Food and Drug Administration (FDA) Medical Device 2012 Quality System Data

FDA Inspectional Observations (Form 483) and Warning Letter Citations

Why is FDA making these data available?

In support of the FDA Transparency Initiative and Case for Quality, the Center for Devices and Radiological Health (CDRH) is providing data on inspectional observations and warning letter citations issued in 2012.

With this annual presentation of data, the FDA continues to provide information on quality system related inspectional observations and warning letter citations issued to medical device establishments. By releasing this information CDRH intends to:

- Assist industry in improving device quality by sharing common observations from inspections
- Identify possible areas of emerging concern
- Possibly help firms to avoid receiving warning letters

Key Inspection Findings

- The number of routine quality system surveillance inspections has increased by 37 percent overall and for foreign firms it has increased by 93 percent.
- Common inspectional observations include failures in corrective and preventive actions (observed in 30 percent of 483s) as well as inadequate production and process controls (observed in 30 percent of 483s).
- The most frequent inspectional observations in 2012 were:
  - 21 CFR 820.100(a) Corrective and preventive action procedures,
  - 21 CFR 820.198(a) Complaint files, specifically establishing and maintaining procedures for receiving, reviewing and evaluating complaints and
  - 21 CFR 820.22 Quality audits to assure that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system.
- The number of observations related to 21 CFR 820.184 (device history record) increased significantly in 2012.
  - The device history record demonstrates that the device is manufactured in accordance with the Design Master Record and includes dates of manufacture, quantity manufactured, quantity released for distribution, acceptance record, primary identification label and device identification and control numbers.

Key Warning Letter Findings

- The number of warning letters increased in the past two years due to an increase in inspections, increased focus on foreign firms by the foreign device cadre and improved site selection, and fewer official action indicated (OAI) inspections resulting in Untitled Letters due to missed FDA deadlines or insufficient evidence.
- While foreign firms accounted for 300 of the 2748 quality system inspections (10 percent) in 2012, they accounted for 62 of the 195 OAI outcomes (32 percent) and 66 of the 164 warning letters issued (40 percent).
- Consistent with inspectional observations, 21 CFR 820.198(a) and 21 CFR 820.100(a) were the most frequent warning letter citations in 2012.
    - 21 CFR 820.100(a) Corrective and preventive action procedures
    - 21 CFR 820.198(a) Complaint files, specifically establishing and maintaining procedures for receiving, reviewing and evaluating complaints.
- Two violations were observed at higher rates in warning letters than inspectional observations:
    - 51 warning letters included a 21 CFR 820.184 design history documentation violation
    - 49 warning letters included a 21 CFR 820.75(a) process validation violation.

The Quality System Regulation

- In Oct. 1996 the FDA published the final rule for the Quality System (QS) regulation.
- In June 1997 revisions to 21 CFR part 820 (covering CGMP) took effect.
- The QS regulation includes requirements related to the methods used in, and the facilities and controls used for, designing, manufacturing, packaging, labeling, storing, installing, and servicing of medical devices intended for human use.
- The QS regulation established a framework for device manufacturers to follow and gave them greater flexibility in achieving quality requirements. This action was necessary to add preproduction design controls and to achieve consistency with quality system requirements worldwide.

Quality System (QS) Subsystems

P&PC	Production and Process Controls
CAPA	Corrective and Preventive Actions
MGMT	Management Controls
DES	Design Controls
DOC	Document Controls

Descriptions of Quality System Subsystems

Corrective and Preventive Actions (CAPA) Each manufacturer shall establish and maintain procedures for implementing corrective and preventive action Each manufacturer shall maintain processes to address non-conforming product and establish and maintain complaint files. Each manufacturer shall establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit. The related sections of the CFR include 21 CFR 820.90, 820.100, 820.198)

Production and Process Controls (P&PC) Each manufacturer is required to develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications. Where deviations from device specifications could occur as a result of the manufacturing process, the manufacturer shall establish and maintain process control procedures that describe any process controls necessary to ensure conformance to specifications. In addition to process controls, this subsection includes purchasing controls, labeling, packaging, handling, storage, and installation. The related sections of the CFR include 820.50, 820.60, 820.65, 820.70, 820.72, 820.75, 820.80, 820.8, 820.120, 820.130, 820.140, 820.150, 820.160, 820.170, 820.200, and 820.250).

