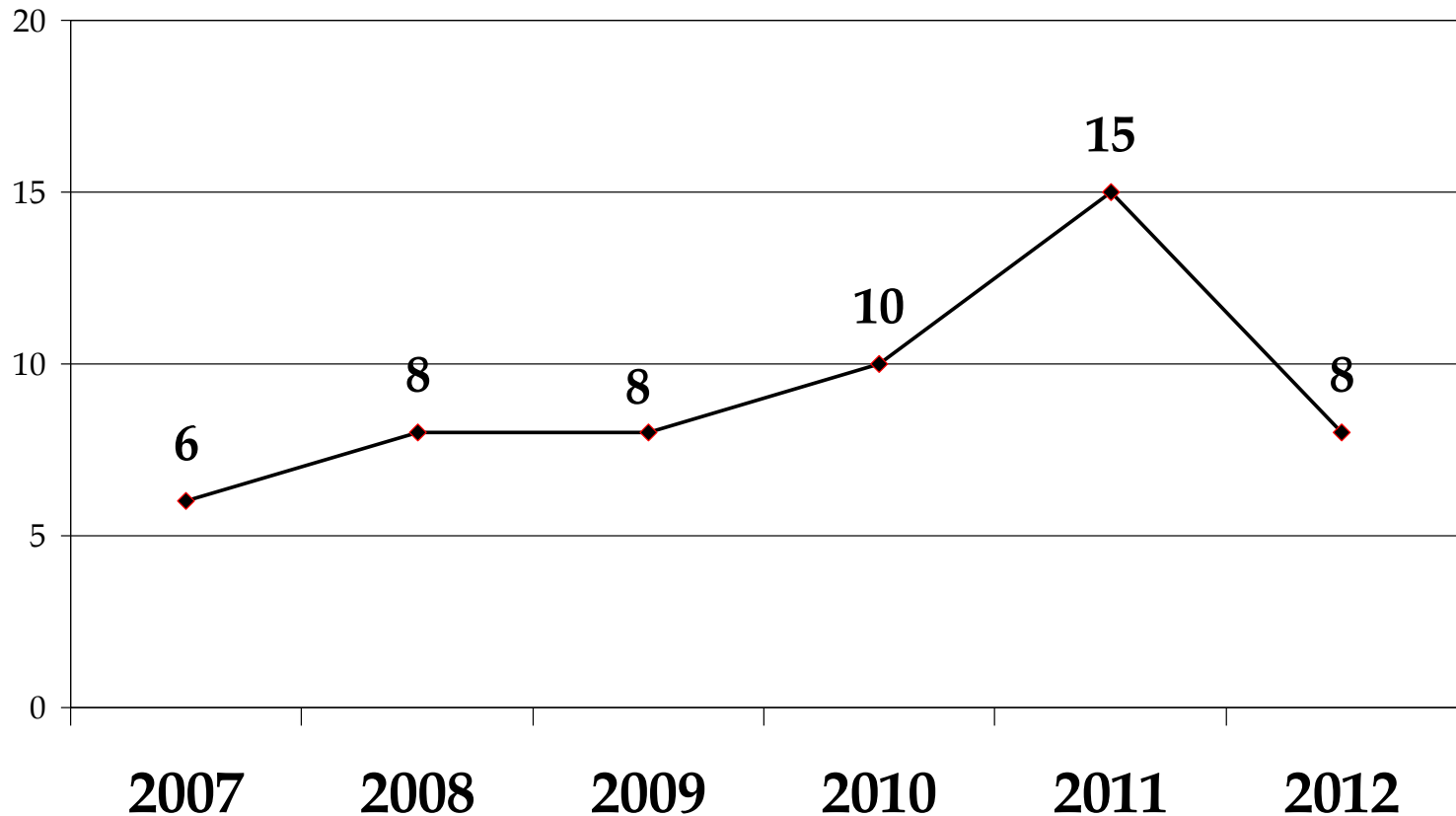
Seizures	8
Injunctions	17
Warning Letters	4,882
Recall Events	4,075
Recalled Products	9,469
Debarments	20

