FDA Compliance Trends

What's Old is New Again

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BD

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Agenda

- Highlights of the FDA/CDRH Report 10/31/2011 *Understanding Barriers to Medical Device Quality*
- Inspections
- 483 Observations
- Warning Letters
- Recalls & Adverse Event Reports

Understanding Barriers to Medical Device Quality Report Observations*

- General comments:
  - The medical device industry has experienced growth in both revenues and complexity of its products over the past 10-20 years
  - Adverse event reports related to IVDs and medical devices have outpaced industry growth by 8% per annum since 2001
  - “Quality risk” is unevenly distributed across the industry; 20 of the 1189 active product codes (1.7%) account for 65% of all serious adverse events reports in recent years
  - Failures in product design and manufacturing process control are the root cause of more than half of all product recalls

*Understanding Barriers to Medical Device Quality, FDA/CDRH Report 10/31/2011

Understanding Barriers to Medical Device Quality Report Observations

- In this report, FDA makes their “Case for Quality”
- The Agency takes the position that it is their responsibility to help the diagnostic and device industry
  - create an ongoing culture of quality
  - implement strong quality systems based on best practices rather than “reactively waiting” for deficiencies to be discovered during FDA inspections to make corrections
- Three focus areas were identified
  1. Focus on quality while maintaining compliance
  2. Improve transparency through publically available information
  3. Better communication between FDA, industry, and stakeholders to share expectations and solicit changes or improvements

Trends in Medical Device Quality

- FDA identified seven opportunities for improving quality
  1. Design and reliability engineering - validation of actual product use, reliability, manufacturability, and software robustness
  2. Robust post-production monitoring/feedback - design and manufacturing that goes beyond base compliance requirements
  3. Supplier management - material and process control
  4. Quality metrics – beyond regulatory compliance
  5. Quality organization - cross-functional integration of quality principles, not focused solely on compliance
  6. Performance management - measure individuals in key roles design roles around quality performance
  7. Quality culture – improve proactively to severe quality-related issues as opposed to reactively

Inspection Strategy

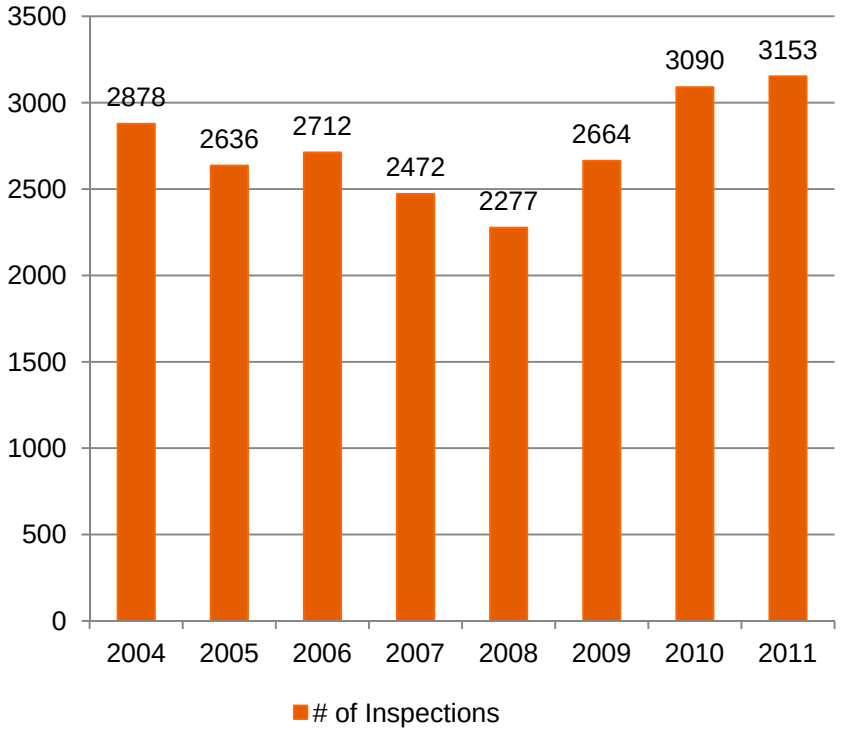
- The QS inspectional goal remains the same; to assess the firm's quality management system for compliance with the appropriate regulations
- Five inspectional strategies continue to be used:

Inspection Level	Type of Inspection	Guide to Inspections
1	Abbreviated	QSIT – Two subsystems; Corrective and Preventive Actions (CAPA) plus Production and Process Controls (P&PC) or Design Controls
2	Comprehensive	QSIT - The four major subsystems; Management Controls, Design Controls, CAPA and P&PC
3	Compliance Follow-up*	As directed by inspectional guidance and elements of QSIT
Special	For Cause*	As directed by inspectional guidance and elements of QSIT
Special	Risk Based Work Plan	As directed by CDRH inspection assignment and elements of QSIT

* Understanding Barriers to Medical Device Quality, FDA/CDRH Report 10/31/2011

Inspections & 483 Observations

QS Inspections Metrics

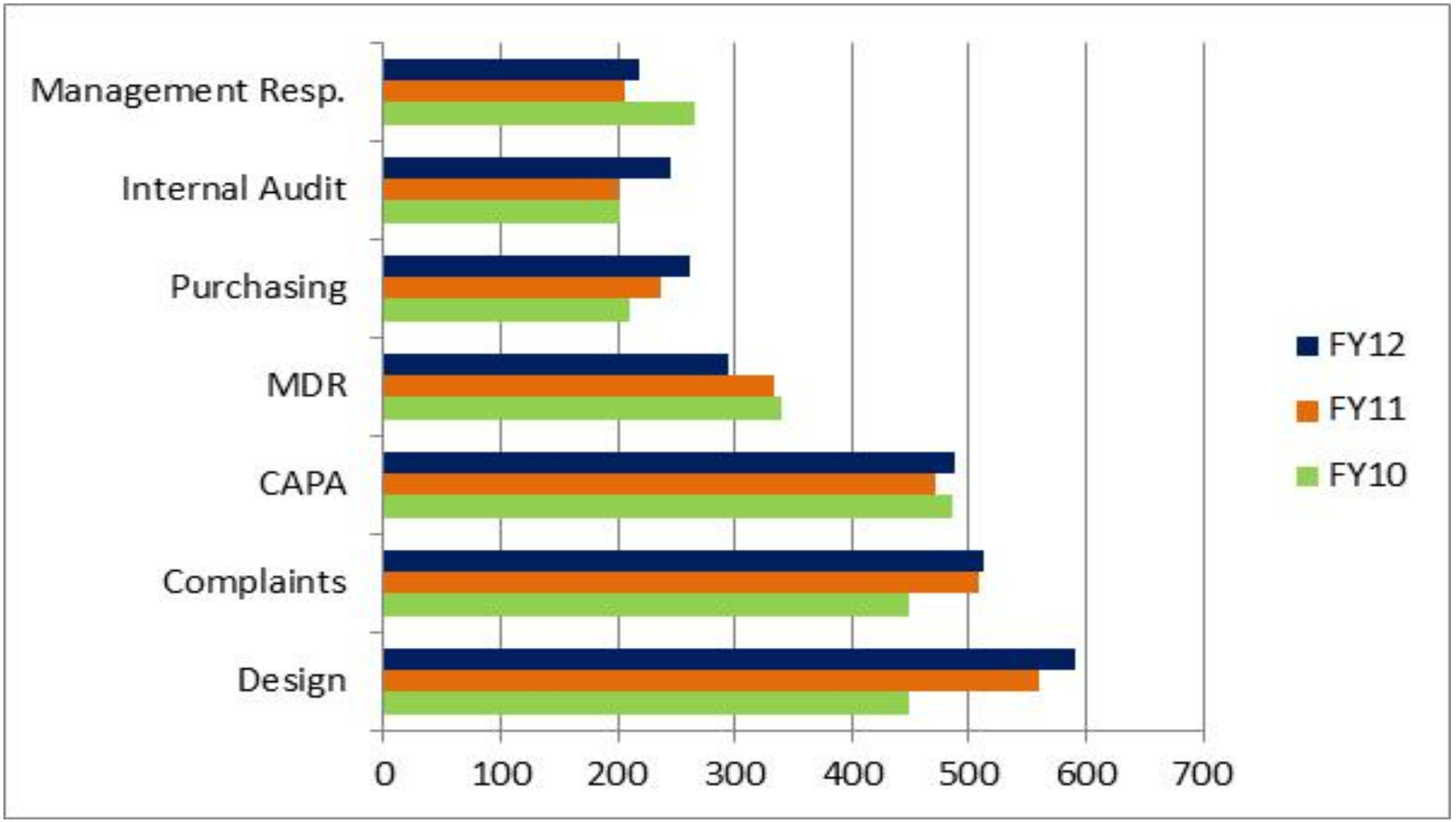


Year	Inspections
2011	3153
2010	3090
2009	2664
2008	2277
2007	2472
2006	2712
2005	2636
2004	2878

- The number of QS inspections has grown steadily over the past 5 years reflecting the agency's focus on quality