Management Controls (MGMT) Management is responsible for establishing policy and objectives for, and commitment to, quality. The QS regulation requires that each manufacturer establish and maintain an adequate organizational structure to ensure that devices are designed and produced in accordance with the GMP requirements. To meet these regulatory requirements, manufacturers are required to provide adequate resources, including the assignment of trained personnel for management, performance of work, and assessment activities, including internal quality audits. The related sections of the CFR include 21 CFR 820.5., 820.20, 820.22 and 820.25.

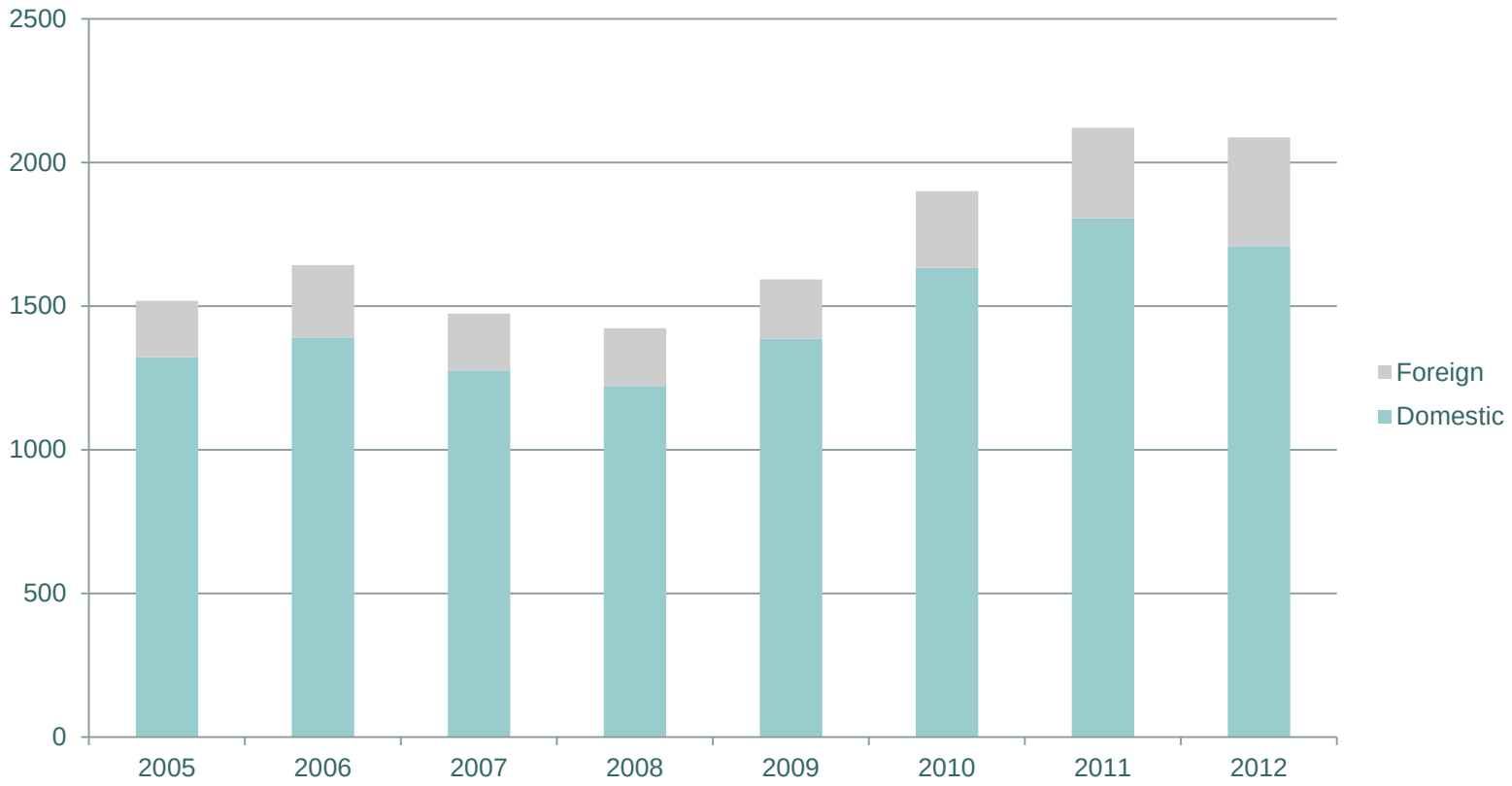
Design Controls (DES) Each manufacturer is required by regulation to establish and maintain design control procedures for any class III or class II device, and a selected group of class I devices. The design control procedures ensure that specified design requirements are met. The Design Control regulation is 21 CFR 820.30.

