Common Audit Findings
Root Cause Analysis
Corrective & Preventive Actions

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Objectives

01 Review common audit findings and solutions

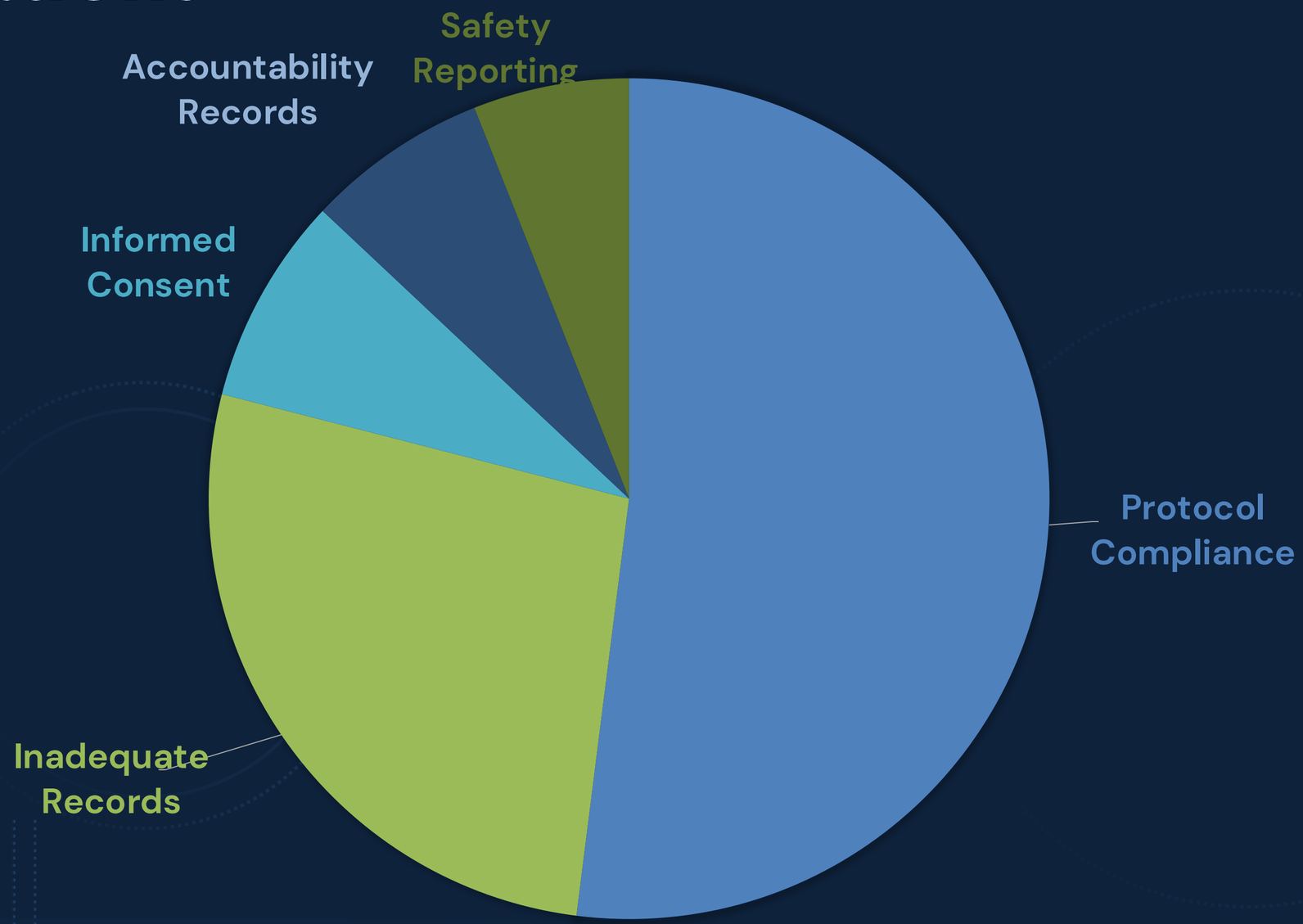
02 Overview of conducting a root cause analysis

