Implement an Effective Corrective Action and Preventive Action (CAPA) Program that Adheres to FDA’s New Initiative

Presented By:

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QUALITY METRICS AND MANAGEMENT WEEK

February 22 - 24, 2016
San Diego, CA
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Welcome to the 2010 IVT CAPA Workshop!

Areas covered today:
Part 1: Regulatory Expectation
Part 2: Addressing CAPA Challenges
Part 3: Re-defining CAPA System
Part 4: Important CAPA Requirements
Part 5: CAPA Recommended Guidelines
Part 6: CAPA Quality Metric
Part 7: CAPA Summary
Regulatory Expectation

Part 1:
Planning is Key
“To address this mistake we need to utilise our thorough system of root cause analysis. I will begin, if I may, by pointing out that it’s not my fault”
Quality System Inspection Technique (QSIT) Inspections

Top Four FDA 483 Items

- CAPA (30%)
- Records (10%)
- PAPC (20%) - Production and Process Controls
- Mgmt (40%)
Top FDA 483 Items

- Records (20%)
- CAPA (50%)
- PAPC (30%)
- Non-QSIT Inspections
QSIT Study Findings

(Population 42 Firms)  
QSIT Objectives

- Procedures
- ID existing problems
- Data challenge
- Analysis techniques
- Failure Investigation
- Actions taken
- Actions effective …
- Actions implemented …
- Info disseminated
Two Different Approaches

We use a risk-based approach

We always initiate a CAPA

Quality Issues

Risk Analysis

Trend Analysis

Formal CAPA

Quality Plan
CAPA requirements are described in detail in FDA 21 CFR § 820.100 and ISO 13485:2003 Chap. 8.5.

You must fulfill these requirements in order to be able to sell medical device products worldwide.

Compliance with these requirements also helps your business by achieving better product quality and higher customer satisfaction.
• Very similar is the U.S. FDA’s regulation for pharmaceutical manufacturers 21 CFR Part 211.22 (Quality Control Unit)…
  – responsibilities of a quality control unit...to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated.
  – The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, an purity of the drug product

• …and in Part 211.92 (Production Record Review)
  – Any unexplained discrepancy…or the failure of a batch or any of its components to meet any of its specifications shall be thoroughly investigated…The investigation shall extend to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy. A written record of the investigation shall be made and shall include the conclusions and follow-up.
Numerous source areas for CAPA
Scope of “problems” that drive CAPAs go beyond nonconforming product
Any process that affects product quality is included
Regardless of where the problem originates, or what type it is, it must follow a process.

**Identify & Triage**
- Identify problem
- Assess impact
- Quality / Regulatory / Management Notification
- Investigation Process?

**Investigate, Root Cause, Action Plan**
- Complete Investigation
- Determine Root Cause
- Proposed Corrective / Preventive Actions
- Plan effectiveness

**Change Control**

**Verify Effectiveness**
- Measure to ensure problem has been resolved
- Monitor to ensure it is not re-occurring
Addressing CAPA Challenges

Part 2: There no Perfect System
Typical CAPA Challenges

- **Challenges in Problem Identification**
  - Missing view of the big picture
  - Lack of ownership and accountability
  - Inability to link related problems
  - Insufficient tools for trending and analysis

- **Challenges in Investigation**
  - Quality of investigations is poor
    - Missing & incomplete information
    - Inability to easily review similar past investigations
  - Inconsistent investigation process & Root Cause
  - Not determining root cause
  - Past due investigations, not being closed, get lost

- **Challenges in Planning**
  - Vague root cause analysis
  - Confusion over what is “corrective” and what is “preventive” action
  - Inability to relate corrective actions to source problems
  - Lack of integration to Change Control System
Typical QMS Challenges (cont.)