Document Controls (DOC) Each manufacturer is required to establish and maintain procedures to control the documents for *approval and distribution as well as changes.* Manufacturers are also responsible for creating and maintaining the device master record, the device history record and the Quality System Record. The related sections of the CFR include 820.40, 820.180, 820.181, 820.186 and 820.184).

QS Regulation Cites by Subsystem

P&PC	CAPA	MGMT	DES	DOC
820.50	820.90	820.5	820.30	820.40
820.60	820.100	820.20		820.180
820.65	820.198	820.22		820.181
820.70		820.25		820.186
820.72				820.184
820.75				
820.80				
820.86				
820.120				
820.130				
820.140				
820.150				
820.160				
820.170				
820.200				
820.250				

Routine Quality System Surveillance Inspections

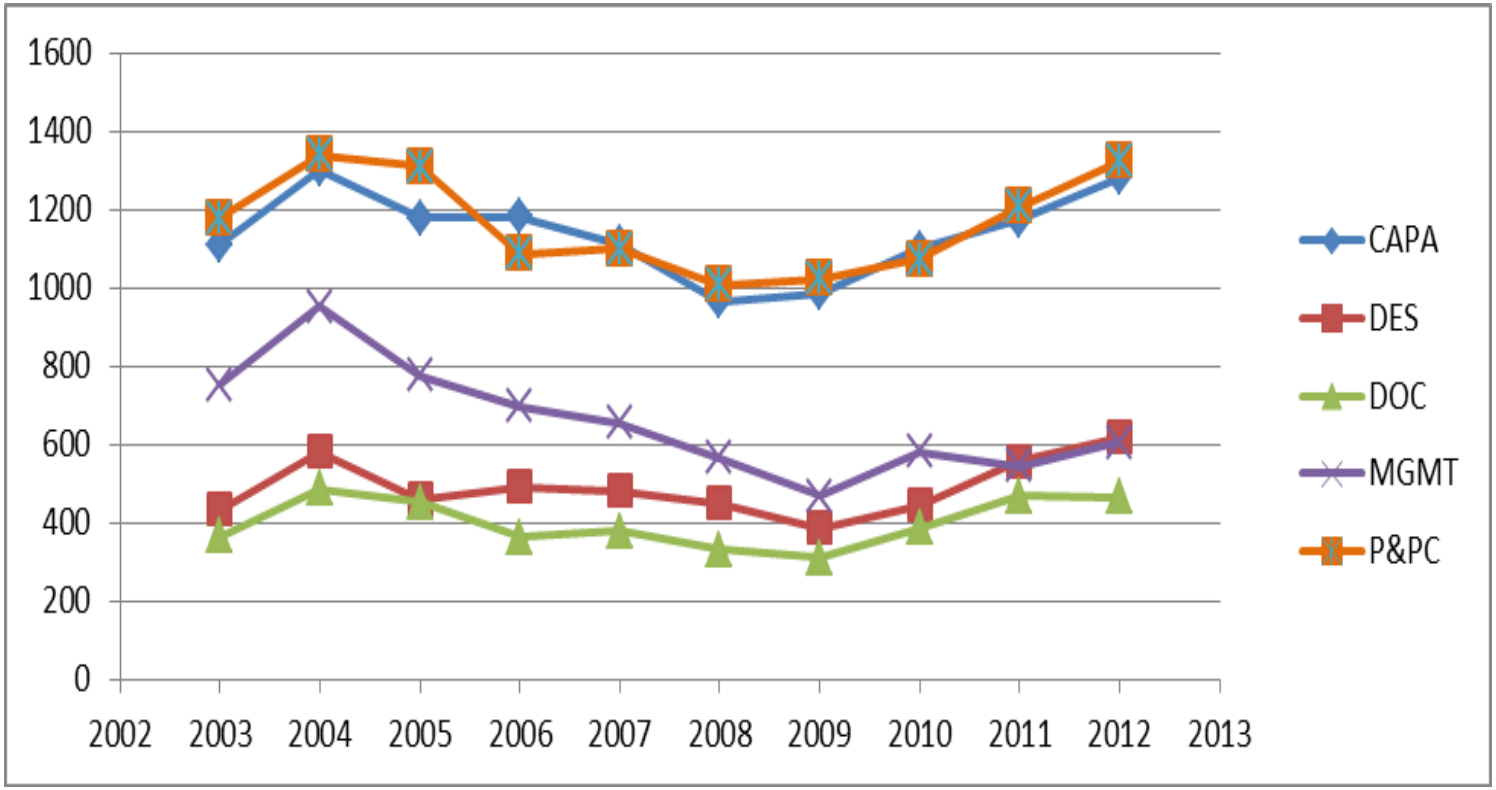


2012 FDA Inspectional Observations (Form 483) Data

- Source of data - FDA's Turbo Establishment Inspection Reporting (EIR) Database
- Time frame 1/1/2012 to 12/31/2012
- **4243** FDA Form 483 observations cited for 21 CFR 820 (Quality System regulation*) deficiencies

*http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820&showFR=1

Inspectional Observations 2003-2012 by Quality System Subsystem



2012 483 Observations Data

QS Subsystem	Number of Observations	Percentage
CAPA	1258	30%
P&PC	1303	30%
DES	630	15%
MGMT	583	14%
DOC	469	11%
Total: 4243		

Most Frequent QS 483 Observations

2011 2012

2011 Citations	No. of Observations	2012 Citations	No. of Observations
21 CFR 820.100(a)	367	21 CFR 820.100(a)	378
21 CFR 820.198(a)	301	21 CFR 820.198(a)	349
