Best Practices in Preparing for an FDA Inspection

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Agenda

- Developing a successful plan to ensure compliance with FDA protocols
- Tips for how to best prepare for an FDA audit
- Implementing a strategy that will aid in the preparation and managing the inspection
- Utilizing best practices to prepare for FDA inspections while ensuring successful outcomes
- How to navigate high risk areas with complaint handling systems
- Group Discussion
Types of Inspections – Directed vs. Routine

QSIT 4 Main sub-Systems and Satellite Systems

- Management Control
- Corrective and Preventative Actions
  - (CAPA)
- Medical Device Reporting
- Corrections and Removals
- Medical Device Tracking

Design Controls

Production and Process Controls (P&PC)
- Sterilization Process Controls

Types of Inspections:

- **Level 1 (Abbreviated)**
  - CAPA + 1 other sub-system
- **Level 2 (Baseline)**
  - Management Controls, Design Controls, CAPA, Production and Process Controls, then return to Management Controls
- **Level 3 (Compliance Follow-up)**
Preparing for a FDA Inspection

• Develop and Use Audit checklist:
  − Items that can be prepared in advance e.g. procedures, training records, data pulls; list of frequently asked questions)

• Conduct Mock Audits

• Review previous inspection and compliance history

• Review Warning letters; Compliance Programs, Guidance Documents, Guides to Inspection, QSIT, Investigators Operations Manual (IOM)

• Train all management with executive responsibility, whom investigators will seek to interview:
  − Internal procedures and their requirements
  − FDA Regulations and requirements for the relevant area of inspection
  − Quality System (QSIT)
  − Front and Back room protocols
  − What to say and not to say

   Be Audit Ready All the Time!
Audit Preparation Hints

You should communicate and demonstrate how you run your business in compliance with the regulations and within the framework of your Quality management System.

- Know your Company policy/procedure and the FDA’s
- Be honest, direct, and communicate clearly
- Stop when the question is fully answered
- Use procedures to avoid uncertainty
- DO not provide “hearsay” or anecdotal information
- Never guess or speculate
- Maintain eye contact and be aware of body language
- Generally do not volunteer information
- Be prepared to be challenged on the science –
  - Why did you test / not test; what the results mean?
  - How are they related to the your design files?
  - Test Linkages with CAPAs and Field Actions.
FDA Inspection Approach

- FDA views complaints as a primary indicator of product performance
- Expect FDA to analyze complaints for significant trends and issues presenting with patient harm
  - Investigators will attempt to identify the probable causes of the problem
    - e.g. Was it a supplier quality issue? Was it a failure in design validation? This review may serve as inputs for other avenues in the inspection
  - May be concurrent with a review of hazards identified in the risk file and complaints with the same hazard to assess whether mitigations were effective
  - FDA will evaluate complaint trends to determine if they were acted upon in a timely manner. This could lead to an evaluation of the trending process
- FDA investigators will assess adequacy and depth of complaint investigations, actions taken, whether these actions were aligned with the seriousness of the issue from a harm perspective, and whether the actions were effective.
  - These may serve as entry points into the CAPA process
FDA Investigator

• “Public health” Law Enforcement official – compliance focused
• Scientifically trained
• Objective observer – fact witness
• Typically not an “expert”; FDA can and does use “experts” for certain inspections
• Mission oriented – Want the inspection to go smoothly
• Not seeking to “trap” anyone; want you to get it right the first time
• Expect most people to be honest and forthcoming; trained to detect deception
• Understand that firms prepare their employees for inspections
• May believe that firms do not want to voluntarily divulge adverse information
What to expect?

Review:
• Records: Complaints; MDRs; Adverse events; CAPAs; FCAs
• Procedures; Protocols; Agreements; Device traceability; supplier quality; lab and inspection results

Interview:
• Confirmation by collecting inputs from multiple sources.
• Interview Questions:
  ➢ Direct – “Do you have a procedure for …..?” Can I see the training record for ….?”
  ➢ Leading – “Why did / didn’t you …..?” “Who else does ….. ?”
  ➢ Open-ended – “ How do I know that you corrected ……?” Why would I believe that xyz action you took was effective?” “Tell me more about that ….”
  ➢ Hypothetical – “What would you do if …?”
Regulatory Inspection Process

