International Journal of PharmTech Research
CODEN (USA): IJPRIF, ISSN: 0974-4304
Vol.9, No.3, pp 406-414, 2016

Corrective and Preventive Action: A Key to Pharmaceutical Industry

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Abstract: CAPA is an essential management tool that should be used in every quality system. This program provides a simple step by step procedure for carrying out and verifying corrective or preventive actions. The main objective behind corrective action and preventive action (CAPA) in any pharmaceutical or medical device industry is to decide the weakness, deviation or failures and to complete its investigation with proper actions so that such difficulties are not repeated again. CAPA is also a process in which preventive procedures are taken in the commencement itself so that manifestation of any incidence can be prevented**.** It is a part of overall Quality Management System (QMS) and also a regulatory requirement in a pharmaceutical company. The result will be a complete, well documented investigation and solution that will satisfy regulatory requirements and form the basis for an effective continuous improvement plan for any company. The risk-based CAPA requirements demand a well-documented system that determines the root cause of nonconformance's, system failures, or process problems, corrects the problems, and prevents them from recurring.
Keywords: Corrective action, Preventive action, Root cause analysis, Quality management system (QMS), Corrective and Preventive action (CAPA).

Introduction[1]:

CAPA is an essential management tool that should be used in every quality system. This program provides a simple step by step procedure for carrying out and verifying corrective or preventive actions. The result will be a complete, well documented examination and solution that will fulfill regulatory requirements and form the base for an effective constant improvement plan for any company. Properly documented activities provide significant historic data for a constant quality improvement plan and are vital for any product that must meet regulatory requirements required by FDA and ISO and other quality systems. This is the reason for the implementation of a correct Corrective Action / Preventive Action (CAPA) program. CAPA is a major area of concern for both FDA, ISO 9000.

CAPA relationship with Quality Subsystems[1]:

The CAPA system is a critical component of an effective QMS and it must maintain a close relationship with other quality subsystems. The ultimate goal of any regulated company must be to have a CAPA system that is compliant, effective and efficient. All relevant subsystems that may produce non-conformances must be part of the process. Internal processes encompass both non-conformance and in-conformance results, internal audits and assessments, management reviews and so on. External sources of CAPA process inputs are supplier audits and assessments, customer feedback and results from external audits and assessment such as regulatory agencies, ISO and so on.

Corrective Action[2]:

A corrective action is a term that encompasses the process of reacting to product problems, customer complaints or other nonconformities and fixing them. The process includes:

1. Reviewing and defining the problem or nonconformity
2. Finding the cause of the problem
3. Developing an action plan to correct the problem and prevent a recurrence
4. Implementing the plan
5. Evaluating the effectiveness of the correction.

Preventive Action[2]:

A preventive action is a process for detecting potential problems or nonconformance's and eliminating them. The process includes:

1. Identify the potential problem or nonconformance
2. Find the cause of the potential problem
3. Develop a plan to prevent the occurrence.
4. Implement the plan
5. Review the actions taken and the effectiveness in preventing the problem.

Difference between Corrective and Preventive Action[2]:

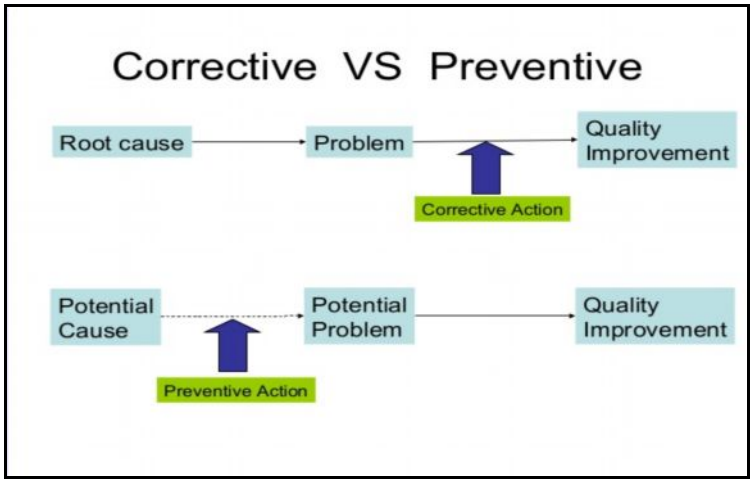
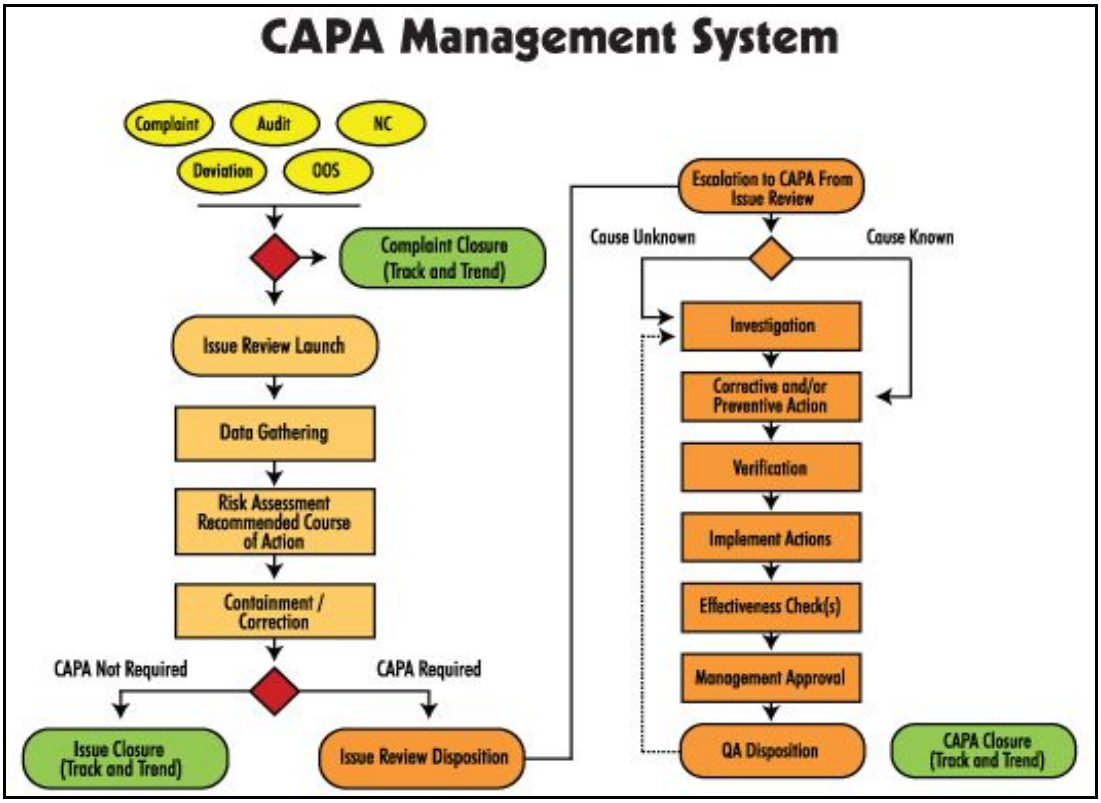


Figure 1: Difference between corrective and preventive action

Capa Procedures[2,3]:

Implementing an effective corrective or preventive action capable of satisfying quality assurance and regulatory documentation requirements is accomplished in seven basic steps:

1. The **Identification** of the problem, nonconformity, or incident or the potential problem, non- conformity, or incident.
2. An **Evaluation** of the magnitude of the problem and potential impact on the company.
3. The development of an **Investigation** procedure with assignments of responsibility.
4. Performing a thorough **Analysis** of the problem with appropriate documentation
5. Creating an **Action Plan** listing all the tasks that must be completed to correct and prevent the problem.
6. The **Implementation** of the plan.
7. A thorough **Follow up** with verification of the completion of all tasks, and an assessment of the appropriateness and effectiveness of the actions taken



1. **Identification:**

The initial step in the process is to clearly define the problem. It is important to accurately and completely describe the situation as it exists now. This should include the source of the information, a detailed explanation of the problem, the available evidence that a problem exists.