21 CFR 820.22	207	21 CFR 820.22	234
21 CFR 820.75(a)	173	21 CFR 820.30(g)	214
21 CFR 820.30(g)	154	21 CFR 820.184	190
21 CFR 820.90(a)	147	21 CFR 820.75(a)	166
21 CFR 820.100(b)	127	21 CFR 820.90(a)	145
21 CFR 820.25(b)	117	21 CFR 820.100(b)	126
21 CFR 820.20(c)	112	21 CFR 820.25(b)	119
21 CFR 820.50	105	21 CFR 820.20(c)	109
21 CFR 820.40	101	21 CFR 820.40	101

2012 CAPA Observations

Observation	Count	Percentage
21 CFR 820.100(a)	378	30%
21 CFR 820.198(a)	349	28%
21 CFR 820.90(a)	145	12%
21 CFR 820.100(b)	126	10%
21 CFR 820.198(c)	93	7%
21 CFR 820.90(b)(2)	50	3%
21 CFR 820.198(b)	33	3%
21 CFR 820.198(e)	33	3%
21 CFR 820.90(b)(1)	24	1%
21 CFR 820.198(d)	22	1%
21 CFR 820.198(a)(3)	2	<1%
21 CFR 820.198(f)	2	<1%
21 CFR 820.100(a)(5)	1	<1%
	1258	**100%**

2012 DES Observations

Observation	Count	Percentage
21 CFR 820.30(g)	214	34%
21 CFR 820.30(i)	100	16%
21 CFR 820.30(f)	77	12%
21 CFR 820.30(a)	58	9%
21 CFR 820.30(e)	38	6%
21 CFR 820.30(j)	38	6%
21 CFR 820.30(h)	34	5%
21 CFR 820.30(c)	29	5%
21 CFR 820.30(b)	23	4%
21 CFR 820.30(d)	19	3%
	630	**100%**

2012 DOC Observations

Observation	Count	Percentage
21 CFR 820.184	190	40%
21 CFR 820.40	101	22%
21 CFR 820.181	96	20%
21 CFR 820.40(a)	41	9%
21 CFR 820.40(b)	19	4%
21 CFR 820.180	11	2%
21 CFR 820.186	6	1%
21 CFR 820.184(e)	3	<1%
21 CFR 820.180(b)	1	<1%
21 CFR 820.184(f)	1	<1%
	469	**100%**

2012 MGMT Observations

Observation	Count	Percentage
21 CFR 820.22	234	40%
21 CFR 820.25(b)	154	26%
21 CFR 820.20(c)	109	19%
21 CFR 820.20(e)	33	6%
21 CFR 820.20(a)	24	4%
21 CFR 820.25(a)	15	3%
21 CFR 820.20(d)	14	2%
	583	**100%**

