CAPA

Reignite your passion for quality investigations

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Agenda

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

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What is CAPA & why do we Investigate?

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What is CAPA?

"... CAPA is a quality assurance system, which addresses quality events, which have occurred or could be anticipated to occur during healthcare products manufacturing."

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

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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

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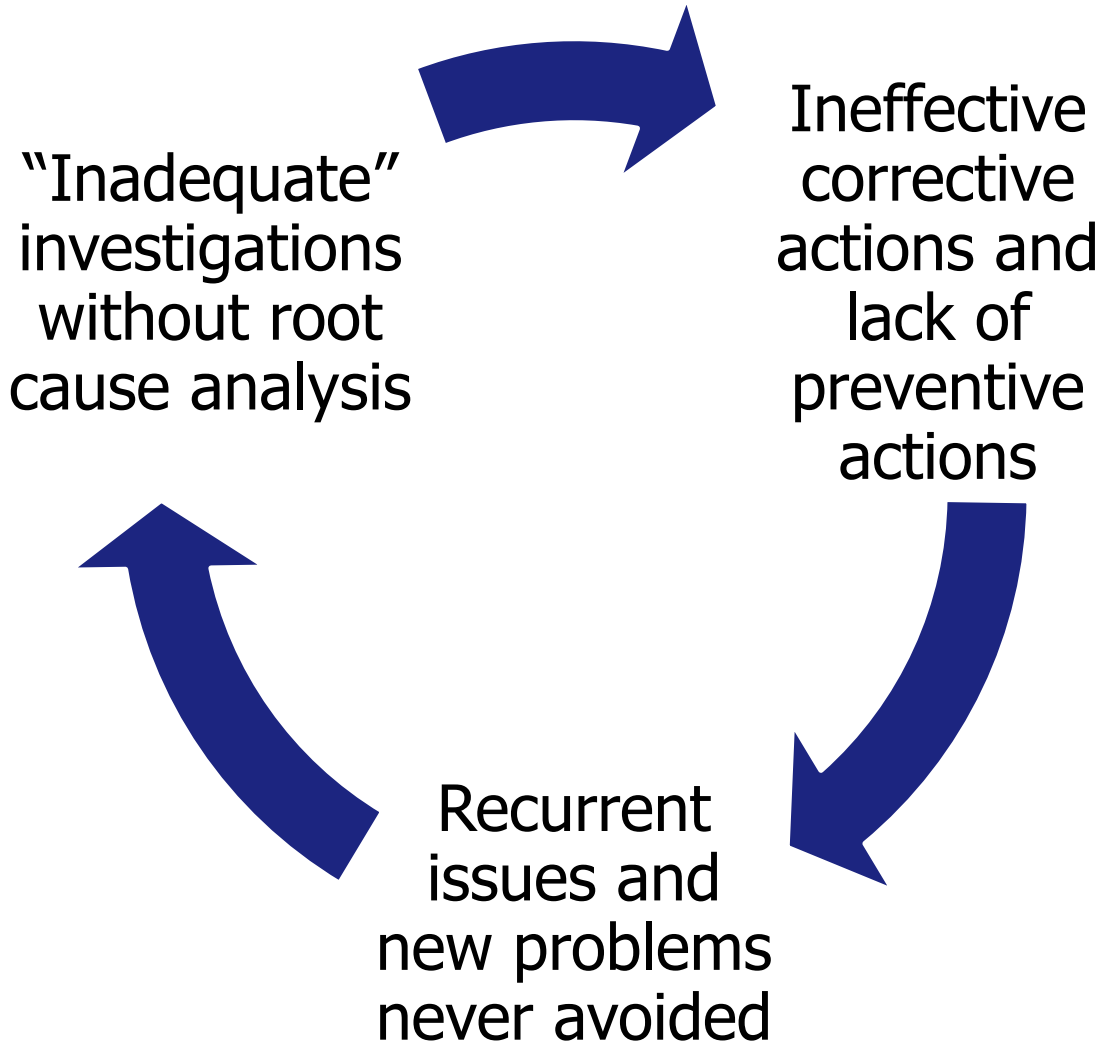
"CAPA death spiral"



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What do the Regulations Say?

