

FDA Medical Device Inspections

**FDA Small Business
Regulatory Education for Industry (REdI)
Silver Spring, MD
September 28, 2016**

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Learning Objectives

- Learn how to prepare for your next inspection
- Review the Quality System Inspection Technique (QSIT)
- Review keys for reducing 483 observations
- Discuss Post-inspection correspondence

Purpose of the Inspection

- To assess compliance with CFR, Title 21, Parts:
- 820 (Quality System)
- 803 (Medical Device Reporting)
- 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 provides a Class 1 high risk list

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
- This investigator is _____



Before the Inspection - Investigator

- Call five days before the inspection to preannounce
- May request procedures to review ahead of time to facilitate the inspection
- Review the firm's inspectional history, MDRs, recalls, 510(k)s, PMAs, standards that apply to products, Registration & Listing information and total product lifecycle (TPLC) reports

Before the Inspection - Firm

- Are you registered?
- Are your listings updated?
- Coordinate easy retrieval of documents
- Coordinate resources for inspection (scribes, support staff, etc.)
- Be prepared to talk about risk
 - What is your most critical design output?
 - Why didn't you open a corrective and preventive action (CAPA) for this?
 - Why was this corrective action not reported to FDA?

Poll Question

D2S5-1

View Votes

Edit

End Poll

D2S5-1: Which activities has your firm performed to get ready for a FDA inspection?

<input type="radio"/> Purchased FDA Form 483s previously written by the investigator.		0%	(0)
<input type="radio"/> Looked up the investigator's background on a professional website.		0%	(0)
<input type="radio"/> Called colleagues from other firms/sites about your investigator.		0%	(0)
<input type="radio"/> Checked out his/her photos on Facebook.		0%	(0)
<input checked="" type="radio"/> No Vote			

☒ Broadcast Results

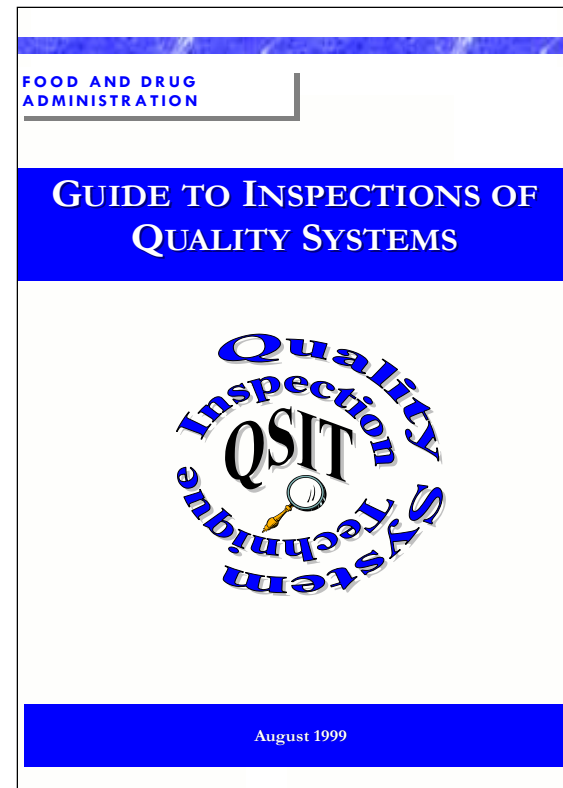
FDA investigator arrives. Now what?

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

What is QSIT?

