Root Cause Revealed – Finding and Fixing the Real Problem

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Quality Assurance

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Agenda

- CAPA overview
- Defining the problem
- Types of Causes
- Root Cause Analysis Tools
- How to use them for a Corrective Action

5 Steps of CAPA

DETECTION

The first step is to identify the incident or problem

INVESTIGATION

Determining and analysing the root cause of the incident

CORRECTION

Appropriate corrective actions are identified and implemented

REVIEW

The effectiveness of the corrective actions taken is reviewed and evaluated

INCIDENT RESOLVED

The incident is resolved and the documentation is completed

REASONS TO START A CORRECTIVE ACTION

1. **Protocol deviations**: Any deviation from the approved protocol, such as missed assessments, incorrect dosing, or failure to follow study procedures, could trigger a CAPA. Deviations may be identified during monitoring visits, data review, or site self-reporting.

2. **Safety issues**: Any potential safety concerns or serious adverse events (SAEs) that occur during the trial may prompt a CAPA. These could include unexpected adverse reactions, medication errors, or issues with the investigational product itself.

3. **Quality control issues**: Deviations from Good Clinical Practice (GCP) guidelines, standard operating procedures (SOPs), or quality control systems could trigger a CAPA. Examples include issues with study documentation, data management, or laboratory procedures.

4. **Equipment or facility problems**: Any issues with the equipment used in the trial, such as malfunctioning devices or instruments that produce inaccurate results, or problems with the study site facilities, such as temperature excursions or inadequate storage conditions, could necessitate a CAPA.

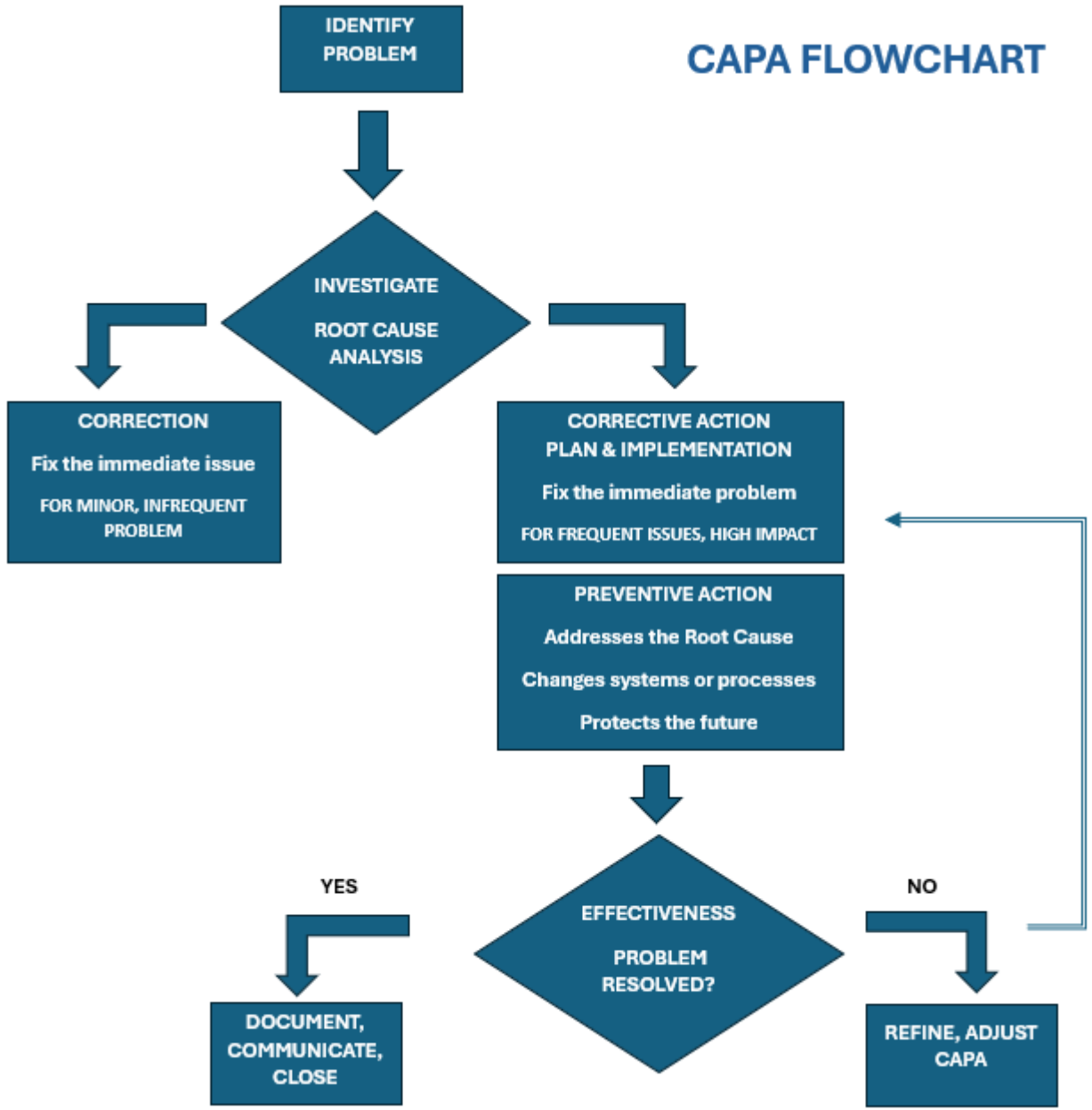
REASONS TO START A CORRECTIVE ACTION

5. Personnel issues: Concerns regarding the qualifications, training, or performance of study personnel, such as investigators, coordinators, or laboratory staff, could prompt a CAPA. This could include inadequate training, non-compliance with study procedures, or failure to follow GCP guidelines.