Human Error

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 of such actions should be monitored and assessed, in line with Quality Risk Management principles;

1. Root Cause Analysis
2. Quality Risk Management
3. Don't just put down Human Error as the Root Cause
4. Implement the right Corrective Action and/or Preventive Action
5. Effectiveness checks

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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.

Clauses in PIC/S GMP – Part I

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

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Clauses in PIC/S GMP – Part I

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.

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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

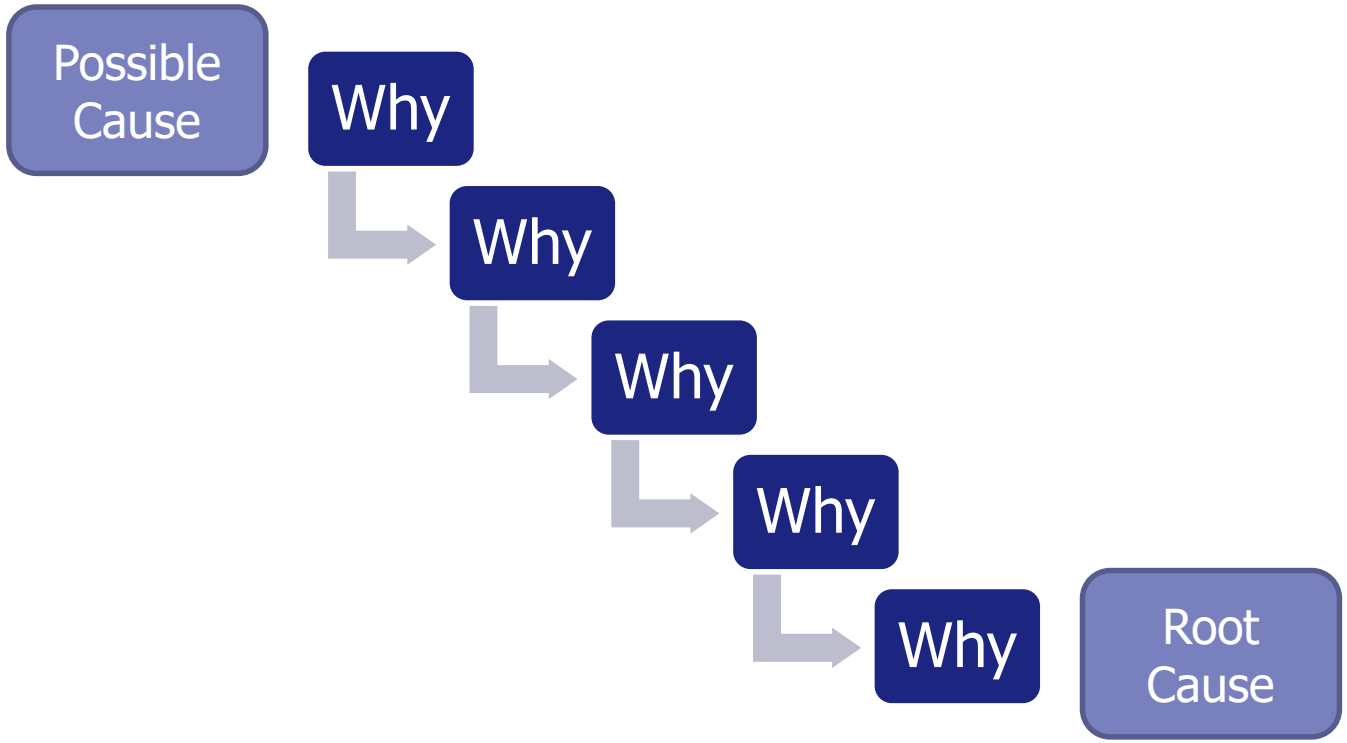
- Brainstorming can be used in association with other Root Cause Analysis tools
- Brainstorming is a method for generating a large number of creative ideas in a short period of time

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



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5 Why's

Step 1:

Establish a problem statement

E.g. "I was late to the PDA dinner tonight"

