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Corrective and Preventive Action – Background & Examples

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Overview

- Background on Corrective and Preventive Action (CAPA) Requirements
- Quality System (QS) CAPA (21 CFR 820.100)
- Link Between CAPA and Other QS Regulation Requirements
- Examples on CAPA
- Guidance and Other Resources

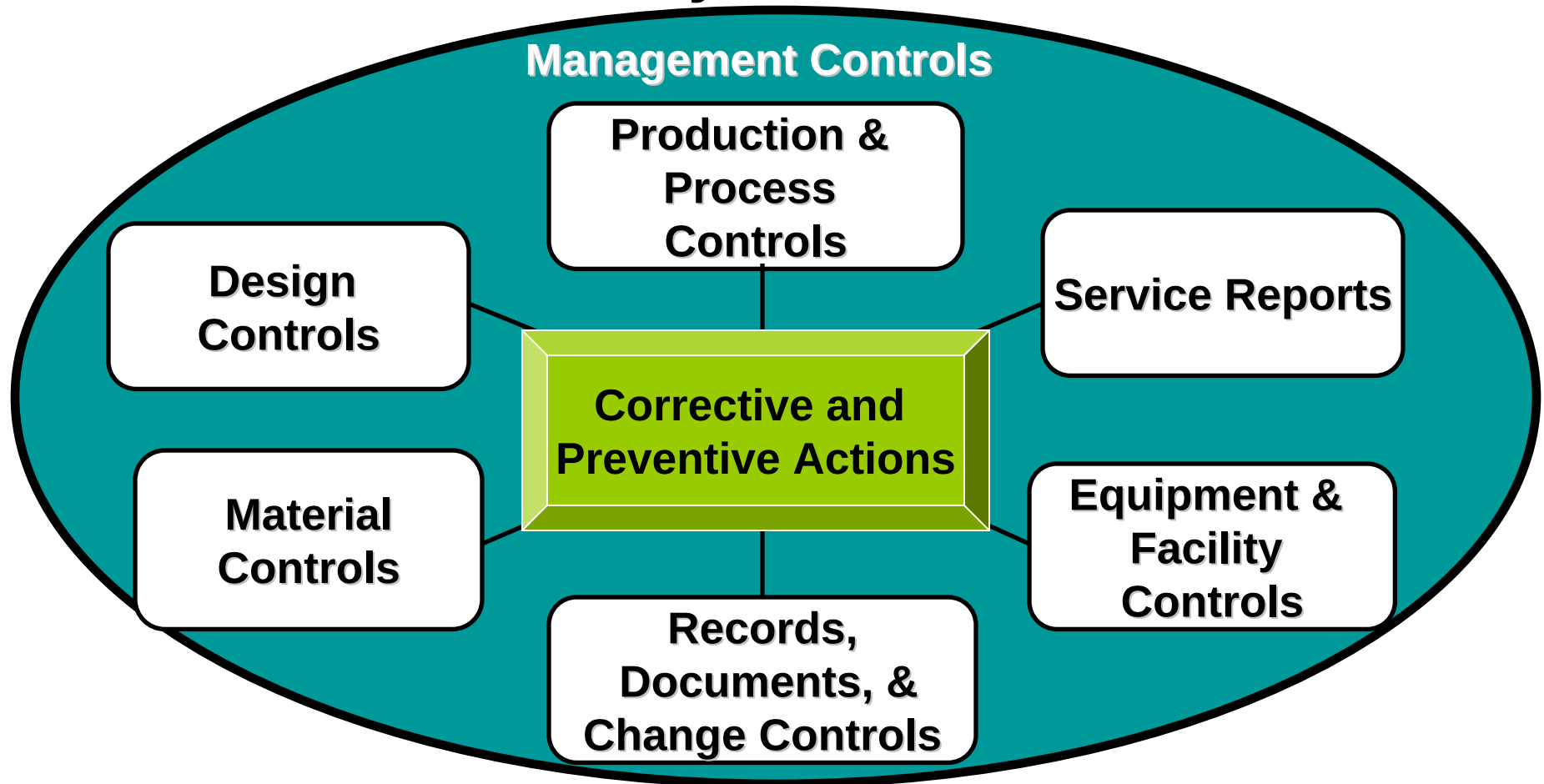


Purpose of the CAPA Subsystem

- Collect and Analyze Information based on appropriate Statistical Methodology as necessary to detect recurring quality problems
- Identify and Investigate Existing and Potential Product and Quality Problems
- Take Appropriate, Effective, and Comprehensive Corrective and/or Preventive Actions



CAPA Subsystem in Context





When Does FDA Review CAPA?