Seizures by FDA Center Fiscal Year 2012

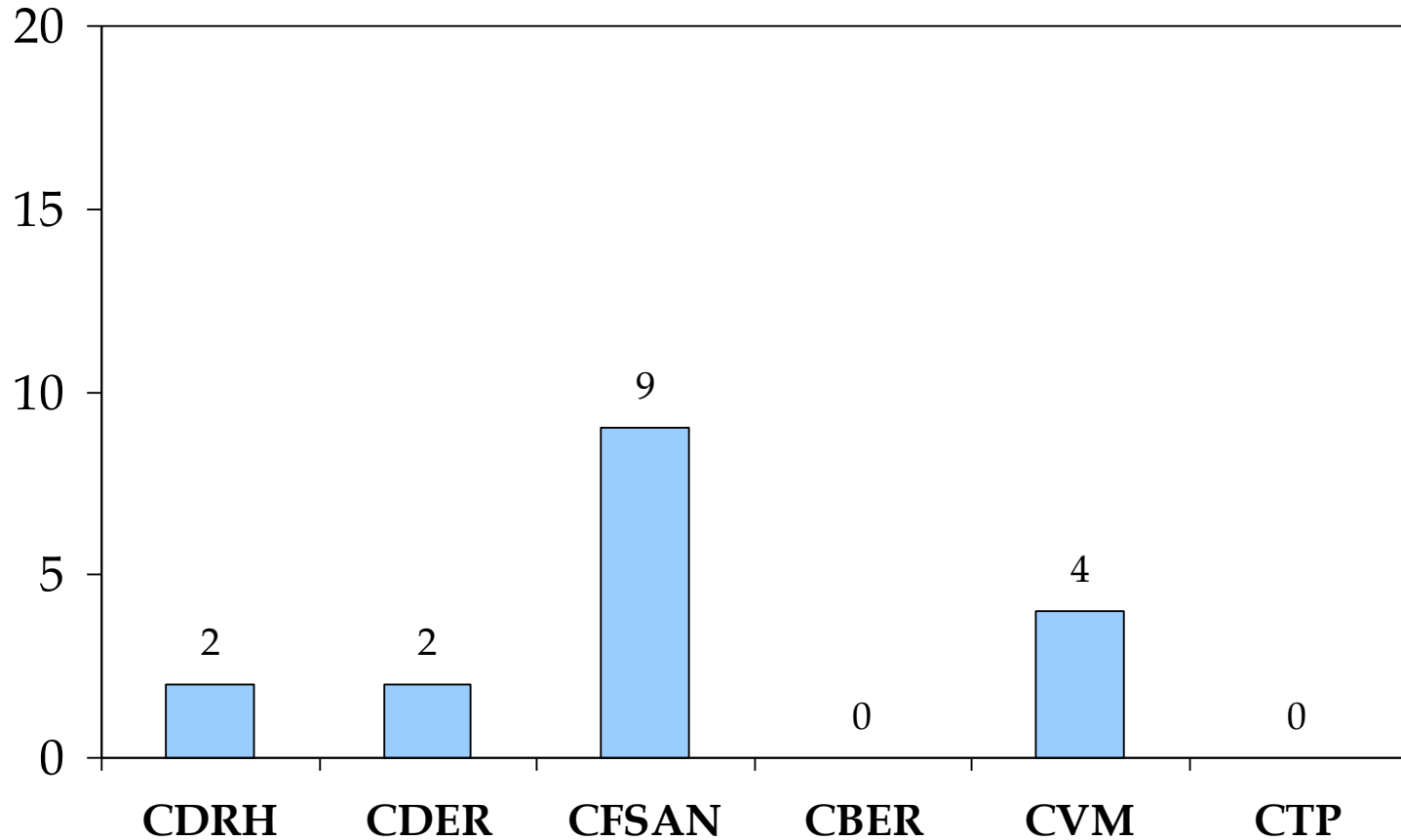


FDA Seizures

Fiscal Years 2007 - 2012

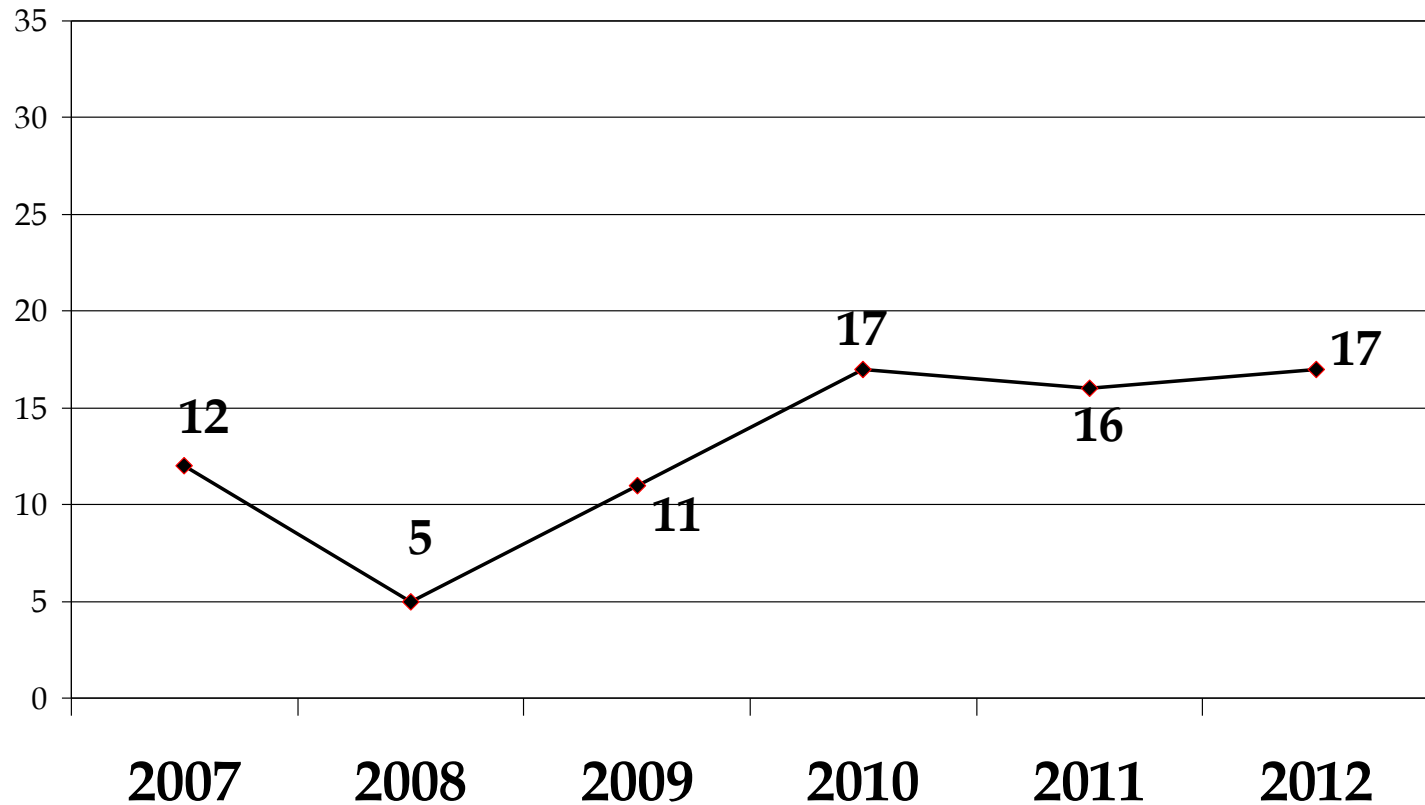


Injunctions by FDA Center Fiscal Year 2012

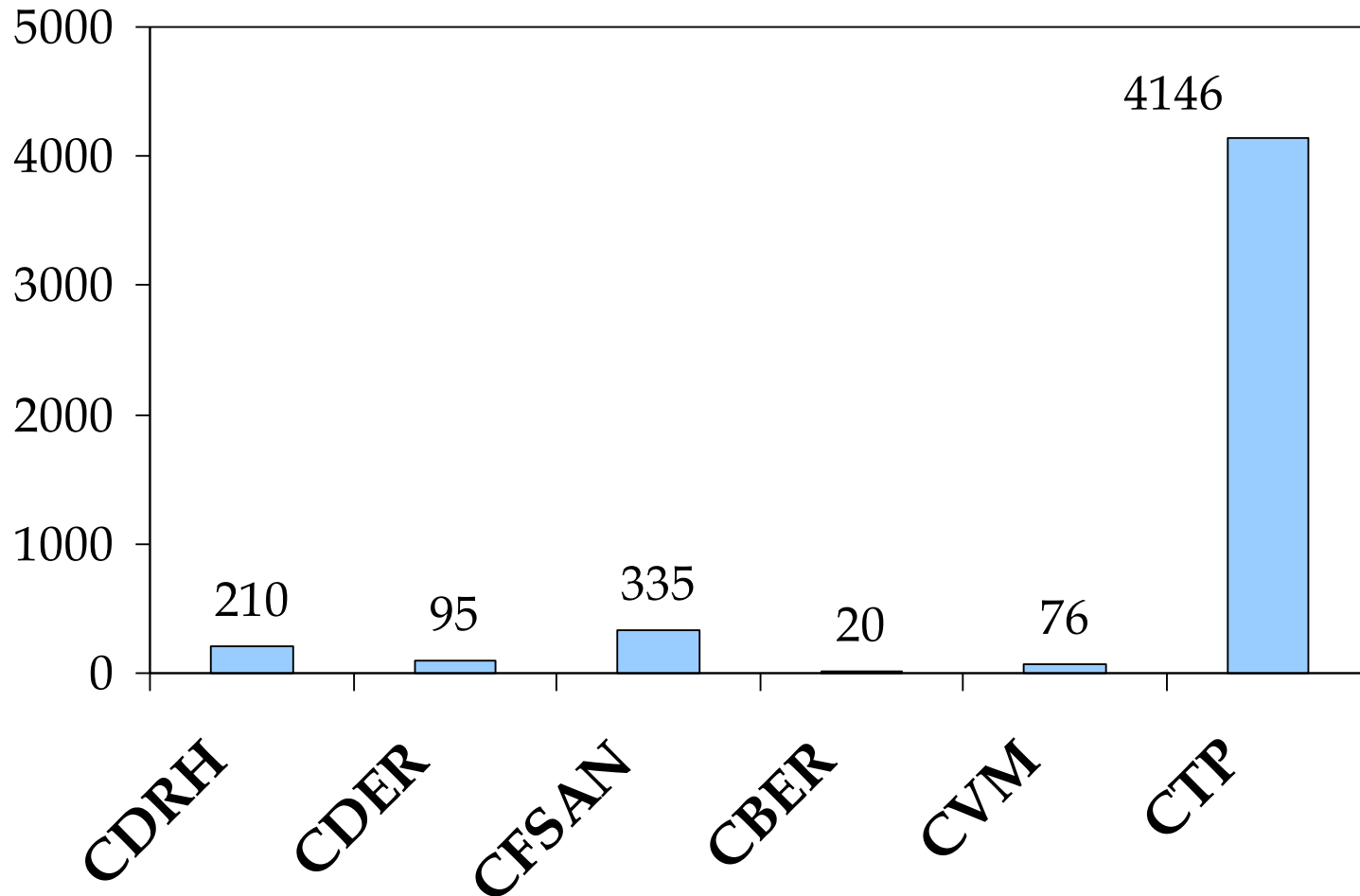


FDA Injunctions