Source: Current FDA Inspection, Enforcement Trends, and Field Issues, Melissa Torres

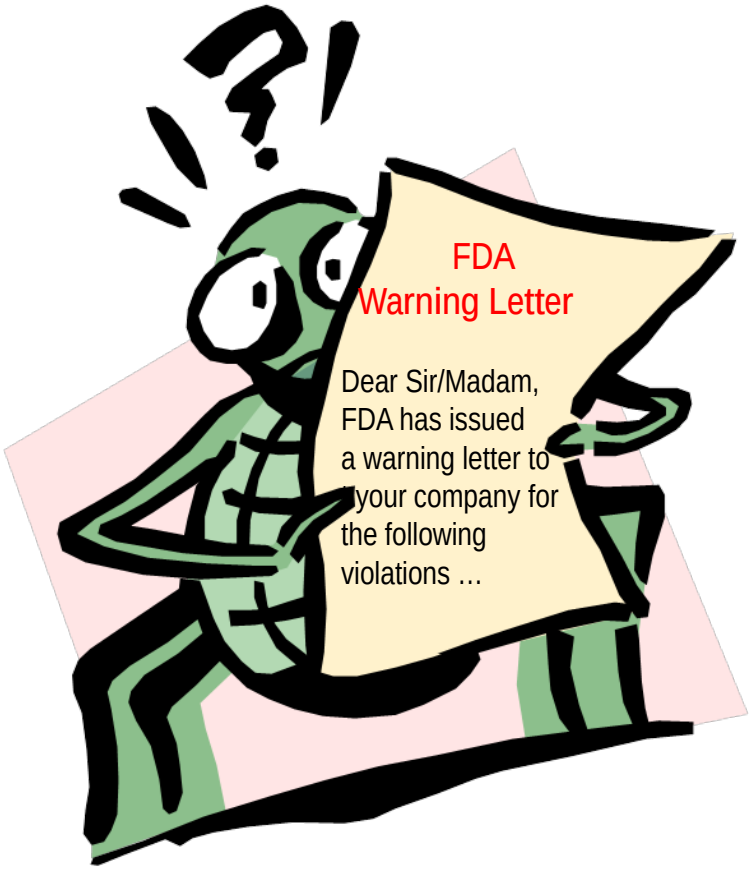
Top FDA 483 Observations 2010-2012



Source: BD Corporate Compliance team

Note: categories total observations by major element (e.g. Design includes all 820.30x subparts)

Warning Letter Analysis



Warning Letter Historical Data

- Quality System (QS) Inspections and Warning Letters with QS Citations

Year	Inspections	# WLs	% WL
2011	3153	122	4%
2010	3090	89	3%
2009	2664	77	3%
2008	2277	98	4%
2007	2472	74	3%
2006	2712	79	3%
2005	2636	97	4%
2004	2878	113	4%

Source: Current FDA Inspection, Enforcement Trends, and Field Issues, Melissa Torres

2011 Warning Letter Analysis

- FDA issued a total of 122 Warning Letters to diagnostics & medical device firms for QS deficiencies from January – December 2011

• CAPA	104/122	85%
• P&PC	97/122	80%
• Design	70/122	57%
• Management	58/122	48%
• Documentation	43/122	35%

