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*Review*

# A review on corrective action and preventive action (CAPA)

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**The primary objective behind corrective action and preventive action (CAPA) in any pharmaceutical or medical device industry is to determine the weakness, deviation or failures and to carry out its investigation with appropriate actions so that such problems are not repeated again. CAPA is also a method in which preventive measures are taken in the beginning itself so that occurrence 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.**

**Keywords:** Corrective action, preventive action, corrective action and preventive action (CAPA), action plan, root cause determination.

## INTRODUCTION

Corrective actions and preventive actions (CAPAs) are a very important part of pharmaceutical quality systems and industry producing medical devices. Once it is discovered that there are weaknesses, including failures in the production and/or testing of drugs, investigations into the cause(s) should commence. Actions should be taken to correct the existing product non-conformity or quality problems (corrective actions) and to prevent the recurrence of the problem (preventive actions). FDA (Food and Drug Administration) investigators and compliance officers often refer to the practice of addressing only the immediate problem as the “band-aid approach,” which often results in a warning letter. CAPA is part of the overall Quality Management System (QMS) (Denise, 2001; ISO, 9000, 2005; US FDA website).

### Regulatory expectations

#### *International Conference on Harmonization (ICH) Q10 (Pharmaceutical Quality System)*

The pharmaceutical or medical device company should have a system for implementing corrective actions and preventive actions resulting from the investigation of complaints, product rejections, non-conformances, recalls, deviations, audits, regulatory inspections and findings, and trends from process performance and product quality monitoring. A structured approach to the investigation process should be used with the objective of determining the root cause. The level of effort, formality and documentation of the investigation should be

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commensurate with the level of risk, in line with ICH Q9 (Quality Risk Management). CAPA methodology should result in product and process improvements and enhanced product and process understanding (Code of Federal Regulations CFR, 2015) (Figure 1).

## CORRECTION

It is an action to eliminate a detected non-conformity. A correction can be made in conjunction with a corrective action. A correction can be, for example, rework or regrade. ISO 9000: 2005 (E). (Michael, 1997; James and Terry, 2000)

## CORRECTIVE ACTIONS

A corrective action is to eliminate the cause of a detected non-conformity or other undesirable situation. There can be more than one cause for non-conformity. Corrective action is taken to prevent recurrence. Corrective action may arise from manufacturing deviations, OOS (Out Of Specification) investigations, complaints, audit findings, recalls, etc (ICH, 2005; US FDA website, Michael, 1997; Corrective Action Preventive Action, 2015). The process includes:

1). Reviewing and defining the problem or non-conformity.
2). Finding the cause of the problem.
3). Develop an action plan to correct the problem and prevent a recurrence.
4). Implementing the plan.
5). Evaluating the effectiveness of the correction.

## PREVENTIVE ACTIONS

A preventive action is a process to eliminate the cause of a potential non-conformity or other undesirable situation. There can be more than one cause for a potential non-conformity. Preventive action is taken to prevent occurrence. Preventive action may result from trending of in process data, of analytical data, of audit findings, trending of root causes for non-conformities or complaints, from annual product reviews, quality risk analyses, etc (ICH, 2005; US FDA website, Michael, 1997; Corrective Action Preventive Action, 2015). The process includes:

1). Identify the potential problem or non-conformance.
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.

**Note:** Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence. (ISO 9000:2005)

## PROCESS OF CAPA

There are 7 basic steps of CAPA for pharmaceutical or medical devices industries (Joseph, 2006; Kimberly Lewandowski-Walker, 2008; MarliseGyger, 2012):

1). Identification - Define the problem.
2). Evaluation - Appraise the magnitude and potential impact.
3). Investigation - Identify the root cause of the problem.
4). Analysis - Perform a thorough assessment with documentation.
5). Action Plan - Define corrective and preventive actions.
6). Implementation - Execute the action plan.
7). Follow UP - Verify and assess the effectiveness.

## 21 CFR (Code of Federal Regulations) 820 regulatory requirements (Procedures)

They establish and maintain procedures for implementing corrective and preventive action (Code of Federal Regulations CFR, 2015).

### Preamble on procedures

The procedures (for implementing corrective and preventive action) must provide for control and action to be taken on devices distributed, and those not yet distributed, that are suspected of having potential non-conformities (Preamble, comment 158).

## ESTABLISHING DATA SOURCES

Data can be established from internal sources as well as external sources. Examples of internal data sources are: Process control data, test/inspection data, device history records, internal audits, non-conforming material reports, rework and scrap/yield data and training records. Examples of external data sources are: Supplier controls, customers, complaints, servicing repairs, adverse event reporting (MDR), FDA and similar devices from competitors.