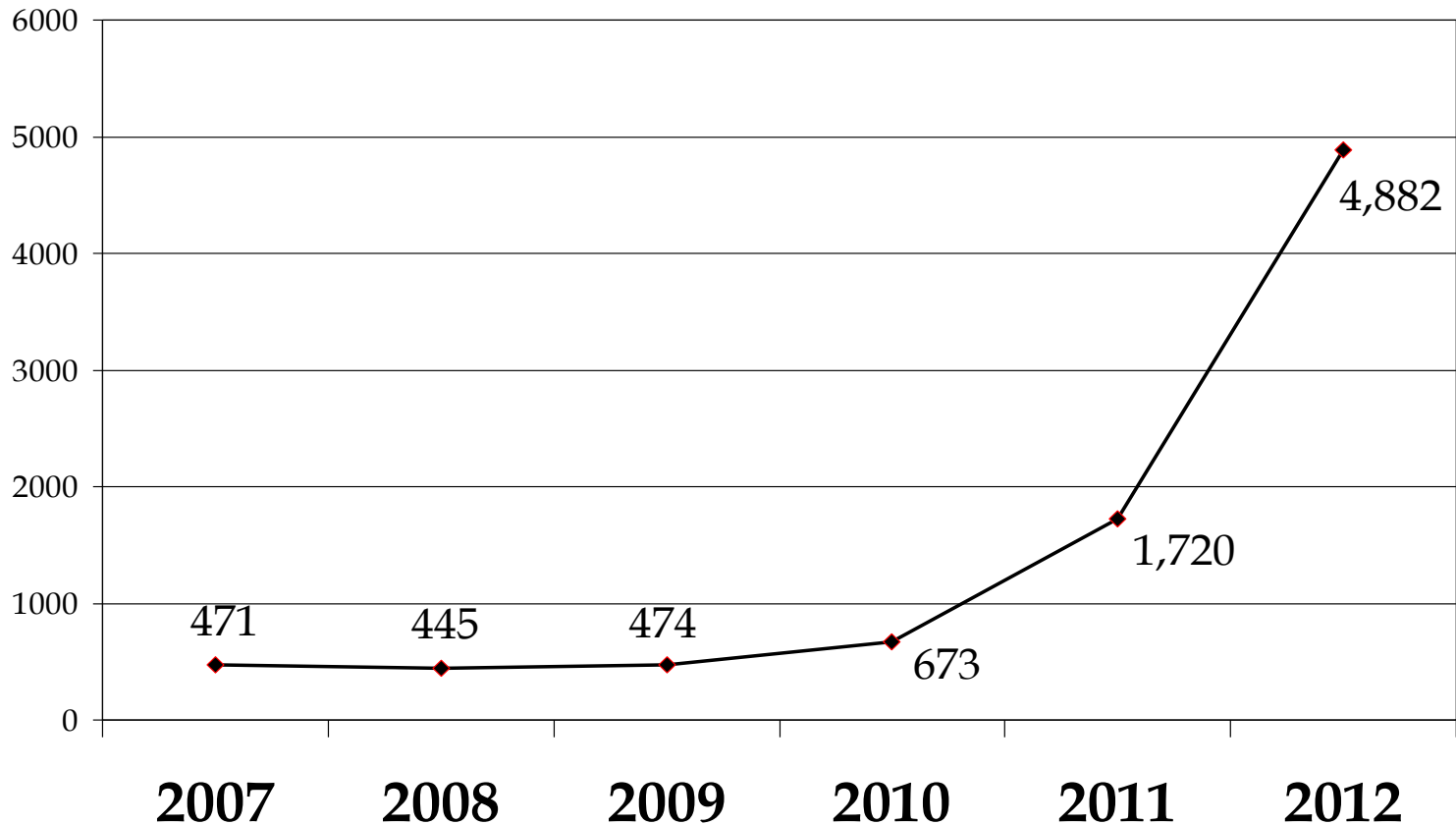
Fiscal Years 2007 - 2012



Warning Letters by FDA Center Fiscal Year 2012

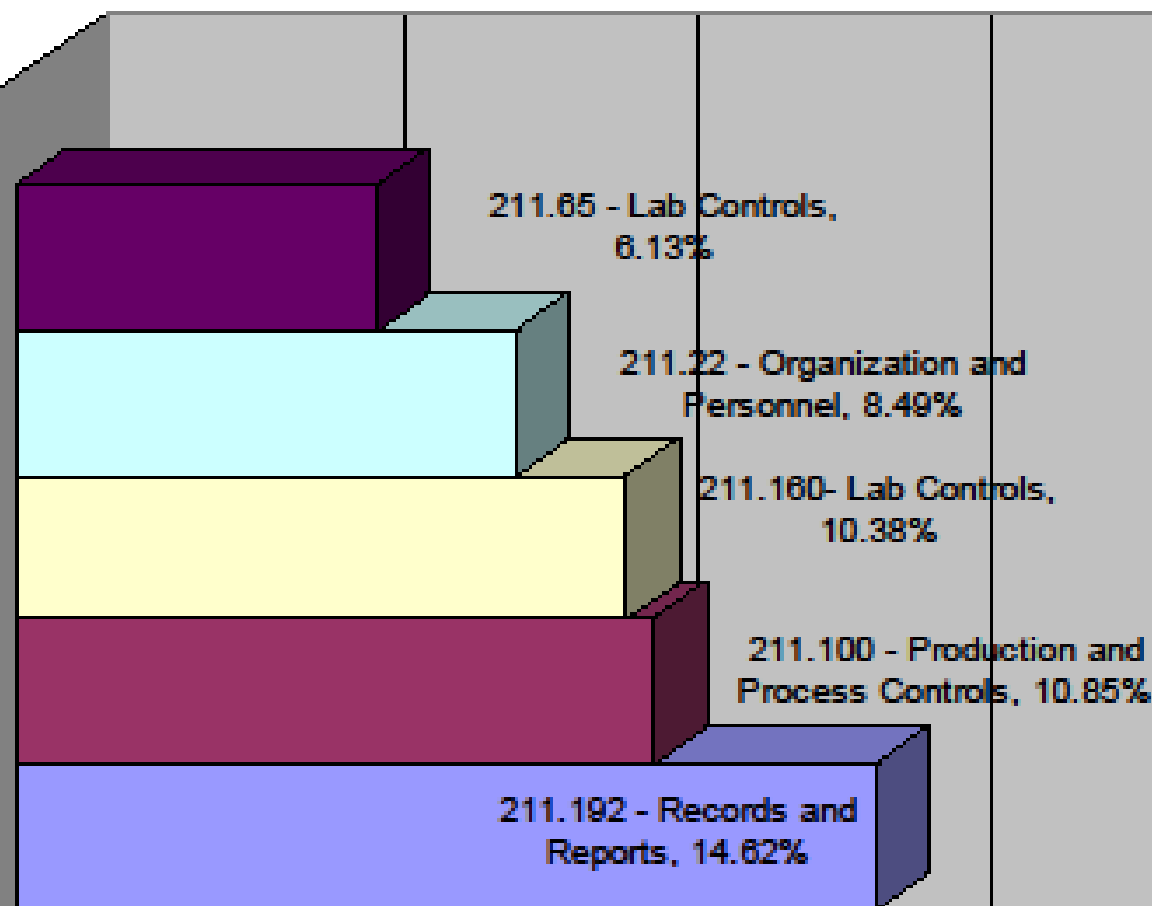


FDA Warning Letters Fiscal Years 2007 - 2012



Top 5 GMP Regulatory Violations and in 2010 WLs

(Domestic and Foreign)