Source: Silver Sheet Publication

Warning Letters with CAPA Citations

➢ CAPA Subsystem Warning Letter Data Summary

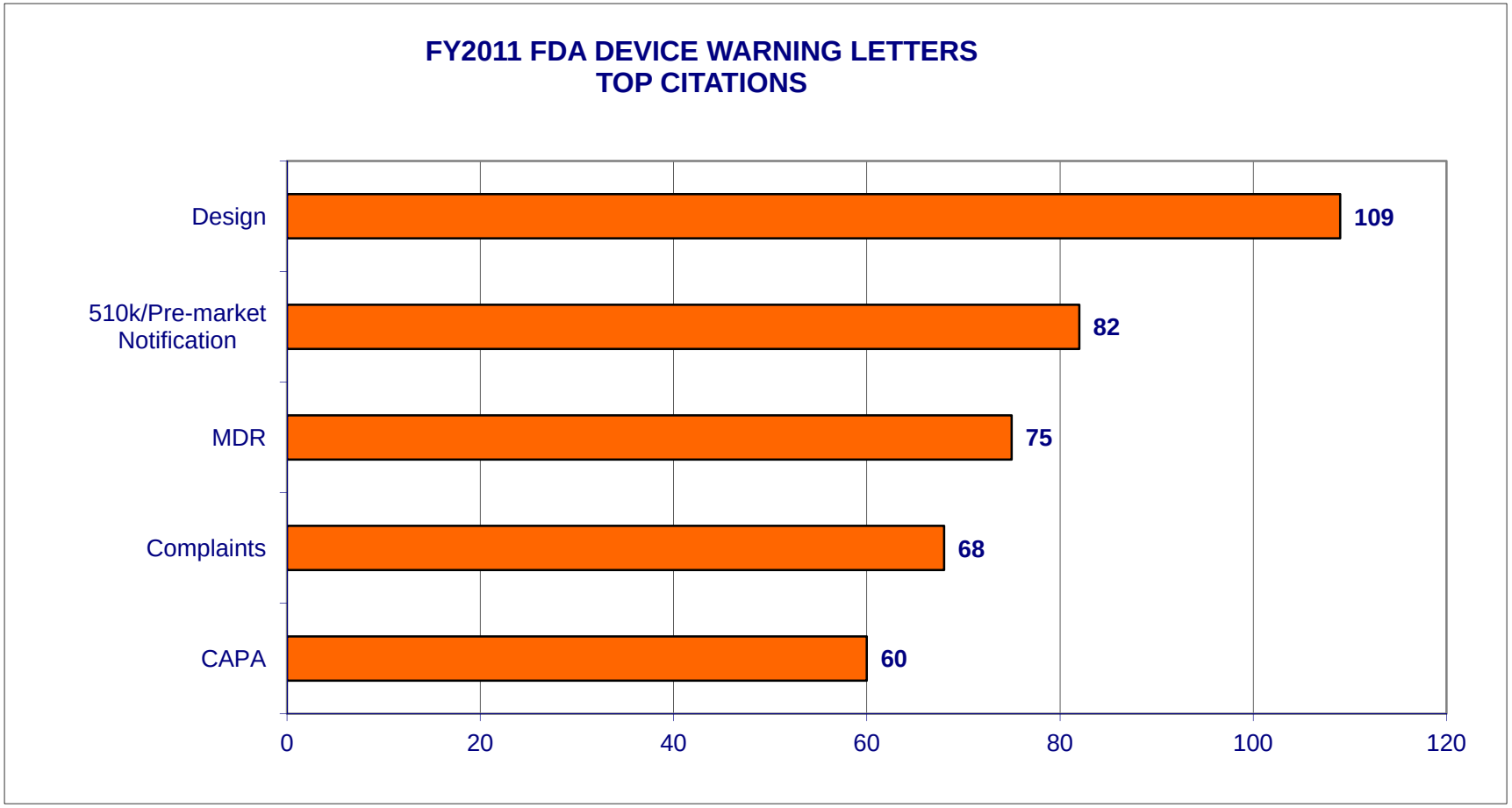
Year	#WL	#CAPA Citations	%
2011	122	104	85
2010	89	81	91
2009	77	68	88
2008	98	86	88
2007	74	62	84
2006	79	69	87
2005	97	85	88
2004	113	89	79