- Quality System Inspection Technique

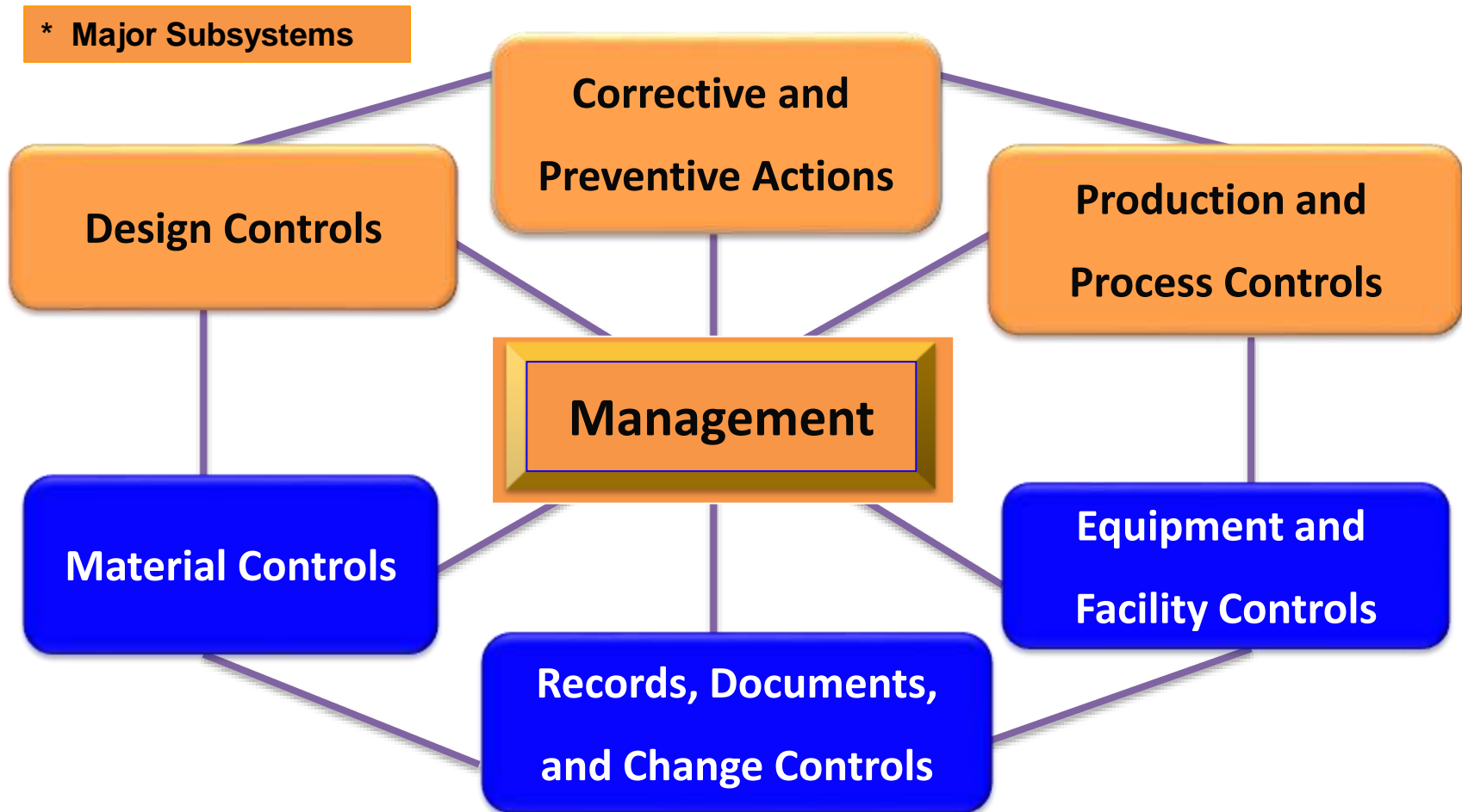
www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074883.htm



QSIT continued

- 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?
- Investigators don’t always follow QSIT.

The 7 Subsystems of a QSIT



Different Medical Device Inspections

- Level 1 – Abbreviated QSIT – CAPA + Design Controls or Production & Process Controls
- Level 2 – Baseline QSIT – all 4 subsystems
- Compliance follow-up – may include elements of QSIT
- “For Cause” – more in depth than QSIT

Management Controls (MC)

- What records can we review in MC?
- Answer: Discussed in 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 a written request is made
- However, we will review raw data that feeds into Management Reviews (MR) and any CAPAs opened as a result of audits/MR

Hints to Reduce MC 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
- Audits need to cover FDA Quality System Regulation (not just ISO)
- Reaudit when necessary
- Perform adequate data analysis for management review

Management Representative: 17 years and counting



Design Controls (DC)

- CDRH - 510(k) clearance and PMA approval
- Districts – review design inputs, outputs, risk analysis, verification, validation, design reviews and changes
- Verification – does output meet the input
- Validation – specifications conform with all user needs and all intended uses

Hints to Reduce DC 483s

- Predefined acceptance criteria for all V&V testing
- Outputs need to be measurable and characterized
- Recently bought another company's device?
 - Due diligence/design review on their design history file (DHF)
- Software?
 - Black-box validation - function
 - White-box validation - code
 - Track and prioritize defects during design & postmarket
 - Guidance Document: General Principles of Software Validation, Version 1.1, dated June 9th, 1997.

