

## Review Article

**Corrective Action and Preventive Action: Management and Applications in Pharmaceutical Industry****M.P. Venkatesh\*, Angela Philip, H.V. Gangadharappa**

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**ABSTRACT**

Corrective and Preventive Actions (CAPA) is essential for the improvement and increasing the quality of the final product or service. It is a key component for the continuous development of any industry. It is a regulatory requirement in a pharmaceutical company as well as a comprehensive part of Quality Management System. The corrective actions are taken after the occurrence of non-conformity whereas a preventive action is taken to control or avert non-conformity and its recurrence. This review gives an insight to the corrective and preventive actions as well as the series of action involved in the CAPA plan.

**Keywords:** CAPA, Corrective action, Preventive action, Risk Management System.**INTRODUCTION**

Corrective and Preventive Action (CAPA), is a subsystem that harmonize all quality subsystems, thereby closing a "quality loop." CAPA represents one among many mechanisms that ensures continuous improvement within an organization along with customer satisfaction measurements, internal audits, trend recording, and non-conforming product control. On reaching the intended performance, a new performance criterion is set to achieve continuous improvement with increased priority on quality. In this way, CAPA effectuates the philosophy of the spiral helix depicted by the International Organization for Standardization (ISO) 9001: 2000. A CAPA program is a robust and incessant element for the improvement of product, process, and quality systems. CAPA is assumed to be a quality improvement tool which works on a two-loop system – a reactive loop and a proactive loop. Utilizing a CAPA program must be proactive according to the Food and Drug Administration's (FDA) new systemic audit inspection approach and its emphasis on risk-based management.<sup>1</sup>

CAPA is a fundamental management tool that can be implemented in every quality system. It provides a simple step-by-step process for completing and documenting corrective or preventive actions. The result will be a complete, well-documented investigation and solution which satisfies most regulatory requirements and form the basis for an effective continuous improvement plan for any Company.<sup>2</sup>

**DISCUSSION**

A CAPA program should be SMARTER: Specific, Measurable, Attainable, Results-oriented, Time-based, Evaluated, and Reviewed. All seven attributes of a SMARTER program are equally important. If performance criteria and established metrics (measurable actions) do

not exist for analysis and monitoring, program effectiveness cannot be evaluated.<sup>3</sup>

The fundamental objective behind corrective action and preventive action (CAPA) in any pharmaceutical or any industry is to determine the weakness, discrepancy or failures and to execute investigation with befitting actions to prevent the problem from recurring. CAPA is a proactive method in which preventive measures are taken in the initial stage itself so that occurrence of any discrepancy can be avoided. It is a part of overall Quality Management System (QMS) and as well a regulatory requirement in a pharmaceutical company.<sup>4</sup>

The core value of such a program is to determine the root cause of any quality issue resulting from an investigation into a non-conformance, complaint or other undesirable situation. Once determined, the root cause is addressed by a two-pronged approach. The first is the corrective action, which is implemented to address the cause of a detected issue. The second is the preventive action, which is implemented to prevent the detected issue from recurring. In the context of manufacturing drug products, GMP principles outlined in the ICH Q10 document are applied to ensure that the products are consistently produced and controlled in such a way as to meet the quality standards appropriate for their intended use, as required by the marketing authority. The CAPA program, when implemented properly, should result in a greater understanding of the product and processes and, therefore, their improvement. The most efficient way to implement a sustainable and robust CAPA management system is by applying a closed loop system, which typically includes seven basic steps:

- The identification of the problem/potential problem, nonconformity or incident;
- An evaluation of the amplitude of the problem and the likely impact on the company;



- The development of an investigation procedure with specific responsibility assigned to people;
- Conducting a thorough (root cause) analysis of the non-conformity with proper documentation;
- Implementing an action plan quoting all the tasks that must be accomplished to correct and prevent the problem from recurring;
- The execution of the plan;
- A thorough follow-up confirming completion of all tasks, and an assessment of the aptness and effectiveness of the actions which have been taken.<sup>5</sup>

In the Pharmaceutical Industry, the CAPA management system is a key element of QMS, and it is also the heart and driving force for Quality improvements. The CAPA management system backup the Quality System to improve processes, procedures, organization and business in an efficient, well-documented and actionable way.

There is a strong link between QUALITY and OPERATIONAL EXCELLENCE, as a well-established CAPA management system which will result in a high Return on Investment (ROI) and benefits for the business, for instance:

- Improved safety and security
- Infrastructure efficiency gains
- Avoiding cost of regulatory non-compliance (fines, business closure, reputational and brand damage)
- Increased productivity, as a smarter process might require less personnel
- Better product quality
- Improved customer satisfaction

CAPA management systems are well documented indicators of problems and how they are resolved and hence CAPA systems are a primary target for scrutiny at every audit or regulatory inspection.

