Principles of Lean Six Sigma and CAPA

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Agenda : Part 1 – Lean Six Sigma

- Overview
- Lean and 6 Sigma integration
- Work shop + Quiz
- Take away:
- Closing
Agenda: Part 2 - CAPA

- Objectives of course
  - Med Dev + Pharmaceuticals
- Operations Overview
- Statistics regarding CAPA issues: FDA 483, Warning Letters + Consent Decree.
- What is an effective CAPA program important for your business
- CAPA regulation in detail
- CAPA inputs
- Effective approach
  - Problem Solving
  - Technical Writing
  - Tracking and F/U
  - Ownership – your way of making business.
Objectives of course

- Awareness on how critical is for your operations the compliance to regulations.
- To provide a solid understanding of the CAPA requirements as set by the FDA and how these can be integrated into the normal business activities with effective results.
- Direct recommendations will be provided to improve your current practices, including the link to 2 mayor initiatives, Lean Manufacturing and 6 Sigma.
CAPA (Correction and Preventive Action)

Controles de Gerencia

Design Control  Process Control

Material Control  Facilities Control

Corrective And Preventive Action  Documentation & Change Control
Operations Overview

Purpose of any business is…

Making Money through meeting some customer needs.

1. This requires:
   - resources capable of producing the required goods,
   - at the right rate and
   - cost to make it profitable.

2. Continuous improvement is the call of the day on almost any organization.
   - Because is intended to make more with less resources, but maintaining the competitive edge.
Operations Overview

- To achieve this; firms are moving into programs to improve their business in different areas.
  - Cell Manufacturing
  - Theory of Constraints
  - Lean Manufacturing
  - 6 Sigma
  - Integrated Learning systems.
  - SAP or other similar MRP programs.

- Also are driving to automate as much as possible.

- This requires highly talented human resources, with their minds focused on continuous improvement and capable of managing multiple activities with a high level of effectiveness.
Operations Overview

- While doing all this, each firm needs to comply with regulatory agencies like:
  - OSHA
  - FDA
  - ISO
  - And some other guidelines too, depending on the type of business or supporting services required.

- Some of these regulations put a heavy burden over the companies. Burden that traduces into cost but needed to continue on business.

- Reality; when not fully integrated the Regulatory aspect of the business and the Operations needs, both of them might collide.
Operations Overview

- In order to reduce collisions and take advantage of all the requirements, management must understand what each element is capable to provide and how can get in conflict with other requirements.

- The concept to integrate these apparent conflicting requirements is what I call, “Operations Systems”.
Operations Overview

- Operations Systems = Operations requirements integrated with/to the Quality System.

- As of today, is being introduced just as an integration concept, because the focus of this course is to talk about CAPA and how we can use it in benefit of the firm.

- Benefits not only in terms of compliance but also in terms of process improvement.
CAPA Management Controls

- Design Control
- Production & Process Control
- Material Controls
- Preventive and Corrective Action
- Records, Documents & Change Control
- Equipment & Facilities Control
QSIT audit findings

- Firms with Observations
- QSIT Objectives (Population of 42 firms)

Legend:
- Procedures
- ID existing problems
- Data Challenge
- Analysis techniques
- Failure Investigation
- Actions taken
- Actions effective
- Actions implemented
- Info disseminated
CAPA in details...

CHAPTER I - FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
PART 820--QUALITY SYSTEM REGULATION

Subpart J--Corrective and Preventive Action
Sec. 820.100 Corrective and preventive action.
(a) Each manufacturer shall establish and maintain procedures for implementing corrective and preventive action. The procedures shall include requirements for:

(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;

(2) Investigating the cause of nonconformities relating to product, processes, and the quality system;

(3) Identifying the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems;
CAPA in details…

(a) Each manufacturer shall establish and maintain procedures for implementing corrective and preventive action. The procedures shall include requirements for:

   (4) Verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device;
   (5) Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems;
   (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; and
   (7) Submitting relevant information on identified quality problems, as well as corrective and preventive actions, for management review.