1.1Report Source:

The specific origin of the information that initiated this action is recorded. Documenting the source of the information can be very useful when conducting an investigation into the problem and implementing the action plan that is created. It will also provide data for evaluating the effectiveness of the quality system and facilitate communicating the completion of the action to the appropriate individuals or departments. This information may come from many possible sources. For example, situations that require corrective actions may come from external sources such as customer concerns or service requests. Internal quality audits, staff observations, quality assurance inspections, trending data, and management review are all examples of possible internal sources of information.

Examples of Internal Data Sources:

- Process Control Data
- Test/Inspection data
- Device History Records
- Internal Audits
- Nonconforming material reports
- Rework and Scrap/Yield Data
- Training records

Examples of External Data Sources:

- Supplier Controls
- Customers
- Complaints
- Servicing repairs

- Adverse Event Reporting

1.2 Explanation of the Problem:

A complete description of the problem is written. The description should be concise but must contain sufficient information to assure that the problem can be easily understood from reading the explanation.

1.3 Evidence:

List the specific information available that demonstrates that the problem does exist. For example, the evidence for a product defect may be a high percentage of service requests or product returns. The evidence for a potential equipment problem may be steadily increasing downtime.

1.4 Corrective/Preventive Action Request form:

A sample form is provided "Corrective/Preventive Action Request that can be used to initiate a CAPA action and collect the initial information.

2. Evaluation:

The situation that has been described and documented in the "Identification" section should now be evaluated to determine first, the need for action and then the level of action required. The potential impact of the problem and the actual risks to the company and/or customers must be determined. Essentially, the reasons that this problem is a concern must be documented.

2.1 Potential Impact:

Part of the evaluation is a specific explanation of specifically why the problem is a concern. This may include the possible impact that the problem may have in terms of costs, function, product quality, safety, reliability, and customer satisfaction.

2.2 Assessment of Risk:

Using the result of the impact evaluation, the seriousness of the problem is assessed. The level of risk that is associated with the problem may affect the actions that are taken.

2.3 Remedial Action:

The actions that are taken are documented. This documentation will become part of the 'Action Implementation' and 'Follow Up' sections of the CAPA action. In some instances it may be determined that the remedial action is all that is needed. In that case, a rationale is written for that decision, appropriate follow up is done and the CAPA closed out.

2.4 Remedial Action form:

A sample "Remedial Action" form is included. This form should be used to explain the steps that must be taken to avoid any further adverse effects.

3. Investigation:

In this step of the process a procedure is written for conducting an investigation into the problem.

A written plan helps assure that the investigation is complete and nothing is missed. The procedure should include: an objective for the actions that will be taken, the procedure to be followed, the personnel that will be responsible, and any other anticipated resources needed.

3.1 Objective:

The first step in the investigation is to state an objective for the action. In the "Identification" section the problem was defined and the current situation stated. The objective is a statement of the desired outcome of the corrective or preventive action. State what the situation will be when the action is complete. This may be a

statement in the form of: "the problem will be corrected, all effects of the problem identified, rectified, and controls will be in place to prevent the situation from happening again.'

3.2 Investigation Procedure:

A set of specific instructions are created that outline what must be done to determine the contributing and root cause of the problem. The investigation procedure will vary depending on the circumstances, but must incorporate a comprehensive review and analysis of all of the circumstances related to the problem.

3.3 Responsibilities:

An important part of the investigation procedure is to assign responsibility for conducting each aspect of the investigation. Any additional resources that may be required is also identified and documented. For example, specific testing equipment or external analysis may be required.