6. Regulatory observations: Findings from regulatory inspections or audits conducted by health authorities, such as the FDA, may require a CAPA to address any observations or deficiencies identified.

In essence, any issue that has the potential to impact the safety, integrity, or quality of the clinical trial data, or that deviates from established standards and regulations, could trigger the need for a CAPA to investigate the root cause, implement corrective actions, and prevent similar occurrences in the future.

Understanding the Corrective Action process



Corrective Action Template

Corrective Action / Preventive Action Plan

The following form is used to document a single or a series of related deficiencies and the corresponding CAPA plan. The fields included in this form may be modified or deleted based on the organization's specific needs.

Protocol Title / Code	
Qualified / Principal Investigator	

ISSUE			
Date Occurred[1]	Click here to enter a date.	**Date Identified**[1]	Click here to enter a date.
Description	Describe the deviation / deficiency / non-compliance.		
Impact	Describe the impact of the issue on participant safety, rights, and well-being, as well as data integrity. Include a list of affected participants, if applicable.		
References	List any regulation, policy, procedure, or section of the protocol that the issue deviated from.		
Root Cause	Outline the root cause to the issue.		

All changes have been saved

CORRECTIVE ACTION			
Date Implemented	Click here to enter a date.	**Date Completed**[2]	Click here to enter a date.
Description	Describe the corrective action plan in detail.		
Attachments	List documents attached that help support the corrective action.		
Person(s) Responsible	List names of individuals who are responsible for carrying out the corrective action.		
☐ **N/A**	In the event there can be no corrective action, specify the reason.		

PREVENTIVE ACTION			
Date Implemented	Click here to enter a date.	**Date Completed**[2]	Click here to enter a date.
Description	Describe the preventive action plan in detail.		
Attachments	List documents attached that help support the preventive action.		
Person(s) Responsible	List names of individuals who are responsible for carrying out the corrective action.		
☐ **N/A**	In the event there can be no preventive action, specify the reason.		

ADDITIONAL COMMENTS
Include any additional comments or information not noted above. If applicable, outline any plan / procedure to evaluate the effectiveness of the CAPA.

1. If a distinct date is not available, a rough range of dates may be entered.
2. Date may be a projected date if the plan is written prior to implementation / completion. Write "N/A" if not applicable.

CAPA Written By (Print Name & Title)	CAPA Written By (Signature)	Date (dd-MMM-yyyy)
CAPA Approved By (Print Name & Title)	CAPA Approved By (Signature)	Date (dd-MMM-yyyy)

Defining the Problem

Defining the problem statement is much more difficult than it seems

Often focuses on **apparent causes** or beliefs

- “The coordinator forgot to submit the SAE report
- “The PI was out of town and didn’t review it”
- “ The coordinator didn’t notice the serious event”

A typical response might be

- “Tell coordinator to be more careful”

These solutions might help temporarily, but the same problems keep coming back.
Because we haven’t addressed what’s really causing them.

GATHERING "PROBLEM" INFORMATION

5W 2H	Typical questions	Contains
Who?	Who are the people directly concerned with the problem? Who does this? Who should have been involved but was not? Was someone involved who shouldn't be?	Roles and Departments
What?	What happened?	Action, steps, description
When?	When did the problem occur?	Times, dates, place In process
Where?	Where did the problem occur?	Location
Why is it important?	Why did we do this? What are the requirements? What is the expected condition?	Justification, reason
How?	How did we discover it? Where in the process was it?	Method, process, procedure
How Many? How Much?	How many things are involved? How often did the situation happen? How much did it impact?	Number, frequency

Common Issues with Problem Statements

Vague Problem Statements

- We have data quality issues
- The team isn't following procedures
- There are compliance problems

"Apparent Cause" Problem Statement

- Coordinator forgot to report SAE
- Coordinators aren't managing their time well to respond to queries
- Staff needs more training on data entry

Solutions from an apparent cause problem statement

When we stop analyzing at the apparent cause problem statement, we end up with solutions like:

(Problem) Coordinator forgot to report SAE in a timely manner

(Solution) "Tell Coordinator to be more careful"

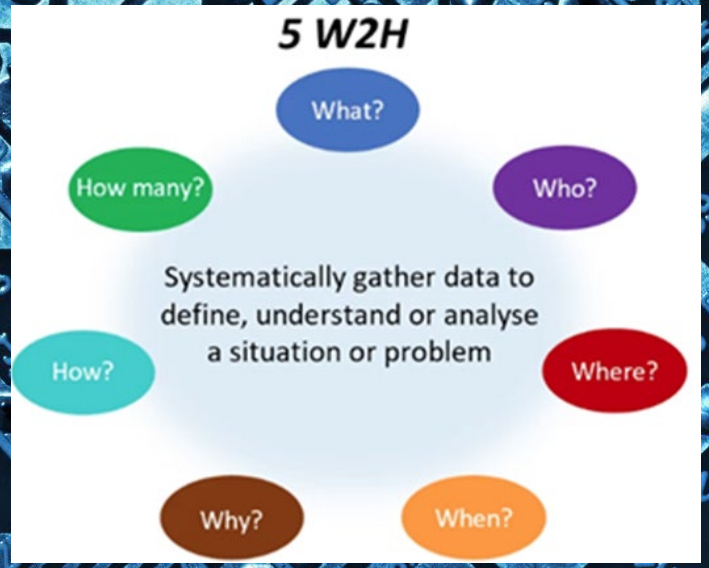
(Problem) Coordinators aren't timely in responding to queries

(Solution) "Remind sites to check email more often"

(Problem) Staff needs more training on data entry

(Solution) "Train staff to double-check their work"

These solutions might help temporarily, but the same problems keep coming back because we haven't addressed what's really causing them.