(b) All activities required under this section, and their results, shall be documented.
CAPA in Details…

**Subpart J Corrective and Preventive Action: Recall what we said before.**

- We need to identify existing and potential causes of non-conformances and correct and prevent. Statistics should be used. Reoccurrence should be prevented. The corrective action should be verified that it was effective.

- The FDA really wants you to do three things. If you did these three things you would fulfill most FDA regulations and be in good standing with them:
  1. **Find your problems**
  2. **Fix you problems**
  3. **Prevent your problems**

- Why?
CAPA in detail…

- Critical Definitions:
- Correct ("correction") nonconforming products and other quality problems.
- Prevent re-occurrence ("corrective action") of nonconforming products and other quality problems.
- Eliminate the potential causes of potential nonconforming product ("preventive action") and other quality problems.
Inputs to the CAPA system – traditional translation.

- Repetitive or critical Nonconformities
- Process Issues
- Audits or Complaints
- Incomplete or deficient procedures
- Equipment Issues

Corrective And Preventive Action
CAPA in details…

Inputs to the CAPA program:

- Internal Audits**
- Customer Complaints
- Lean Audits
- 5 S audits
- Safety Group audits (ergonomic issues)
- Process improvement projects
- Negative variances
- Non conformance reports
- Waste/Rejection rates
- Rework rates
- Employee complaints or observations
- FMEA
- Third party audits

Any weird observations from this list?
CAPA in details...

- What is an effective approach:
  1. Your procedure must address each single detail of the regulation and must be controlled.
  2. Your procedure must provide clear direction on how the system is managed, tracked and reviewed by upper management.
  3. Your personnel must be:
     - trained to the procedure.
     - trained on how to perform investigations.
     - trained in the correct way to document the investigation.
  4. Your reviewing personnel must understand how to review a document.
  5. All personnel must understand the implications of their signatures in a record.
  6. All personnel must feel ownership of the system.
1. Your procedure must contain clear definitions, responsibilities, instructions to manage the system, to fill forms, to follow up, to review and to perform investigations.

2. Must indicate clear expectations regarding review periods, information escalation/reporting.

3. Prevent adding too restrictive timeframes, or mentioning disciplinary actions as enforcement methods for compliance.
CAPA in details…

1. Managing the system:
   1. Designate a resource to manage the CAPA program.
   2. Control access to the CAPA progress reports.
   3. Perform regular meetings for F/U on open items, evaluate new proposed items, share knowledge.
   4. Have a CAPA index, Manual log, Electronic Log, Canned solution software “watch out”.
   5. Rise status to upper management.
   6. Deal with slow progress issues, don’t let them age.
   7. Do not assign a CAPA investigation to a non-trained resource.
   8. Review for closing, considering if there are loose ends.
   9. Audit closed CAPA to verify effectiveness. Set a schedule.
CAPA in Details…

1. Training in the CAPA procedure must include:
   1. Reading of the procedure
   2. Test to verify understanding
   3. Workshop on how to fill forms and perform investigations
   4. Review pre-requisites for participants of the CAPA programs
CAPA in details...

Investigations and documentation:
  - Problem solving Techniques?
  - 6 Sigma?
  - Lean Manufacturing?
  - Technical Writing?
  - Review and Approval?
CAPA in details…

Problem Solving Steps
6 Sigma Approach
Lean Approach
CAPA in details…

- Upon completion of the CAPA information, the last topic which is a very critical one is related to review of documents.
- This apply to CAPA investigations and in fact to must of the documents created as part of the quality system requirements.
Review and Approval of documents

- This single act of review and approval is the most important action in the entire validation process.
- Yet in most firms’ this action is rushed, given no thought and is the most error prone of all actions within the validation life cycle.
- The purpose of this presentation today is to change this paradigm.
- Focus is on validation documentation but this presentation applies everywhere.
COMPLIANCE

What does review and approval have to do with compliance?