3.4 Investigation Procedure form:

A sample "Investigation Procedure" form is included. This is a written plan of action for the investigation into the problem. It should include the overall objective and the instructions for conducting the investigation. The persons responsible for the investigation and an expected completion date should also be entered.

4. Analysis:

The investigation procedure that was created is now used to investigate the cause of the problem.

The goal of this analysis is primarily to determine the root cause of the problem described, but any contributing causes are also identified. This process involves collecting relevant data, investigating all possible causes, and using the information available to determine the cause of the problem. It is very important to distinguish between the observed symptoms of a problem and the fundamental (root) cause of the problem.

4.1 Possible Causes / Data Collection:

A list of all possible causes is created. This will form the basis for collecting relevant information, test data, etc. There are many possible causes for this condition including: operator error, incorrect software, a dull or broken tool, an incorrect or obsolete print, a material problem, a design problem, etc. By considering all possible causes, appropriate information and data can be collected that will be ultimately be used to determine the root cause of the problem.

4.2 Results and Data:

The results of the data collection are documented and organized. This may include a combination of testing results and/or a review of records, processes, service information, design controls, operations, and any other data that may lead to a determination of the fundamental cause of the problem. The resulting documentation should be complete and address all of the possible causes that were previously determined. This information is used to determine the root cause of the problem.

4.3 Root Cause Analysis:

Determining the root cause often requires answering a series of 'why?' questions and digging deep into the situation until the fundamental reason for the problem is found. The root cause of the problem is documented. This will be essential for determining the appropriate corrective or preventive actions that must be taken.

4.4 Problem Analysis form:

A sample "Problem Analysis" form is included. This form is optional but is intended to be used for recording information related to the analysis of the problem. The form can be used as a collection point for the information discovered during the analysis and any supporting data or documentation can be attached.

5. Action Plan:

By using the results from the Analysis, the optimum method for correcting the situation and an action plan developed. The plan should include, as appropriate: the items to be completed, document changes, any process, procedure, or system changes required, employee training, and any monitors or controls necessary to prevent the problem or a recurrence of the problem. The action plan should also identify the person or persons responsible for completing each task.

5.1 Actions to be completed:

List all of the activities and tasks that must be accomplished to either correct the existing problem or eliminate a potential problem. For a CAPA program to be effective, it is very important to take a very global approach. Make sure to identify all actions that will be required to address everything related to the situation.

5.2 Document or Specification changes:

List any documents that will be modified and describe in general terms what the modifications will be.

5.3 Process, Procedure, or System changes:

If any changes to processes, procedures, or systems must be made they are described. Enough detail should be included so that it is clearly understood what must be done. The expected outcome of these changes should also be explained.

5.4 Employee Training:

Employee training is an essential part of any change that is made and should be part of the action plan. To assure that the actions taken will be effective, any modifications made to documents, processes, etc. must be effectively communicated to all persons or departments that will be affected.

5.5 Action Plan form:

A sample "Action Plan" form is included. This should provide a set of written procedures that detail all of the actions that must be done to resolve the problem and prevent it from recurring. This includes corrective and preventive activities, document changes, training, etc. The person or persons responsible and an expected completion date should also be entered on the form.

6. Action Implementation:

The corrective / preventive action plan that has been created is now implemented. All of the required tasks listed and described in the action plan are initiated, completed, and documented.

6.1 Implementation Summary:

All of the activities that have been completed as required in the "Action Plan" should be listed and summarized. This section should contain a complete record of the actions that were taken to correct the problem and assure that it will not recur. This includes changes, preventive measures, process controls, training, etc.

6.2 Documentation:

All documents or other specifications that have been modified are listed. Typically the documentation would be attached to a final printed report of this CAPA action. This will facilitate verification of the changes for the follow up.

