READY ROOM

How to Talk to Your Clinical Study Teams about Data Integrity

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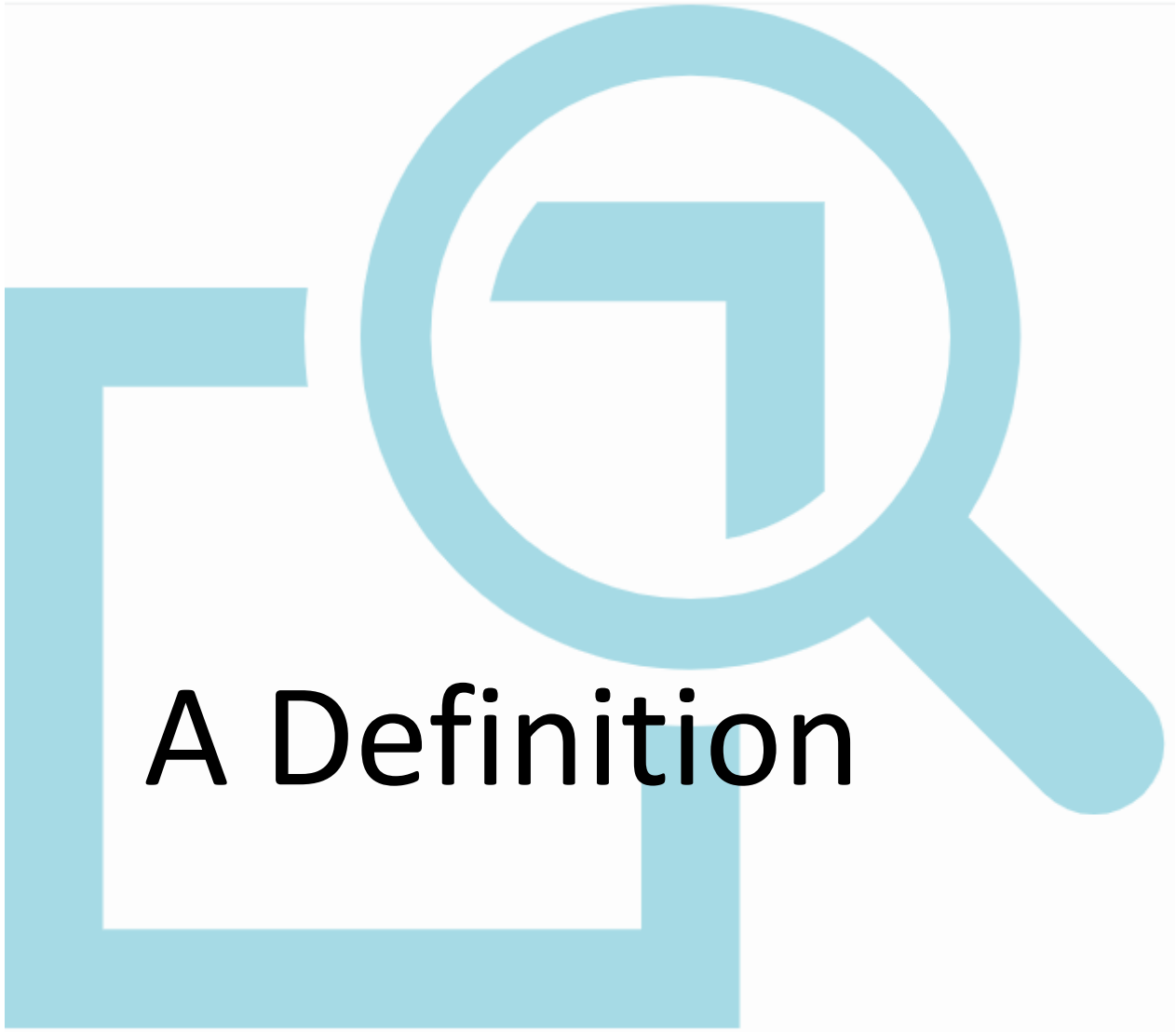
9 April 2024

Society of Quality Assurance
40th Annual Meeting & Quality College
6-11 April 2024 Aurora, Colorado, USA

How do we make the concept of data integrity concrete for our clinical study teams?