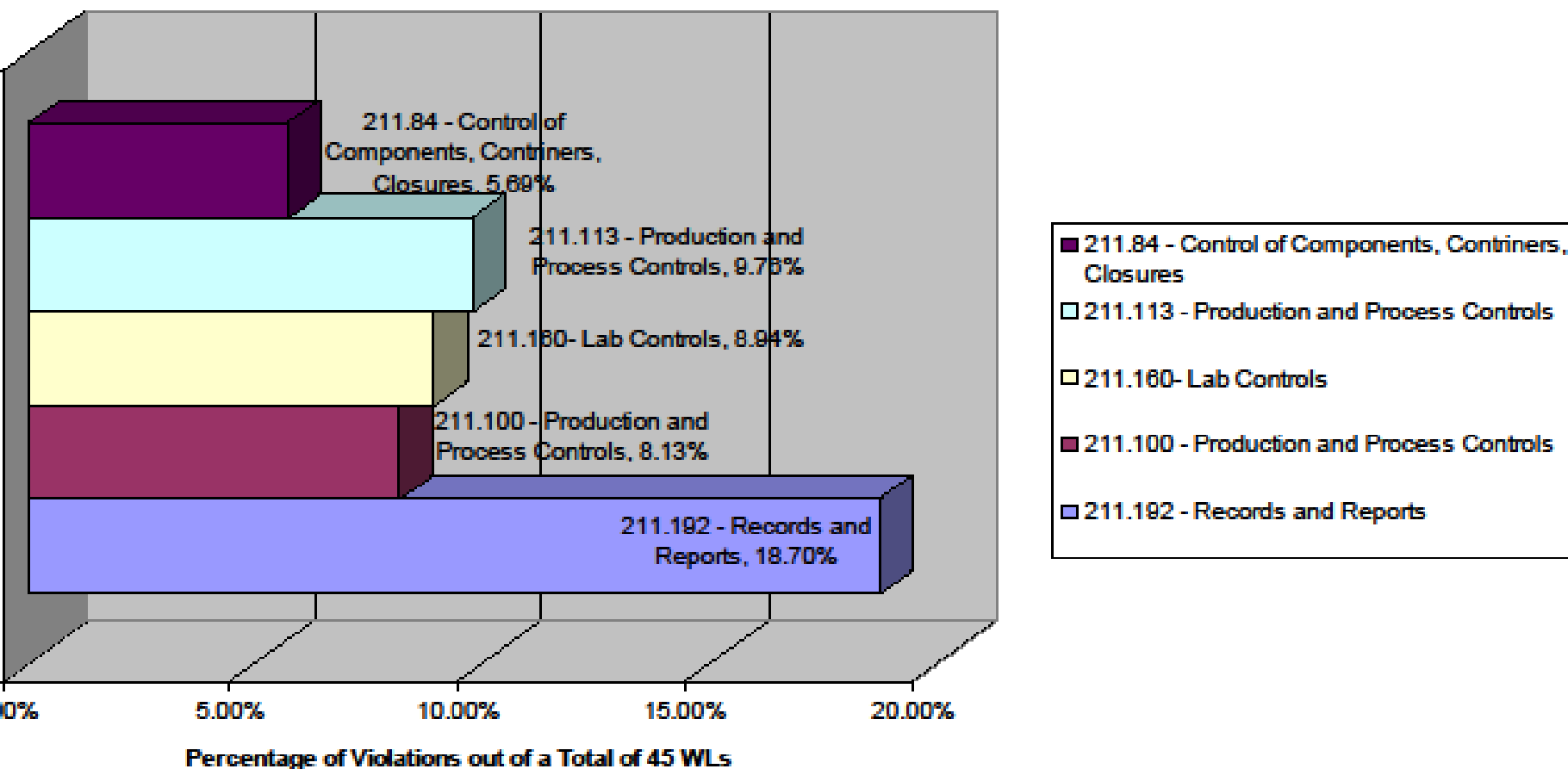
- 211.65 - Lab Controls
- 211.22 - Organization and Personnel
- 211.160 - Lab Controls
- 211.100 - Production and Process Controls
- 211.192 - Records and Reports

PQ

5 GMP Regulatory Violations found

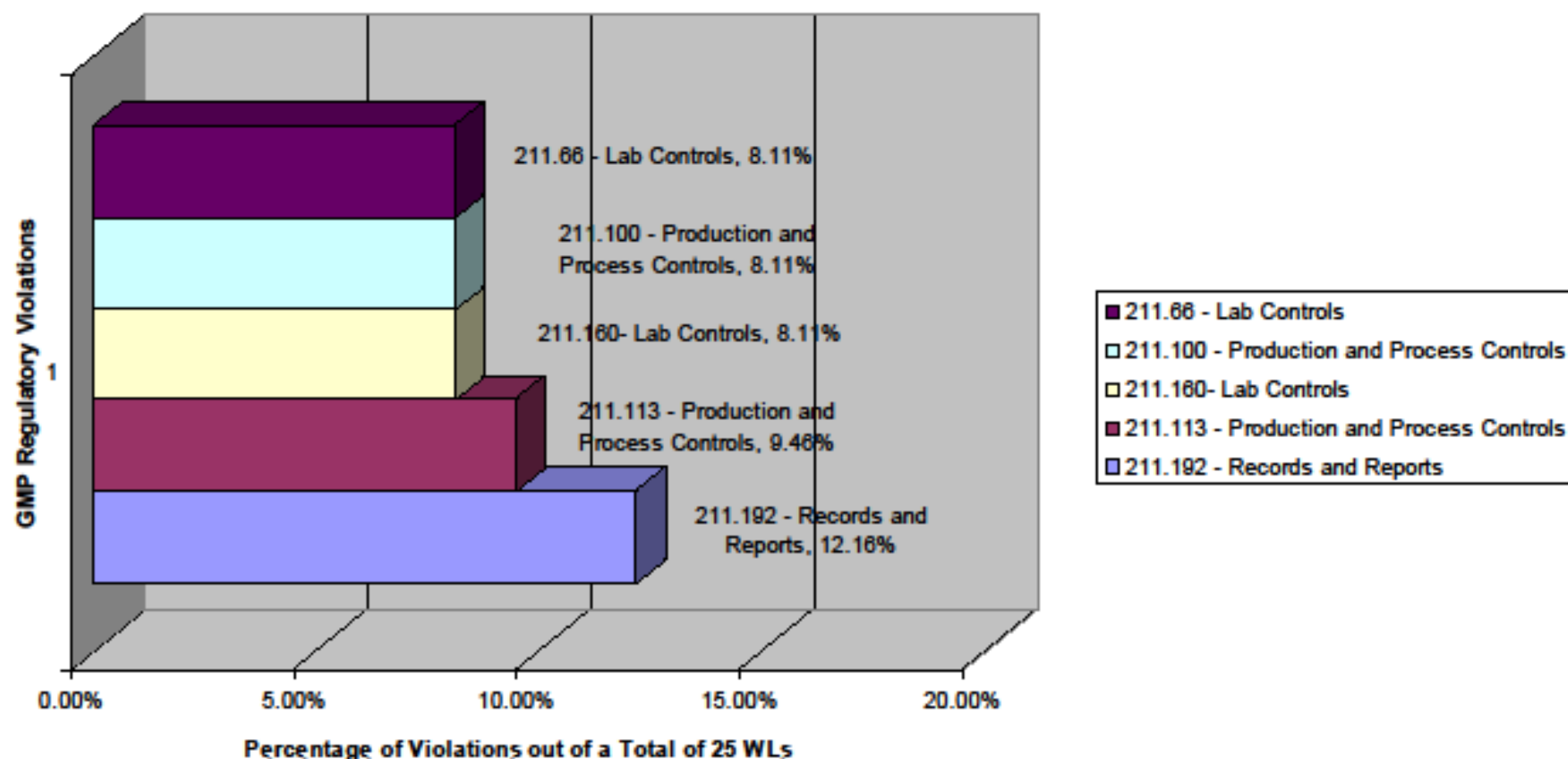
2011 WLS (Domestic and Foreign)

Top 5 GMP Regulatory Violations found in 2011 WLS



Top 5 GMP Regulatory Violations found in 2012* WLs (Domestic and Foreign)