- Manage Investigator requests for records; provide what is asked for in a reasonable timeframe.
- Subject Matter Experts (SMEs) trained on their respective roles in the inspection. All SMEs and supporting information should be prepared and ready in the back room before going to the front room.
- Define Roles and responsibilities - Escorts; Runners; Front room; Back room personnel. Train everyone (Front gate guard; receptionist; Quality and Manufacturing personnel)
- Back Room and Front Room Setup (Seating for multiple streams; Computers, Printers, Copiers, Supplies)
- Daily updates to Sr. Management; Backroom personnel; prep for next day inspection
- Have prepared frequently requested information and have ready in back room.
  - Lists of Complaints, (defined fields); CAPAs; Non-conformances; Field Actions.
  - Design changes (time-frame since the last inspection but be prepared to adjust depending on what the investigator requests)
  - “Golden” examples of complaints; Ready to show electronic complaint system
  - Any previous 483 and WL responses; list of commitments and associated CAPAs
Inspection Do’s and Don'ts

When speaking with Investigators

- Be confident - Know your procedures and the applicable FDA Regulations
- Focus on Facts: procedures, systems, and records
- Key phrases “As per our procedure” “Following approved procedures
- Carefully listen to the question before answering; Seek clarification if you don’t understand
- Pause to think before you answer – If you don’t remember say so and look it up in your procedure
- Answer the question that is asked and don’t play the card “I’ll have to get someone to discuss that” too often
- Ask for break if you need – “…I need to verify this…” to step out of the room
- Silence is OK - don’t feel compelled to fill the “void” by talking
- Do not make commitments on how something will be resolved.
- Note in some cases, management may decide to resolve certain issues or make changes to procedures prior to inspection closeout but this requires discussion in the backroom.
- Always be civil and professional
- ALWAYS TELL THE TRUTH!
Opening Meeting..

- Front room & Full Backroom support
  - Inspection Team (Escorts; Note Taker; Runners, etc.)

- FDA Form 482 Notice of Inspection
  - Ask the Investigator:
    - Purpose and anticipated duration of the inspection
    - Assure the investigator that firm intends to facilitate a smooth inspection and cooperate with the investigator

- Short presentation given by the most senior Quality Associate during the opening meeting:
  - Org charts (indicating who is the management representative),
  - Presentation about the facility/layouts, plan tour ahead of time.
  - Products manufactured (registered) at the facility; Hours of operation
  - High Level organization chart
  - Since last inspection what are the new products that are launched
  - Any significant changes since the last inspection
Managing the Inspection…

• Control documents provided to Investigator: Keep a log of requests and their status, review at the end of each day to see trends, Determine if “confidential” and mark appropriately, keep a copy of all documents (records and procedures).

• Present the records which are requested but if you are able to choose the records select “good samples” that clearly represent the process.

• Inspection behaviors: Do not guess at the answer. Say you do not know rather than say “I assume” or “I think”, Do not respond or allow others to respond outside of their area, Stick to the question, do not embellish or volunteer information

• Daily wrap up: Be sensitive to their time, no arguments, Regroup and try to address the concerns,  
  − Ask the investigator if there are any open issues from that day, if there is a concern, and what they would like to cover on the next day.  
  − Ask the investigator to confirm they are done with that topic.  
  − If collecting some documents would be problematic, give an estimate of when they would arrive..

• After FDA leaves for the day: Review daily summary report, Prep documents, Determine what is outstanding and anticipate what’s next.
FDA Investigator Will Look For…

- Complaints with hazards that result in patient harm
- Examine the mitigations in the risk file
  - Trace to mitigations by design, protection, labeling and assess adequacy
  - Trace mitigations to Design V/V – assess adequacy
  - Trace mitigations to design inputs & outputs and assess if they are clear and adequately addressed by the mitigations.

- Special focus on complaints leading to field actions and whether the appropriate corrective and preventive actions were completed.
  - Could also lead to a review of how the issue(s) were managed within the Management controls subsystem.
Typical Questions

- Quality Policy: How applies to your function in post market surveillance?
- How do you know what is required of you in your job?
- Complaints Review - MDRs Submitted? Timely? Investigator may request to view records electronically.
- What are the complaint trends? How used?
- Non Conformance System: What are the trends? How related to Complaints, product, design?
- Supplier Quality: Process, Qualified, Scars? Information from other subsystems
- Design Changes? Compliance with the regulations? Process Validation? P&PC:
- Management Review, Frequency? Agenda, Participants?
- Training: There should be no gaps in training. Address before the inspection.
- 3’rd party / distributors / consultants. If doing work on behalf of the company – they should be trained.
- Labs / Areas: Walkthroughs; Instrument Calibrations; test method validations
Top Mistakes