03 Activity: identify the root cause

04 Discuss corrective and preventive actions for protocol deviations

Common Audit Findings

Top Citations



Protocol Compliance

Missed visits

Missed procedures

Out of window visits

Ineligible participants

Changes made to protocol without IRB approval

Failure to report or document deviations

Protocol Compliance: Solutions

Read the protocol before starting the study

- Does the protocol require anything new/different or outside standard practice

Follow the protocol as submitted and approved by the IRB

- The protocol is the complete map and procedure guide to conducting the study
- Submit additional treatment plans and procedures to the IRB if not already included in the protocol

Build visit checklists, visit flowsheets, or data collection forms following the approved protocol

If a deviation occurs more than once, determine if a protocol modification is appropriate

Document all deviations and investigator review and assessment of deviations

- Report deviations as applicable

Eligibility Example

Protocol inclusion criteria includes:

- Ages 13-17
- Diagnosed with social anxiety
- No prior cognitive behavioral therapy for anxiety

Visit checklist includes:

- Confirm age between 12-18
- Confirm participant has social anxiety symptoms
- Confirm parental permission

Online screening survey includes:

- Open text entry for the participant's age
- No questions about prior diagnoses or therapy

There is potential to enroll ineligible participants (age, diagnosis, and prior therapy) due to inconsistent study materials and incomplete screening information.

Participant Protections & Adverse Events

- Lack of documentation of adverse events
- Lack of documentation of adverse event review, assessment and attribution by an investigator
  - Relationship (related, unrelated) and expectedness are essential for AE documentation and reporting requirements
  - Incomplete documentation/management of participant complaints
  - Incomplete DSMP requirements
- Discrepancies between source and case report forms (e.g., and AE was noted in the source record but not recorded on the AE log)
- Failure to follow reporting requirements

Participant Protections & Adverse Events: Solutions

Evaluate the AEs in real-time

Review the reporting requirements

- IRB reporting requirements
- DSMP requirements
- Funder requirements

Participant Records

Missing source documentation

Incomplete questionnaires

Incomplete assessments

Discrepancies in records

Participant Records: Solutions

- Read the protocol and review the case report forms (CRFs)/database carefully before starting the study
  - Ensure the CRFs capture the necessary study data
  - Ensure study source captures the necessary study data

- Review data regularly (assigned team members and the PI)
  - Set up regular research team meetings to review data and protocol conduct

- Avoid “CRF build-up”
  - Complete data forms in real-time

- Ensure maintenance and access to records as required

Data Management

- Untimely data entry
- Changes made to data without documentation
- Changes to forms in the middle of study
  - Ensure previous data is not affected or corrections are documented
- Monitoring efforts not documented
- Sharing log-in credentials

Documentation Practices

- Making changes without documentation
- Documents signed by someone other than the persons involved
- Unsigned Notes to File
- Back-dating documentation
- ALCOA-C Principals
  - Attributable
  - Legible
  - Contemporaneous
  - Original
  - Accurate
  - Complete
- Incomplete forms and checklists

Informed Consent

- Use of incorrect version
- Changes made from IRB-approved version
- Lack of re-consent providing new information when required by the IRB
- Inadequate documentation of consent (or the process)
  - Missing participant signature or date
  - Missing personnel signature or date
  - Lack of documentation of participants receiving a copy of the signed consent form
  - Checkboxes left blank
- Missing consent

Informed Consent

- Study procedures performed prior to consent
  - Ensure there is documentation if procedures were completed as part of another study
- Consents signed by personnel not involved in the consent process or not approved personnel
- Consent signatures back-dated
- Consent signatures by someone other than the participant
- Missing required elements of consent

FUN Study Consent Session	**Invitees**
Monday, March 24, 2025 from 5:00 PM to 6:00 PM	*Accepted*
Please join us to learn more about the FUN study.	Cassandara Myers (Organizer)
	Rachel Green
	Phoebe Buffay
	Ross Geller
	Joey Tribbiani
	Declined
	Marisa Corbett
	Monica Geller

Statement of Consent:

Your signature documents your consent to take part in this research.		
Ross Geller		
Printed Name of Participant		
Ross Geller		3/24/2025
Signature of Participant		Date
Marisa Corbett		
Printed Name of Person Obtaining Consent		
Marisa Corbett		4/18/2025
Signature of Person Obtaining Consent		Date

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Printed Name of Participant		
Ross Geller		3/24/2025
Signature of Participant		Date
Cassandra Myers		
Printed Name of Person Obtaining Consent		
Cassandra Myers		4/18/2025
Signature of Person Obtaining Consent		Date

Informed Consent Process Documentation:

The participant attended the FUN Study Consent Session on 3/24/2025 which provided a detailed overview of the study procedures and review of the consent form in a group meeting setting. The participant signed the informed consent form at the conclusion of the session on 3/24/2025 after being provided ample time to review the document and ask questions. Study personnel, Cassandra Myers, led the group consent session on 3/24/2025 but signed this informed consent form on 4/18/2025. No study procedures were completed prior to the consent form being signed by both parties. The participant was provided a copy of the signed informed consent form.

Document the Process

How do you show that participants went through the consent discussion, were given time to consider participation and ask questions, that they signed the form before completing other procedures?

_____Yes	_____No	Participant and/or the participant's legally authorized representative (LAR) was given a copy of the consent document/HA to read.
_____Yes	_____No	Ample time was provided for reading the consent document/HA, and the participant (or participant's LAR) was encouraged to ask questions.
_____Yes	_____No	All questions and concerns were addressed to the satisfaction of the participant (or participant's LAR) prior to signing the consent document/HA.
_____Yes	_____No	The PI or Co-I was available for questions prior to the subject signing the consent/HA.
_____Yes	_____No	The subject (or subject's LAR) agreed to participate in the study and signed/dated the consent document/HA.
_____Yes	_____No	A copy of the signed consent document/HA was provided to the participant (or participant's LAR). ❑ Verbal consent was obtained (per IRB approved consent process). Documentation of the process and the individual(s) witnessing the process is described below.
_____Yes	_____No	No procedures specifically related to the study were performed prior to the participant signing the consent document.

Investigational Product

- Lack of drug diaries to determine participant adherence
- Lack of documentation addressing accountability
  - Dispensing
  - Compliance by participant
  - Product returned
  - Discrepancies between product returned and product taken
  - Education and training (initially and ongoing)
- Storage area not secure
- Incorrect dose prescribed

Subject ID # and/or initials	Lot or Kit Number	# Bottles, Vials, etc.	Amount of Study Drug per Bottle, Vial, etc.	Total Amount Dispensed	Initials	Date Dispensed	Date Returned	# of Bottles, Vials, etc. Returned	Total Amount Returned	Balance: Number Dispensed Less Number Returned	Comments: Subject lost, discarded, etc.	Initials

Regulatory Administration

Missing essential documents, including but not limited to:

Delegation of Authority Log
Screening/Enrollment Log
CVs/resumes
Medical Licensures
Study Correspondence
Source Documents
Protocols
IRB Submissions/Approvals

Regulatory Administration

- Implementing changes prior to IRB approval of amendments
- Discrepancies between the protocol and the informed consent form
- Missing or incomplete delegation of authority log
- Use of materials not approved by the IRB
  - All participant-facing materials, including templates and verbal scripts must be IRB-approved
- Regulatory maintenance and storage

Training & Staff Qualifications

- Lack of training documentation
  - Study start-up and initiation
    - Intervention procedures
    - Data management
  - GCP
  - Protocol amendments
  - Protocol-specific procedures or specialized training
- Delegation of study tasks to personnel not licensed or qualified to perform those tasks
- Personnel not approved by IRB

Documentation of Training

Description of Completed Training	Training Date	Method*	Staff Signature

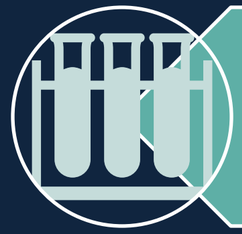
**Method: Should describe what type of training was completed. Examples include Self-Review which could include completing online video-based training or document reading or Guided which includes when a trainer or other individual is leading a training.*

