FDA Medical Device Inspections

FDA Small Business
Regulatory Education for Industry (REdI)
Silver Spring, Maryland
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Call to Action

- Better communication/more efficient inspections
- Efficient – be able to review multiple high risk issues during a 2-3 day QSIT inspection

Learning Objectives

- Preparation for your next inspection
- Overview of QSIT inspection
- Keys for reducing 483 observations
- Post inspection correspondence

Purpose of the Inspection

- To assess compliance with CFR, Title 21, Parts:
- 820 (QS)
- 803 (MDR)
- 821 (Tracking)
- 806 (Corrections and Removals)
- 807 (Registration and Listing)
- To assess compliance with Electronic Product Radiation Control requirements

How are Firms Selected for Inspection?

- Biennial: Class II and III manufacturers
  - Includes contract manufacturers, design specification developers, repackagers, relabelers, and contract sterilizers
- Reduced resources = risk-based approach.
- Each year CDRH selects a few high risk Class I firms

High Risk Firms

- Class III > II > I
- Pre-Market and Post-Market (PMA)
- Initial inspections of III
- Compliance Follow Up*
- For Cause Inspections*
- Consumer Complaint/Whistleblower*
- Manufacturers of high risk devices

*Inspections that don't require preannouncement from FDA

Assumptions

- I'm ISO certified, you won't find anything
- I'm a contract manufacturer, you don't belong here
- The last investigator only took a day
- The last investigator said this …
- That's your subjective opinion, you can't cite this
- All FDA investigators are created equal

Two Different Inspections

Veteran

Newbie

You

Before the Inspection - Investigator

- Call five days before the inspection to preannounce
- Request procedures to review ahead of time to facilitate inspection.
- Review firm's inspectional history, MDRs, recalls, 510(k)s, PMAs, standards that apply to products, Registration & Listing information.

Before the Inspection - Firm

- Are you registered?
- Listings updated?
- Coordinate easy retrieval of documents
- Coordinate resources for inspection (scribes, support staff, etc.)
- Review your procedures, documents, open CAPAs. File any MDRs.
- Perform a complete makeover of your quality system …

Before the Inspection – Starting Today

- What is a DHR, DMR, DHF, MDR, CAPA, correction and removal?
- Don't know? Quiz each other on 21 CFR Parts 820, 803, 806, 807, 821, 1000, or:
  - CDRH Learn
  - Read the regs/preamble
  - Attend a conference
  - Read the QSIT Guide
  - Hire a consultant

FDA investigator arrives. Now what?

- Identify the top management official
- Present credentials
- Issue an FDA 482, Notice of Inspection
- Conduct an opening meeting
- Walk-through the facility

QSIT = Quality System Inspection Technique

FOOD AND DRUG ADMINISTRATION

GUIDE TO INSPECTIONS OF QUALITY SYSTEMS

QSIT

- An FDA validated method for investigators to conduct medical device inspections.
- Uses the “top down” approach – look at procedures and ask questions - then review records
- Procedures need to be established = defined, documented, and implemented
- Did management with executive responsibility adequately provide resources to setup and maintain an effective quality system?

QSIT Systems

Management Controls

- What records can we review in MC?
- Answer: Read the QSIT Guide, 21 CFR Part 820 regulations and preamble.
- FDA won't review your internal or supplier audit reports, or management review meeting minutes unless they make a written request.
- However, we will review raw data that feeds into Management Reviews and any CAPAs opened as a result of audits/MR.

MC Hints to Reduce 483s

- Choose a good Management Representative
  1. Detail oriented, analytical, good documentation
  2. Understand the regulations (read preamble)
  3. Can challenge the MER for more resources
- Provide adequate training for internal auditors
- Avoid the blue light special for external auditors
- Reaudit when necessary
- Perform adequate trending for management review

Video: Time for Bloopers!