- Inspections
 - Quality System Inspection Technique (QSIT) – Corrective and Preventive Action (CAPA) Subsystem
 - Compliance Program (7382.845) – Inspection of Medical Device Manufacturers
- Premarket Approval Applications (PMAs)
 - Original PMAs
 - Some PMA supplements (Site changes, 30-Day Notices)
- CAPA is NOT Reviewed in 510(k) applications
- Recalls (corrections and removals)



Why is CAPA Important?

- Linked to many other requirements.
 - 820.198 Complaint Files
 - 820.90 Nonconforming Product
 - 820.80 Acceptance Activities
 - 820.200 Servicing
 - 820.22 Audits
 - 803 Medical Device Reporting (MDR)
 - 806 Reports of Corrections and Removals (“Recalls”)
 - ... And many more
- Ensures problems are detected AND resolved.





Definitions

- Correction: repair, rework, or adjustment and relates to the disposition of an **existing** nonconformity.
- Corrective Action: the action taken to eliminate the causes of an **existing** nonconformity, defect or other undesirable situation in order to prevent recurrence.
- Preventive Action: action taken to eliminate the cause of a **potential** nonconformity, defect, or other undesirable situation in order to prevent occurrence.
- Nonconformity: non-fulfillment of a specified requirement.



Correction, Corrective Action, or Preventive Action?

- Replacing the label on a device that had the wrong label applied?
- Revising process parameters in response to complaints?
- Rewelding a contact that does not meet visual inspection requirements?
- Auditing all vendors of a key component after quality issues with only one vendor are identified?
- Revising equipment maintenance procedures to reduce drift in process specifications?



CAPA Procedures – 21 CFR 820.100(a)

Each manufacturer shall **establish and maintain procedures for implementing corrective and preventive action.**

Procedures must ensure all requirements of CAPA subsystem are met

Establish: define, document (in writing or electronically), and implement.

Number and complexity of procedures vary based on the organization



The CAPA Process

INPUTS

Internal/
External
Sources

ELEMENTS

- Analyze Data, 820.100(a)(1)
- Investigate Cause, 820.100(a)(2)
- Identify Action, 820.100(a)(3)
- Verify/Validate Effectiveness, 820.100(a)(4)

OUTPUTS

Implement Changes,
820.100(a)(5)

Disseminating Information,
820.100(a)(6)

Submit for Management
Review, 820.100(a)(7)

Document, 820.100(b)



CAPA Procedures – 21 CFR 820.100(a)

- What is your firm's process for events that “trigger” a CAPA
 - Not every complaint is a CAPA
 - Not every nonconformance is a CAPA