Principal Investigator		IRB Number	
Protocol Number		Study Title	

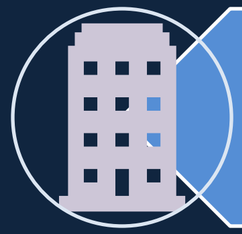
Trainee Name	Training Title/Topic	Training Format (include trainer name if applicable)	Training Date	Trainee Signature

Facilities & Equipment

Lack of documentation of laboratory inspections/certifications



Inadequate specimen handling



Inadequate facilities for specimen collection, processing, and storage

Other Area Observations

- Use of external electronic systems, not approved by Drexel or TPRM
- Use of personal devices (computers, cell phones) to store or transmit study information
- Use of personal or non-Drexel email accounts to store or transmit study information
- Umbrella studies or add-on studies
- Oversight documentation
  - PI has overall responsibility
  - Review deviations
  - Review adverse events
  - Review complaints
  - Evaluate training and training needs
  - Faculty Investigator and Student Investigator roles

Root Cause Analysis (RCA)

What is an RCA?

A Root Cause Analysis is a systematic process to investigate problems, such as adverse events or protocol deviations, to find the underlying, fundamental causes, rather than just the surface level symptoms.

The goal of an RCA is to move beyond assigning individual blame and identify system failures in order to develop and implement effective solutions to prevent recurrence and improve the safety and integrity of the research.

5 Whys

Ask “Why?” until you reach the underlying cause:

Problem: An ineligible participant was enrolled.
Why? → Eligibility checklist indicated ages 12–18
Why? → Checklist not updated with protocol
Why? → No version control system
Why? → Staff were unaware of the new protocol
Why? → Inadequate communication process