7. Follow Up:

One of the most fundamental steps in the CAPA process is an evaluation of the actions that were taken. Several key questions must be answered:

1. Have all of the objectives of this CAPA been met?
2. Have all recommended changes been completed and verified.

3. Has appropriate communications and training been implemented to assure that all relevant employees understand the situation and the changes that have been made?
4. Is there any chance that the actions taken may have had any additional adverse effect on the product or service?

7.1 Verification Results:

The implementation and completion of all changes, controls, training, etc. must be verified. The evidence that this has been done must be recorded. Appropriate information should have been entered to document that all actions have been completed successfully.

7.2 Results / Effectiveness of the Actions:

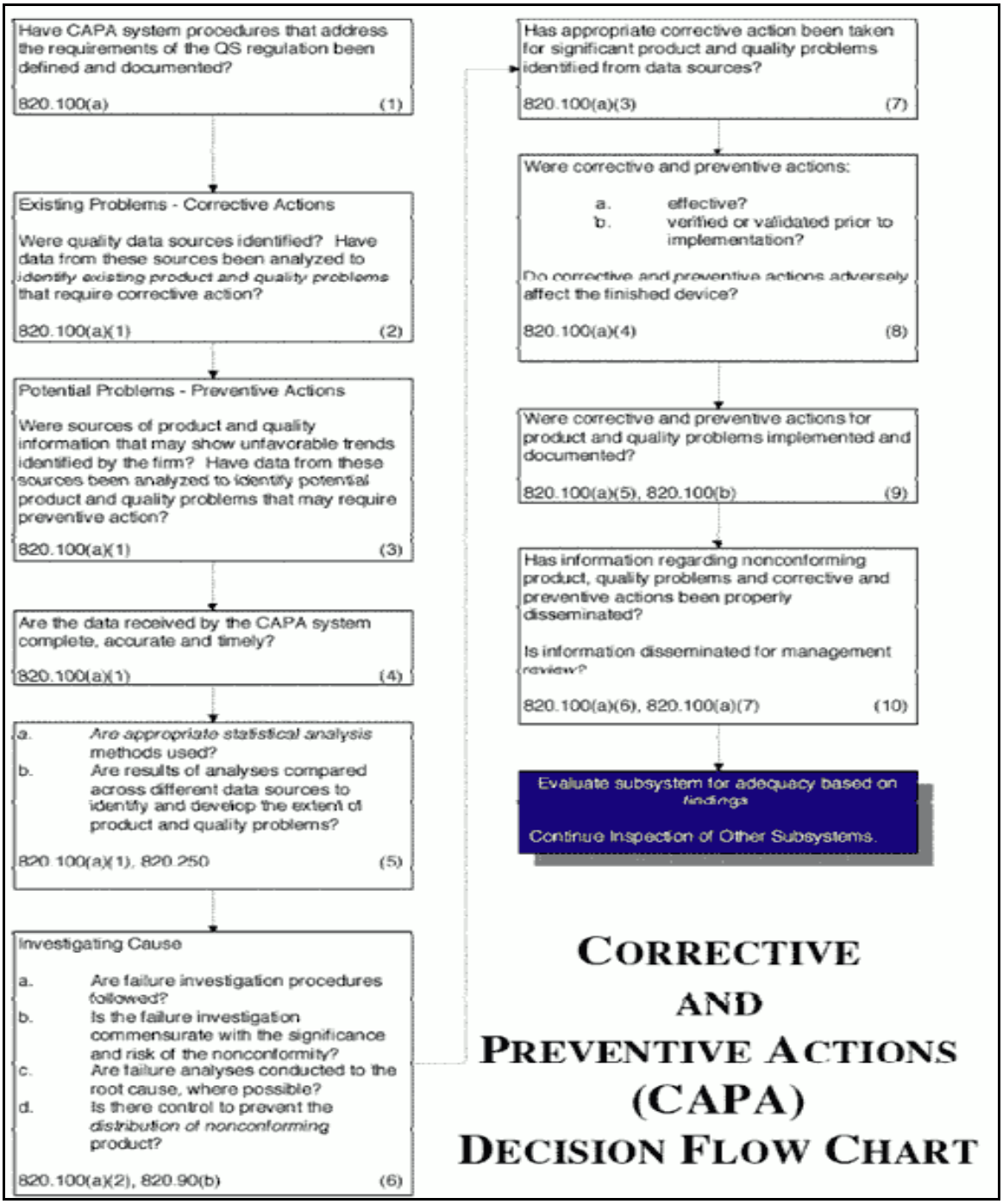
Another important aspect of any CAPA action is to make sure that the actions taken were effective. A thorough evaluation must be done to make sure that the root cause of the problem has been solved, that any resulting secondary situations have been corrected, that proper controls have been established, and that adequate monitoring of the situation is in place. This evaluation must also include an investigation to determine if the actions taken could result in any other adverse effects. This investigation and the results should be documented.