## DATA ANALYSIS

Analyze processes, work operations, concessions, quality

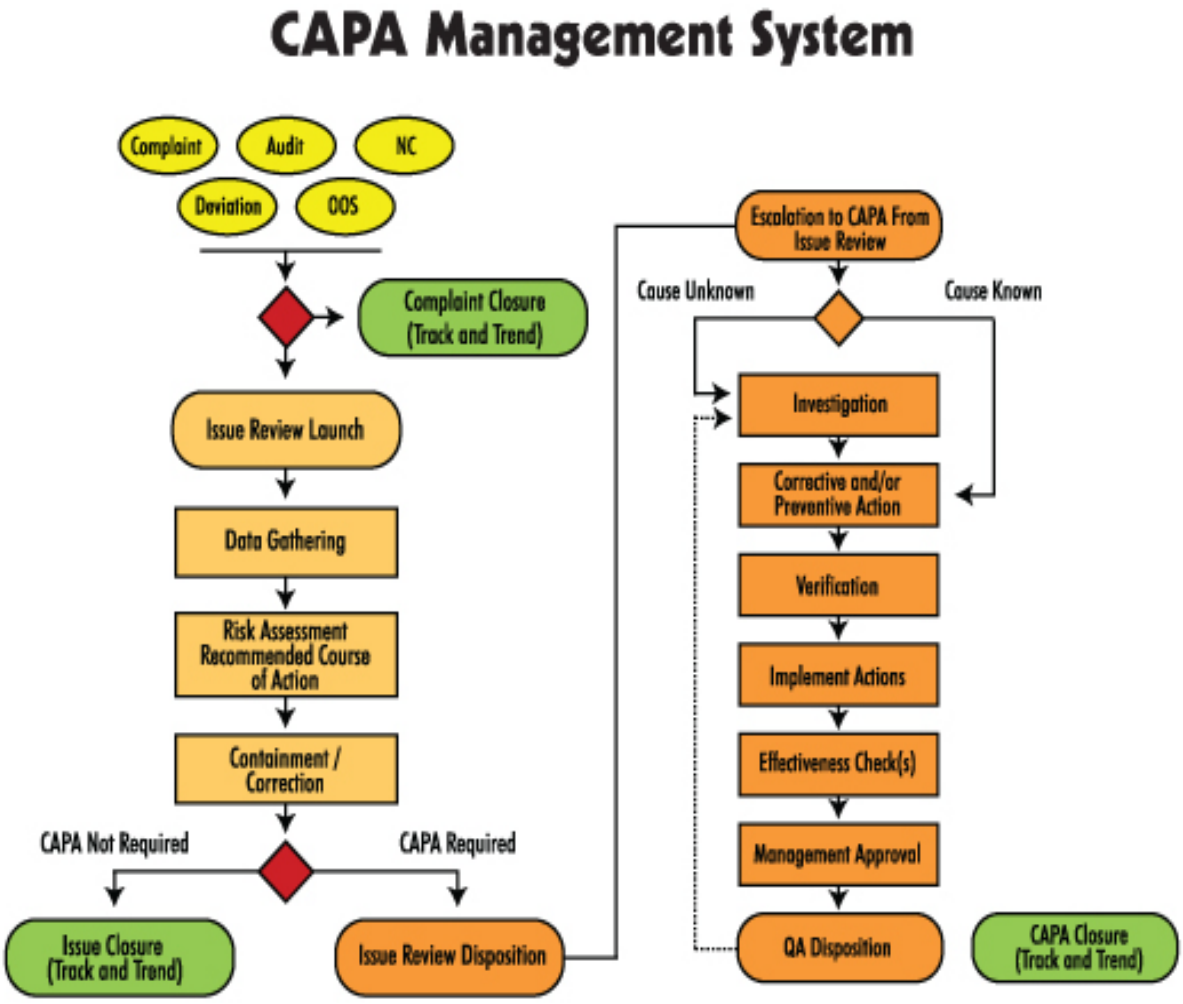


**Figure 1.** reference: www.mastercontrol.com/capa-software/corrective-action-capa-software.html

audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of non-conforming product, or other quality problems. 21 CFR 820.100 (a) (1).

**Approach to data analysis: Non-statistical and statistical techniques**

1). Use a risk-based approach to rank areas, select items with major impact, that is, product related or process related. Proceed with items from high to low impact and eventually assure all areas are addressed.
2). Use of Statistical Methodology; 21 CFR 820.100 (a) (1). Appropriate statistical methodology shall be employed where necessary to detect recurring quality problems (Code of Federal Regulations CFR, 2015).

**Investigation to determine root cause**

Investigate the cause of non-conformities relating to product, processes, and the quality system. 21 CFR 820.100 (a) (2).

**PREAMBLE ON INVESTIGATIONS**

The requirement in this section is broader than the requirement for investigations under section 820.198, because it requires that non-conforming product discovered before or after distribution be investigated to the degree commensurate with the significance and risk of the non-conformity. The requirement in this section applies to process and quality system non-conformities, as well as product non-conformities. If a molding process with its known capabilities has a normal five percent

rejection rate and that rate rises to ten percent, an investigation into the non-conformance of the process must be performed (Preamble Comment 161) (How to create a corrective and preventive action plan, 2015; Code of Federal Regulations CFR, 2015).