**CAPA Definitions**

**Corrective action**– Corrective Action is a reaction to a non-conformity or undesirable situation that has already happened. A non-conformance or problem occurred and has been reported by either internal or external sources. The initiated actions designed to prevent the recurrence included the following steps:

- Correct the problem
- Modify the quality system so that the process that resulted in the non-conformity is monitored to prevent the recurrence

- The documentation for the corrective action taken provides evidence that the problem was recognized, corrected and proper controls were installed

“Corrective action is the process to eliminate the cause of detected non-conformity or other undesirable situation”.<sup>6</sup>

**Preventive action**– A Preventive Action is a proactive approach and process for detecting non-conformances or undesirable situations that may happen and prevents them before occurring. The process includes:

- Identify potential problems or non-conformances
- Find the cause of the potential problem / non-conformance
- Develop a plan to prevent the occurrence
- Implement the plan
- Review the actions taken and the effectiveness in preventing the problem

“Preventive actions are the process undertaken for eliminating the cause of a potential nonconformity or other undesirable situation”.<sup>5</sup>

**Differences between corrective and preventive action<sup>9</sup>**

Corrective action	Preventive action
<ul style="list-style-type: none"> <li>• A corrective action is a reaction to a problem that has already occurred</li> <li>• It assumes that a non-conformance or problem exists and has been reported by either internal or external sources.</li> <li>• The actions initiated are intended to:                             <ol style="list-style-type: none"> <li>1. fix the problem</li> <li>2. Modify the quality system so that the process that caused it is monitored to prevent a reoccurrence.</li> </ol> </li> <li>• The documentation for a corrective action provides evidence that the problem was recognized, corrected, and proper controls installed to make sure that it does not happen again</li> </ul>	<ul style="list-style-type: none"> <li>• A preventive action is initiated to stop a potential problem from occurring</li> <li>• It assumes that adequate monitoring and controls are in place in the quality system to assure that potential problems are identified and eliminated before they happen.</li> <li>• If something in the quality system indicates that a possible problem is or may develop, a preventive action must be implemented to avert and then eliminate the potential situation.</li> <li>• The documentation for a preventive action provides evidence that an effective quality system has been implemented that is able to anticipate, identify and eliminate potential problems.</li> </ul>

From a business perspective, Preventive Actions are much more powerful than Corrective Actions as they are proactive rather than a reactive approach.

Companies must ensure that appropriate corrective actions include both short-term actions to address the immediate problem and long-term actions to prevent the



recurrence of a problem. To successfully manage the CAPA system, companies need to simplify their procedures, and to filter and prioritize the corrective and preventive actions. Senior management must allocate proper resources to identify and remove the root causes of recurring problems.

### More comprehensive approach of CAPA

Not having adequate CAPA management is considered a serious compliance weakness. CAPA investigations are usually initiated by a customer complaint, a regulatory or internal audit, a manufacturing inconsistency or a laboratory investigation. Most companies initiate their CAPA processes after a complaint or product failure has been discovered.

Generally, this is not a good sign for any pharmaceutical business, as it signals a lack of awareness as to the causes of identified problems. While CAPA involves more than just addressing issues that arise in production, at times it seems that problem-solving is the main issue. CAPA experts describe investigations as following a multi-step process – identify the problem, evaluate its magnitude, investigate to assign responsibility and analyze the root cause of the problem.

CAPA management further involves analyzing the root cause analysis and upgrade the processes with proper training to stakeholders to prevent the same problem in future. CAPA methodology is meant to manifest product and process improvements. Effective CAPA management needs consistent process requirements and written procedures.

An inconsistency across laboratories or facilities leads companies to have recurring problems at multiple operation sites simultaneously, according to Pharma Manufacturing. Smaller pharmaceutical firms are sometimes better able to instate successful CAPA systems and utilize a systematic approach to dealing with problems or complaints because single-site operations generally have more team collaboration and less problems caused by long-distance information management. CAPA requires that consistent requirements and written procedures be in place, and when this is the case, a pharmaceutical company operates more efficiently – especially when aided with powerful technology solutions.<sup>7</sup>

Still most of the companies are manually executing CAPA practices and facing many complexities like:

- Improper or error prone investigation
- Multiplying issues because of unstructured fixing of problems
- Desperate quality system and data sources
- Increase non-conformities, complaints or recall
- Reactive approach rather than proactive

These seven steps in cycle for effective execution of CAPA starts with:

### Identification – Clearly define the problem

It is important to accurately and completely describe the situation as it exists now.

