CAPA

Reignite your passion for quality investigations

Presented by Maria Mylonas
August 2019
Agenda

What is CAPA & why do we Investigate?
What do the Regulations Say?
Handy Tools & Techniques
Common deficiencies & how to fix them
What is CAPA & why do we Investigate?
What is CAPA?

A Continuous Improvement (CI) tool used within Quality Management system

Aims to prevent a recurrence (corrective action) or to prevent issue occurrence (preventive action)

CAPA is the core of continuous improvement systems and better quality of product or service

“… CAPA is a quality assurance system, which addresses quality events, which have occurred or could be anticipated to occur during healthcare products manufacturing.”
Key CAPA Definitions

Correction

Corrections typically are one-time fixes. A correction is an immediate solution such as segregate, quarantine, repair or rework

- Also known as remedial or containment action.

CAPA - Corrective and Preventive Action

A systematic approach that includes actions needed to correct (correction), avoid recurrence (corrective action), and eliminate the cause of potential non-conforming product and other quality problems (preventive action)
Key CAPA Definitions

**Symptom**
- Obvious or detectable manifestation of a causal factor

**Causal factor**
- The condition that directly caused the problem, allowed it to occur, or allowed the consequences to be worse

**Root causes**
- The basic reasons why the causal factors occur or persist
The value of CAPA

- Helps determine the actions needed to correct or fix the causes of identified problems
- A structured approach to eliminate the causes of problems that affect systems, processes and products
- Mechanism to recognise existing or potential quality issues, take steps to investigate them, resolve the issues, and stop the issues from occurring again.
- CAPA systems can help to identify gaps in the QMS and assist in recognising and resolving important quality issues
“CAPA death spiral”

“Inadequate” investigations without root cause analysis

Ineffective corrective actions and lack of preventive actions

Recurrent issues and new problems never avoided
What do the Regulations Say?
1.4 (xiv) An appropriate level of **root cause analysis** should be applied during the investigation of deviations, suspected product defects and other problems.

This can be determined using **Quality Risk Management** principles. In cases where the true root cause(s) of the issue cannot be determined, consideration should be given to identifying the most likely root cause(s) and to addressing those. Where **human error** is suspected or identified as the cause, this should be justified having taken care to ensure that process, procedural or system based errors or problems have not been overlooked, if present. Appropriate corrective actions and/or preventive actions (CAPAs) should be identified and taken in response to investigations. The **effectiveness check** of such actions should be monitored and assessed, in line with Quality Risk Management principles;
1.8 GMP for Medicinal Products

(vii) Any significant deviations are fully recorded, investigated with the objective of determining the root cause and appropriate corrective and preventive action implemented;

Issues Observed:
- CAPA that has no link to the identified Root Cause (RC).
- Investigations where it is very clear that the RC is determined before the investigation even started and then everything is directed to proving that RC is valid.
Product Quality Review – Clause 1.10, 1.11

(iv) A review of all significant deviations or non-conformances, their related investigations, and the effectiveness of resultant corrective and preventive actions taken;

(ix) A review of adequacy of any other previous product process or equipment corrective actions;

1.11 The manufacturer and, where different, Marketing Authorisation holder should evaluate the results of the review and an assessment made as to whether corrective and preventive action or any revalidation should be undertaken, under the Pharmaceutical Quality System. There should be management procedures for the ongoing management and review of these actions and the effectiveness of these procedures verified during self-inspection. Quality reviews may be
Chapter 9 – Self - Inspection

9.3. All self inspections should be recorded. Reports should contain all the observations made during the inspections and, where applicable, proposals for corrective measures. Statements on the actions subsequently taken should also be recorded.
Handy Tools & Techniques
Use of Standard Checklists

Checklists are beneficial in providing a standard, consistent list of potential sources of error.

For example:

- Was the correct procedure followed?
- Was the person trained in the procedure?
- Does the procedure match actual practice?
- Is this a recurring issue?
- Was there an equipment problem?
- Was the equipment calibrated?

If the checklist does not identify the root cause, there are a number of other tools that you can use.
Brainstorming

- Brainstorming can be used in association with other Root Cause Analysis tools
- Brainstorming is a method for generating a large number of creative ideas in a short period of time

Approach:
- Unstructured shout-out ideas
- Thinking “outside the box”
- Structured rotation around the room for ideas
5 Why’s

• Simple tool to identify causal factors and illicit possible root cause
5 Why’s

Step 1:
Establish a problem statement
E.g. “I was late to the PDA dinner tonight”

Step 2:
Ask (and answer) the question “Why” 5 times

Step 3:
The root cause usually becomes apparent at or before the 5th Why
Fishbone Diagram

- Simple tool looking at exploring key areas that may have led to the problem

Diagram:

- People
  - People
  - People
  - People

- Materials
  - Materials
  - Materials
  - Materials

- Method
  - Method
  - Method
  - Method

- Measurement
  - Measurement
  - Measurement
  - Measurement

- Machine
  - Machine
  - Machine
  - Machine

- Environment
  - Environment
  - Environment
  - Environment

- Problem
Common Deficiencies & How to Fix Them
## TGA Common Deficiencies – Sterile Medicines

<table>
<thead>
<tr>
<th>Deficiencies</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of Issues</td>
<td>• Failure to immediately assess the criticality of issues</td>
</tr>
<tr>
<td></td>
<td>• Failure to expeditiously progress the CAPA based on risk</td>
</tr>
<tr>
<td></td>
<td>• Poor management, completion and effectiveness checks of CAPA’s (e.g. Deviations, OOS &amp; Customer Complaints)</td>
</tr>
<tr>
<td></td>
<td>• Recurrence of similar issues not addressed</td>
</tr>
<tr>
<td>Investigation Quality</td>
<td>• Poor identification of issues and assessment</td>
</tr>
<tr>
<td></td>
<td>• Lack of appropriate severity assessment</td>
</tr>
<tr>
<td></td>
<td>• Incomplete resolution of sterility issues</td>
</tr>
<tr>
<td></td>
<td>• Lack of urgency in addressing significant issues</td>
</tr>
<tr>
<td>No.</td>
<td>Chapter</td>
</tr>
<tr>
<td>-----</td>
<td>---------</td>
</tr>
<tr>
<td>1</td>
<td>1.4 (Xiv) – Root Cause Analysis – (Deviations/CAPA)</td>
</tr>
<tr>
<td>2</td>
<td>1.8 (vii) – Significant Deviations – (RCA/CAPA)</td>
</tr>
<tr>
<td>3</td>
<td>4.8 – Record in real-time (traceability)</td>
</tr>
<tr>
<td>4</td>
<td>4.1 – Control of documentation</td>
</tr>
<tr>
<td>5</td>
<td>4.2 – Generation of documentation</td>
</tr>
</tbody>
</table>
Top 2 Clauses

Findings Chapter 1 per Section

Number of findings

PQS

GMP
Timeliness
(or lack of)
Issue

Variability regarding timeframes that regulated companies establish to deal with CAPA processes.

Examples:
- No time limits
- Fortnight limit
- 30-day limits

The only guidance is ‘reasonable’.

When timelines are getting close, management puts pressure on investigators, and the end result may be inadequate.
Best Practices

Perform a risk assessment on the issue

- Allocate timeframes according to the risk involved
  - High risk situations have 20 days
  - Medium risk situations have 30 days
  - Low risk situations have one week

- High risk investigations should be given priority
Correcting the Symptom & not the cause
Issue

• Most companies don’t differentiate between a correction (spot fix) and a corrective/preventive action (attack on the root cause)
Best Practices

- Train both the investigators as well as general employees on the difference between correction and CAPAs
  - Ensure they can distinguish between symptoms and root causes
- When verifying a CAPA, ask: will this corrective action avoid the cause occurring again? If the answer is no, you simply have a correction
Lack of Interim Corrective Actions
Companies take time to implement CAPAs e.g. writing a new procedure or validating a piece of equipment. This allows a very long lapse before implementation; with no interim action to stop the issue.
Before you approve corrective actions, always ask whether the process will be run again prior to the implementation of that action.

If the answer is yes, you must request some interim action.
Lack of Effectiveness Checks
Effectiveness v Implementation Check

Some companies only measure effectiveness by asking:

“Has the CAPA been implemented?”

and not assessing whether the action has actually worked
Discussion: CAPA Effectiveness

Imagine a tap is dripping 5 ml per hour due to a leaky washer.

A CAPA is undertaken to replace this washer and implement more regular maintenance.

How do you measure the effectiveness of this action?
Discussion: CAPA Effectiveness

Most people would say 'when the tap stops dripping' This does not measure effectiveness as it is linked to the symptom not the root cause.

Effectiveness should be measured by ensuring the root cause does not recur (i.e. the washers don’t become leaky)

This is because symptoms can have multiple causes, and a tap being leaky could be due to another reason!
Best Practices

- Clearly define evaluation as the effectiveness of CAPAs
- Ensure effectiveness measures the occurrence of the root cause, not the symptom
Many companies blame issues on human error, and then implement retraining as their only Corrective Action.

Humans are involved in all processes, and we can’t change the fact that they could make errors.

We can change the conditions people work in.

E.g. Root causes of human error may be vague procedures, or inadequate systems.
Best Practices

There is only one: do not allow the use of human error as a root cause.

Always ask why the human made the mistake.
Summary

01 Focus on improving your RCA techniques (use a tool)

02 Ensure you conduct your investigations in a “timely” manner

03 Know the difference between a causal factor and true root cause

04 Implement the right effectiveness check
Thank you for your time.
Questions?

Maria Mylonas
Learning and Development Director

maria.mylonas@pharmout.net
www.pharmout.net