2012 P&PC Observations

Observation	Count	Percentage
21 CFR 820.75(a)	166	13%
21 CFR 820.50	129	10%
21 CFR 820.70(a)	92	7%
21 CFR 820.72(a)	77	6%
21 CFR 820.80(d)	68	5%
21 CFR 820.80(b)	67	5%
21 CFR 820.80(e)	44	3%
21 CFR 820.50(a)(1)	41	3%
21 CFR 820.70(c)	40	3%
21 CFR 820.50(a)	39	3%
21 CFR 820.70(i)	38	3%
21 CFR 820.80(c)	37	3%
21 CFR 820.50(b)	36	3%
21 CFR 820.80(a)	36	3%
21 CFR 820.70(b)	35	3%

2012 P&PC Observations (cont.)

Observation	Count	Percentage
21 CFR 820.120	28	2%
21 CFR 820.250(b)	26	2%
21 CFR 820.75(c)	24	2%
21 CFR 820.60	21	2%
21 CFR 820.70(g)(1)	21	2%
21 CFR 820.250(a)	18	1%
21 CFR 820.150	17	1%
21 CFR 820.200(a)	17	1%
21 CFR 820.50(a)(3)	15	1%
21 CFR 820.120(b)	14	1%
21 CFR 820.50(a)(2)	14	1%
21 CFR 820.160(a)	13	1%
21 CFR 820.86	13	1%
21 CFR 820.75(b)	12	<1%
21 CFR 820.75(b)(2)	12	<1%

2012 P&PC Observations (cont.)

Observation	Count	Percentage
21 CFR 820.120(d)	10	<1%
21 CFR 820.70(e)	10	<1%
21 CFR 820.70(g)	9	<1%
21 CFR 820.72(b)	9	<1%
21 CFR 820.200(b)	8	<1%
21 CFR 820.200(d)	8	<1%
21 CFR 820.70(f)	5	<1%
21 CFR 820.130	4	<1%
21 CFR 820.140	4	<1%
21 CFR 820.160(b)	4	<1%
21 CFR 820.170(a)	4	<1%
21 CFR 820.70(g)(2)	4	<1%
21 CFR 820.70(h)	4	<1%
21 CFR 820.120(a)	3	<1%
21 CFR 820.200(c)	2	<1%