Objective

- By the end of this session, GCP QA personnel will be able to utilize five key concepts to promote understanding of record integrity with their study teams



A Definition

EMA Defines Data Integrity in GDP Terms

- Achieved when data are collected, accessed, and maintained such that ALCOA++ principles are maintained:
  - Attributable
  - Legible
  - Contemporaneous
  - Original
  - Accurate
  - Complete
  - Consistent
  - Enduring
  - Available
  - Traceable

EMA Guideline on Computerized Systems and Electronic Data in Clinical Trials, March 2023

Possible New Acronyms

- Cat Cloacae
- A Celt Cacao
- Caecal Taco

Suspicious Minds

Suspicious Minds

- One objective of an audit or inspection is to rule out scientific misconduct and fraud
- ALCOA++ principles provide some assurance that data and documents have not been falsified

How Does Lack of ALCOA+ Adherence Raise Suspicion?

If information is not…	Meaning…	Then inspector might think…
Attributable	Person who generated the record signed it via wet ink or validated e-sig	Someone falsified the record
Legible	All information is clear, no information is obscured	Someone is trying to hide a piece of evidence
Contemporaneous	Record was signed at the same time as the activity it documents	Someone generated the record later on to cover up a gap
Original	The record is a paper original; an electronic original from a validated system; or a certified copy	Record may have been corrupted or truncated as it was emailed, transferred, or copied
Accurate/Consistent/ Traceable	Info in record is internally and externally consistent	Record cannot be relied upon as evidence
Complete	All pages are present, all docs are filed, all identifiers are present	Someone is trying to hide a piece of evidence
Enduring/Available	We can't locate it	Someone is trying to hide a piece of evidence

"Provide evidence that the site monitor was trained on all versions of the protocol"

Training Record

1. TRAINING

Training Topic	Training Date	Method
Protocol v1.0 21-JAN-2019	30-JAN-2019	Self-study
Protocol v2.0 03-MAR-2020	15-MAR-2020	Self-study
Protocol v3.0 17-JUL-2022	30-JUL-2022	Self-study
Protocol v4.0 05-MAR-2023	15-MAR-2023	Self-study

2. TRAINEES

Printed Name	Job Title	Signature	Date
Suzy Q. Monitor	Clinical Research Associate		20-NOV-2023

3. TRAINER Check here if N/A ☒

Printed Name	Job Title or Role	Signature	Date
N/A			

Which Principles Were Impacted?

- **C**ontemporaneous
- **A**ttributable
- **E**nduring
- **C**omplete
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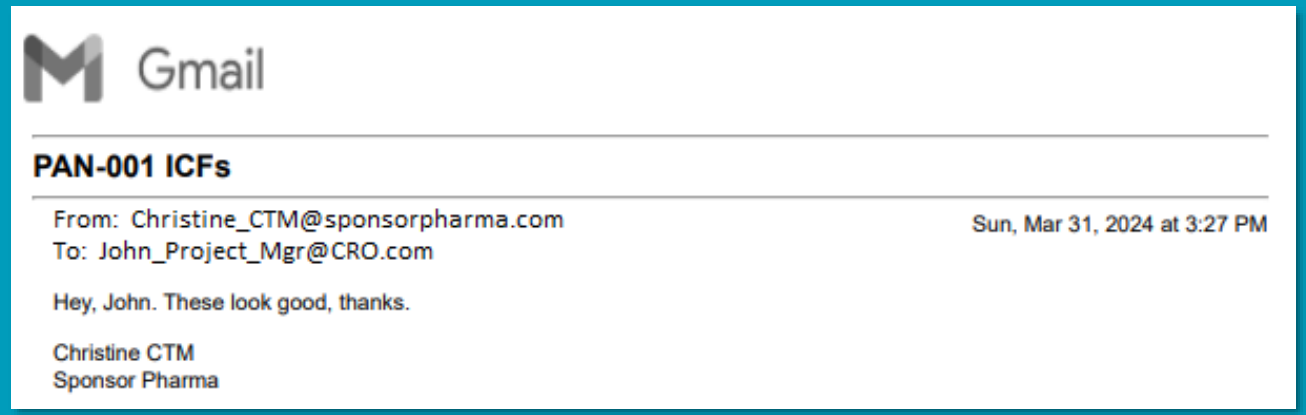
"Provide evidence that the sponsor approved the ICF templates."