Step 2:

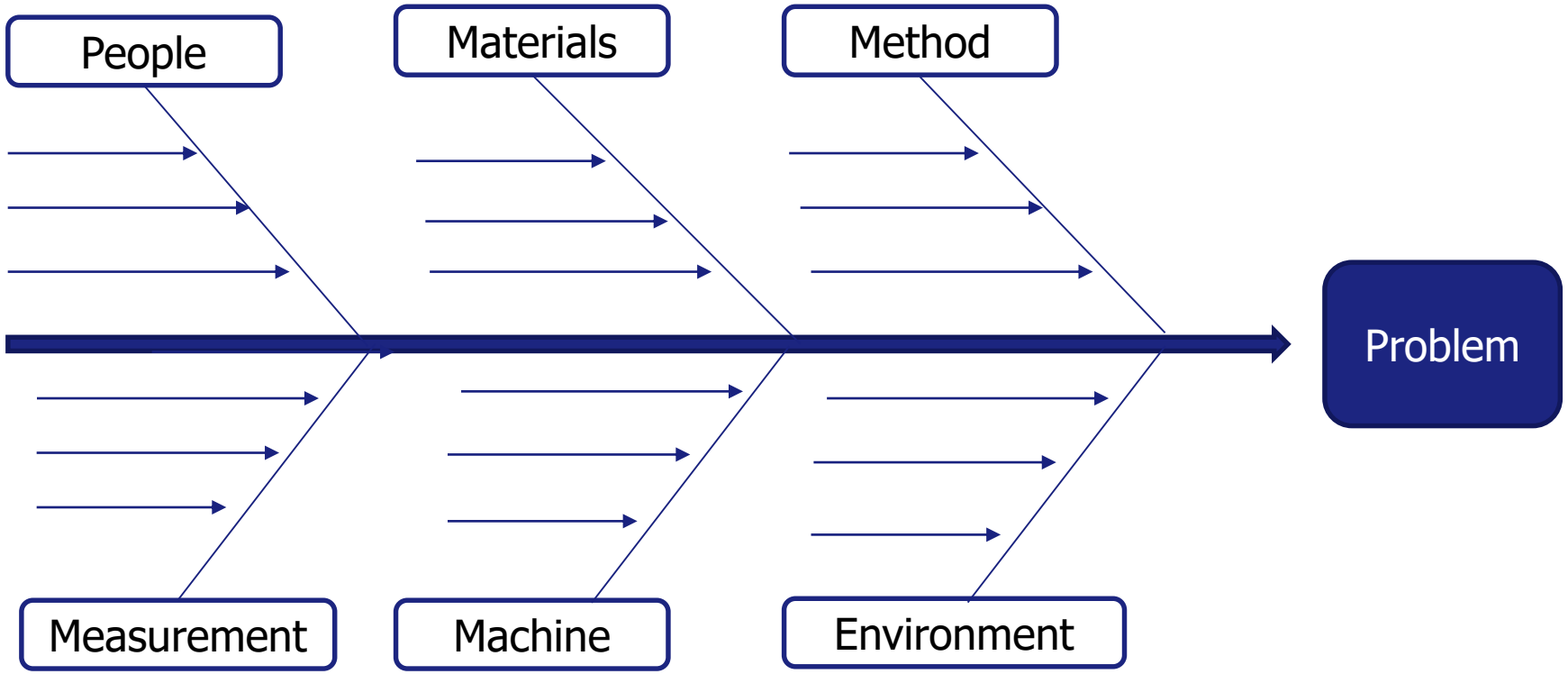
Ask (and answer) the question "Why" 5 times

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



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Common Deficiencies & How to Fix Them

Deficiencies	
Management of Issues	• Failure to immediately assess the criticality of issues • Failure to expeditiously progress the CAPA based on risk • Poor management, completion and effectiveness checks of CAPA's (e.g. Deviations, OOS & Customer Complaints) • Recurrence of similar issues not addressed
Investigation Quality	• Poor identification of issues and assessment • Lack of appropriate severity assessment • Incomplete resolution of sterility issues • Lack of urgency in addressing significant issues