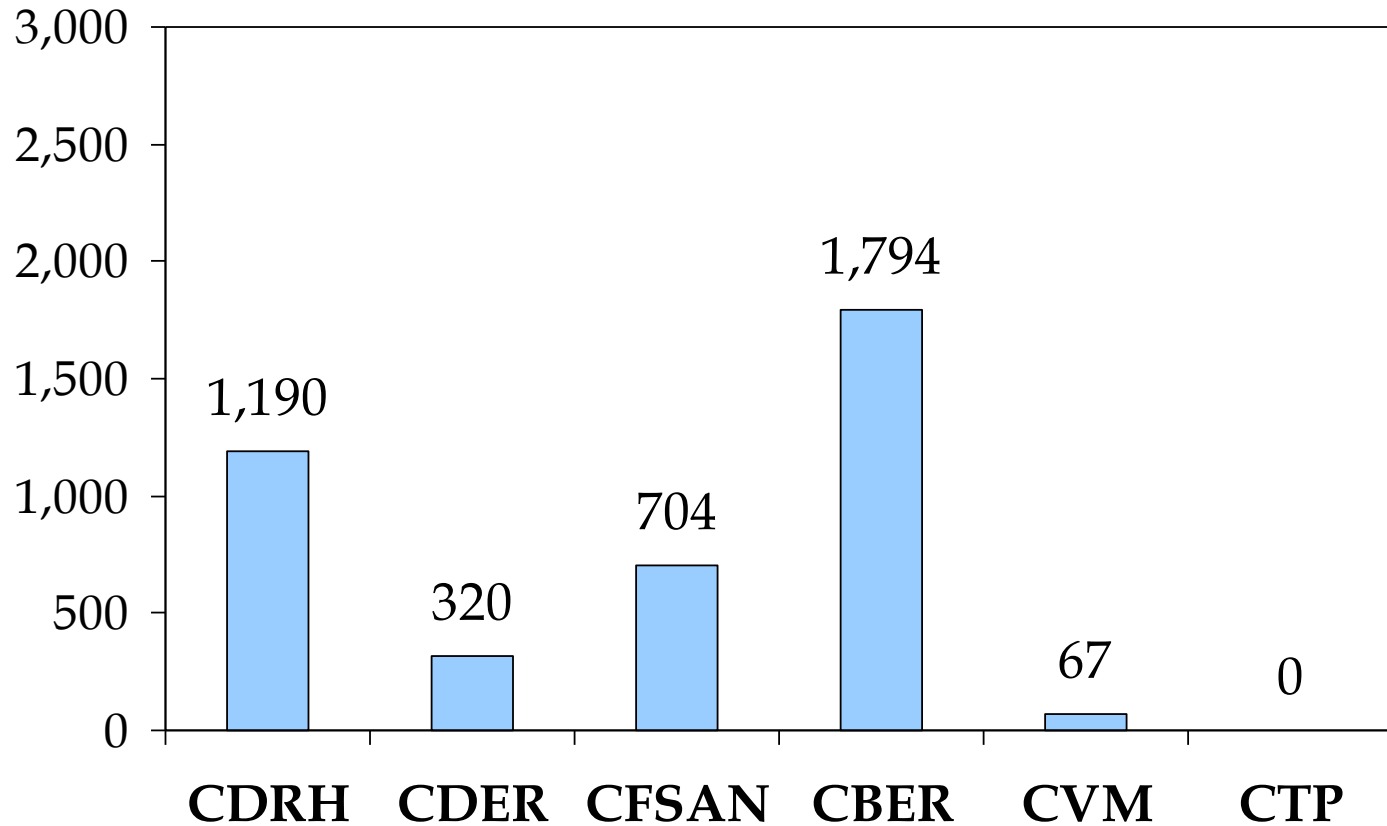
Top 5 GMP Regulatory Violations found in 2012 WLs as of August 2, 2012



OMPQ List of GMP Regulatory Violations found in WL FY 2010-2012* (as of August 2012)

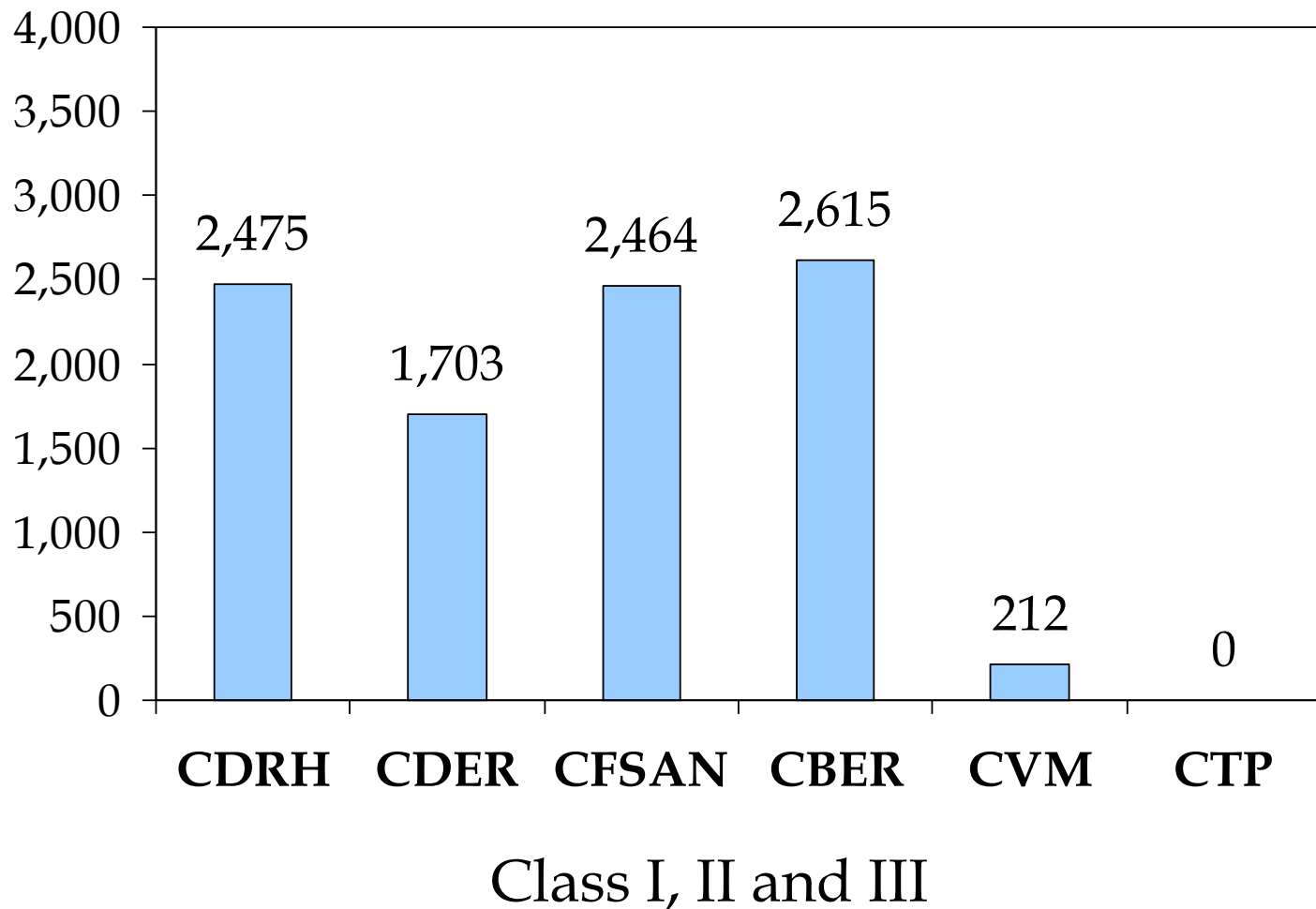
21 CFR 211	Subpart Name	Regulation Section Title (description)
211.22	B. Organization and Personnel	Responsibilities of QC Unit (QC Unit to maintain and follow SOPs RE: QC responsibilities and authorities)
211.84	E. Control of Components, Containers, Closures	Testing and approval or rejection
211.100	F. Production and Process Controls	Written procedures; deviations (designed to assure that DPs have the characteristics they claim to have)
211.113	F. Production and Process Controls	Control of microbiological contamination
211.160	I. Laboratory Controls	General Requirements (Scientifically sound specs. established by appropriate org unit, designed to assure appropriate standards)
211.165	I. Laboratory Controls	Testing and Release for Distribution (Must use appropriate tests and know DPs meet specs before release.)
211.166	I. Laboratory Controls	Stability Testing
211.192	J. Records and Reports	Production Record Review (includes investigation of any failures to meet specs)

