THE UNIVERSITY OF ARIZONA Research & Partnerships

IS / IS NOT ANALYSIS

1. Purpose

The Is / Is Not technique is a problem-scoping tool used to define the boundaries of a problem by systematically comparing what IS occurring against what IS NOT occurring. It is designed to eliminate assumptions, narrow the scope of investigation, and identify distinguishing characteristics that point toward the root cause of a deviation, adverse event, or quality issue.

2. Definitions

Is / Is Not Analysis	A structured problem-scoping technique that compares what IS observed (the problem) with what IS NOT observed (a similar but unaffected comparator) across five dimensions: What, Where, When, Who, and How Much.
IS Statement	A precise description of the problem as it actually exists — the specific defect, incident, or deviation that has been observed.
IS NOT Statement	A description of comparable situations, populations, locations, or time periods where the problem could plausibly occur but does not.
Distinction	A characteristic or factor that differentiates the "Is" from the "Is Not." Distinctions are key clues that help identify the root cause.

3. Procedure

3.1 Initiation

An Is / Is Not Analysis shall be initiated whenever a deviation, adverse event, audit finding, or quality issue meets one or more of the following criteria:

- The issue is complex, recurring, or cannot be attributed to an obvious single cause.
- Multiple sites, subjects, or processes are involved, and the scope is unclear.
- A CAPA is required and root cause has not yet been identified.

3.2 Defining the Problem Statement

Begin by developing a concise, factual problem statement. The problem statement must:

- Describe what is happening — not why.
- Be based on observable, verifiable facts.
- Avoid assumptions, diagnoses, or implied causes.
- Reference specific data points where possible (e.g., subject ID, visit number, date, site).

- Example: "Three subjects at Site 04 were randomized in January 2026 prior to the signed informed consent form being filed in the Investigator Site File."

3.3 Completing the Five Dimensions

Work through each of the five dimensions in order. For each dimension, populate both the IS and IS NOT columns, then identify the key distinction(s):

WHAT — Define the specific nature of the problem (IS) and contrast it with what is not occurring (IS NOT). Focus on the precise defect, not general categories.

WHERE — Identify the physical location (site), anatomical location (patient), and process location (workflow step) where the problem does and does not occur.

WHEN — Establish the timeline: when the problem first appeared, how frequently it occurs, and during which periods it does not occur. Cross-reference with known changes such as protocol amendments, staff changes, or system updates.

WHO — Identify which subjects, patient populations, investigators, or staff are involved in the problem versus those who are not, despite similar exposure.

HOW MUCH — Quantify the extent of the problem: number of affected subjects, percentage of documents impacted, severity grades, frequency of occurrence. Compare against the unaffected comparator.

3.4 Identifying Distinctions and Changes

Once the IS and IS NOT columns are complete for all five dimensions, the team shall review the distinctions column. For each distinction identified, the team must ask:

- What is unique or different about the IS compared to the IS NOT?
- Has anything changed recently (process, personnel, equipment, software, protocol) that correlates with the IS?
- Could this distinction plausibly cause, trigger, or contribute to the problem described in the IS column?

Distinctions and associated changes become the hypotheses to be tested in the subsequent root cause analysis phase (e.g., 5-Why analysis, fishbone diagram).

Study / Project	Site	Date Initiated

Problem Statement
Describe the specific, factual problem here. Avoid assumptions.

Below are examples of questions and scenarios that can be used during this analysis.

Create a blank template to populate information based on your analysis.

Question	IS ✓	IS NOT ✗	Distinction / Clue
WHAT	What is the specific issue, incident, or defect? What is the precise nature of the deviation? (e.g., Patients randomized before informed consent signed; Inclusion criteria 4.2 violated)	What similar issues are NOT occurring? (e.g., This occurred only in January 2026, not other months) What could have been affected but was NOT? (e.g., Informed consent was missing for Dose 1 only; drug dispensed correctly)	Look for what makes the affected group different from a closely related but unaffected group. Finding these gaps narrows the potential cause.
WHERE	**Physical**: Which study site is the incident occurring at? **Anatomical:** Where on the patient's body is the AE observed? (e.g., Left arm injection site) **Process**: At which workflow step does the data inconsistency occur? (e.g., Upon eCRF entry; Lab A analysis)	**Physical**: Which similar sites are NOT having this issue? **Anatomical:** Where else could the reaction be, but isn't? (e.g., Systemic rash, right arm) **Process**: Where is the workflow functioning correctly? (e.g., Source data collection; Lab B)	A location difference can point to site-specific training gaps, equipment issues, or process failures at one node.
WHEN	When did the deviation/event first occur? **(Date and time)** When in the study timeline did this problem first arise? (e.g., At study initiation? After EDC transition?) Is this a constant issue (every time) or intermittent (specific days/cycles)?	When, after the first occurrence, did the event NOT recur? During which periods or visits was the process functioning normally? What is the expected duration in unaffected patients?	Timing differences help distinguish a one-time error from a systemic failure, and correlate events with changes such as staff turnover, system updates, or protocol amendments.

Question	IS ✓	IS NOT ✗	Distinction / Clue
WHO	Which **subjects** are experiencing the AE or deviation? (e.g., Cohort, age group, sex) Which **investigators, coordinators, or pharmacists** handled the affected cases?	Who is demographically similar but NOT experiencing the problem? (e.g., Rash in females >60; NOT in males >60 or females <60) Which personnel, following the same SOPs, had no issues? Who is taking the same intervention but is unaffected?	Personnel or population differences can reveal training deficiencies, biological risk factors, or protocol adherence issues limited to a specific group.
HOW MUCH	How many subjects/patients exhibit this specific AE or deviation? Is the issue in one cohort (e.g., 50 mg arm only) or across all study arms? What % of source documents contain this missing data point? What is the average severity of reactions? (e.g., Grade 3) How many doses were missed or administered incorrectly? Is this a one-time or recurring error across multiple visits?	How many subjects with similar demographics are NOT affected? What % of data from the same site is accurate and compliant? What is the maximum severity seen in the control group? How many doses were administered correctly per protocol?	Magnitude comparisons reveal whether the problem is isolated or widespread, and whether it correlates with dose level, visit frequency, or data volume.

Completed By	Reviewed By	Approved By
Name: _____	Name: _____	Name: _____
Role: _____	Role: _____	Role: _____
Signature: _____	Signature: _____	Signature: _____
Date: _____	Date: _____	Date: _____