- **Challenges in Review & Approval**
  - Not sure who needs to approve
  - Approvals in serial, not parallel
  - Approval process takes long time
  - Lack of key stakeholder input

- **Challenges in Implementation**
  - No way to track issues through workflow
  - Lack of visibility to open items
  - Lack of visibility to related items
  - Changes to plan mid-stream
  - Compliance risk

- **Challenges in Effectiveness**
  - Easy to “forget” to measure effectiveness
  - Difficult to gather necessary metrics
  - No means to generate metrics
  - Inability to measure effectiveness does not give us any assurance if we are addressing the root cause of the problems
Best Approach to Quality Management

- Globalize (harmonize) around a common philosophy and approach to CAPA and source Events
- Obtain full compliance with cGxPs, as well as regulatory & customer expectations
- Use quality metrics as a basis for continuous improvements
  - Trending – Problem Analysis
  - Thorough Investigations and Root Cause Analysis
  - Ensuring CAPA effectiveness
  - Bring attention to risk areas to prevent problems

Implement a centralized Quality Management System:

- Manages all inputs and outputs as well as the actual actions
- Scalable to be deployed on a global basis
- Functionality / Flexibility to meet business requirements
Re-defining CAPA System

Part 3:
Define the Inputs & Process
Re-defining CAPA System

• Definitions
  – Standardize definitions across the organization
  – Terms like “deviation”, “event”, “nonconformance”, correction”, “corrective action”, “preventive action”, “discrepancy” must be consistent for each operating unit
  – The same term should have the same meaning everywhere, and drive the same process
  – CAPA sources include: Complaints, Audits Observations, Trends can feed CAPA

• Determine, scope identification & impact of new system
  – Where does the process need to change?
  – Who will the system affect?
  – What existing policies may change?
  – Understand the difference between the “what” and the “who”
Record the Event

- Capture all related data of any event regardless of the type
  - Source
  - Date & Time of Event
  - Type
  - Description
  - Department

- For issues surrounding Events, utilize a quality evaluation:
  - Quality Event only
  - Quality Event + CAPA
  - Quality Event + Investigation + CAPA + Change Control

- Log observations / trends to implement pro-active changes
Perform Assessment & Investigation

• Assign Investigator
  – Use “Push” or “Pull” concept
  – Assess impact, consider decision tree approach

• Create Investigation Plan
  – Use Parent-Child concepts – track each investigation “task”
  – Use Investigation Templates

• Track & Complete Investigations
  – Use workflow, due dates and reminders
  – Escalation of past due investigations
  – Search & Reporting
  – User Dashboards

• Analyze Root Cause
  – Structure Root cause Analysis Tree
  – Use Root Cause to Drive CAPA process
• Review currently in progress CAPAs
• Create CAPAs and link to root cause
  – If multiple CAPAs identify which ones resolve which root cause?
  – Which actions must be closed to close the deviation?
• Create an Effectiveness Plan at this time
• Determine Approvers
  – Use pre-set approver functions if possible
• Route Investigation & CAPA plan for approval
  – Email alerts, reminders
  – Dashboards
• Obtain Approval
  – Ability to reject to various previous workflow states
Each CAPA record should have its own record and workflow

Use Parent-child relationships to break up the process into “smaller bites”
  - Action Item Tracking

Track completion and verification of each CAPA
  - Use workflow, due dates and reminders
  - Escalation of past due investigations
  - Search & Reporting
  - User Dashboards

Measure effectiveness according to the plan -> evidence that root cause has been eliminated (This is a key component of the CAPA system. This is where a lot of companies get writing up on.)
Important CAPA Requirements

Part 4: Control and Structure
### Defining the Requirements

- Centralized database
- Handles all process areas - modular
- Workflow driven
- Proactive user notification and escalation
- Action items management
- Querying & Reporting
- Elaborate security by user-group
- Management reports
- Performance Metrics & Trending
- Part 11 Compliance

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"O.k., and now you'll do exactly what I'm telling you!"
Management of all Data

• Modular approach to handling all source areas but maintains individual requirement
  – Multiple “Record Types” to handle all process areas
  – Ability to create user defined fields
  – Configurable data entry forms
  – Validation and business rules