Total Recall Events by FDA Center Fiscal Year 2012



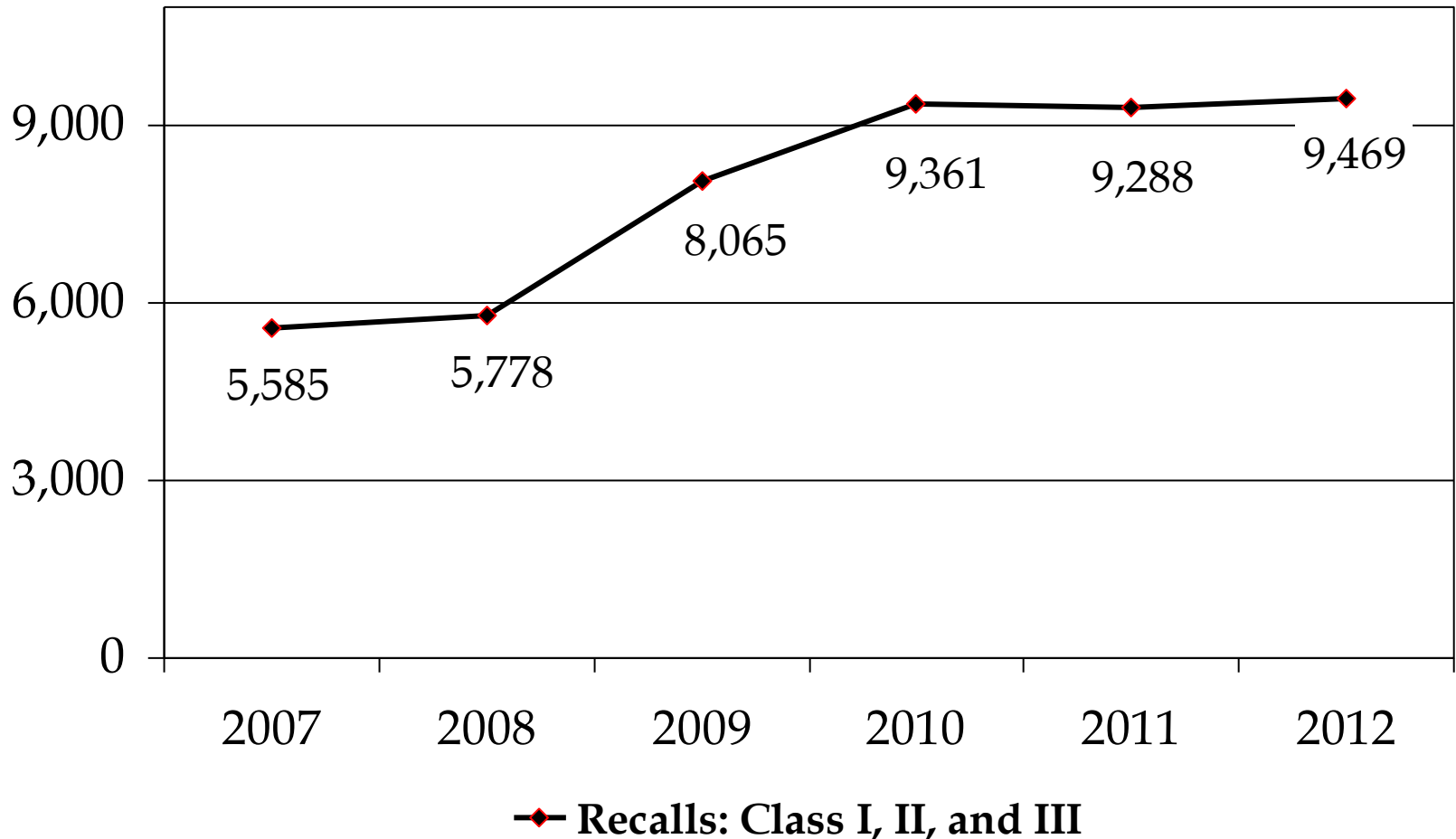
Class I, II and III

Total Recalled Products by FDA Center Fiscal Year 2012

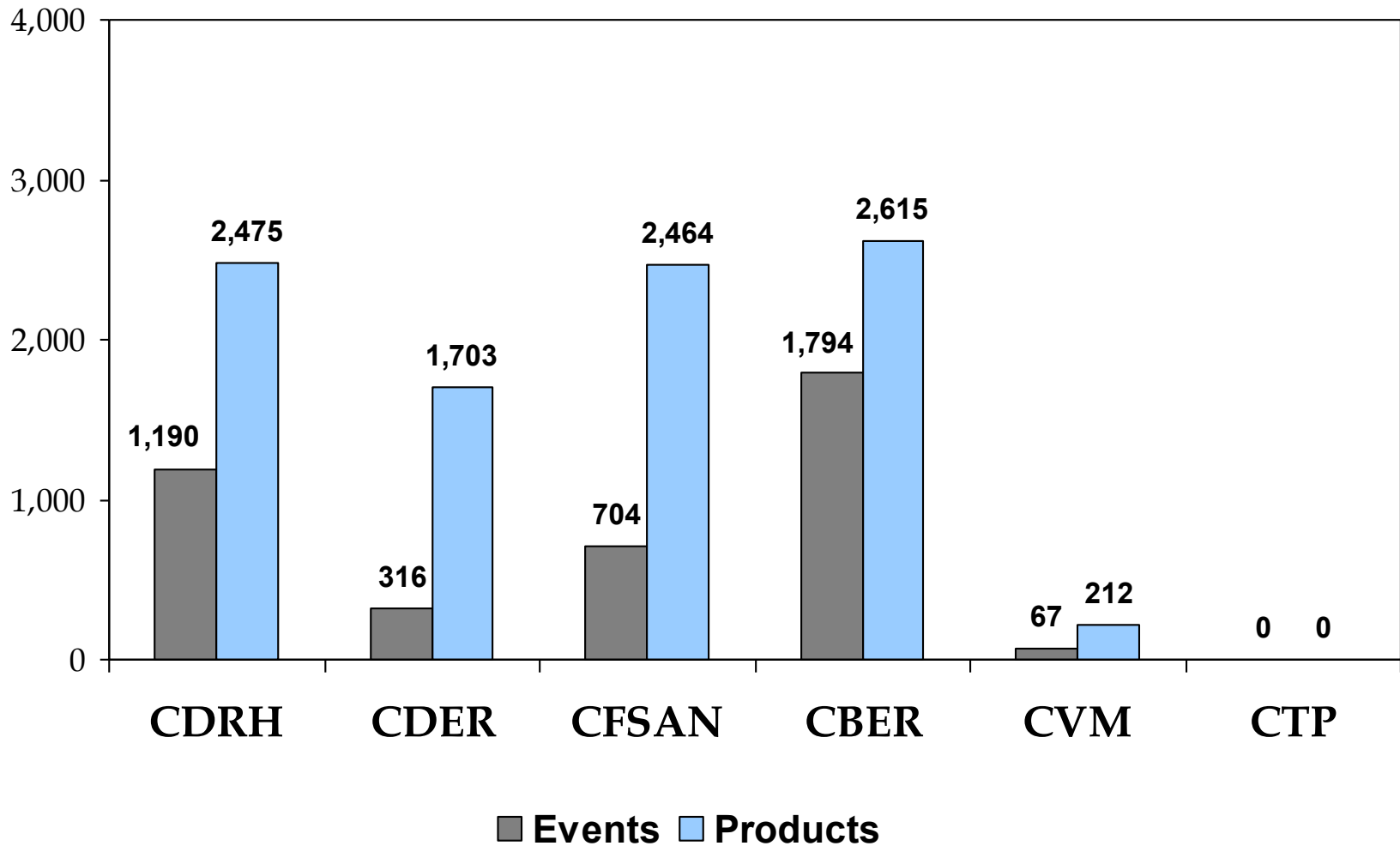


Recalled Products - All Centers

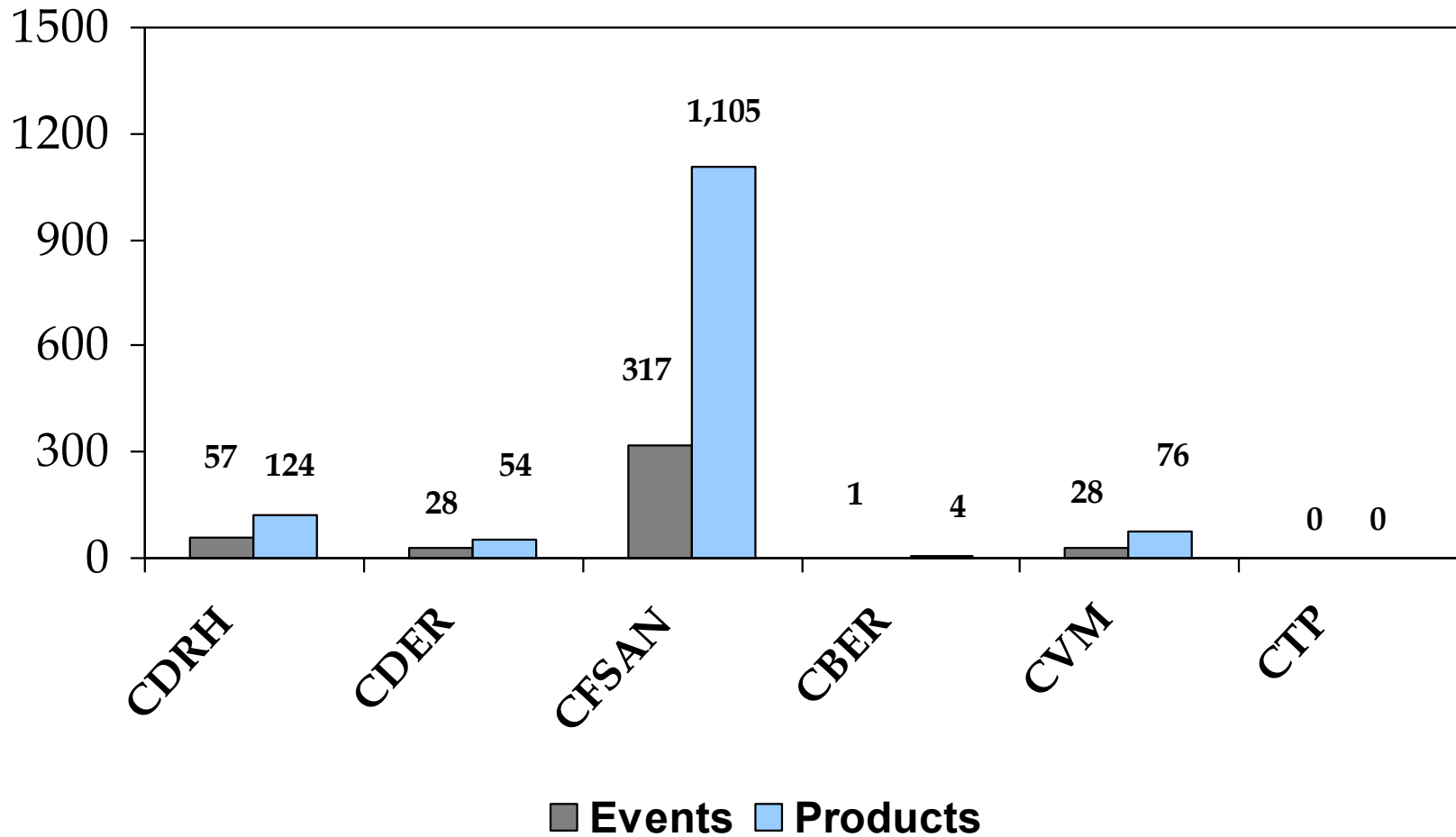
Fiscal Years 2007 - 2012



FDA Recalls By Center - All Classes Fiscal Year 2012

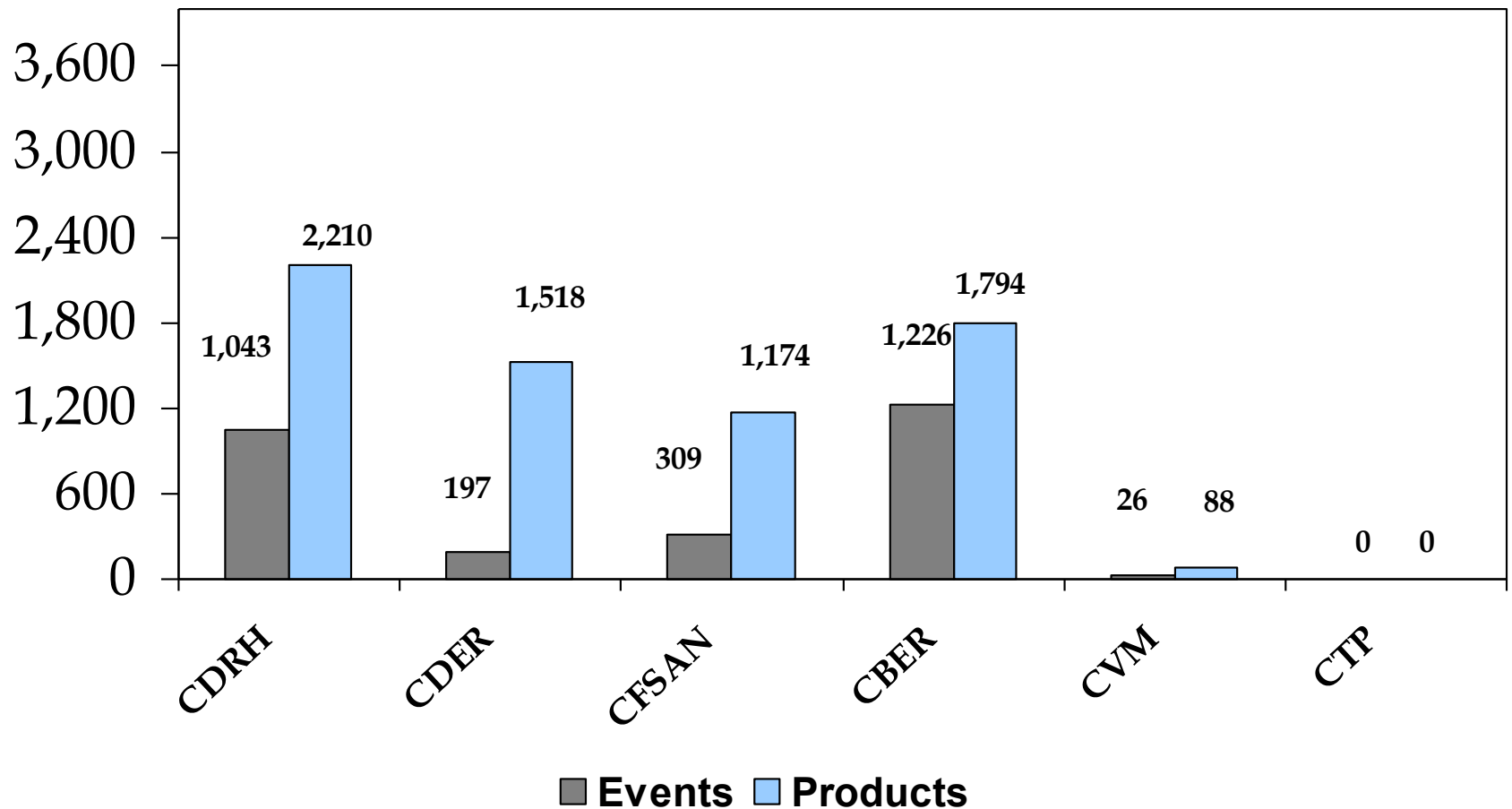


FDA Recalls - Class I By Center Fiscal Year 2012



FDA Recalls - Class II By Center

Fiscal Year 2012



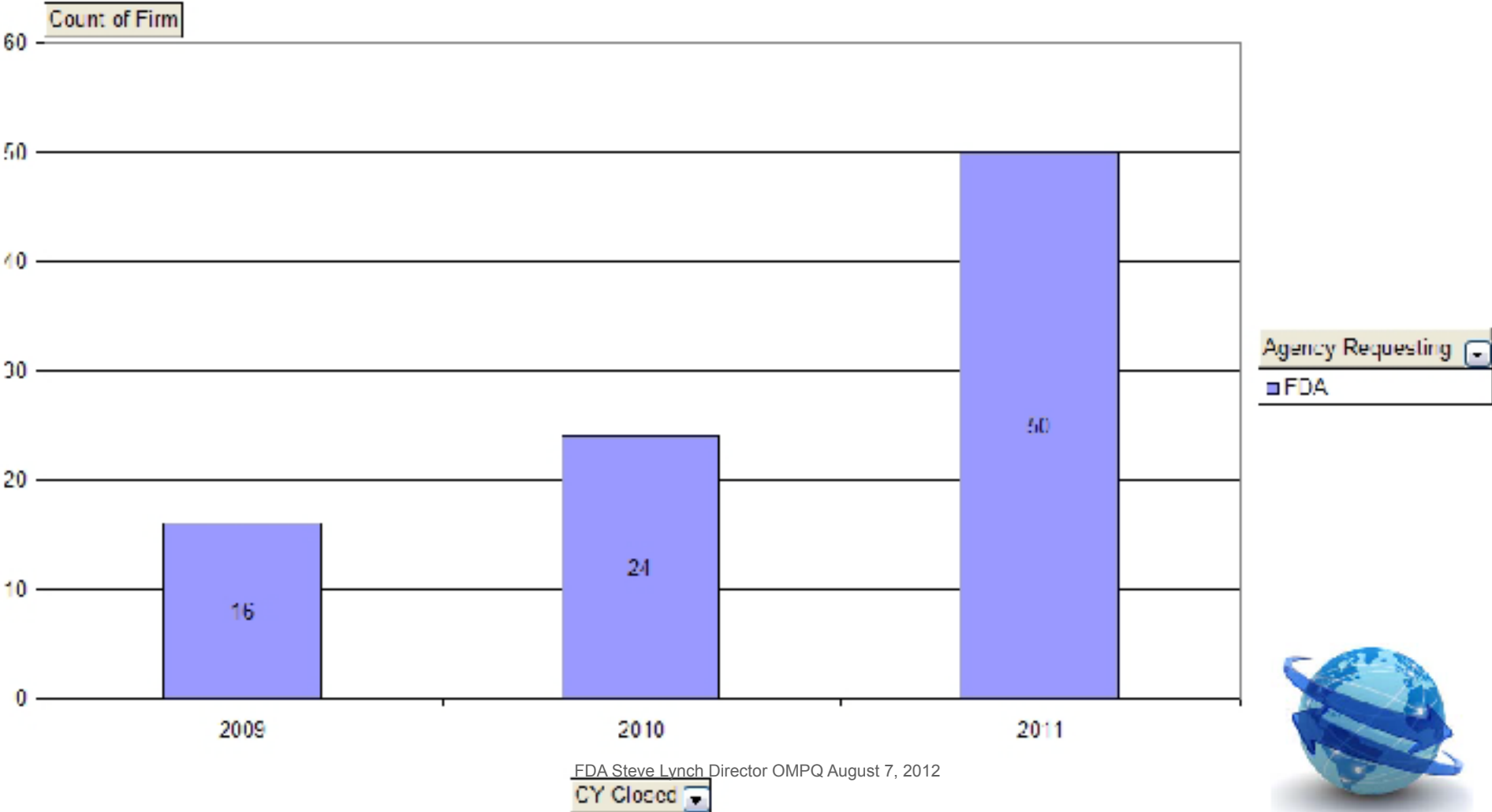
ODSIR

Major reasons for recalls

(OTC and Rx) - FY 2010 - 2012*

<u>Year</u>	<u>Top Reasons</u>
2010	GMP Deviations Temperature Abuse Marketed without an Approved NDA/ANDA
2011	Penicillin Cross Contamination GMP Deviations Marketed without an Approved NDA/ANDA
2012*	Penicillin Cross Contamination Microbial Contamination of Non-Sterile Products GMP Deviations

Foreign Agency Reports Received and Reviewed by the Agency



Data Source: CMS as of 2012-01-06

FDA/EMA Good Clinical Practices (GCP) Initiative

CDER & European Medicines Agency

Started as a pilot program in 2009

- Sharing inspectional information
- Performed Joint inspections
 - Clinical investigators
 - Sponsor monitors
 - Contract Research Organizations
- Bilateral training of investigators/inspectors

Possible expansion of the initiative to other areas such as Bioequivalence (BE)

Possible expansion to include working with CBER

FDA's HSP/BIMO Initiative

- Better protect the rights, safety & welfare of clinical subjects involved in FDA regulated clinical trials.
- Increase the accuracy of the data submitted in support of a marketing application.