1. 21 CFR 820.75 requires the review of validation
2. 820.30 requires the approval of design control segments no less than 5 times.
3. 820.40 requires review and approval of documents, 2 times mentioned.
4. 820.50 Purchasing controls mentions it once
5. 820.70 Production processes mentions review and approval once
6. 820.80 mentions it once
7. 820.90 mentions it once
8. 820.100 mentions it once
9. 820.186 mentions it once
10. 820.198 mentions it once
COMPLIANCE

- A total of 15 times it is mentioned in the CGMP’s! And it is inferred a host of others. Does it appear to be important to the FDA?

- Remember FDA spend the majority of their time reviewing documents.

- Do you think maybe we should give reviews some importance too?
The signing of the document is an act of regulatory compliance. Moreover the review is an act of regulatory compliance.

You can not separate the two. You can not sign if you did not review.

The act of signing implies:

1. You read what you signed
2. You understand what you read
3. You have the experience or training
4. You are authorized to sign
If signing merely meant that we just wanted someone to sign. We could drive our documents to the local elementary school and have a bunch of students in the first grade sign! This would be cost effective as we can only pay them 25 cents.

The firm and the FDA expects much more than a signature.

It is like signing a contract. Would you sign a contract for employment if you knew nothing and employer said just to sign? What is my salary, how many holidays do I get, what are the terms of my employment. You would read then.

Neither would we expect you to sign something that you did not read nor read and did not understand.
VALUE ADDED

- Signing should be value added. Meaning the firm should get something for the time it took you to read it. What is value added:

1. In the case of a protocol you find out about the problems with the validation before it is run. Thereby saving materials, time, the loss of time having to repeat and being quicker to market a new item.

2. In the case of a validation result-final report, prevention of FDA problems, prevention of recalls, less waste/scrap.
NON VALUE ADDED

If you just sign the document without reading what is non-value:

1. **You allow the FDA to become your reviewer.** Chance are since they have all the time they need you can be sure they will find your problems for you.

2. **The consequences of the FDA being your reviewer are 483’s, warning letters, possible recalls and more.**

3. If data indicated that the validation should have been rejected and was approved due to a review error a recall may be initiated. A health hazard analysis may need to be performed to assess if the failed validation represents a health risk and if so, recalls would be required.
NON-VALUE ADDED

- If one just signs then there is one more name on the signature list that is unnecessary thus taking more time for the documents to be reviewed.
- Other regulatory action could occur because if one signed without reviewing this is a violation of CGMP.
- From a business perspective we do not find out about the problems before the process is approved so we have to live with scrap and rework. Additionally we may have to repeat the validation.
INGREDIENTS OF A PROPER REVIEW—VALIDATION

- The rationale is clear
- The documentation in the protocol is in the same order as the final report
- There is no ambiguities
- The testing strategy is clear
- No miscellaneous documents are present including Post-its®
- The writing is legible
- The document speaks for itself and needs no help translating.
- Justifications are given
- There is no testing into compliance
INGREDIENTS OF A PROPER REVIEW-VALIDATION

- That the results meet the acceptance criteria
- That the data supported the result and all data was reviewed thoroughly.
- That the sampling plan made sense and was based on a statistically valid plan.
- That proper documentation techniques were used, no pencil etc.
- People were trained
- The protocol and result would make sense to someone that did not know the subject.
- That the protocol was followed
- That all required data was given
INGREDIENTS OF A PROPER REVIEW-VALIDATION

- That the interface systems were clearly outlined and validated-cleaning, HVAC etc.
- That the protocol met our SOP requirements.
- All aspects of FDA regulations have been met.
- That technically the validation makes sense.
- That the validation proves that the process is operating to the maximum capacity with little to no break downs (OEE)
- That the process is capable (CpK, PpK)
- This is not all
OUTSIDE CONTRACTORS

- At times validation are performed by outside contractors on site (never should be off site).
- The firm is still responsible from an FDA perspective for their work done.
- Some staff person that is qualified should be present during the execution.
- The validation still should be sign off as reviewed and approved by the firm’s staff.
- FDA will hold you responsible for the outcome of the validation.
PLANNING

- The start of review and approval is to determine who should perform this function for what documents.