Management Control Blooper

- Inadequate resources
- Software firm
- Software designed to update blood classification at midnight everyday (quarantine, expired, etc.)
- Software bug – system actually updates at 4:00 AM
- Maintenance contractor – “It’s a cheap fix.”
- Firm does not own source code and cannot get it from the development contractor

Design Controls

- CDRH - 510(k) clearance and PMA approval
- Districts – review design inputs, outputs, verification, validation, and changes
- Verification – does output meet the input
- Validation – specifications conform with all user needs and all intended uses
- Software – validate code (white-box testing) and functionality (black-box testing)

Hints to Reduce DC 483s

- Predefined acceptance criteria for all verification and validation testing
- Inputs need to measurable; how else can you test them?
- Recently bought another company's device? Do due diligence/design review on their DHF.
- Software? Do whitebox (code) and blackbox testing (functional). Track and prioritize defects during design & development and postmarket.

Design Control Blooper

- Inadequate design validation
- Company buys 510(k)
- Product – biodegradable facial implants
- Design – degradation profile, sterilization
- Sterilization validated at 25 kGy (gamma)
- Contract sterilizer uses 25 – 40 kGy
- “Can you show me in your validation the test reports for 40 kGy?”

CAPA

- Covers 820, 803 (MDRs) and 806 (corrections and removals), and 821 (tracking)
- CAPA is the heart of an effective quality system.
- Not all complaints need CAPAs – data analysis
- Corrections ≠ corrective or preventive actions
- Investigations: NCR < complaints < CAPA
- All CAPAs need verification – date game
- Verification = corrective/preventive action solves problem and it doesn't have an adverse effect.

Hints to Reduce CAPA 483s

- Did you analyze your data sources for CAPAs?
- Perform adequate investigations/verification
- Document everything into CAPA record
- Have established MDR and C&R procedures?
- If you have no MDRs, I'll ask:
  - Are MDRs filed only for cases of death or serious injury?
  - Can you hypothetically give an example of issue that would be MDR reportable for your product?

CAPA Blooper

- Inadequate corrective action
- Complaint - software bug found in Version 2
- Bug – cancels the wrong medication in an ICU environment
- Firm corrects bug in Version 3 and 4
- During FDA inspection – “How many customers are still using Version 2?”
- Firm surprised to find 5 customers including the original complainant

Production & Process Controls (P&PC)

- Records are important – device master record, device history record
- Define acceptance criteria for incoming, in-process, and final inspection
- Incoming inspection vs purchasing controls (↑↓)
- Process validation vs verification
  - Required – Destructive testing
  - Optional – to reduce sampling plan for verification
  - Validation – look at all process parameters

Hints to Reduce P&PC 483s

- Predefined acceptance criteria for process validation
- Sampling plans based on sound statistical rationale (risk-based)
- All automated production or quality control software needs to be validated (i.e. AOI cameras – automated optical inspection).
- Validation only as good as calibration, preventative maintenance, and employee training records

P&PC Blooper

- Inadequate process validation
- Contact lens packager – dailies
- Complaints – power on box doesn't match power on daily blister packs inside box
- Automated optical inspection AOI camera
- Validated 17 lines but did not open the box to verify the blister packs during validation

Purchasing Controls

- A large source for recalls
- Maintain an approved supplier list
- For each supplier/contractor/consultant on list:
  1. Define requirements that need to be met
  2. Qualify
  3. Monitor their performance

During the Inspection

- Multiple walk-throughs of facility
- Point out 483 observations in real time
- Provide daily updates
- Interview the person who does the work.
- We are not allowed to consult
- We take our green journals with us at all times

Observations vs Discussion Items

- Observations
  - Documented on an FDA 483 Form, Inspectional Observations
  - FDA 483s can be requested by FOI Act
  - Corrections to FDA 483s reviewed during next inspection

- Discussion Items
  - Not placed on the 483
  - Documented in final report
  - Can lead to observations during next inspection