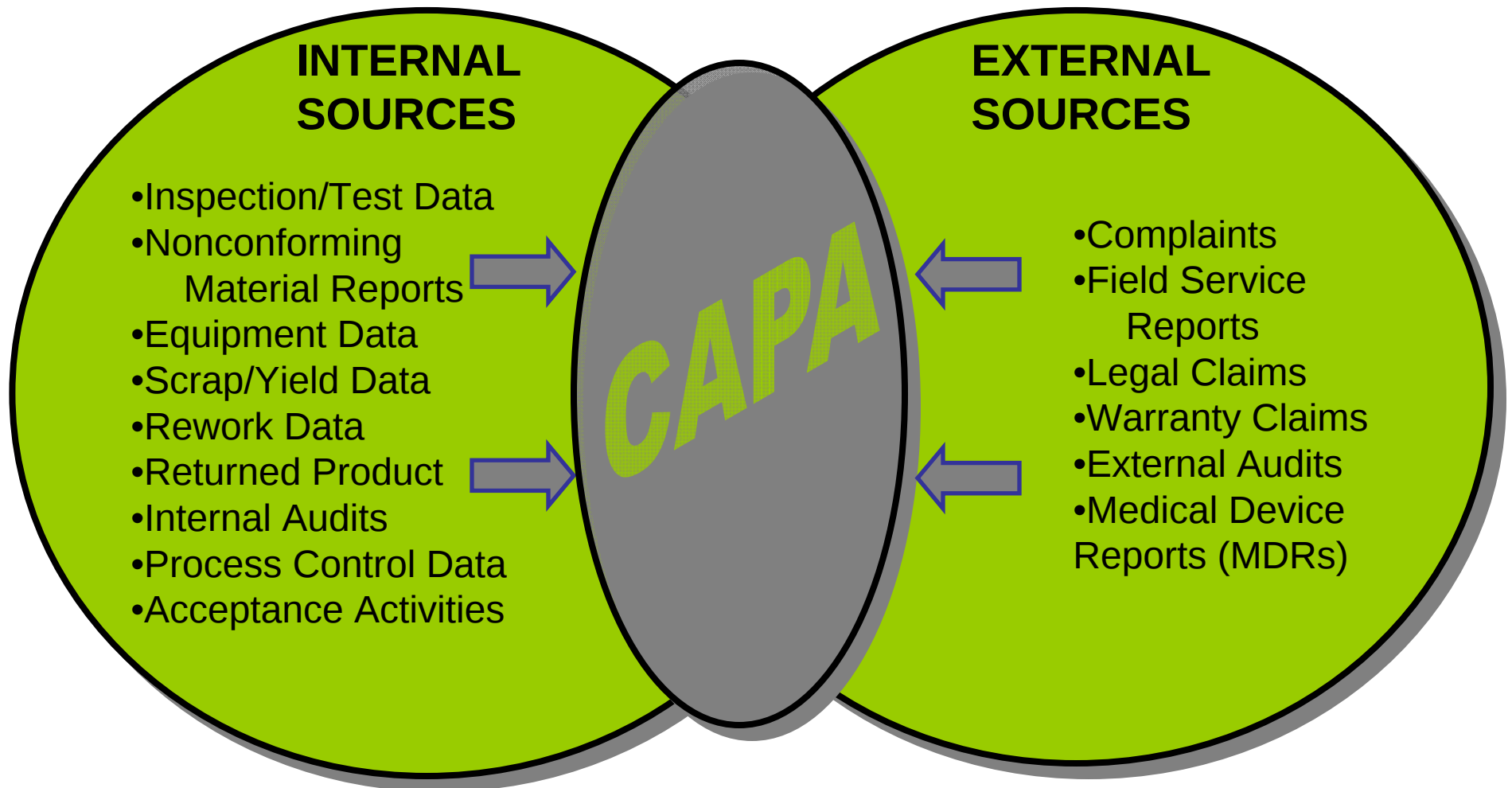


CAPA Data Analysis – 21 CFR 820.100(a)(1)

Analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other **sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems. Appropriate statistical methodology shall be employed** where necessary to detect recurring quality problems.



Data Sources





CAPA and Statistical Analysis

“FDA emphasizes that the appropriate statistical tools must be employed when it is necessary to utilize statistical methodology. FDA has seen far too often the misuse of statistics by manufacturers in an effort to minimize instead of address the problem. Such misuse of statistics would be a violation of this section.”



Common Statistical Techniques

- Pareto charts
- Run charts
- Control charts
- Mean and standard deviation
- T tests for comparisons
- Experimental design (DOE)
- Graphical methods (fishbone diagrams, histograms, scatter plots, spreadsheets, etc.)



Other Analysis Techniques

- Management reviews
- Quality review boards
- Material review boards
- Other internal reviews



CAPA Data Analysis – 21 CFR 820.100(a)(1)

- Ensure all quality data sources are defined and analyzed to identify existing product and quality problems
- How is the data is captured and maintained?



CAPA Data Analysis – 21 CFR 820.100(a)(1)

- How does your firm categorize and group data and perform the analysis?
 - Expect FDA to verify your firm is using appropriate analysis techniques
 - Analysis of data should also include a comparison of the same problem type across different data sources



CAPA Data Analysis – 21 CFR 820.100(a)(1)

- Is the data received by the CAPA system is complete, accurate, and timely?
- Trend analysis is one type of data analysis



CAPA Investigation – 21 CFR 820.100(a)(2)

Investigating the cause of nonconformities relating to product, process, and the quality system.

21 CFR 820.198, Complaint Handling, also requires investigations for the device involved, but the CAPA requirement is broader to cover the process and the quality system.





Typical Investigation Steps

- Identify problem and characterize.
- Determine scope and impact.
- Investigate data, process, operations and other sources of information.
- Determine root cause, if possible.



Possible Root Causes

- Training
- Design
- Manufacturing
- Management
- Change Control
- Purchasing/Supplier Quality
- Testing
- Documentation
- Maintenance

Many manufacturers tend to overuse training as a corrective action and do not adequately address the systemic corrective action.



Root cause analysis tools

- Commonly used tools
 - Fishbone diagrams
 - 5 “whys”
 - Fault-tree analysis
 - Among others



CAPA Investigation – 21 CFR 820.100(a)(2)

- Is the depth of the investigation sufficient?
- Expect FDA to evaluate the adequacy of your firm's rationale for determining if a corrective or preventive action is necessary
 - Decision process may be linked to risk analysis



CAPA Investigation – 21 CFR 820.100(a)(2)

- What controls does your firm have over devices suspected of having potential nonconformities?
 - Justification for concessions should be well documented and appropriate to the product risk



Identify Required Actions – 21 CFR 820.100(a)(3)

Identify the action(s) needed to correct and prevent recurrence of non-conforming product and other quality problems.