Common CAPA Issues

- Procedures do not address the CAPA requirements
- No CAPA procedures
- Lack of verification, validation, effectiveness
- Inadequate implementation of corrective actions

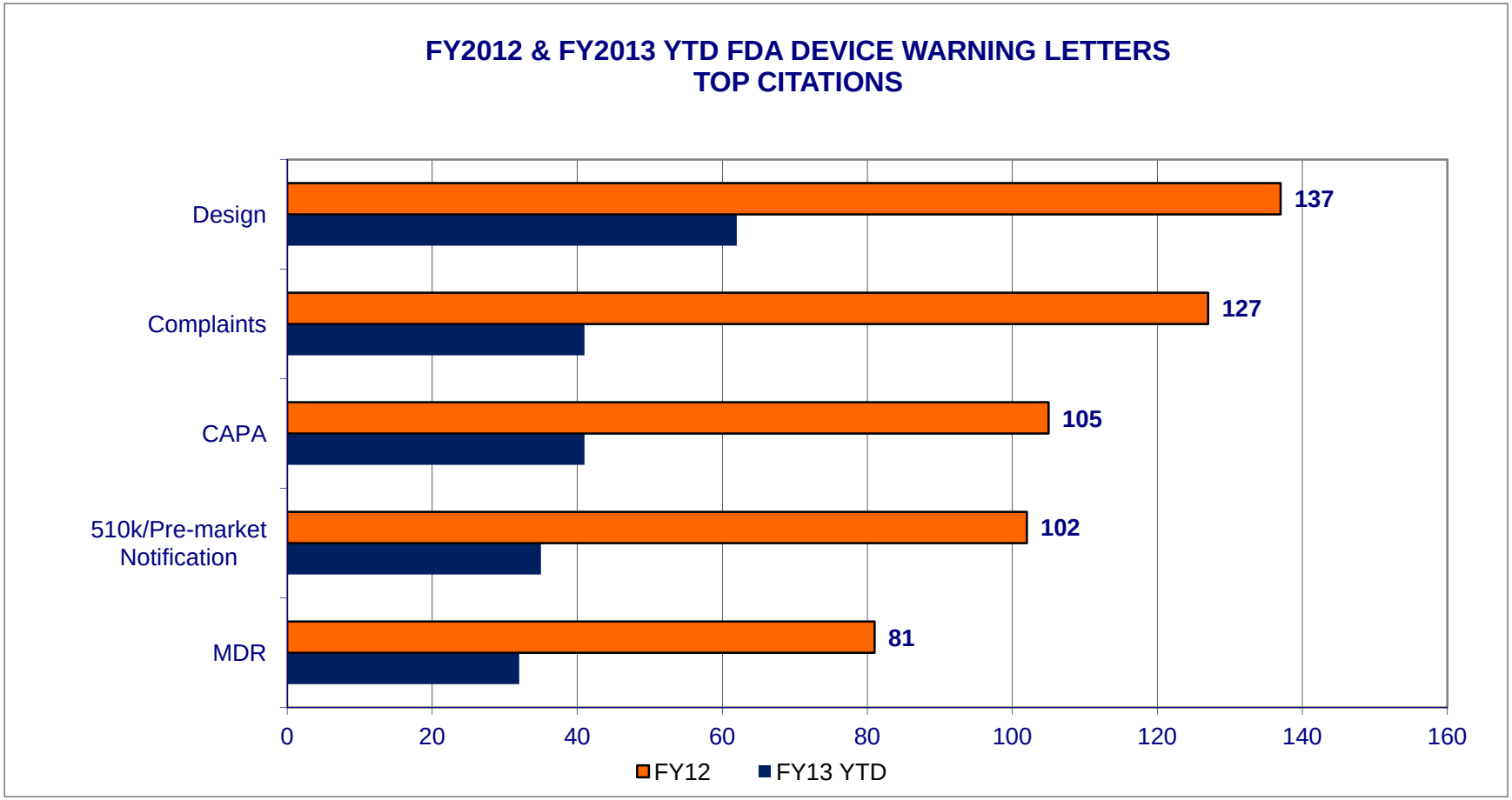
Source: Current FDA Inspection, Enforcement Trends, and Field Issues, Melissa Torres