End of Inspection – Close-out Meeting

- Issue an FDA 483
- Explain the annotation process – voluntary process that allows firm to comment on observations
- Discuss any observations
- Discuss any discussion items

You have 15 business days to respond to the FDA district office regarding the FDA 483 content

FDA Form 483

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER

6000 Metro Drive, Suite 101
Baltimore, MD 21215
(410) 779-5455 Fax:(410) 779-5707
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

07/16/2015 [redacted]

FEI NUMBER

[redacted]

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: [redacted]

FIRM NAME

[redacted]

STREET ADDRESS

[redacted]

CITY, STATE, ZIP CODE, COUNTRY

[redacted]

TYPE ESTABLISHMENT INSPECTED

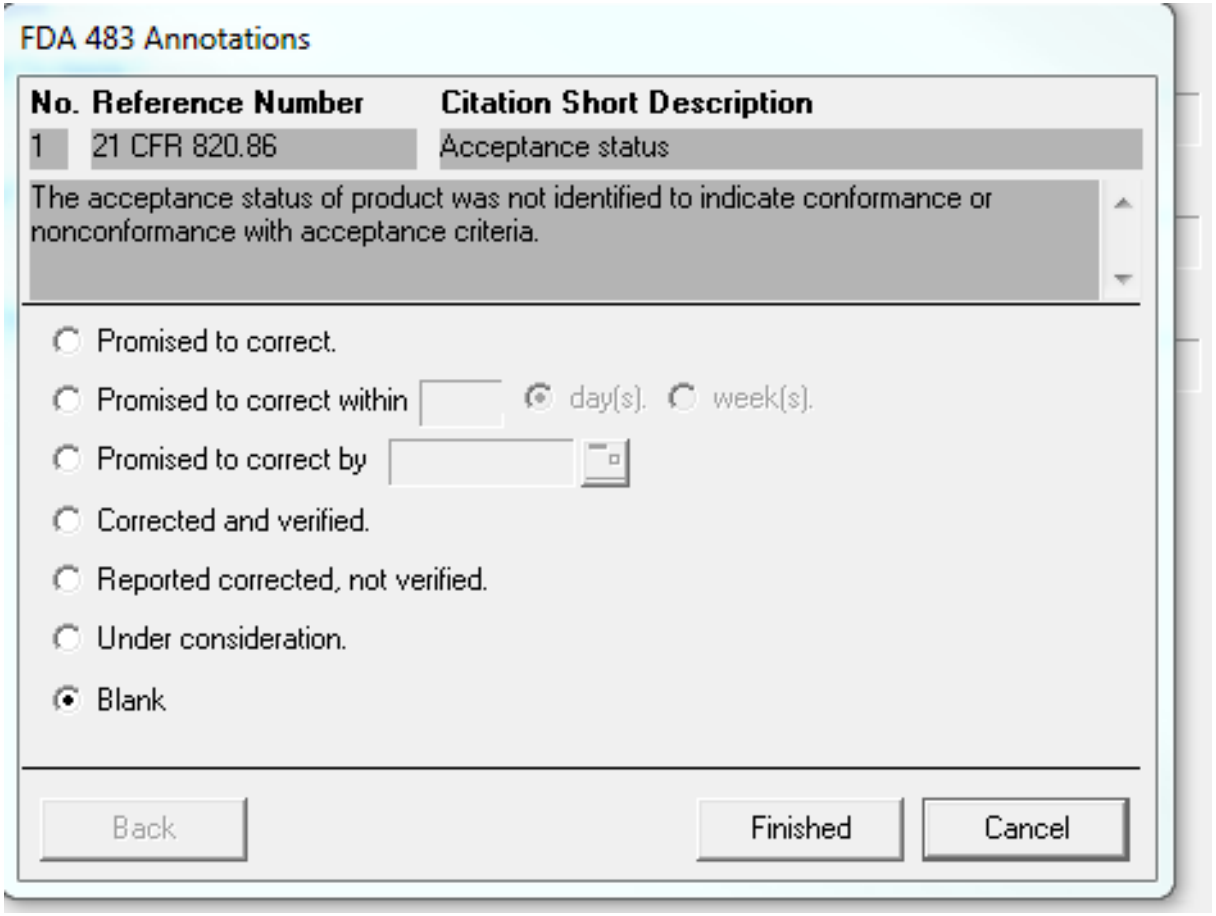
Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

