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CAPA and Root Cause Analysis

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AGENDA

Corrective and Preventative Action (CAPA) Basics
When to implement a CAPA
Typical CAPA Process
Root Cause Analysis (RCA)
RCA Methods
Case study
What is expected from a CAPA
What Problems to Avoid

CAPA Basics

- What is a CAPA used for
  - Addresses deviations or non-compliance that have already occurred and puts measures in place to avoid them from happening again in the future.
- What does a CAPA do?
  - Aims to collect information regarding an incident
  - Analyzes the information
  - Identifies and investigates quality problems
  - Takes appropriate and effective corrective and preventive action to prevent recurrence

CAPA Basics

- **Corrective Action**
  - Action to eliminate the cause of a detected problem or situation
  - A reaction to a problem
  - Includes defining the problem and correcting it

- **Preventative Action**
  - Action to eliminate the cause of a **potential** problem or situation
  - Implementation of processes to stop future recurrence

When to implement a CAPA

- **When there are deviations from the study's protocol or noncompliance with regulations and institutional policies.**
- Examples:
  - A study visit conducted outside of the protocol window
  - Missing consent signature
  - Enrollment of a subject who did not meet eligibility criteria
  - Implementing changes to the protocol without IRB approval

Typical CAPA Process

- **Begin with a detailed problem description**
  - Describe the problem in detail and ensure it is documented accurately. What occurred, when it occurred
- **Perform a Root Cause Analysis**
  - Determine the problem's root cause, 5 Whys (RCA technique)
- **Implement**
  - Take immediate action to correct the specific problem
  - Create the CAPA and remedy the root cause and ensure the problem does not occur again
- **Check for effectiveness**
  - Ensure the CAPA is successful, if not proceed with an additional CAPA or modify the existing CAPA to make more effective

Root Cause Analysis

- It is a structured process to help identify the underlying reason or reasons why a problem occurred.
- The goal is to find the true cause, so the corrective and preventive actions (CAPA) address the right issue.
- It is possible for there to be multiple causes that contribute to a problem and multiple methods to resolve each cause. The root cause is the most basic cause of a problem that may trigger a chain of additional causes.

RCA Methods

The 5 Whys Method

- Write the problem statement at the top.
  - Example: Adverse events are submitted later than required
- Ask “Why did this happen?” and record the answer.
- For each answer ask “Why?” again.
- Repeat until you have asked at least 5 times or have reached a logical root cause.
- Avoid stopping at human error and look for other weaknesses.

Case Study

ABC Medical Center conducts clinical trials on experimental devices. According to the protocol and regulatory requirements, all serious adverse events (SAEs) must be reported to the sponsor within 24 hours of site awareness.

During a routine audit, it was discovered that three SAEs were reported 5-7 days late.

5 Whys

- Problem: Adverse events are being submitted later than required by the protocol.
  - Why 1: Why were they not submitted per protocol?
    - Because researchers were unsure whether the events met the definition of serious adverse events and waited for confirmation.
  - Why 2: Why did they need to wait for confirmation before escalating?
    - Because researchers did not receive recent training on SAE definitions and escalation procedures.
  - Why 3: Why hadn't they received recent training?
    - Because adverse event training is only including during onboarding and not reinforced regularly.
  - Why 4: Why isn't training included more regularly?
    - Because there are not standardized recurring compliance training programs or ownership for maintaining adverse event reporting.
  - Why 5: Why isn't there standardized ongoing training or ownership?
    - Because adverse event training and oversight were not formally assigned.
- Root Cause: Lack of formal assignment of responsibility for adverse event reporting training oversight.

Corrective and Preventative Actions

Corrective Actions (Fix the cause)

- Implement regular mandatory AE/SAE reporting training for all staff
- Consult the protocol's SAE decision guide and escalation flowchart
- Assign an owner for monitoring reporting timelines

Preventative Actions (Stop future risk)

- Quarterly audits of AE reporting timelines
- Practice SAE scenarios/case studies with staff
- Automated reminders for event documentation

What is expected from a CAPA

A regulator or auditor should be able to answer the following by looking at the CAPA.

1. What happened?
2. What did you do immediately?
3. Why did it happen?
4. What did you change?
5. How do you know it worked?

Problems to Avoid

- Fixing the mistake without addressing why it happened
- Blaming individuals instead of systems
- Vague or generic CAPA language
- No effectiveness check
- Unreasonable Timelines or Deadlines
- Stating that a problem cannot be corrected or prevented due to the availability of staff

Resources

- Corrective and Preventive Action (CAPA): The Definitive Guide (2026)
- Corrective and Preventive Actions (CAPA) | FDA
- CDRH-Learn-Presenation--Corrective-and-Preventive-Action-Basics.pdf

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Thank you

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CAPAs: Researcher's Perspective

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Outline

- When is a CAPA required
- Real world examples of CAPAs
- CAPA best practices

When is a CAPA required?