- I would also on occasion test to ensure that people do review the documents. Test by sticking in the center of the document a phrase such as call your extension if they read the phrase. Those who did not are removed from the review process as they add no value.

- Time for validation review should be part of the validation process. Each person should have a day to review and since your document is not the only piece maybe two or three days.
POOR REVIEWS

- Poor reviews are easy to detect
- Multiple signatures the same day
- Obvious mistakes are not caught
- You call for 6 days and finally the 6\textsuperscript{th} day it is delivered to you an hour after you call.
- FDA finds numerous issues when they visit.
- The process validated has numerous problems running despite being validated.
NEVER

- Never-Review a document that you are not qualified to do.
- Never sign your own work e.g.: you were asked to calibrate an instrument and you signed it as performed and reviewed. Why? Because you were so close to it you will miss important information.
- Never sign work that you did not perform e.g.: you had to sign a check made on a temperature but it was lunch time and you did not want to be late so you signed the check even though you did not perform it. Not only is this a CGMP violation it is forgery; serious penalties personally result.
NEVER

- Never rush a review for any reason.
- Never sign a empty folder without the document
- Never assume that QA will catch everything that you do not catch. QA has its role and so do you. If that was true then we would only need QA to review and approve.
CHECKLIST

- Checklists’ are helpful. They are used in many firm’s Device History Records to ensure nothing is missed.

- Checklists’ in validation can not only show what is missing but remind one of what is important to review.
SUGGESTED REVIEW RESPONSIBILITIES:

Suggested General Reviewing Responsibilities:

- **All parties:** The testing is clear and not ambiguous to the person performing the validation. The expected outcome is well defined.
SUGGESTED REVIEW RESPONSIBILITIES:

Suggested General Reviewing Responsibilities:

- **Engineering/R&D/Manufacturing:** That all interface systems, utilities and equipment are indicated either in flow charts or in the body of the protocol. The protocol meets our VMP and SOP requirements. All key process input variables have been determined (if applicable). That the design of the test is scientifically sound.
SUGGESTED REVIEW RESPONSIBILITIES:

- **QA/RA**: The review should ensure that all regulations and guidance requirements have been met. Does the protocol make sense to an outside auditor. The test: “The document must speak for itself”

- **Statistician/ Black Belt/ Green Belt**: The protocol is based on statistically valid methods and sampling.
WHAT CAN I DO TO HELP?

- If you find something wrong in someone else’s area tell them and QA.
- Make sure your area is clean, free from contamination and orderly.
- Make the CGMP’s a way of life not just some words to know.
- Ensure your equipment is working properly, preventive maintenance is performed to the schedule.
- All equipment you are using is calibrated and is not expired.
WHAT CAN I DO TO HELP?

- Read SOP’s carefully.
- Document results carefully.
- Make sure you follow-up on everything that you said you would do. If a protocol says that you run 10 minutes at 350 degrees F then you run at 350 F for 10 minutes not 9 minutes and document the temperature and time.
- Look at the gauges. They are there for a reason. If they tell you that your are not running to specification you can not run until that is fixed.
- If you are asked to review something review it like your own money was involved because it is. The more money we waste on non-compliance the more we lose as a company.
WHAT CAN I DO TO HELP?

- BE CAREFUL: ACT AS THOUGH YOU ARE MANUFACTURING THE MEDICAL DEVICE OR DRUG FOR YOU OR YOUR CHILDREN OR PARENTS.

- LETS MAKE A GOAL TO BE THE HIGHEST COMPLIANT SITE.

- IF WE ARE, WE ALSO WILL END UP THE SITE WITH THE HIGHEST QUALITY AND EFFICIENCY.
References

Free online resources:

- The Lean Enterprise –
  http://www.freeleansite.com/
Preguntas