Key Elements of an Effective Problem Statement

1. Specific and Measurable : Include quantifiable data
2. Time-bound : Define when the problem occurs
3. Impact-focused : Describe consequences
4. Observable : Based on factual evidence
5. Scope-defined : Clear boundaries of the issue

Example Problem Statement
" We are having problems with SAE reporting with multiples studies.

Specific and Measurable

Instead of saying problems with SAE reporting , get specific!

- SAE reports are being submitted late.
- How late? An average of 6.5 days after the 24-hour deadline
- How many? 78% of all SAE report in Q1 2025

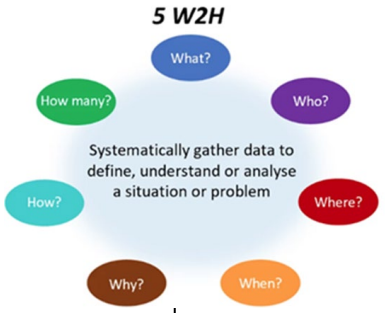
Time bound

- When is this happening?
- This occurred during Q1 2025 (Jan – Mar)
- The pattern started in mid Jan and has continued

Impact – focused

What are the consequences?

- Resulting in 23 protocol deviations
- Potential regulatory citations during upcoming inspections
- Increased monitoring burden requiring additional site visits



Observable

Based on facts, not opinions Be Objective

- Data on hand: submission timestamps, regulatory deadlines, deviation reports
- Not: Sites seem careless, or Staff appears overwhelmed.

Scope – Defined

State clear boundaries

- Affecting 4 out of 12 sites in the cardiology study
- Specifically serious adverse events, not non serious AE's or other safety reports

Our improved problem statement

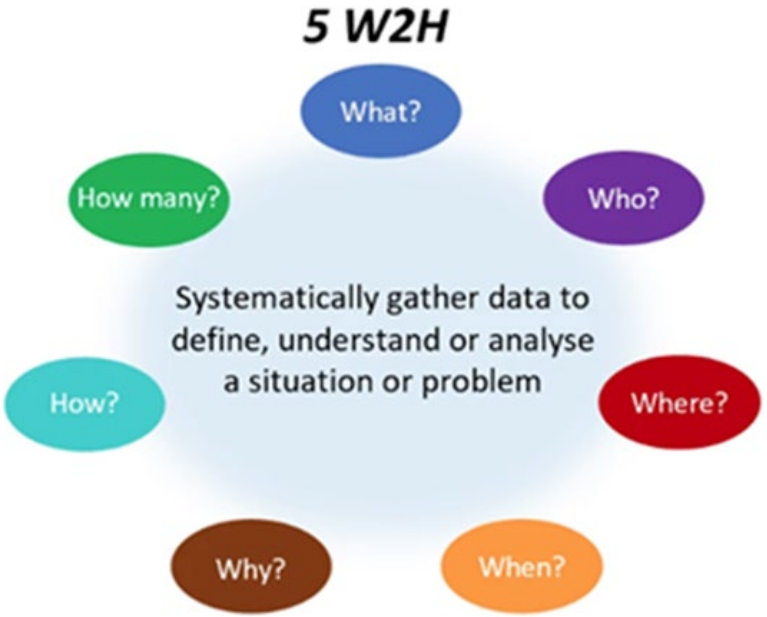
"Four sites in the cardiology study submitted 78% of SAE reports an average of 6.5 days late during Q3 2024, exceeding the required 24-hour reporting deadlines and resulting in 23 protocol deviations with potential regulatory impact.