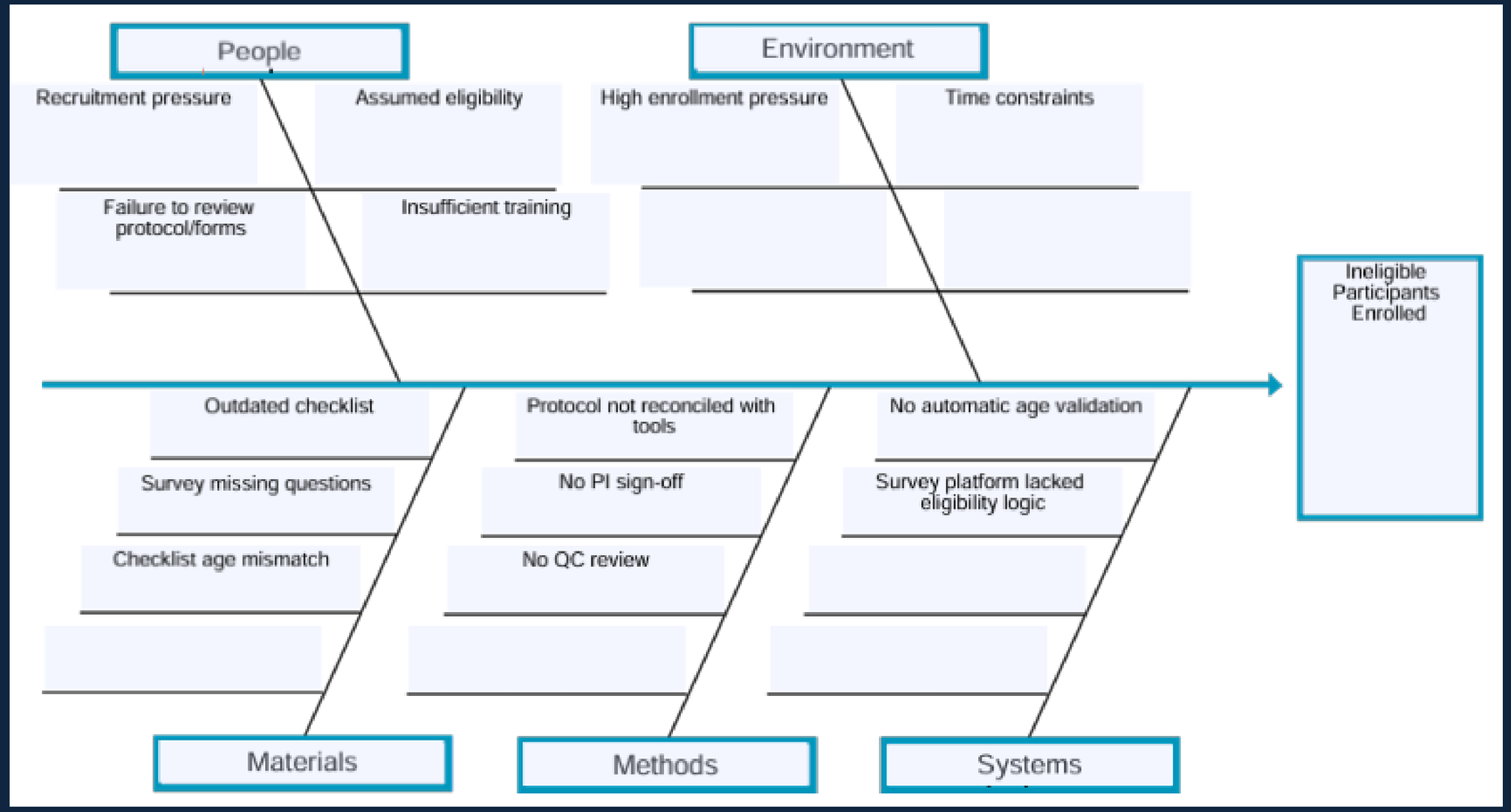
5 Whys

Drexel University
Research Quality Assurance Program
Root Cause Analysis – Documentation Form

1.	**Protocol #/Title** **THE EVENT** : Describe what happened **PROBLEM STATEMENT:**	RCA Team Members: Team Leader:
2.	**BACKGROUND & FACTORS SUMMARY**	
	What was the sequence of events that was expected to take place? Attach flowchart if available.	
3.	**Documentation of 5 Why's** (Add sections as necessary)	
3.1		

Fishbone Diagram

Categorize potential causes (e.g. People, Methods, Materials, Environment) and brainstorm under each.



Failure Mode and Effects Analysis (FMEA)

Scoring Definitions (1-10)