7.3 Additional Comments:

It is always a good idea to add any additional information or other appropriate comments concerning the problem, investigation, actions, or follow up that may be helpful in understanding anything that has been done for a CAPA action. Documenting the complete process involved in a corrective or preventive action from identifying the problem to a successful completion is important for all companies, but absolutely essential for meeting current regulatory requirements. Following the steps outlined in this document will provide a complete, well documented CAPA action that will meet regulatory requirements and can significantly improve the quality process in an organization.

Inspectional Objectives[3]:

1. Verify that CAPA system procedure that address the requirements of the quality system regulation have been defined and documented.
2. Determine if appropriate sources of product and quality problems have been identified. Confirm that data from these sources are analyzed to identify existing product and quality problems that may require corrective action.
3. Determine if sources of product and quality information that may show unfavorable trends have been identified. Confirm that data from these sources are analyzed to identify potential product and quality problems that may require preventive action.
4. Challenge the quality data information system. Verify that the data received by the CAPA system are complete, accurate and timely.
5. Verify that appropriate statistical methods are employed (where necessary) to detect recurring quality problems. Determine if results of analyses are compared across different data sources to identify and develop the extent of product and quality problems.
6. Determine if failure investigation procedures are followed. Determine if the degree to which a quality problem or nonconforming product is investigated is commensurate with the significance and risk of the nonconformity. Determine if failure investigations are conducted to determine root cause (where possible). Verify that there is control for preventing distribution of nonconforming product.
7. Determine if appropriate actions have been taken for significant product and quality problems identified from data sources.
8. Determine if corrective and preventive actions were effective and verified or validated prior to implementation. Confirm that corrective and preventive actions do not adversely affect the finished device.
9. Verify that corrective and preventive actions for product and quality problems were implemented and documented.
10. Determine if information regarding nonconforming product and quality problems and corrective and preventive actions has been properly disseminated, including dissemination for management review.



Application of Corrective Action and Preventive Action System Throughout the Product Lifecycle[4]:

Pharmaceutical Development	Technology Transfer	Commercial Manufacturing	Product Discontinuation
Product or process variability is explored. CAPA methodology is useful where corrective actions and preventive actions are incorporated into the iterative design and development process.	CAPA can be used as an effective system for feedback, feedforward and continual improvement.	CAPA should be used and the effectiveness of the actions should be evaluated.	CAPA should continue after the product is discontinued. The impact on product remaining on the market should be considered as well as other products which might be impacted

Conclusion:

In order to resolve problems every group must know how to conduct an actual investigation, detect root causes and implement effective corrective and preventive action in a timely manner. The CAPA process must provide a common model and language within the organization, which lets investigators to master the process quickly and easily. Management of non-conformances and CAPA processes are essential for pharmaceutical companies, although scope of business, culture and existing processes will heavily impact the quality of the product. An efficient CAPA process is a great tool to improve quality systems and processes; the initial effort is worthwhile if it is well planned and performed correctly.

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