TGA Common Deficiencies – Sterile Medicines

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No.	Chapter
1	1.4 (Xiv) – Root Cause Analysis – (Deviations/CAPA)
2	1.8 (vii) – Significant Deviations – (RCA/CAPA)
3	4.8 – Record in real-time (traceability)
4	4.1 – Control of documentation
5	4.2 – Generation of documentation

Good Manufacturing Practice
MHRA Top 5 Deficiencies

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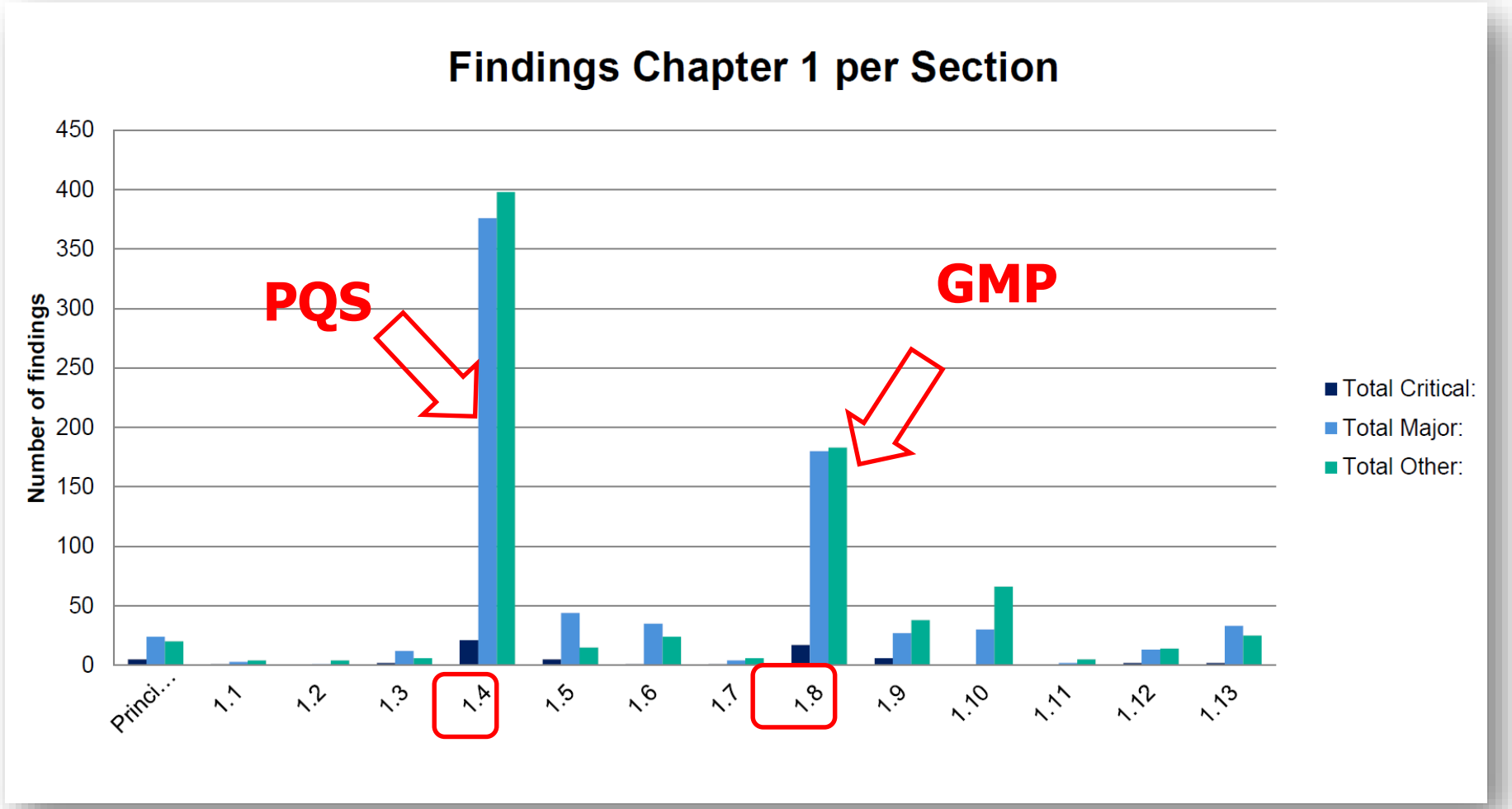
Top 2 Clauses