*Beware of terminology!
A Preventive Action is **NOT** required for all situations; however, a Corrective Action to prevent recurrence is required.*





“Other Quality Problems”?

“... The objective of § 820.100 is to correct and prevent poor practices, not simply bad product. ... Correction and prevention of unacceptable quality system practices should result in fewer nonconformities related to product. ... For example, it [CAPA] should identify and correct improper personnel training, the failure to follow procedures, and inadequate procedures, among other things.”

61 Fed. Reg. at 52633-52634, Comment 162



Taking Action

- Identify solutions.
- Develop action plan for corrective action and/or preventive action.
- Should consider the risk posed by the problem.
 - Not all problems require the same level of investigation and action.
 - It is appropriate to “elevate” some issues at the expense of others



CAPA and Risk Management

“FDA agrees that the degree of corrective and preventive action taken to eliminate or minimize actual or potential nonconformities must be appropriate to the magnitude of the problem and commensurate with the risks encountered...FDA does expect the manufacturer to develop procedures for assessing the risk, the actions that need to be taken for different levels of risk, and how to correct or prevent the problem from recurring, depending on that risk assessment.”

61 Fed. Reg. at 52633-52634, Comment 159



CAPA and Risk Management

- Risk analysis allows a manufacturer to:
 - Determine priorities
 - Assign resources
 - Determine the severity of impact
 - Determine the depth of investigation
- Common tools
 - Hazard analysis
 - Used early for potential problems
 - Failure Mode Effects Analysis (FMEA)
 - Bottom up
 - Fault Tree Analysis (FTA)
 - Top down



Identify Required Actions – 21 CFR 820.100(a)(3)

- Expect FDA to review the actions taken
- Be prepared to discuss the appropriateness of the action taken
 - Why was corrective action taken?
 - Does the corrective action extend to include any additional actions (component suppliers, training, acceptance activities, field actions) if necessary?



Verify and Validate – 21 CFR 820.100(a)(4)

Verifying or validating the corrective and preventive action to **ensure that such action is effective and does not adversely affect the finished device.**

Effectiveness:

Did my solution work?

*Did it create other
potential nonconformances?*





Verify and Validate – 21 CFR 820.100(a)(4)

- Verify that verification/validation protocols were established
- Review data associated with verification or validation activities
- Review the effectiveness of the corrective and preventive actions by reviewing data to determine if similar quality problems exist after implementation



Implement and Record Changes – 21 CFR 820.100(a)(5)

Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems.



Implementing Changes

- Tie CAPA implementation to:
 - Document control for products and processes (DMR – 820.181)
 - Change control (820.40)
- Ensure that controlled documents are reviewed and approved if changes are made.



Implementing Changes

- Expect FDA to verify implementation of changes by viewing actual processes and equipment
- Implemented changes may directly link to design or production and process controls



Disseminate Information – 21 CFR 820.100(a)(6)

Ensuring that information related to quality problems or nonconforming product is disseminated to **those directly responsible for assuring the quality of such product or the prevention of such problems**



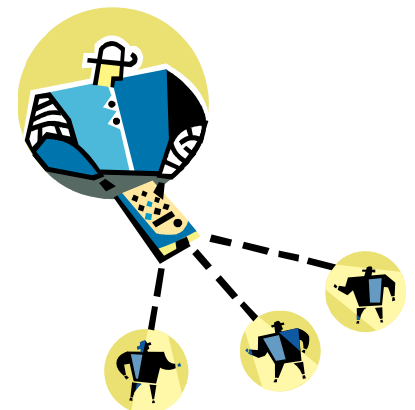


Management Review – 21 CFR 820.100(a)(7)

Submitting relevant information on identified quality problems, as well as corrective and preventive actions, **for management review**

The significance of the problem impacts the level of management review.

Need management awareness and buy-in so that resources are allocated, etc.





Documentation – 21 CFR 820.100(b)

All activities required under this section, and their results, shall be documented.



CAPA Subsystem – Other Requirements

- 21 CFR 820.90, Nonconforming Product
- 21 CFR 820.198, Complaint Files



What is Nonconforming Product?