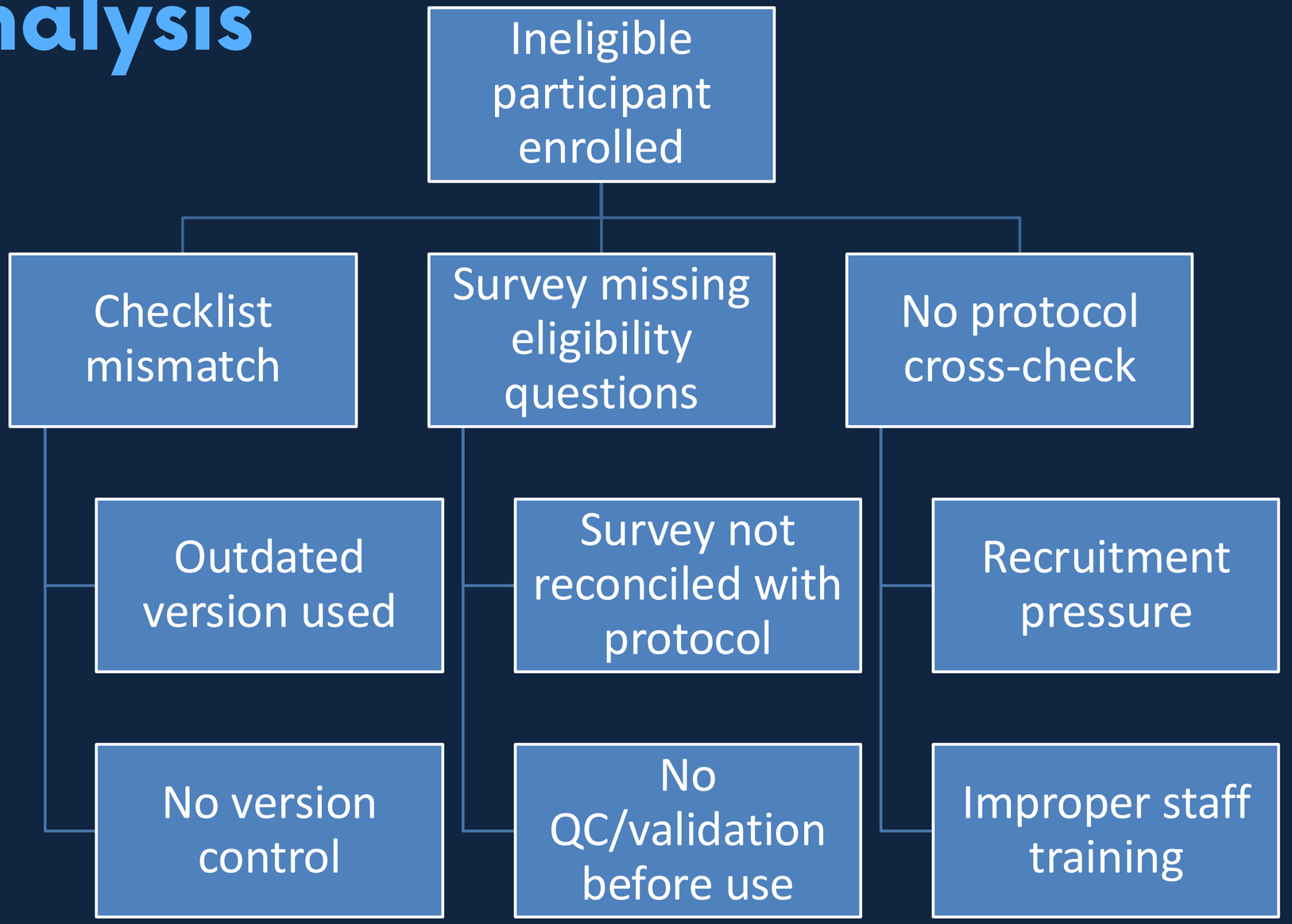
- **Severity (S)** – impact on participant safety, data integrity, regulatory exposure (1-negligible, 10-significant)
- **Occurrence (O)** – likelihood the failure will occur (1-very unlikely, 10-very likely)
- **Detectability (D)** – likelihood the failure will not be detected before harm/data use (1-easily detected, 10-undetectable)
- **Risk Priority Number (RPN)** = S x O x D
  - Higher RPN = higher priority

Failure Mode and Effects Analysis (FMEA)

Failure Mode	Effect	S	O	D	RPN
Survey missing prior therapy Q	Enrolled participant with prior therapy (bias)	7	7	6	294
No version control	Staff use outdated tools (eligibility errors)	6	7	7	294
Staff assumption (no cross-check)	Enrolled ineligible participant	6	6	8	288

Fault Tree Analysis

A top-down diagram that maps out logical pathways leading to a problem (using and/or logic)



RCA Activity

Noncompliance Example

Event: Three participants were enrolled and began study activities prior to signing the informed consent form.

Additional Context:

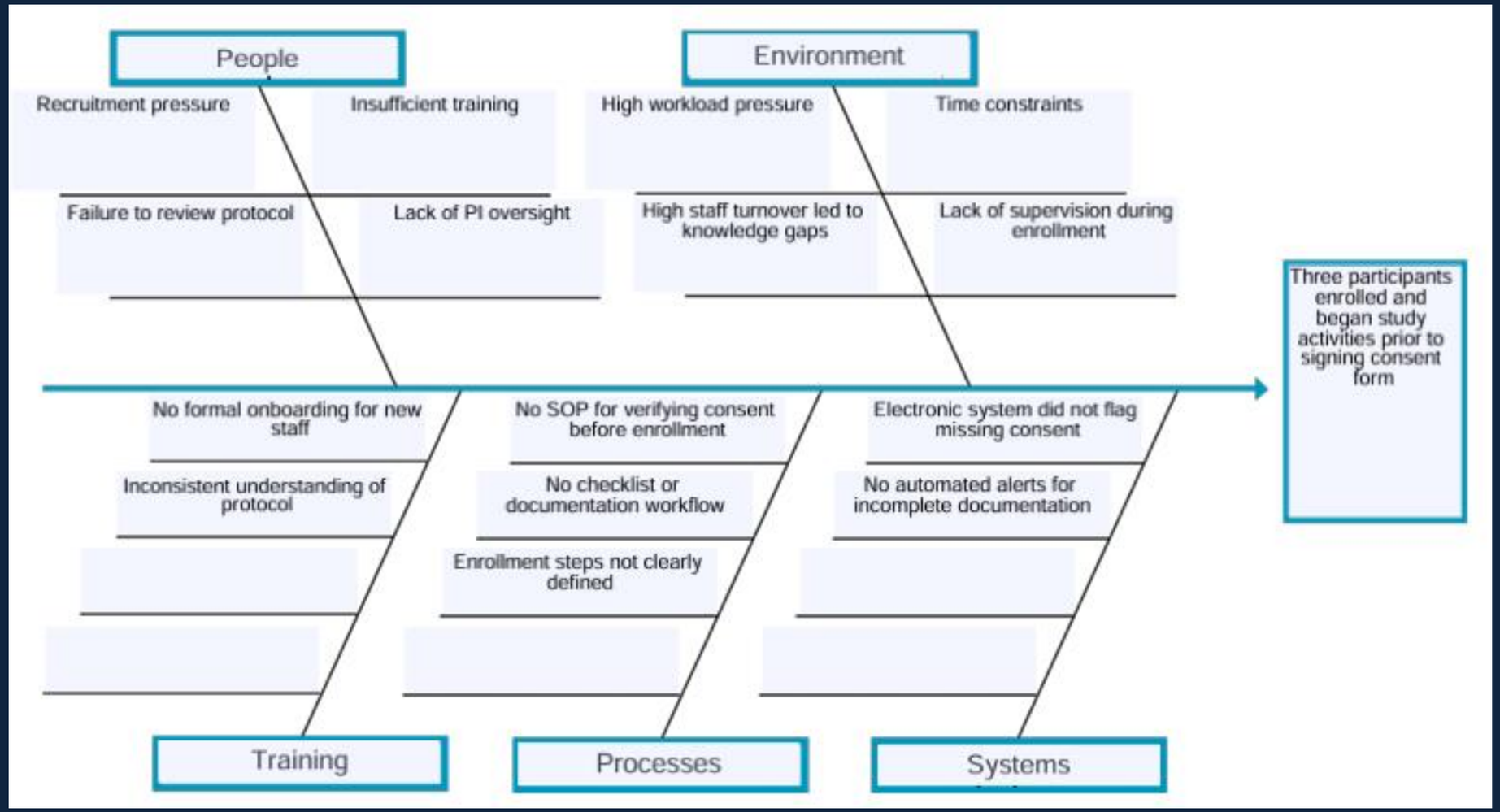
- The study includes a verbal pre-screening consent process.
- The participants were enrolled by a research assistant who started working on the study a few weeks ago.
- The previous study coordinator left the institution prior to the new research assistant starting at the site.

5 Whys

Problem: Three participants were enrolled and began study activities prior to signing the informed consent form.

Why? → The research assistant assumed verbal consent was sufficient.
Why? → Misunderstanding of protocol requirements & IRB policies.
Why? → Inadequate training on consent procedures & regulatory requirements.
Why? → No formal onboarding training for new staff.
Why? → Lack of standardized procedures for staff training and lack of investigator oversight.

Fishbone Diagram



Importance

- Prevents recurrence and continuing noncompliance
  - A superficial fix might patch the issue temporarily, but addressing the true underlying cause will prevent recurrence
- Protects participant safety
- Strengthens regulatory defense
- Saves time and resources

Corrective & Preventive Actions

Corrective Actions

Corrective actions are reactive measures taken to address and fix the root cause of an identified problem, noncompliance, or protocol deviation.