- Increase the reliability/integrity of the data submitted in support of a marketing application.
 - Identify key clinical sites for inspection.
 - Develop a risk-based model to prioritize inspections of CROs, IRBs and bio-analytical sites.

First two inspections performed in China

Operation Pangea V

Annual effort

FDA works in partnership with international regulatory and law enforcement agencies to shutdown internet pharmacies that illegally sell potentially dangerous unapproved drugs to consumers

- Shutdown more and 18,000 illegal websites
- Seized approximately \$10.5 million worth of pharmaceuticals worldwide
- FDA itself sent out 4,100 Warning Letters to Websites
- F/U letters to Internet Service providers
- F/U letters to Domain Name Registrars
 - Informing them that these websites were in violation of US law.

2013 FDA Pharmacy Inspection Initiative

Purpose: Critical look at the surveillance and enforcement of pharmacies that produce sterile drug products

Reason: Response to New England Compounding Center

High risk drug products that potentially pose a significant threat to public health from poor sterile production practices.

Plan: Risk-based model to identify sites

- **Serious Adverse events**
- **Historical inspection data**
- **Reports of drug product quality issues**

2013 FDA Pharmacy Inspection Initiative

Identified 29 firms that were inspected over a seven week period from February to April 2013.

Covered 18 different states

Applied 21 CFR Parts 210 & 211

Many inspections conducted jointly with State Boards of Pharmacy

Due to question of regulatory authority