Warning Letter Metrics
2011 Top Citations



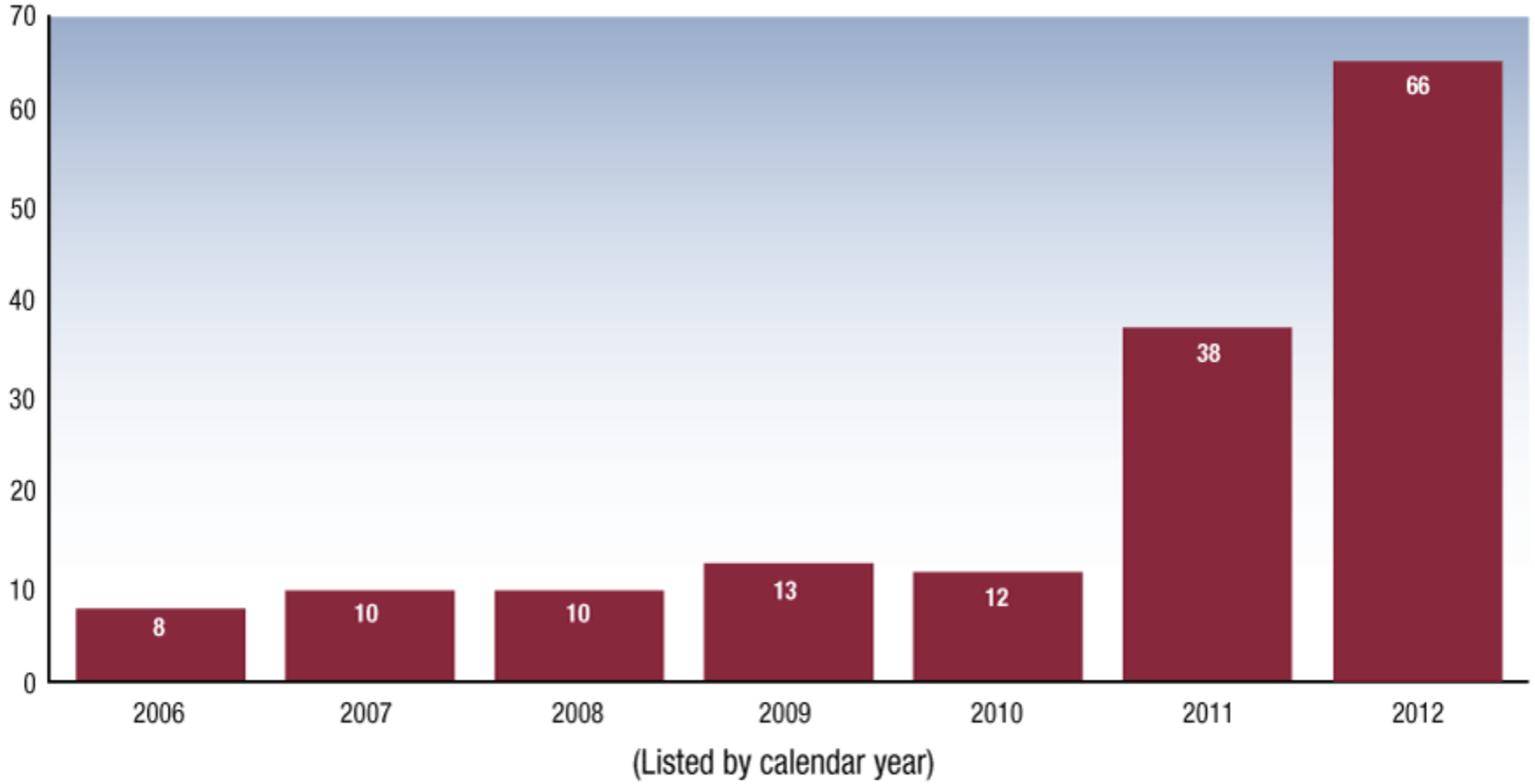
Source: BD Corporate Compliance analysis of 2011 Warning Letters using BD citation categories