• Integration to external systems
  – E.g., Create deviations automatically from ERP
  – E.g., Create OOS Investigation from LIMS
  – Master data (customer, product/item, etc.)
Workflow Management

• Configurable workflow
  – Automate review and approval process based on meta data
  – Business-rule based workflows
  – Parallel Approvals
  – Process changing activity
  – E-mail notifications

• Integrated source areas process to Corrective Action process
  – Parent – child relationships
  – Cross referencing
Escalations and Business Rules

- **Business rules enforcement**
  - Date Due, Milestone Dates
  - Automatically assigning investigators, reviewers, approvers
  - Automatically scheduling tasks based on type of Record

- **Escalation**
  - “Reminders” of tasks reaching expected completion date
  - Escalation of CAPA past due
Querying
- Ability to query on all fields
- Full text / search engine functionality
- Ability to save searches

Reporting
- Customizable report format
- On screen view, print, email, save
- Status reporting

Trending
- Across all sites
- Across all source areas
- Root cause analysis
- Identify occurrence rate decrease / increase
- Ability to detect trends automatically
Compliance with Part 11

• Is your CAPA system software driven if so;
  – Does the system conform with your firm’s Part 11 requirements?
  – Has the software “passed” the test, i.e., has it gone through FDA audits at another firm?
  – Can it be validated?
  – How confident are you in the above assessment?

- Full audit trail
- Reporting features
- Configurable security groups
- Complete record of created and modified data
- Enforced workflow sequencing
- Password composition rules
- Electronic Signatures made up of two unique components

- Password aging/expiration
- Cannot re-use previous password
- Account Locking and Admin Notification after failed log-in Attempts
- Session time-out
- Requirement of “reason” for data modification
- Administrator / Configuration Audit Trail
CAPA Recommended Guidelines

Part 5: Control and Structure
A CAPA case due date is based on the estimated length of time required to investigate and resolve the issue. The task doer, with justification, may negotiate the task completion due date. If the task doer is unable to meet the agreed upon assigned task completion date, an extension for the task completion date may be approved through the CAPA coordinator.
• For the investigation and proposed disposition task, the CAPA coordinator allows 15 days for task completion.
• For any task with a completion date greater than 90 days from assignment, the task doer must provide a report detailing the progress on the task every 90 days.
• The task doer task cannot be closed until all required document updates are approved and implemented, if applicable.
• Past due CAPA tasks are escalated to Senior Management.
• CAPAs are monitored to detect recurrence of nonconformities and for timely completion of tasks assigned
• A Look-Ahead report listing all tasks due within the next 30 days is distributed bi-monthly
• PAST DUE reports are issued to management for follow-up once a month
• A report of the CAPA system is presented to Management at the quarterly Management Review
CAPA Quality Metrics

Part 6:
How well is your CAPA system working?
Trend/data analysis is performed on historical data to identify adverse trends or data that require corrective action.

- Examples are
  - Overall nonconformance/deviation activity levels
  - Corrective action types
  - Past due corrective actions
  - Defect code analysis
  - Root causes
Challenges

• Inputs not clearly defined or established
• Trigger thresholds not established
• Focus on reactive metrics (Nonconformances, Complaints, Audit Observations)
• Data not easily retrievable
• Data not easy to analyze for trends
Quality Metric Suggestions:

- Implement predictive metrics/indicators
  - Routinely review and act on sources of product and quality data
  - Use a risk assessment process that allows CAPAs for Preventive Action
  - Improve linkage between CAPA into Design Controls
  - Take a holistic view of issues
  - Does CAPA system link to other Quality Systems, systems, and/or processes?
Internal Sources that should be considered:

- Acceptance activities
- Calibration and Maintenance records
- Design Control system
- Management Reviews/Annual Product Reviews
- Nonconformances (product and non-product)
- Packaging and Labeling materials
- Quality Audits
- Returned products
- Risk Management documents
- Service and Installation records
- Process Excellence programs
- SPC monitoring
- Stability studies
- And more...