Some resisted inspection based upon FDA's lack of inspectional jurisdiction.

FDA obtained administrative inspection warrants in some cases

In the end, joint inspections were performed.

2013 FDA Pharmacy Inspection Initiative

Using investigators trained in aseptic processing

Inspection focus:

- SOPs
- Interviews with technicians
- Sterilization methods
- Stability data
- Review failures of potency, sterility, endotoxins
- Laminar airflow

2013 FDA Pharmacy Inspection Initiative

All but one site received an FDA-483

FDA Listed the following types of observations:

“Incomplete and/or inadequate drug product batch failure investigations”

“Inappropriate and/or inadequate clothing for sterile processing”

“Lack of appropriate air filtration systems”

“Insufficient microbiological testing”

And other practices which, “create a risk of contamination.”

2013 FDA Pharmacy Inspection Initiative

What's next?

Pharmacies that are operating beyond the, “bounds of traditional pharmacy compounding and who had significant production issues,” FDA intends to, “take aggressive action, including through enforcement actions.”

However: FDA admits that it, “may not be able to take enforcement action against firms that meet certain criteria and are operating within the bounds of traditional pharmacy compounding, unless certain provisions of the law are violated, such as producing or distributing a contaminated drug product.”

GMP Site Selection Model

RISK BASED APPROACH

- Facility Size
- Recalls (Class 1)
- Last three District Inspections
- Establishment type
- Therapeutic Class of drugs
- Profile Classes being manufactured
- Time since the last inspection
- Processes used in manufacturing