Corrective and Preventive Action

- 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
- 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/Reference everything in CAPA record
- Have established MDR, Complaint and Recall 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?

Production & Process Controls (P&PC)

- Device History Records
 - Documentation shows requirements of DMR are met
 - Copy of the labeling for each DHR
- Not adequately controlling NCRs (nonconformance)
 - Worst case – recall situation
- Sampling plans
 - based on sound statistical rationale
 - adequately implemented (i.e. # of samples)
- Software validation (P&PC and Quality)
 - If off-the-shelf (OTS) software: perform black-box validation
 - If coded in-house: perform black-box and white-box

Process Validation

- Required – destructive testing
- Optional – to reduce sampling plan for verification
- Predefined acceptance criteria
- Look at all process parameters
- If parameter not important – document rationale
- If validated process involves chemicals (i.e. coating)
 - Expiration dating and worst case usage
 - Functional testing on aged samples?
- Continuously monitoring process parameters?

Purchasing Controls

- Maintain/update Approved Supplier List
- For each supplier/contractor/consultant on list:
 1. Define requirements that need to be met
 2. Qualify
 3. Monitor their performance
 4. Risk based
 5. Contracts

Common 483s/Quick Fixes

- No or inadequate Device History Record SOP
 - a copy of labeling not included in DHR
- No or inadequate MDR SOP
 - Internal mechanism for timely reporting
 - MDR supplemental reporting
- CAPA analysis
- Complaint investigations
 - no documented rationale why an investigation is not performed

Poll Question

D2S5-2

View Votes
Edit
End Poll

D2S5-2: Has your firm been cited with one of these observations?

<input type="radio"/> DHR doesn't include copy of labeling		0%	(0)
<input type="radio"/> No or inadequate MDR SOP		0%	(0)
<input type="radio"/> No or inadequate CAPA analysis		0%	(0)
<input type="radio"/> P&PC and/or Quality System software not validated for its intended use		0%	(0)
<input checked="" type="radio"/> No Vote			

☒ Broadcast Results

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
 - Labeling, lack of 510(k) and registration

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
- Firms are encouraged to respond to 483s within 15 business days

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 FEI NUMBER
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED TO:	
FIRM NAME	STREET ADDRESS
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED Manufacturer
<p>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.</p> <p><i>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.</i></p>	
DURING AN INSPECTION OF YOUR FIRM I OBSERVED:	


Annotations

FDA 483 Annotations

No.	Reference Number	Citation	Short Description
1	21 CFR 820.86	Acceptance status	The acceptance status of product was not identified to indicate conformance or nonconformance with acceptance criteria.

☐ Promised to correct.

☐ Promised to correct within ☒ day(s). ☐ week(s).

☐ Promised to correct by 

☐ Corrected and verified.

☐ Reported corrected, not verified.

☐ Under consideration.

☒ Blank

Back Finished Cancel

Corrected and verified is generally not an option

- unless firm's management provides a correction or corrective action.

and

- It is verifiable by the investigator.

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.
- OAI – Official action indicated
 - FDA 483 + Warning letter, seizure, injunction, civil money penalties, prosecution.
 - FDA typically won't preannounce next inspection (<2 years)

Questions?

Please complete the session survey:

surveymonkey.com/r/DEV-D2S5

Call to Action

- Better communication between manufacturers and investigators lead to more efficient inspections
- More efficient inspections help manufacturers to better utilize their time.
- More efficient inspections allow FDA to be able to review multiple high risk issues in a timely fashion