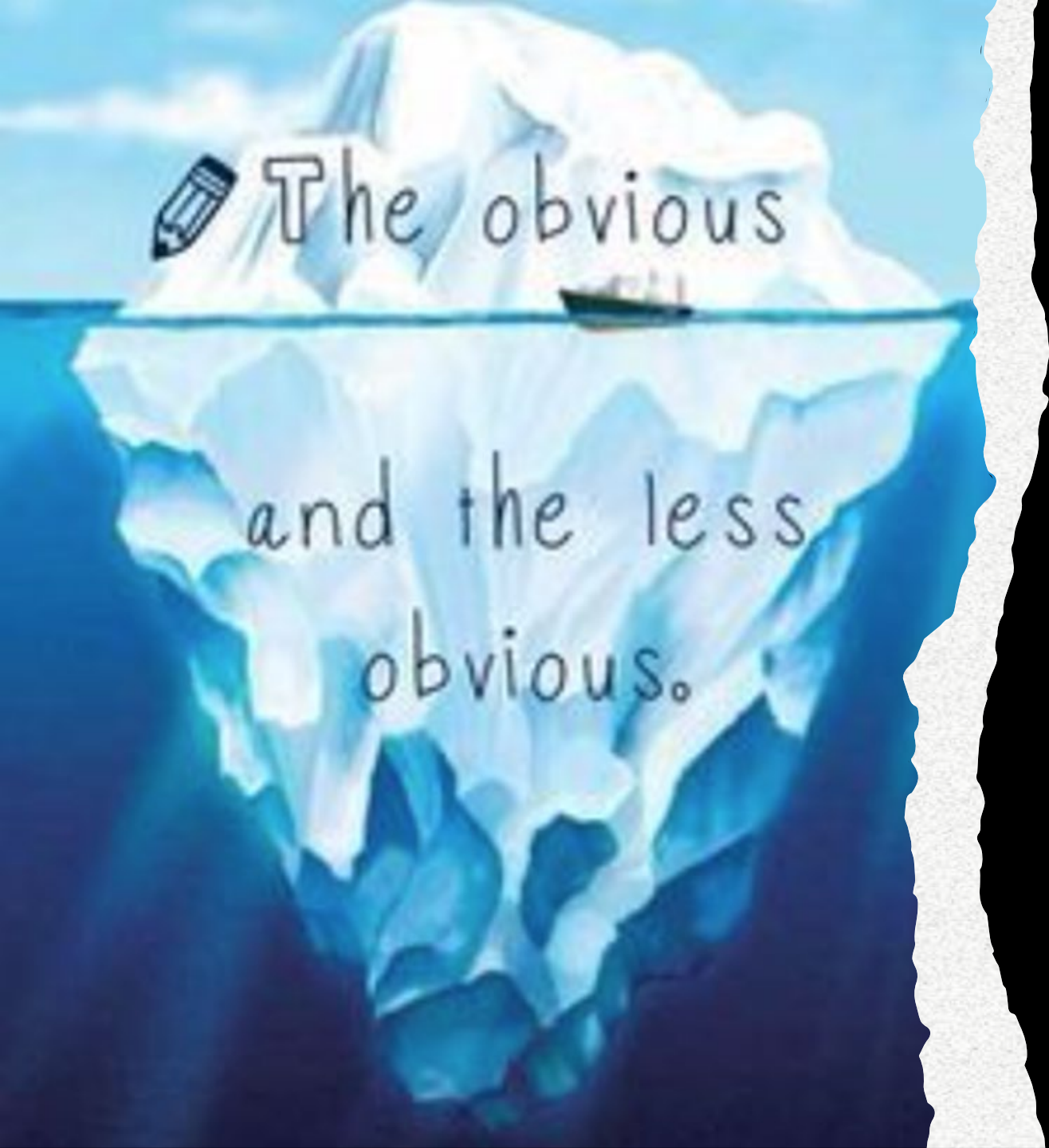
Improved Problem Statements

- **OLD** CCR forgot to report SAE in a timely manner
- **NEW** Submitted SAE reports averaged 8.2 days late over the last quarter. This exceeds the 24-hour regulatory requirement in 73% of the cases.

- **OLD** Coordinators aren't managing their time well to respond to queries
- **NEW** Data monitoring queries remain unresolved for an average of 45 days, with 34% exceeding the 30-day response target

- **OLD** We have data quality issues
- **NEW** Source data verification identified discrepancies in 12% of patient records, primarily in vital signs and concomitant medication documentation.





Moving beyond apparent causes

Understanding Multiple Root Causes

Problem: **Site consistently fails to report SAEs within 24 hours**.

Layer 1 Apparent Causes
- CRC forgets to complete report
- Weekend/holiday coverage gaps
- Unclear reporting procedures

Root Cause Layers

Layer 2 Contributing Causes
- High staff workload and competing priorities
- Inadequate training on safety reporting requirements
- Poor communication between clinical and safety teams

Layer 3 Systemic root causes
- Lack of integrated technology solutions
- Insufficient staffing for study
- Inadequate safety culture and accountability measures

Layer 4 Organizational root causes
- Budget constraints limiting adequate staffing
- Lack of continuous improvement processes
- Inadequate risk management and mitigation planning

Determining Most Probable Root Causes

PICKING THE RIGHT ROOT CAUSE

How strong is the evidence?

- Do you have clear proof this is causing the problem
- Is this just a guess, or do you have data to back it up?

How much impact will this have ?

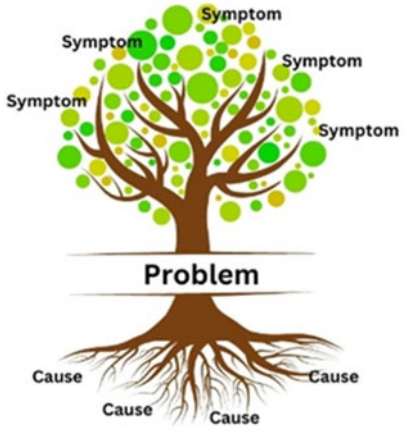
- If we solve this, will it make a big difference?
- Will it prevent the problem from happening again?
- Are we solving a major contributing factor or just a minor piece.

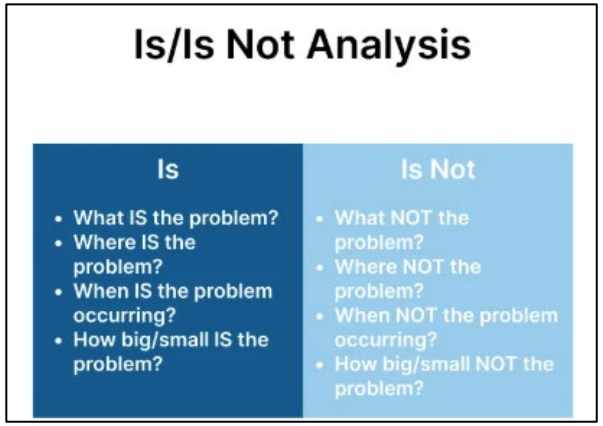
Organizational Control - Do you have the authority to change this?

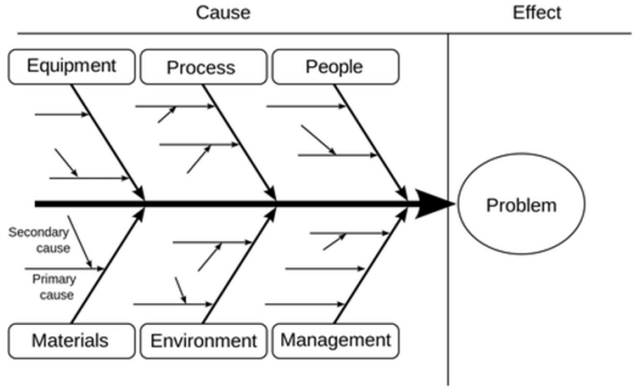
- Do we have the resources, time, money, people to address it.
- Is it something we can influence or is it completely out of our control.