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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

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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

Issue

- 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

Best Practices

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

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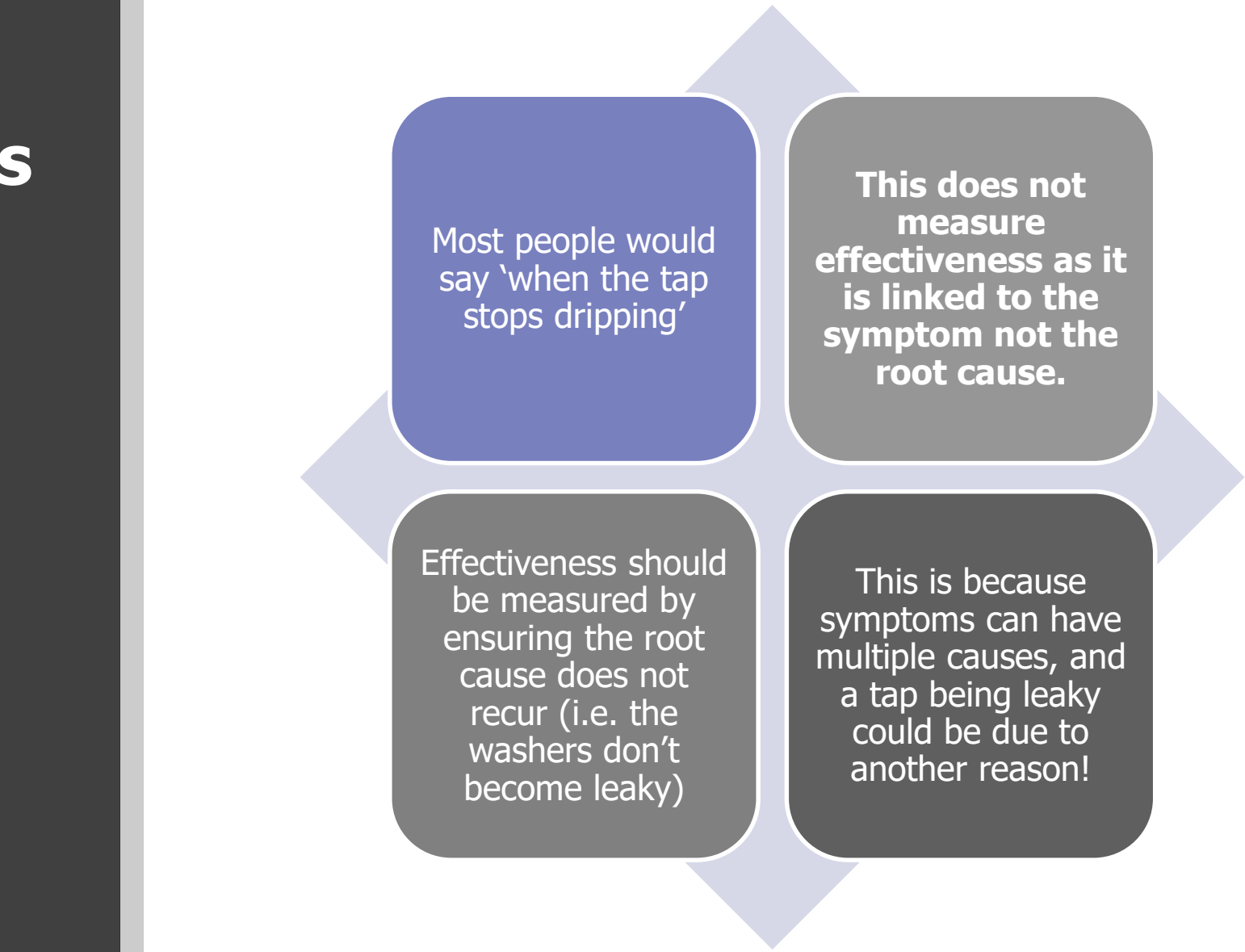
Discussion: CAPA Effectiveness