- Assuming only Subject Matter Experts (SMEs) will be questioned. Management and Lower level employees may be called to the front room.
- Thinking you are in charge of the inspection agenda. Your role is to facilitate a smooth inspection and respond to requests in a timely fashion.
- Failing to provide requested documents or giving the impression that you are not going to provide them.
- Failing to review documents before providing them.
- Assuming discussions are off the record.
- Complacency when things are going well.
Audit Prep Hints

• Assemble talking points and/or storyboards that can be used to help describe complaint, investigation, and MDR processes in an audit.
• Provide a chart showing linkage between Call center, complaint management center; Investigation Site
• Ensure procedures mapped to FDA QSR regulations
• Complaints Review – MDRs Submitted? Timely? Electronic record requests
• What are the complaint & non-conformance trends? Does the Company trend data? How used?
  – Are ALL trend triggers taken to resolution? If there is a re-open (effectiveness) trigger, verify that all excursions above that trigger are addressed.
• Effective? Verification/validation?
• Supplier Quality: Process, Qualified, Scars? Information from other subsystems
• Change Control Review for 510(k)/PMA supplement?
• Design Changes? Compliance with the regulations? P&PC: Observe? Process Validation?
• Management Review, Frequency? Agenda, Participants?
Closing Meeting.

- Request a closing meeting – whether or not a Form 483 is issued.
- Confirm date and time with investigator; invite management.
- Brief attendees on inspection and meeting etiquette (not the time to argue with the investigator);
- Ask questions as needed to clarify any observations or understand the concerns being presented by the FDA Investigator.
- Request that corrections appear in the EIR.

- Know your policy for annotating the Form 483
  - Corrected and verified
  - Corrected and not verified
  - Promised to Correct
  - Under Consideration
After Inspection..

- If Form 483 is issued:
  - Respond to agency within 15 days
  - Ensure corrective actions taken are systemic (global) and go beyond the specific issue.
  - Include objective evidence of corrections and corrective actions in response e.g. updated procedures; training records; evidence of effectiveness if possible
  - Review warning letters to find out where FDA may have taken issue with a response.

- If CAPAs opened, provide timeline for CAPA and detail on what is being planned to address the concerns

- After response submitted, provide periodic updates to the agency

- Track all commitments either in the CAPA or Internal Audit System

- Review back-room and front-room performance with SMEs and support personnel and address any gaps identified.

- Goal is continuous improvement and Inspection readiness
Best Practices

• Complaint record must stand on its own. An investigator should have minimal, if any questions regarding what happened and how complaint was dispositioned.

• Complaints –
  ✓ Good documentation practices are critical. Document follow-up requests for additional information. Avoid leaving blanks and explain unknown’s.
  ✓ Ensure closure summary statements match record and self-audit these statements. Avoid conflicts with rest of record.
  ✓ Have clear rationale for not reporting alleged malfunctions. Saying it is not reportable is not enough. Provide rationale re why event is not reportable.
  ✓ Ensure all open records have some level of documented activity at least every 30 days. Be prepared to talk to your open records/backlog and avoid inactive/latent records.
  ✓ Opening an investigation for P1 trips helps avoid any potential inconsistencies. Better to investigate trips than trying to explain why it wasn’t done. If large number of complaints, be able to justify trip decisions.

• Designate at least 1 local person to speak to wing-wing complaint process.

• Review site’s service records – understand timeliness, documentation issues
  ✓ Understand feeder from service to complaints system; Identify service representative supporting inspections.
  ✓ Include representatives of top two or three feeder systems.. Know what percentage of complaints come from which system.
Best Practices

• Best practice for interview on CAPAs – Lead with an overview / executive summary:
  ✓ Here is what you cited us for …
  ✓ Here is what we found as root causes …
  ✓ Here is what we did to correct the problem and prevent recurrence …
  ✓ Here is a summary of the objective evidence why these actions taken were effective …

• Decide what will be printed including attachments (+1 or +2) and full detailed or formal report.

• Remember ALL complaints are evaluated for investigation. If investigation not performed, rationale is documented. Remember ALL complaints are evaluated for reportability.

• Ideally only one person will go to the FR and will speak from complaint conception – CAPA/Risk Process

• Know where to get the most recent releases of relevant docs and how to ensure they’re not an obsoleted version
Questions & Discussion