Tools for Investigation

Quality Tools







IS / IS NOT DIAGRAM

Defining the Problem – Staying Focused

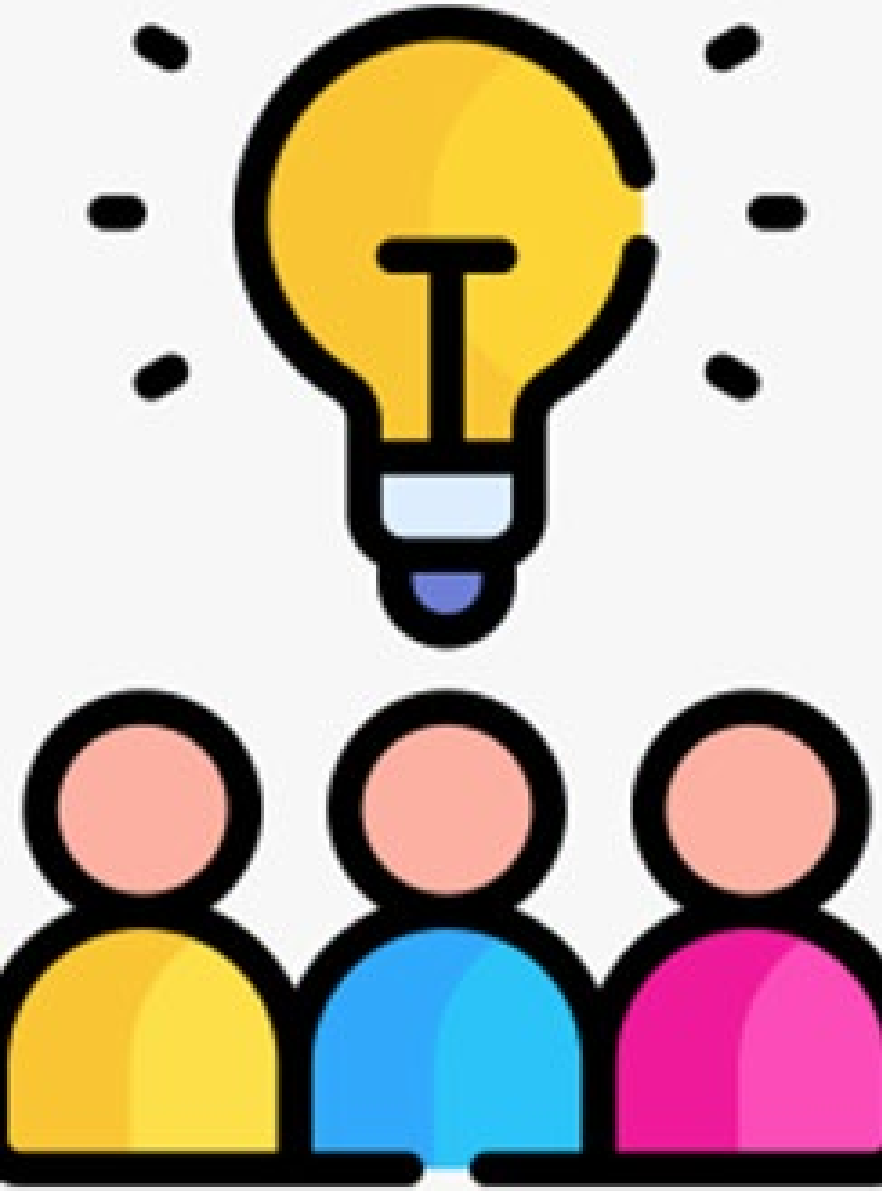
Is / Is-Not

- Helps with scoping
  - Identify concerns
  - Sets a priority
  - Plan next steps

  - Keeps brainstorming from straying
    - What is the deviation
    - Where does it happen
    - When did it start
    - Extent of the issue – How many, How much

  - Other distinctions – Changes
    - What is different
    - What changed

Problem : Late SAE reporting		
Context	**Is**	**Is Not**
What is the problem	**Late submission of SAEs**	Late submission of **AEs.** Protocol deviation reporting delays, annual safety reports
Where is the problem occurring	**Cardiology**	**Radiology**
When is the problem occurring	**Active protocols**	**Inactive** protocols
Who	**PI, Coordinators, RNs**	**Regulatory, Lab**
How	**eIRB, emails**	**Phone call**



Brainstorming

Purpose

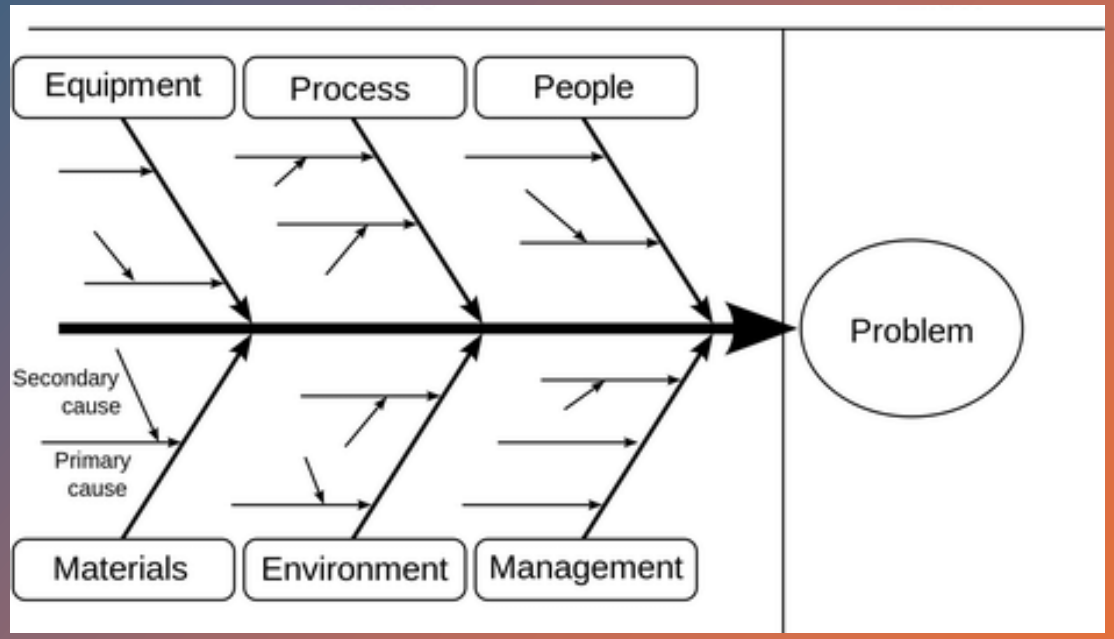
- Generate all possible causes without filtering
- Cast a wide net to map the entire iceberg
- Aim for comprehensive understanding, not immediate answers