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



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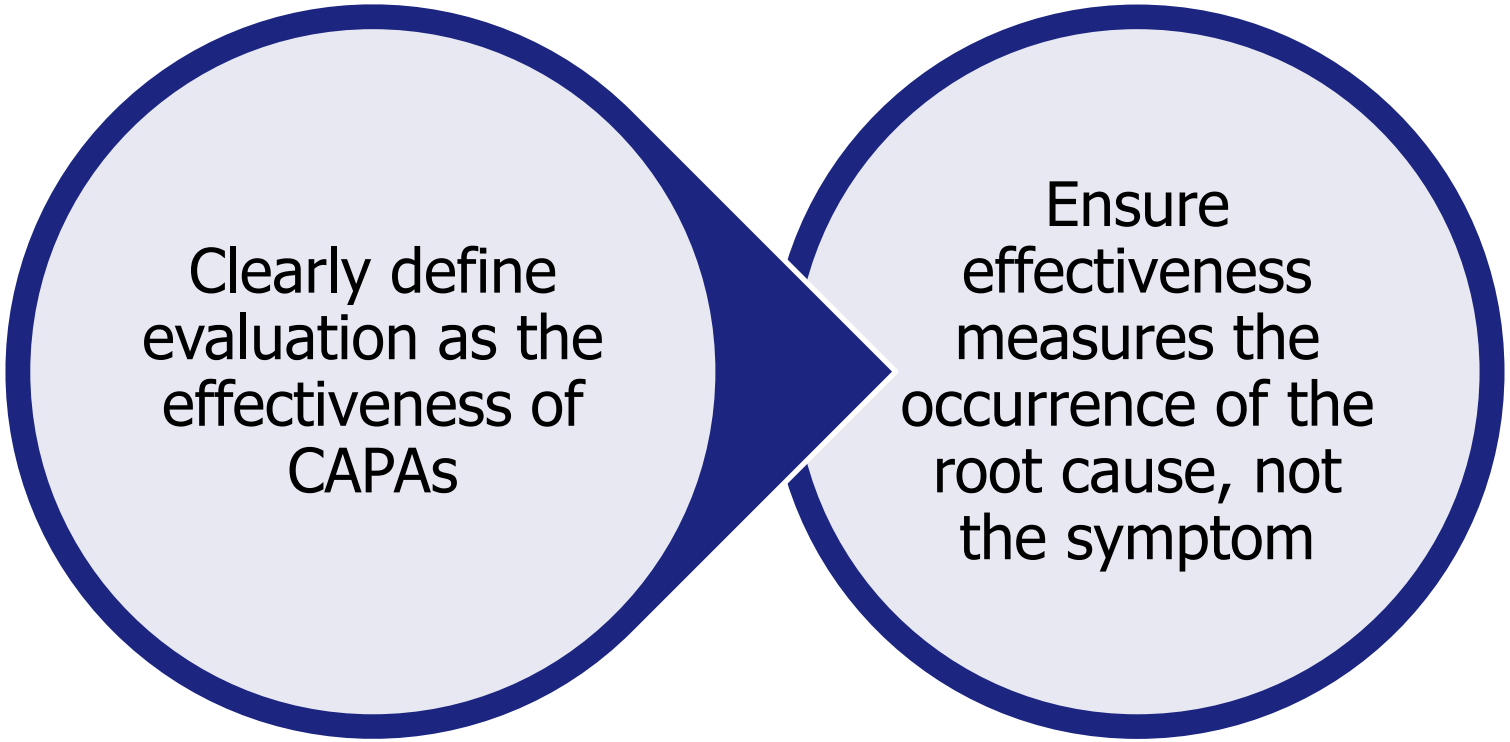
Best Practices



Abuse of Human Error & Retraining

Issue

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

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Thank you for your time.
Questions?

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