Documentation should describe the steps taken to correct the error, identify the person(s) responsible for making the correction and how information was disseminated to study staff, and record the date when the correction was made.

Preventive Actions

Preventive actions are proactive measures taken to avoid the occurrence of potential issues or noncompliance in the future.

Documentation should outline any steps that will be taken to prevent the error or omission from recurring in the future. This could include training, process changes, monitoring, or system upgrades.

Why?

...the investigator should explain the deviation and implement appropriate measures to prevent a recurrence...

Example 1

Deviation: Three participants were enrolled and began study activities prior to signing the informed consent form.

Corrective Actions:

- Immediately consent the affected participants.
- Report the deviation to the IRB and sponsor.
- Document and explain the deviation and actions taken in the source records and the deviation log.

Preventive Actions:

- Develop and SOP for obtaining informed consent.
- Develop standardized onboarding and training procedures.
- Conduct training for all personnel on GCP, IRB policies, and protocol-specific consent procedures.
- Create a visit checklist to verify consent documentation prior to enrollment.
- Schedule weekly meetings with the investigator to review processes, training, and study progress.

Example 2

Deviation: A participant was enrolled who did not meet the study's inclusion criteria as they were 12 years old and had received prior therapy.

Corrective Actions:

- Notify the sponsor and the IRB. Follow guidance on if the participant should be allowed to continue in the study, considering the participant's safety.
- Document and explain the deviation and actions taken in the source records and the deviation log.

Preventive Actions:

- Revise and reconcile the visit checklist and survey to exactly match the protocol criteria.
- Implement an age validation check in the survey.
- Implement an eligibility checklist with dual review/sign-off before enrollment.
- Retrain the study team on verification of inclusion/exclusion criteria.
- Establish a system for version control and communication of changes.

Example 3

Deviation: A participant's follow-up visit was completed more than 10 days later than required in the protocol.

Corrective Actions:

- Document the reason for the delayed visit and assess the impact on the participant's safety and the study data.
- Inform the sponsor and IRB, if required.

Preventive Actions:

- Set automated calendar reminders or use scheduling tools to track participant visits.
- Build buffer time into appointment scheduling, e.g., schedule appointments early.
- Ensure protocol includes appropriate scheduling windows.

CAPA Plan Follow-up

CAPA plan implementation, review, and effectiveness:

- Evaluate if the CAPA plan has been implemented
- Evaluate if the CAPA plan is effective
- Revise and resubmit the CAPA plan if it is unable to be completed or is found to be ineffective

Clinical Research Guidelines & Tools

DREXEL UNIVERSITY
Office of
Research & Innovation

Clinical Research Guideline and Process Roadmap

1 DESIGN & PLANNING

Activities Include:

- Protocol Development Feasibility
- Budget Development
- Medicare Coverage Analysis
- Establish Data Management

2 START-UP

Activities Include:

- Clinical Trial Agreement
- Insurance/Indemnity
- Clinical Trial Registration
- Site Initiation*
- Maintenance of Regulatory Files*
- Delegation of Authority*
- Completion of 1572 (FDA)*

3 CONDUCT & MONITORING

Activities Include:

- Recruitment of Research Participants*
- Enrollment of Participants*
- Financial Management Monitoring
- Quality Assurance

4 ANALYSIS & REPORTING

Activities Include:

- Data Analysis
- Results & Data Sharing
- Sponsor Reporting
- Clinical Trial Reporting

5 CLOSEOUT

Activities Include:

- Study Closeout*
- Site Closure
- Archive Regulatory Files

Resources

- Drexel Clinical Research Guidelines & Tools
- Drexel's Research Quality Assurance Program
  - Root Cause Analysis Template
  - Fishbone Tool for Root Cause Analysis
- ORI-601 Research Quality Assurance Reviews
- HRP-071 Prompt Reporting Requirements
- Drexel Research Integrity
- Drexel Responsible Conduct of Research
- ICH GCP R2
- ICH GCP R3
- Drexel University Compliance Hotline

Questions