Warning Letter Metrics
2012 & 2013 (YTD) Top Citations



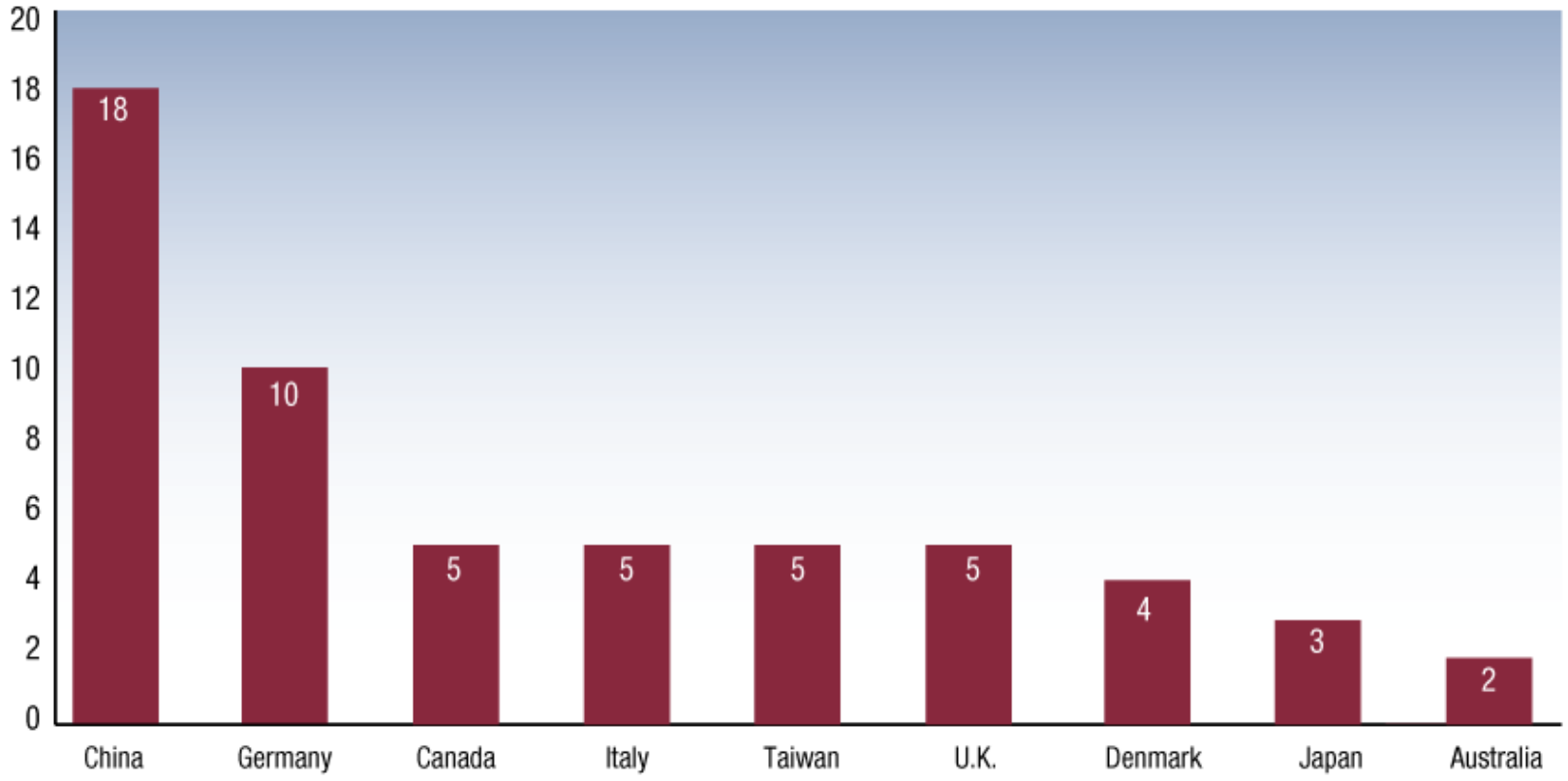
Source: BD Corporate Compliance analysis of 2012 /2013 Warning Letters using BD citation categories, 169 WL issued in 2012