2012 P&PC Observations (cont.)

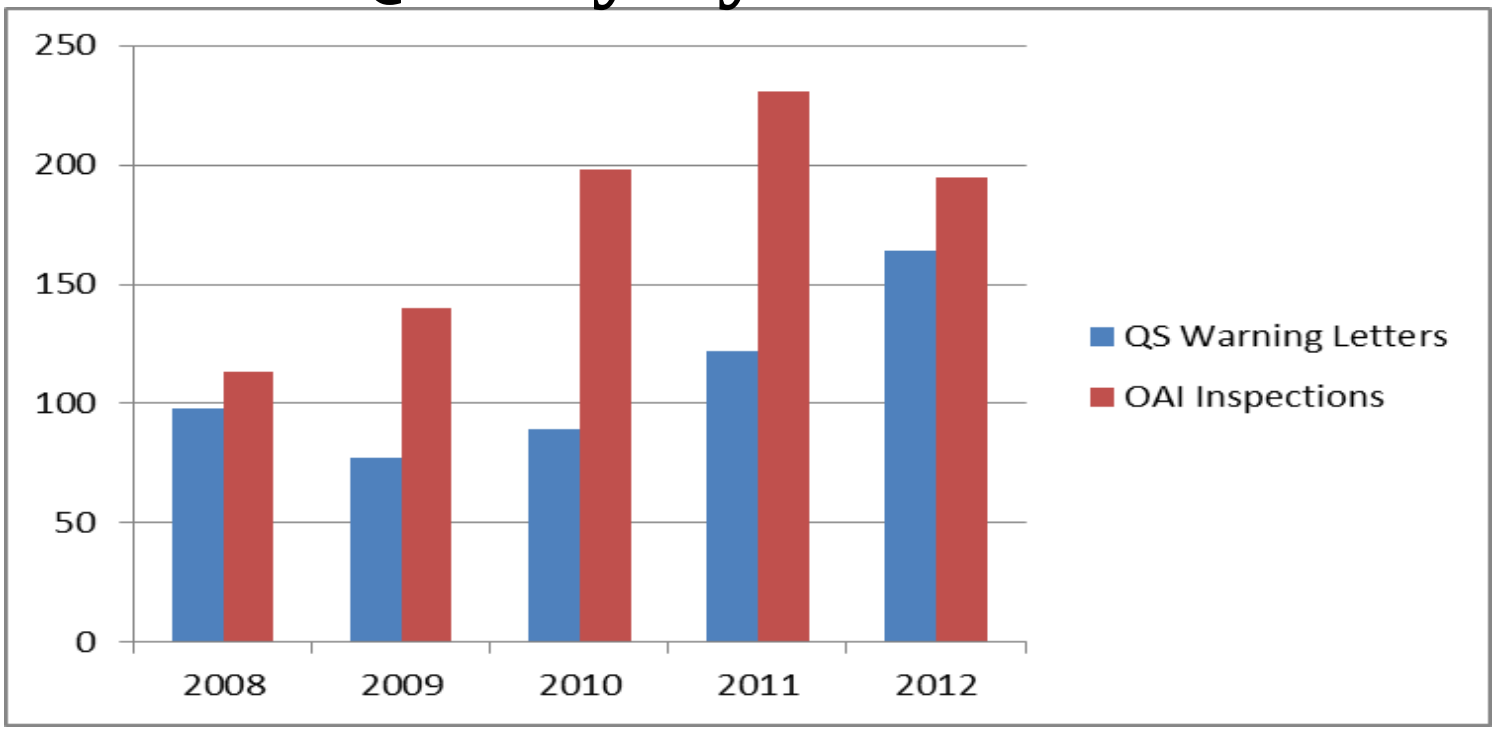
Observation	Count	Percentage
21 CFR 820.72(b)(1)	2	<1%
21 CFR 820.170(b)	1	<1%
21 CFR 820.200(d)(3)	1	<1%
21 CFR 820.70(d)	1	<1%
	1303	**100%**

FDA Warning Letters with Quality System Citations

- Source of data - FDA's Warning letters
- Time frame 1/1/2012 to 12/31/2012
- **164** Warning Letters with 21 CFR 820 (Quality System Regulation*) deficiencies

*http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820&showFR=1

FDA Official Action Indicated Inspections and Warning Letters with Quality System Citations



Warning Letters with QS Citations

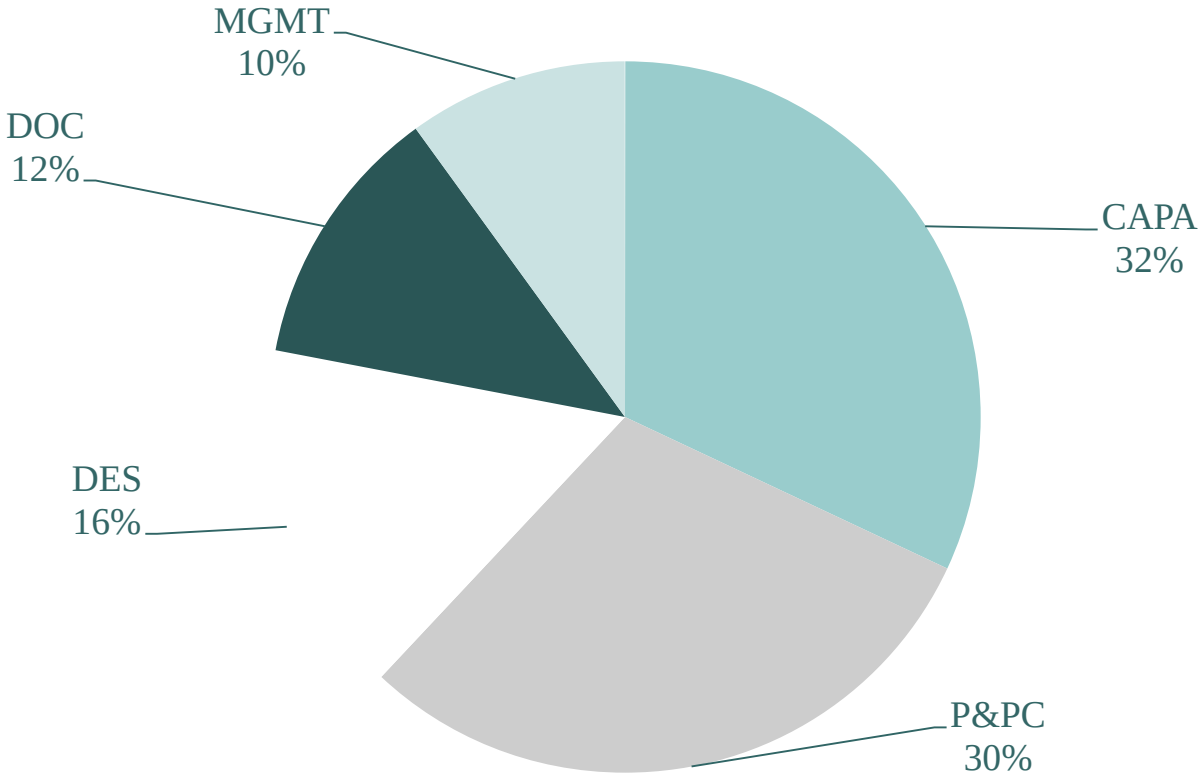
Year	# WL's
2012	164
2011	122
2010	89
2009	77
2008	98
2007	74
2006	79
2005	97
2004	113