- Nonconformity = the nonfulfillment of a specified requirement. [21CFR820.3(q)]

+

- Product = components, manufacturing materials, in-process devices, finished devices, and returned devices. [21CFR820.3(r)]



Examples of Nonconforming Product

- Received components/material that fail incoming inspection.
- Products/components that fail inspection or test steps during manufacturing.
- Product returned to the manufacturer due to defects.





Links Between Nonconforming Product and CAPA

- Identification and monitoring of nonconforming product often “triggers” CAPA activities.
- Nonconforming product investigations can also be leveraged during CAPA investigations.
- Not every nonconformance is a CAPA.



What is a “complaint”?

Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

21 CFR 820.3(b)



Link Between Complaints and CAPA

- Complaints are a required data source to CAPA and may “trigger” CAPA activity.
 - Remember, not every complaint is a CAPA
- Complaint investigations can be leveraged during CAPA investigations.
- Recurrent complaints that involve a health risk may be evaluated by CAPA process and determined to be recalls.



Key Word #1: Nonconformance

- CAPA, nonconforming product, and complaints are all related to identified or potential nonconformances.
- Nonconformances are:
 - A data source for the CAPA system
 - The basis of the nonconforming product requirements
 - A potential cause of complaints



Key Word #2: Investigation

- Investigation is used in CAPA, nonconforming product, and complaints sections of the QS Regulation
- Investigations are:
 - Required for CAPA
 - Done, or justified not done, for complaints
 - May/may not be done for nonconformances, no justification required.



Closing Remarks

- CAPA is a “pulse check” for FDA on how well a firm’s Quality System is operating
 - Strong CAPA systems are usually indicative of strong Quality Systems
- Feedback Loop between CAPA, Complaints, and Nonconforming Product is essential
- CAPA Subsystem is all about identifying and resolving problems that can or have result[ed] in nonconforming product



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Examples Related to CAPA



Example #1 Warning Letter Citation

- Your firm failed to establish, maintain, and implement a corrective and preventive action procedure, as required by 820.100(a). For example,
 - Your firm has no CAPA procedures as defined in the QS regulation including: failure investigation, procedures to analyze quality data...procedures to verify/validate corrections, procedures that ensure that information related to quality problems is disseminated and for submitting relevant information on identified quality problems to management for review.



Example #2 Warning Letter Citation

- The procedures addressing verification or validation of corrective and preventive actions were not implemented as required by 21 CFR 820.100(a)(4). Specifically,
 - CAPA Procedure 100-0025, Rev 4, requires documentation of verification and validation, but this was not completed for CAPA #0225.



Example #3 Warning Letter Citation

- Failure to implement procedures addressing documentation of corrective and preventive action activities as required by 21 CFR 820.100(b). Specifically:
 - The Corrective and Preventive Action procedure (GP.1401, Ver. 6.0) establishes requirements to (i.) " *** Design and implement corrective or preventive action, including verification or validation that such action does not adversely affect the finished device or system" and (ii.) "Demonstrate and document the effectiveness of corrective and/or preventive action(s)." The procedure also states, (iii.) "The corrective action and preventive action changes shall follow design, process, or Quality System change process requirements." However, the validation of patient management recommendations (implemented in CAPA 644 as part of the lead fracture corrective action and October 15, 2007, recall) was not reviewed and documented appropriately.



Injunction Example #1

SOP 040061 Revs. C, D, and E, *Corrective and Preventive Action Procedure*, §4.4 states one of the requirements of a CAPA is “Verifying or validating that the corrective action and/or preventive action is effective and does not adversely affect the finished device.” Form 040061D, *CAPA Form*, dated 3/13/06 describes a CAPA initiated because of a complaint associated with an aortic valve that had a mislabeled size. The firm’s CAPA included a revision of SOP 040002, *Label Control*, to include an additional inspection. The verification/validation activities were stated as “The additional inspection procedure has no bearing on the product quality and will only help to prevent a future occurrence.” As a part of this CAPA, the firm did not ensure that the procedure had been correctly implemented and that employees were retrained on this revised procedure.



References

- 21 CFR Part 820
 - <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=820>
- Preamble to the QS Regulation Final Rule
 - <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/MedicalDeviceQualitySystemsManual/UCM122806.pdf>
- Compliance Program (7382.845) – *Inspection of Medical Device Manufacturers*
 - <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072753.htm>



References, cont.

- Quality System Inspection Technique (QSIT)
 - <http://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074883.htm>
- “Quality System Information for Certain Premarket Application Reviews: Guidance for Industry and FDA Staff” 2003
 - <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070897.htm>
- Global Harmonization Task Force (GHTF) Guidance Document on Corrective and Preventive Action
 - <http://www.gh tf.org/sg3/sg3-proposed.html>



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