What brainstorming is NOT

- Solving the problem
- Debating which causes are “right”
- Assigning blame
- Jumping to solutions

After brainstorming

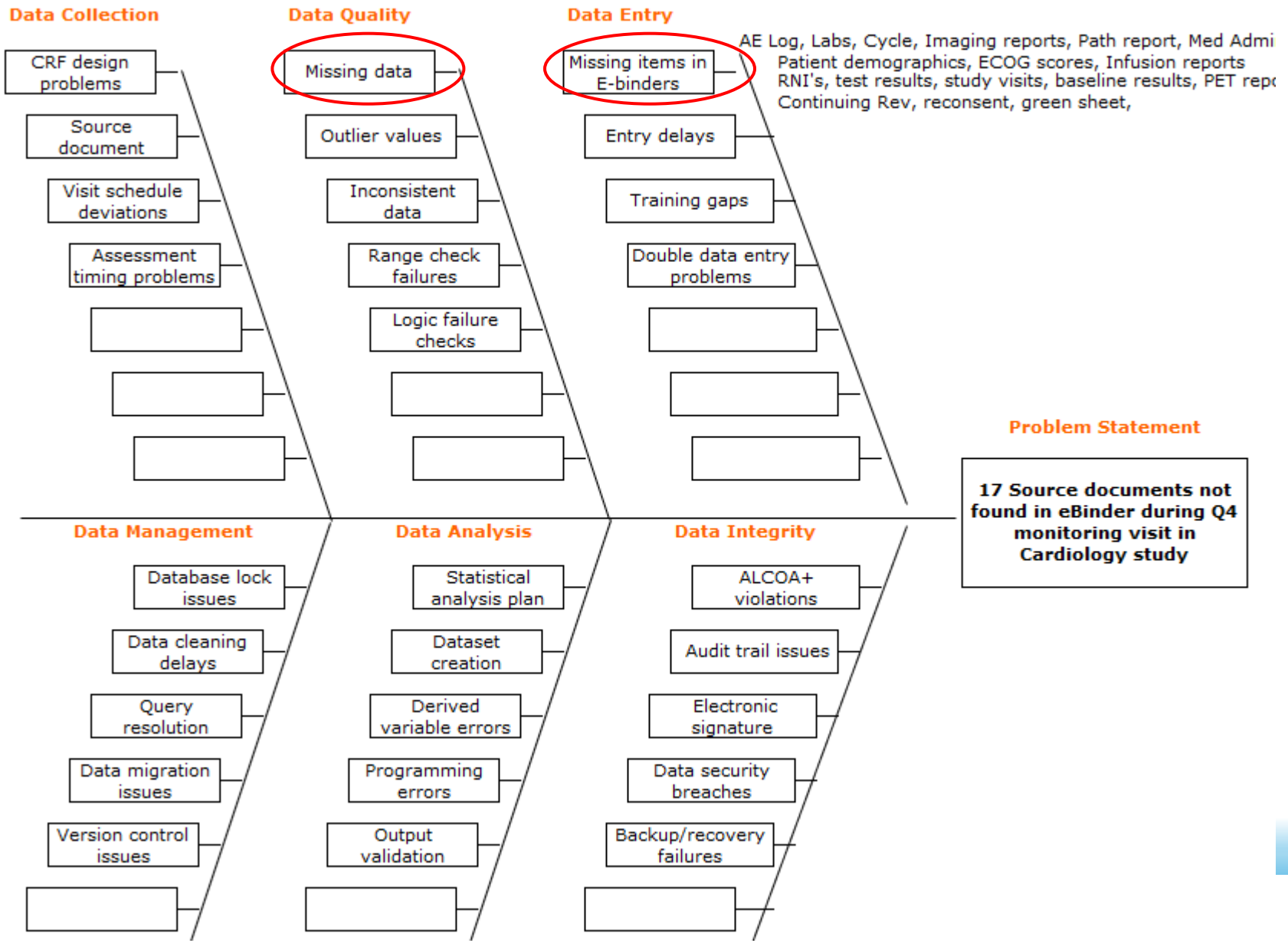
- Analyze using Fishbone diagram or 5Whys
- Determine which causes are root (why its happening) vs symptom (surface issue)
- Evaluate evidence supporting each cause



Cause and Effect Diagram

- Also known as Fishbone diagram
- Helps avoid stopping at the most obvious cause
- Helps to visualize causes vs symptoms