Country	2012 # WL's
USA	98
China	20
Germany	9
Italy	6
UK	6
Denmark	3
Japan	3
Taiwan	3
Canada	2

Numbers of QS citations in 2012 Warning Letters

QS Subsystem	Total Citations	% (1085 Total Citations)
CAPA	342	32%
P&PC	331	30%
DES	174	16%
DOC	131	12%
MGMT	107	10%

Quality System citations in 2012 Warning Letters



Numbers of WLs with QS Subsystem citations in 2012 Warning Letters

QS Subsystem	# WL w/Cite	% (164 Total WLs)
CAPA	143	87%
P&PC	134	82%
DES	91	55%
DOC	78	48%
MGMT	70	43%

Most Frequent QS Warning Letter Cites

Citation	QS Subsystem	Number of WL Cites
21 CFR 820.198(a)	CAPA	82
21 CFR 820.100(a)	CAPA	78
21 CFR 820.184	DOC	51
21 CFR 820.75(a)	P&PC	49
21 CFR 820.22	MGMT	43
21 CFR 820.30(g)	DES	43
21 CFR 820.50	P&PC	36
21 CFR 820.90(a)	CAPA	31
21 CFR 820.181	DOC	31
21 CFR 820.30(i)	DES	30

CAPA Subsystem Warning Letter Cites

Citations	Number of WL Cites
21 CFR 820.198	154
21 CFR 820.100	130
21 CFR 820.90	54
21 CFR 820.86	4
TOTAL: 342	

Design Control Subsystem WL Cites

Citations	Number of WL Cites
21 CFR 820.30(g)	43
21 CFR 820.30(i)	30
21 CFR 820.30(a)	24
21 CFR 820.30(f)	21
21 CFR 820.30(h)	11
21 CFR 820.30(b)	9
21 CFR 820.30(e)	9
21 CFR 820.30(c)	9
21 CFR 820.30(j)	7
21 CFR 820.30(d)	5
21 CFR 820.30	3
21 CFR 820.30(a)	2
21 CFR 820.30(o)	1
TOTAL: 174	

P&PC Subsystem Warning Letter Cites

Citations	Number of WL Cites
21 CFR 820.80	73
21 CFR 820.50	68
21 CFR 820.70	65
21 CFR 820.75	56
21 CFR 820.72	17
21 CFR 820.250	14
21 CFR 820.120	12
21 CFR 820.200	9
21 CFR 820.60	7
21 CFR 820.160	4
21 CFR 820.140	2
21 CFR 820.170	2
21 CFR 820.150	1
21 CFR 820.130	1
Total: 331	

Management Control Subsystem Warning Letter Cites

Citations	Number of WL Cites
21 CFR 820.22	43
21 CFR 820.20	36
21 CFR 820.25	28
TOTAL: 107	

Document Control Subsystem Warning Letter Cites

Citations	Number of WL Cites
21 CFR 820.184	55
21 CFR 820.40	40
21 CFR 820.181	35
21 CFR 820.186	1
TOTAL: 131	