IVD & Device-Related Warning Letters Issued To Foreign Manufacturers



Source: BD Corporate Compliance analysis of Warning Letters

2012 Foreign Warning Letters



Source: BD Corporate Compliance analysis of Warning Letters

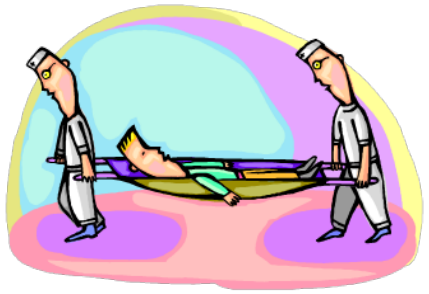
Common Themes of IVD Company Warning Letters 2011-2013

- 15 IVD Company Warning Letters issued 2011 through 2013 were reviewed for themes
- Common citations:
  - Quality Systems - CAPA, complaint management, design control, clinical studies (IRB)
  - Process Control – process validation (mapping, critical control points, SPC), specifications (that did not meet product claims), supplier quality
  - MDR Reporting - under reporting, assessment process
  - Adulterated/Misbranded - failure to file premarket notifications/applications (genetic tests, cytology kits, stand-alone software, modifications, new claims)
  - Product Performance – stability, instructions for use

Adverse Event Reports and Recalls

Adverse Event Reports

- As previously mentioned, 20 of the 1200+ active product codes account for 65% of all serious adverse events reports in recent years
  - Blood glucose test systems ranked #3 in total numbers of MDRs reported, behind implantable insulin pumps and coronary drug-eluting stents
  - Adjusted as a percent of units sold, glucose test systems MDRs are still in the top 20
  - Some of the increase in MDR reporting can be attributed to greater FDA emphasis on timely reporting and reporting requirements



Source: Understanding Barriers to Medical Device Quality, FDA/CDRH Report 10/31/2011

IVD & Medical Device Recalls

- Recall reporting has risen slower than adverse event reporting, but has paralleled the IVD/Medical device industry growth over the last 10 years
- In 2003, there were 540 reported recalls - by 2012, this number increased to 1046
- Like adverse event reports, some of the growth can be attributed to greater FDA emphasis on recall reporting requirements for all Classes

Year	Class I	Class II	Class III	Total
2012	56	916	74	1,046
2011	41	873	43	957
2010	51	622	44	717
2009	23	551	52	626
2008	17	726	107	850

Sources: Understanding Barriers to Medical Device Quality, FDA/CDRH Report 10/31/2011, Current FDA Inspection, Enforcement Trends, and Field Issues, Melissa Torres

IVD Recalls

- In 2011, 2 of the top 20 product codes recalled were IVDs
  - #6 – JJE/Chemistry Analyzers
  - #13 – GKZ/Hematology Cell Counters
- When analyzing the reasons for IVD product recalls by value stream components
  - 32% attributed to design
  - 22% attributed to supplier quality
  - 26% attributed to manufacturing
  - 20% attributed to post production and change control issues

Source: Understanding Barriers to Medical Device Quality, FDA/CDRH Report 10/31/2011

Common Themes of IVD Company 2012/2013 Recalls

- Class I Recalls in 2012/2013
  - False positive/negative results
- Class II Recalls in 2012/2013
  - Product Labeling
  - Product Performance Claims
  - Stability
  - Value assignment
  - Device malfunctions (non-safety)
  - Software

Final Thoughts

- Historical data shows increase activity in inspections (foreign and domestic), adverse event reports, and recalls
- Designs, complaints, and CAPA continue to be the most frequent 483 observations, often cited in warning letters
- IVD products do appear in the top product codes recalled, with >50% of causes rooted in design and manufacturing
- Proactive implementation of robust quality systems with strong quality cultures are the shared goals of both the Agency and IVD companies, resulting in safer more effective products for patients and healthcare practitioners