- Identify the source of information

Examples of sources that lead to preventive actions may include: Service Request, Internal Quality Audit, Customer Complaint / Concern, Quality Assurance Inspection, Staff Observation, Trending Data, Risk Assessment, Process Performance Monitoring, Management Review, Failure Mode Analysis.

- Detailed explanation of the problem

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

- Documentation of the available evidence that a problem exists

Documenting the source of the information can be very useful during conduct of an investigation about 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 individual or departments.

- Corrective/Preventive Action request form

### Evaluation – Evaluate its potential impact

- Potential impact of the problem

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.

- 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.

- Remedial action that may be required

Based on the outcome of the impact and risk evaluations above, it may be determined that immediate remedial action is required to remedy the situation until a thorough investigation and a permanent solution is implemented. If remedial actions are necessary, the actions and the resources required are listed. The steps that must be taken immediately to avoid any further adverse effects are explained.

- Remedial action form



**Investigation – In-depth planning for problem research**

- The objectives for the action

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 and rectified, and controls will be in place to prevent the situation from happening again.

- An investigation strategy

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. Consider equipment, materials, personnel, procedures, design, training, software, and external factors.

- Assignment of responsibility and required resources

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.

- Investigation procedure form

**Analysis – Complete documentation after a thorough assessment**

- Thorough root cause analysis with appropriated data collection

A list of all possible causes is created. 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.

- Document your 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

- Root cause analysis form

**Action Plan – Jot down the required tasks**

- List all activities and tasks that must be accomplished to correct the existing problem
- Needed changes to documents, processes, procedures, or other system modifications should be described

- Employee training is an essential part of any change that is made and should be made part of the action plan
- Action plan form

**Implementation – Execute the action plan**

All 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.

**Follow Up – Verify and assess the effectiveness**

- Have all the objectives been met?
- Have all recommended changes been completed and verified?
- Has training and appropriate communications been implemented to assure that all relevant employees understand the situation and the changes that have been made?
- Has an investigation demonstrated that the actions taken have not had any additional adverse effect on the product or service?

**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

**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.

An effective quality management system detects the problems before its occurrence and prevents the problems. According to FDA, CAPA alone responsible for 30 to 50% of non-compliance. Quality management system streamline, simplify and automate all the quality management practices and provide a centralized platform that can effectively execute various quality processes.