- Major unanticipated events – some examples
  - External monitor discovered a participant did not meet one of the inclusion criteria
  - Day 1 research specimens missed, and central lab PK testing is a primary study endpoint
  - Clinic RN accidentally stuck themselves with needle when performing a research blood draw
- Minor unanticipated events – some examples
  - Consent form used had an old expiration date, but content did not otherwise differ from the last version
  - Day 1 research specimens missed for optional ancillary banking for future studies
  - Dose modification was made per standard of care, which differs from the protocol. There was no impact on patient safety or primary study aims

CAPA Example #1

- Description
  - Consent used was not current. Coordinator pulled from a shared drive what they thought was the current consent, but it was hard to tell, because the file names were confusing.
- Corrective Action
  - Coordinator and treating investigator explained the error to the participant at their next clinic visit, presenting the correct consent form. The participant reconsented to ongoing participation in the study.
- Preventative Action
  - Going forward, the regulatory coordinator will always employ a standardized naming convention in the eRegulatory Binder. The coordinators were trained at the June 2025 staff meeting to pull the current consent from the eRegulatory Binder.

CAPA Example #2

- Event
  - The protocol requires a screening CT scan within 6 weeks prior to enrollment. At an external study monitor visit on 1/16/26, the monitor noted that the participant's screening CT scan was performed on 9/1/25, and the participant was enrolled on 11/3/25, greater than 6 weeks later.
- Corrective Action
  - The participant was removed from the study, as the sponsor indicated there are no exceptions to eligibility, and this patient's data collected thus far will be unevaluable. The patient has been informed. The patient was randomized to the control arm and will continue to receive treatment off study. There was no impact on patient safety.
- Preventative Action
  - A mandatory pre-enrollment Eligibility Checklist has been created for this study that includes the following prompts: instructions about the timing of radiology evaluations for screening; a field to document the date the Screening CT scan occurred; and the treating investigator's signature and date.

CAPA Example #3

- Event
  - Direct Bilirubin is required per protocol on Day 1 of all chemotherapy cycles. This was not ordered for Day 1 of the 3 most recent chemotherapy cycles for this participant.
- Corrective Action
  - The error was discovered halfway into Cycle 3. The participant was informed of the error and is being closely monitored for liver toxicity by the treating investigator. This was deemed not to increase risk to the patient, as a liver function test panel was performed on Day 1 of Cycles 1, 2 and 3, and the results were normal, and the patient has not displayed clinical symptoms of liver dysfunction.
- Preventative Action
  - A study-specific OncoEMR treatment plan was created. In addition, the research team has established a new process for all studies, whereby the study staff will remind the treating investigator 2 days ahead of each visit of the protocol mandated procedures via email.

CAPA Example #4

- Event
  - A routine audit performed by the study sponsor 1/12/26 found that all 5 participants audited had a consent form on file, and the consent form was signed correctly. However, 3 of the 5 participants audited were missing documentation of the initial informed consent meeting. All participants enrolled in 2022.
- Corrective Action
  - A consent meeting note template was implemented by the research team for all studies starting in April 2023 on paper, with an electronic option available in Epic July 2024. Research staff and investigators were trained to document consent using the consent meeting note template.
- Preventative Action
  - We feel that the current process for documenting informed consent, if consistently followed, is sufficient, and this problem is unlikely to recur.

CAPA Example #5

- Event
  - The 48-hour CTA scan is research billable and to be paid by the sponsor, as per the consent form and Medicare coverage analysis. The participant underwent the CTA scan 12/1/25 and called Dr. X's office on 1/5/26 to complain that she received a bill for the professional fee from Radiology Associates of the Main Line (RAML).
- Corrective Action
  - The patient was advised not to pay the bill, and the study coordinator contacted RAML 1/5/26 to request that the charge be reversed. RAML confirmed via email on 1/6/26 that the charge had been reversed.
- Preventative Action
  - The research team was re-educated by the research manager about procedures with separate technical and professional fees, including the proper use of the "Acquisition Form for non-Epic Research Billable Procedure." The research manager revised the study's "List of Research Billable Procedures" cheat sheet to include a new column with special billing instructions for relevant procedures.

CAPA Best Practices

- Act fast to address patient safety issues and prevent future events.
- Even non-serious noncompliance events require a CAPA.
- The sooner you report a reportable event, the happier the IRB and sponsor will be, because it means you have already put a CAPA in place.
- Description should include specifics (while keeping it brief): event date, protocol timepoint, protocol procedure, problem, root cause
- Submission to the IRB is not a corrective action
- Education alone is usually not a sufficient preventative action
- Research program should periodically review prior CAPAs to ensure entire team is aware of and continuing to implement preventative actions

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