Remember to include ancillary improvements, project systems, etc.
External Sources:
- **Customer complaints**
- Customer feedback
- External Quality Audit reports
- FDA/ISO/EN/IVDD feedback
- Product warranty
- Recalls/field actions
- Identification of other condition/issue that does not comply with:
  - Your own Quality System and/or
  - ISO/EN/IVDD standards (e.g., ISO 9001, ISO 13485, EN 46001, etc.)
  - FDA regulations (e.g., 21 CFR 820, 21 CFR 210/211, 21 CFR 600, 21 CFR Part 11, etc.)
- And more…

Remember to track & trend, use risk assessment tools
• **Proposed Optional Metric 1:**
  Was each APR or PQR reviewed and approved by the following: (1) the head of the quality unit, 468 (2) the head of the operations unit; (3) both; or (4) neither?

• **CAPA Effectiveness:** A comprehensive corrective action and preventive action program has been identified as a strong indicator of a robust quality culture. Continual improvement is based on preventing the initial occurrence (preventive action) or recurrence (corrective action) of a detected nonconformity or other undesirable situation. FDA has observed that less robust quality systems often rely on preventing recurrence solely through personnel re-training (i.e., the same training has already been provided to the employee(s)), while more robust quality systems consider re-design and re-development of the process. Comments are requested on proposed Optional Metric 2 and alternative approaches.
• **Proposed Optional Metric 2:**
  What percentage of your corrective actions involved re-training of personnel (i.e., a root cause of the deviation is lack of adequate training)?

• **Process Capability/Performance**  FDA recognizes the importance of statistical process control as a tool in understanding and managing variability in both product and processing for application and non-application products. We recommend that a statistician or person with adequate training in statistical process control techniques develop the data collection plan and statistical methods and procedures used in measuring and evaluating process stability and process capability. Procedures should describe how trending and calculations are to be performed and should guard against overreaction to individual events as well as against failure to detect unintended process variability. Frequently, however, manufacturing control elements are developed based upon early estimates of process capability at time of product launch or using control strategies considered appropriate at the time of approval. Knowledge gained during scale-up and commercial manufacturing can be useful in further developing the control strategy. It is important that statistical analysis be used to enable and advance product quality, not to inhibit continuous improvement and application of post-launch learning and experience to the assurance of high quality product and consistent processing. FDA requires manufacturers to apply statistical tools in a manner appropriate to assure that the product and process reproducibly meet specifications on an ongoing basis. Specifications must be meaningful in terms of achieving the desired finished product characteristics. This data enables science and risk-based quality risk management by identifying when manufacturing improvement is needed.
• Proposed Optional Metric 3:

A “yes” or “no” value of whether the establishment’s management calculated a process capability or performance index for each critical quality attribute (CQA) as part of that product’s APR or PQR.

A “yes” or “no” value of whether the establishment’s management has a policy of requiring a corrective action or preventive action (CAPA) at some lower process capability or performance index.

• If “yes” to the above question – what is the process capability or performance index that triggers a CAPA? If “no” to the above question – please do not respond.
Part 7:
CAPA Good Business Practice
Conclusion

• QMS encompasses the overall process related to events / observations from multiple sources, as well as their investigations, and resolutions

• A “best practices” QMS system requires a single, scalable system, which uses a holistic approach

• Implementing a global QMS system may require your organization to change how it defines CAPA as well as it how it conducts the CAPA process

• Implementing a system can be successfully accomplished by using established software, a harmonized approach, and an organized project structure
Benefits for Your Company through CAPA

- Consistent good quality
- Continuous improvement
- Low scrap cost
- Competitive edge
- Satisfied customers
CAPA is much more than just “corrective actions” and “preventive actions”.

Any opportunity to improve quality in your organization is a CAPA!
Any Questions???