Fishbone diagram using different categories




POLL SURVEY - DATA ENTRY

DATA ENTRY POLL

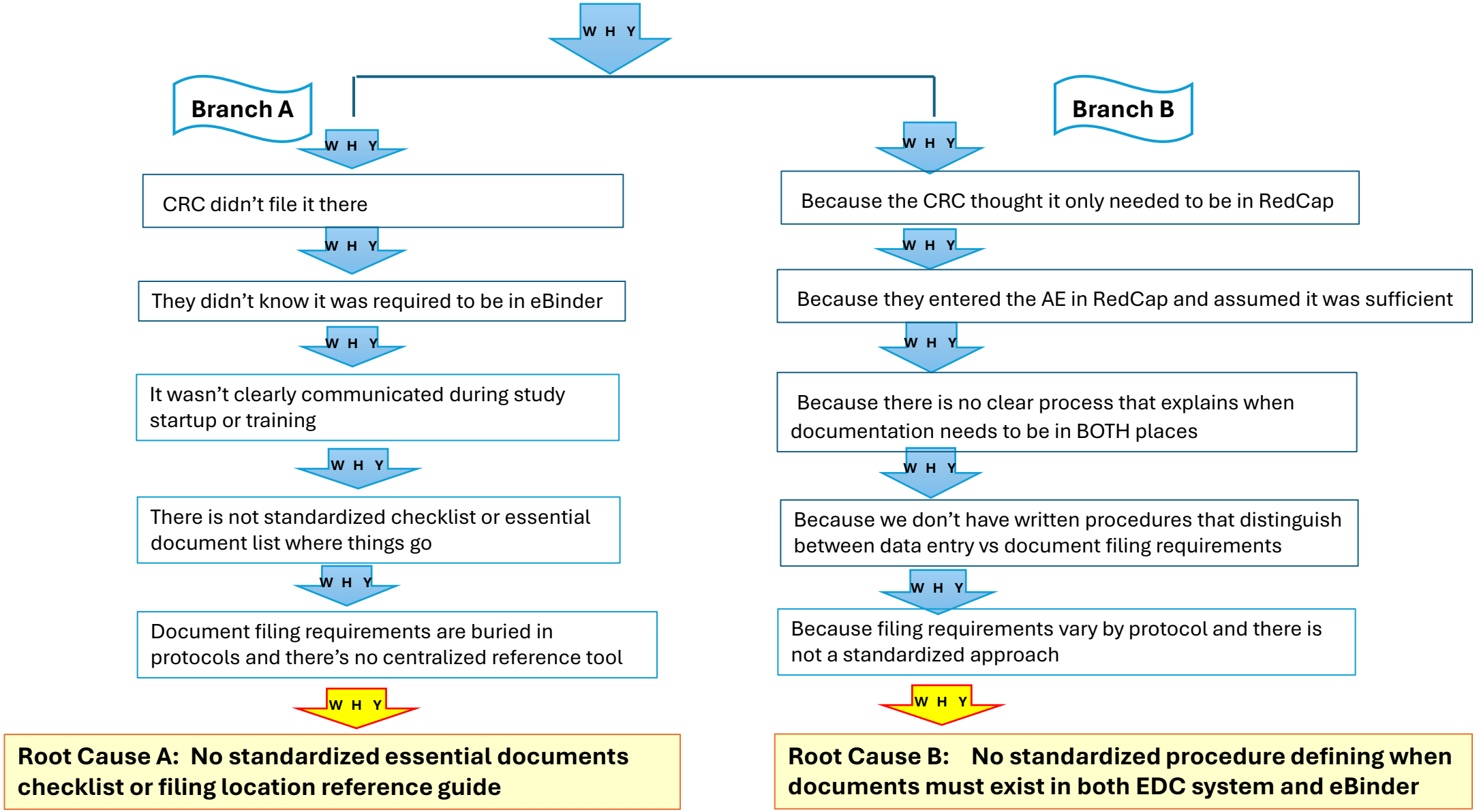
Choose the issues that have impacted data entry accuracy for you (multiple choice)

1. Time pressure / too many tasks at once
2. Unclear or confusing CRF fields / questions
3. Not enough training on the EDC system
4. Different protocols have different data entry requirements
5. Interruptions while entering data
6. No standardized templates or checklists to follow
7. Difficulty understanding what belongs in source vs CRF
8. Difficult to know when documents need to be in both eBinder and REDCap, etc
9. EDC system is slow or has technical problems

5 Whys

5 Whys E BINDER STORAGE

Problem statement: 17 documents were not found in e-Binder



ROOT CAUSE ANALYSIS: BRANCH A

Knowledge/Process Gap

WHY #1	**Why is the AE log not in eBinder?** → *Because the coordinator didn't file it there.*
WHY #2	**Why didn't the coordinator file it there?** → *Because they didn't know it was required to be in eBinder.*
WHY #3	**Why didn't they know it was required?** → *Because it wasn't clearly communicated during study startup or training.*
WHY #4	**Why wasn't it communicated during training?** → *Because there's no standardized study startup checklist that specifies where documents should be filed.*
WHY #5	**Why is there no standardized checklist?** → *Because document filing requirements are buried in protocols and there's no centralized reference tool.*

ROOT CAUSE A: No standardized essential documents checklist or filing location reference guide

ROOT CAUSE ANALYSIS: BRANCH B

Process/Procedure Gap

WHY #1	**Why is the AE log not in eBinder?** → *Because the coordinator thought it only needed to be in REDCap.*
WHY #2	**Why did they think it only needed to be in REDCap?** → *Because they entered the AE in REDCap and assumed that was sufficient.*
WHY #3	**Why did they assume data entry in REDCap was sufficient?** → *Because there's no clear process that explains when documentation needs to be in BOTH places.*
WHY #4	**Why is there no clear process?** → *Because we don't have written procedures that distinguish between "data entry" vs. "document filing" requirements.*
WHY #5	**Why don't we have written procedures?** → *Because filing requirements vary by protocol and we've never created a standardized approach.*