Annotations



Corrected and verified is not an option unless the firm's management provides a correction and a corrective action or preventive action.

What happens after inspection?

- Investigator writes an “Establishment Inspection Report” (EIR)
- Investigations Branch endorses EIR
- Compliance Branch classifies EIR
- Investigation Branch schedules next inspection
- A copy of the EIR is sent to firm (FMD – 145).

How does FDA classify inspection reports?

- NAI – No action indicated
- VAI – Voluntary action indicated
  - FDA 483; need to correct for next inspection.
  - FDA will preannounce next inspection
- OAI – Official action indicated
  - FDA 483 + Warning letter, seizure, injunction, civil money penalties, prosecution.
  - FDA won't preannounce next inspection (<2 years)

Top 10 FDA Device Observations (Jan 2014 – Apr 2015)

RANK #	21 CFR SECTION	CITE DESCRIPTION	TOTAL
10	820.25(b)	Training procedures have not been [adequately] established.	93
9	820.30(i)	Design Change procedures have not been [adequately] established.	117
8	820.100(b)	CAPA activities and/or results have not been [adequately] documented.	121

Top 10 FDA Device Observations (Jan 2014 – Apr 2015)

RANK #	21 CFR SECTION	CITE DESCRIPTION	TOTAL
7	820.22	Procedures for quality audits have not been [adequately] established.	125
6	820.90(a)	Nonconformance procedures have not been [adequately] established.	133
5	803.17	MDR procedures have not been [developed] [maintained] [implemented].	158

Top 10 FDA Device Observations (Jan 2014 – Apr 2015)

RANK #	21 CFR SECTION	CITE DESCRIPTION	TOTAL
4	820.75(a)	A process whose results cannot be fully verified has not been [adequately] validated.	165
3	820.50	Purchasing control procedures have not been [adequately] established.	170
2	820.198(a)	Complaint handling procedures have not been [adequately] established.	350

Top 10 FDA Device Observations (Jan 2014 – Apr 2015)

RANK #	21 CFR SECTION	CITE DESCRIPTION	TOTAL
1	820.100(a)	CAPA procedures have not been [adequately] established.	458

Enforcement Actions

- By Fiscal Year

	2013	2014
Warning Letters	169	108
Foreign	82	39
Domestic	87	69
Seizures	0	0
Injunctions	1	0

Industry Education Resources

Three Resources

1. **CDRH Learn – Multi-Media Industry Education**
   - over 80 modules
   - videos, audio recordings, power point presentations, software-based "how to" modules
   - mobile-friendly: access CDRH Learn on your portable devices

   http://www.fda.gov/Training/CDRHLearn

2. **Device Advice – Text-Based Education**
   - comprehensive regulatory information on premarket and postmarket topics

   www.fda.gov/MedicalDevices/DeviceRegulationandGuidance

3. **Division of Industry and Consumer Education (DICE)**
   - Contact DICE if you have a question
   - Email: DICE@fda.hhs.gov
   - Phone: 1(800) 638-2014 or (301) 796-7100 (Hours: 9 am-12:30 pm; 1 pm-4:30pm EST)
   - Web: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ContactUs--DivisionofIndustryandConsumerEducation/default.htm

Roll the Video!

Call to Action

Better

Communication

More Efficient

Inspections

Thank You!

Please complete the session survey:

surveymonkey.com/r/DEV-D2S8