# CAPA Management System

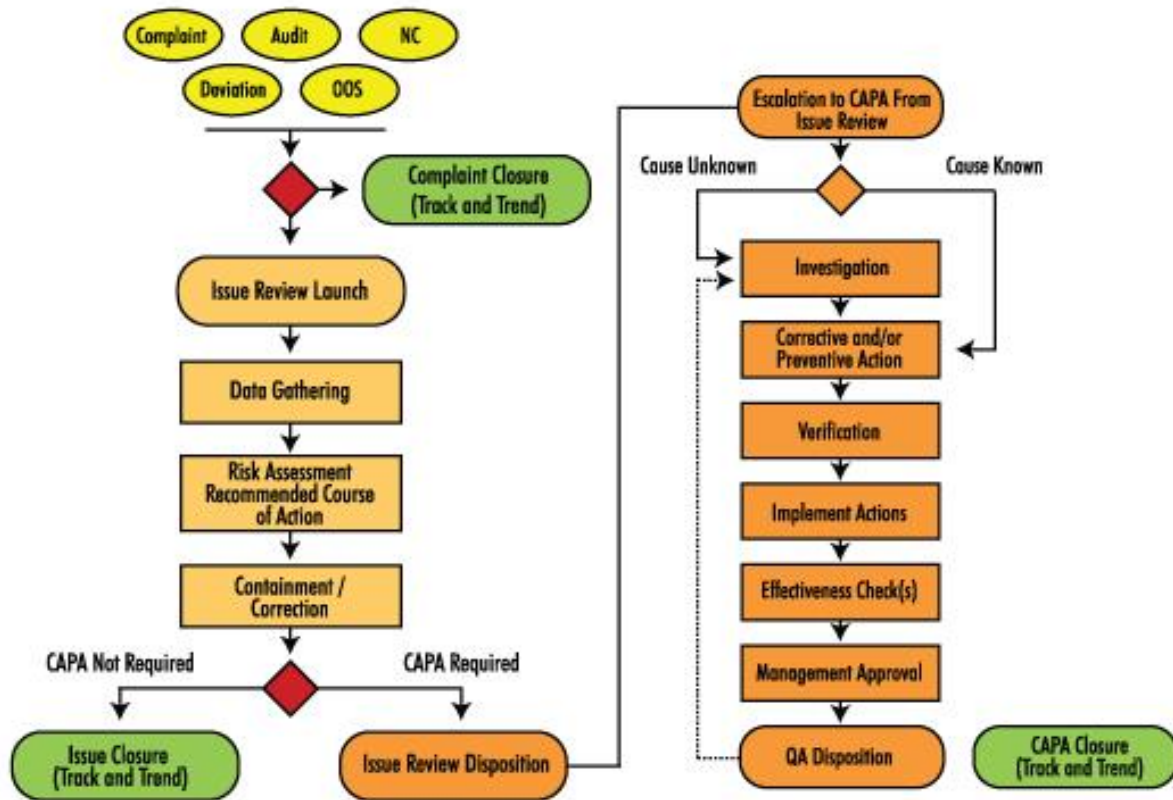


Figure 1: CAPA management flowchart

Reference: [www.mastercontrol.com/capa-software/corrective-action-capa-software.html](http://www.mastercontrol.com/capa-software/corrective-action-capa-software.html)

**Benefits of automated CAPA management:**

- Enhance organization’s compliance quotient
- Reduction in issues, complaints and recall
- More preventive actions over time
- Optimum use of resources
- Facilitate better and more informed decisions by organizations
- Improved customer satisfaction<sup>7</sup>

**Applications of CAPA in Pharma Industry**

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, feed forward 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

**CAPA closure and verification**

- On completion of actions, the department head shall certify that the proposed CAPA is completed and implemented along with associated actions.
- QA shall verify the implementation and completion of CAPA with review of supporting documents and certify the same.
- Any change proposed because of CAPA shall be through the SOP (Standard Operating Procedure) on change control reference; the same shall be mentioned in the CAPA format.
- All change control, deviations, discrepancy, incident reports giving rise to CAPA shall be addressed through CAPA form



- All facility up-gradations, capital purchase requirements, major changes in quality system and compliance to regulatory commitments giving rise to CAPA shall be addressed through CAPA form.
- The record of each CAPA shall be maintained.
- Copy of the completed CAPA shall be provided to the concerned department head by QA.
- QA shall compile the CAPA information and submit the summary to the management during management review meeting.
- Management shall review/verify the same quarterly, in management review meeting.
- Information and documents related to CAPA drawn from internal audits, external/customer audits, and regulatory inspections are considered confidential and can only be made available to regulatory review when approved by director technical and QA head<sup>8</sup>

### CONCLUSION

CAPA is one of the many important tools that ensure quality and continuous improvement for any product and services. It gives a high degree of assurance that the product or services always meet the regulatory and quality requirements throughout. Implementation of CAPA in industry will help in identifying the root cause of non-conformity and prevent further risk in the future as it plays an important role in quality risk management.

### REFERENCES

1. Bodea G. What Companies Should Know and Consider When Designing A CAPA System *Journal of GXP Compliance*, 11(3), 2007, 54-63.
2. Preventive / Corrective Actions (CAPA) Guidelines. R.M Baldwin, Inc. Available from <<http://www.rmbimedical.com/regulatoryaffairs/capa%20guidelines.pdf>>. [Accessed on: 14 July 2017].
3. Nold, L. Be Smart with your Corrective and Preventative Actions (CAPA). *Journal of GXP Compliance*, 7(3), 2003, 35-39.
4. Raj A. A review on corrective action and preventive action (CAPA). *African Journal of Pharmacy and Pharmacology*, 10(1), 2016, 1-6.
5. Hayes R, LeLacheur R, Dumont I, Couerbe P, Safavi A, Islam R et. al. 9<sup>th</sup> GCC closed forum: CAPA in regulated bioanalysis; method robustness, biosimilars, preclinical method validation, endogenous biomarkers, whole blood stability, regulatory audit experiences and electronic laboratory notebooks, *Bio analysis*, 8(6), 2016, 487-95.
6. Pharmaceutical Quality System Q10. 2008 Available from <[http://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/Quality/Q10/Step4/Q10\\_Guideline.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q10/Step4/Q10_Guideline.pdf)>. [Accessed on: 10 July 2017].
7. Contribution of CAPA management in Pharmaceutical production quality. Available from <<http://www.qedge.co.in/contribution-capa-pharmaceutical-production-quality/>>. [Accessed on: 9 July 2017].
8. Raj A. A review on corrective action and preventive action (CAPA). *African Journal of Pharmacy and Pharmacology*, 10(1), 2016, 1-6.
9. Gangadharappa H.V. Tenzin Tashi, Vitalis B. Mbuya. Corrective action and preventive action and its importance in quality management system: A review, *International Journal of Pharmaceutical Quality Assurance*, 7(1), 2016, 1-6.

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