ROOT CAUSE B: No standardized procedure defining when documents must exist in both EDC system AND eBinder

CORRECTIVE / PREVENTIVE ACTION

One Solution Addressing Both Root Causes

CORRECTIVE ACTION

Create Study Document Management Toolkit

aka (New study documents)

Two integrated components:

Component 1: **(Addresses Root Cause A)**	Document Storage Location Map • One-page reference guide listing every document type and its required location(s) • Study-specific, provided at startup
Component 2: **(Addresses Root Cause B)**	Dual Filing Procedure Guide • Clear written procedure explaining when documents must exist in BOTH EDC and eBinder • Decision tree: "Data entry only" vs. "Data entry + document filing" • Examples: AE logs, lab reports, protocol deviations all require dual filing

PREVENTIVE ACTION

- Provide toolkit to all coordinators at study startup
- Include in new staff onboarding checklist
- Update toolkit when eBinder structure or protocol requirements change
- Incorporate document filing verification into the study monitoring visits

Example – Document Storage Location Map

DOCUMENT STORAGE LOCATION MAP

DOCUMENT TYPE	STORAGE LOCATION	TIMELINE
REGULATORY DOCUMENTS		
IRB Approval Letter	e-Binder, eIRB, Oncore	Within 24 hours
Signed Informed Consents	e-Binder, Subject files	Same day
CVs, Medical Licenses	e-Binder, eIRB, Oncore,	Annual update
Sponsor Approval	e-Binder, eIRB	Within 24 hours
Financial Disclosure Agreement	e-Binder, e-IRB	Within 24 hours
Site Initiation Letter	e-Binder, e-IRB	Within 24 hours
CRF & DATA ENTRY		
Adverse Events	AE log, IRB-RNI, Oncore	Within 24 hours
Query Responses	Redcap, e-Binder notes	Per protocol
Demographic data	Redcap	Same day
LAB DOCUMENTS		
Lab reports	e-Binder, subject files	Same day
Lab Data Entry	Redcap	Within 48 hours
PI Review Signature	e-Binder- subject files	Within 72 hours
SOURCE DOCUMENTS		
Progress Notes	e-Binder- subject files	Same day
Subject diary	e-Binder- subject files	Same day
STUDY LOGS		
Screening Log	Regulatory Binder, e-Binder	Same day
Enrollment Log	Regulatory Binder, e-Binder	Same day
Concomitant Med Log	Regulatory Binder, e-Binder	Same day
Protocol Deviation Log	Regulatory Binder, e-Binder	Same day
Unanticipated Event log	Regulatory Binder, e-Binder	Same day
AE log	Regulatory Binder, e-Binder	Same day
Delegation of Authority log	Regulatory Binder, e-Binder	Same day

Updated Corrective Action Plan

Corrective Action / Preventive Action Plan

Protocol Title / Code	Protocol Title
Qualified / Principal Investigator	Wonderful PI

ISSUE			
Date Occurred[1]	20-Oct-2025	**Date Identified**[1]	10-Nov-2025
Description	17 Source documents not found in eBinder during Q4 monitoring visit in Cardiology study. It was 38% of requested documents (17 of 45). .		
Impact	This creates regulatory risk during FDA inspection and added additional hours for CRC locating documents. The monitoring visit was extended for 3 hours locating these documents.		
References	21 CFR Part 312.62 Investigator Record Keeping		
Root Cause	Root Cause A: No standardized essential Document checklist or filing location reference guide. Root Cause B: No standardized procedure that defines when documents must exist in both EDC system and e-Binder		

CORRECTIVE ACTION			
Date Implemented	01-Dec-2025	**Date Completed**[2]	22-Dec-2025
Description	Create document management toolkit. Root Cause A - Create Document Storage Location Map. One page reference guide listing every document type and its required locations. Clearly indicates when dual filing is required. Study – specific, provided at start up. Root Cause B - Dual Filing Procedure Guide Clear written procedure explaining when documents must exist in both EDC and eBinder.		
Attachments	Document Storage Map reference guide. Filing Procedure XX-X-XXX version1		
Person(s) Responsible	Coordinator		
☐ **N/A**	In the event there can be no corrective action, specify the reason.		

PREVENTIVE ACTION			
Date Implemented	07-Jan-2026	**Date Completed**[2]	29-Jan-2026
Description	Provide toolkit to all coordinators at study start up when applicable. Include in new staff onboarding checklist Update toolkit when eBinder or protocol requirements change Incorporate document filing verification into study monitoring visits.		
Attachments	Updated Onboarding checklist .		
Person(s) Responsible	CRC , PI		
☐ **N/A**	In the event there can be no preventive action, specify the reason.		

ADDITIONAL COMMENTS
At the next monitoring visit Feb 2026, document location will be reviewed

1. If a distinct date is not available, a rough range of dates may be entered.
2. Date may be a projected date if the plan is written prior to implementation / completion. Write "N/A" if not applicable.

Principle Investigator

CAPA Written By (Print Name & Title)	CAPA Written By (Signature)	Date (dd-MMM-yyyy)

Using the Tools Together

1

Start with the

Is / Is-Not to define the problem

2

Brainstorming

Generate all possible causes without filtering

3

Build a **fishbone** diagram to visualize the problems. Helps organize the different types of factors that might be contributing to your problem

4

Prioritize most impactful causes

- Use **5 whys** on highest priority targets to dive deeper into causes

Key Take-aways

Move	Move beyond single-cause thinking to multi-causal analysis
Use	Use structured tools consistently and systematically
Invest	Invest time in proper problem definition and investigation
Address	Address root causes at organizational, systemic, and process levels
Monitor	Monitor effectiveness and adjust solutions based on results

Thank You!