**Identify corrective and preventive actions**

Identify the action(s) needed to correct and prevent recurrence of non-conforming product and other quality problems. 21 CFR 820.100 (a) (3) (Preamble Comment 161) (How to create a corrective and preventive action plan, 2015; Code of Federal Regulations CFR, 2015).

**Identify action(s) to be taken**

1). No further action necessary.
2). Correction.
3.) Corrective Action.
4.) Preventive Action.

**The preamble on risk and degree of corrective and preventive action**

The degree of corrective and preventive action taken to eliminate or minimize actual or potential non-conformities must be appropriate to the magnitude of the problem and commensurate with the risks encountered. (Preamble, Comment 159).

**Verify/validate corrective and preventive actions**

Verify or validate the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device. 21 CFR 820.100 (a) (4).

**Preamble on verification and validation**

FDA has revised Section 820.100 (a) (4) to reflect that preventive, as well as corrective, action must be verified or validated (Preamble, Comment 163).

**Implement corrective and preventive actions**

Implement and record changes in methods and procedures needed to correct and prevent identified quality problems. 21 CFR 820.100 (a) (5).

**Communicating CAPA information**

1). Disseminate information related to quality problems or non-conforming products to those directly responsible for assuring the quality of such product or the prevention of such problems. 21 CFR 820.100 (a) (6).
2). Submit relevant information on identified quality problems, as well as corrective and preventive actions for management review. 21 CFR 820.100 (a) (7).

**The preamble on CAPA activities for management review**

Only certain information needs to be directed to management. The manufacturer's procedure should clearly define the criteria to be followed to determine what information will be considered "relevant" to the action taken and why. FDA emphasizes that it is always management's responsibility to ensure that all nonconformity issues are handled appropriately. (Preamble, Comment 164) (US FDA website; Code of Federal Regulations CFR, 2015).

**Documenting corrective action and preventive action activities**

Document all activities required under this section, and their results. 21 CFR 820.100 (b) (US FDA website; Code of Federal Regulations CFR, 2015).

**The preamble on CAPA and internal audits and management reviews**

Two comments stated that the records required under Section 820.100 (b) should be treated as part of the internal audit. FDA disagrees with these comments. FDA has the authority to review such records and the obligation to do so to protect the public health. Manufacturers will be required to make this information readily available to an FDA investigator. (Preamble, Comment 166) (US FDA website; Code of Federal Regulations CFR, 2015)

**FDA inspection**

Manufacturers should consider that their corrective action and preventive action documentation can demonstrate to FDA that the manufacturer's quality system is effective and enables the manufacturer to identify problems quickly and implement effective corrective and preventive actions (US FDA website).

**Initiation of CAPA**

1). The initiation of CAPA requires submission of source document by concerned department head to QA (Quality

Assurance).
2). QA head shall decide the need for CAPA.
3). The department head shall get a CAPA form issued from QA. QA shall write the source document name and source document number on the form before issue of the form to concerned department.
4). Department head shall fill the CAPA form as under:

a). Date CAPA initiated.
b). Proposed completion date.
c). Select the department initiating the CAPA by making a √ mark in appropriate box.
d). Select the relevant system affected by making a √ mark in appropriate box. If none of the systems printed are affected, select "Not Applicable". If any other system, other than those mentioned is affected, write the system in blank spaces provided.
e). Write in brief the CAPA description from the source document and corrective and preventive action details.
f). The department head shall write their names and duly signed with date.

5). The department head shall send the CAPA form to QA.
6). QA shall allot a reference number to the CAPA form and make relevant entries in the CAPA log. Thereafter, QA shall forward the CAPA form to the concerned department.

(Nonconformance and Corrective and Preventive Action-Background and Exhibits, 2015; Ken, 2015; Difference between Containment, 2015).

## CAPA closure and verification

1). On completion of actions, the department head shall certify that the proposed CAPA is completed and implemented along with associated actions.
2). QA shall verify the implementation and completion of CAPA with review of supporting documents and certify the same.
3). Any change proposed as a result of CAPA shall be through the SOP (Standard Operating Procedure) on change control reference; the same shall be mentioned in the CAPA format.
4). All change control, deviations, discrepancy, incident reports giving rise to CAPA shall be addressed through CAPA form.
5). 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.
6). The record of each CAPA shall be maintained.
7). Copy of the completed CAPA shall be provided to the concerned department head by QA.
8). QA shall compile the CAPA information and submit the summary to the management during management review meeting.
9). Management shall review/verify the same quarterly, in management review meeting.
10). 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.

(Tonya, 2013; Difference between Containment, 2015; Larry and Chair, 2010).

## CONCLUSION

Corrective action and preventive action is an important path towards improvement and effectiveness of Quality Management System. It plays an important role in Quality Risk Management System. The root cause analysis of any problem or deviation can be easily done by implementing CAPA. Pharmaceuticals, health care and medical devices industries should strictly adhere to the implementation of CAPA in their organization.

## Conflict of Interests

The author have not declared any conflict of interests.

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