Gmail

PAN-001 ICFs

From: Christine_CTM@sponsorpharma.com
To: John_Project_Mgr@CRO.com

Sun, Mar 31, 2024 at 3:27 PM

Hey, John. These look good, thanks.

Christine CTM
Sponsor Pharma

Which Principles Were Impacted?

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The Clothes Chair

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Regulated records, like clothes, belong in a controlled, specified repository, NOT mixed up with draft/unregulated records in an uncontrolled repository.

Why Must the Repository Be Controlled and Specified?

- Repositories must be
  - Access-controlled so only authorized personnel can upload or take actions with records
  - Validated so records can’t be accidentally lost or corrupted
  - Organized so records can be retrieved
  - Specified so there is documentation of where the record is located

"We can't find the study team list in the TMF."

"We keep it on SharePoint and file it at the end of the study."

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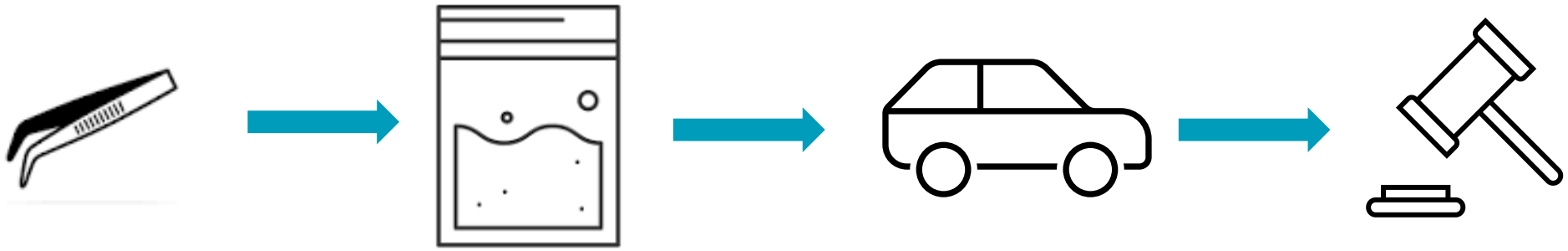
Chain of Custody

Chain of Custody

- Regulated data and documents are like evidence in a police case
- Evidence must be controlled and accounted for at every step; otherwise, it might be corrupted, manipulated, lost, or stolen



How Do We Maintain a Chain of Custody in Clinical Research?

- Records should be moved/copied from one validated system to another, via a validated mechanism…
- OR manual controls should be in place to verify that the original version = the version transmitted/copied

"How do you capture evidence of the Medical Monitors' review of Protocol Deviations?"

"We export the PD data to a spreadsheet and email it to the Medical Monitors who fill it out, and then we consolidate the input in one spreadsheet."

Which Principles Were Violated?

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What’s the Worst That Could Happen?

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- User Acceptance Testing (UAT) is a critical part of validation that should include both “happy path” and “the worst that could happen” scenario testing to ensure data integrity

Why Is UAT Important?

- The vendor that configures an EDC or IRT system tests whether the system performs according to the specifications
- UAT tests the user's perspective: How the system should perform
  - On a typical day, with a typical subject
  - On an atypical day, when everything goes wrong
- UAT should identify whether the study team has a different interpretation of the specifications than the configuration vendor

"The IRT system was programmed such that the randomization scheme was applied incorrectly. Can you provide documentation that UAT was conducted?"

UAT Issues Log

Form	Field	Issue	Comments
Screening	Date	System allowed me to enter a future date.	Fixed MB.
Rescreening	NA	Typo in instructions (should be "rescreening," not "rescrening"	Fixed AC.
Day 3	Weight	Edit check does not fire for weights entered with incorrect units	Fixed MB.

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Risk-Based Controls

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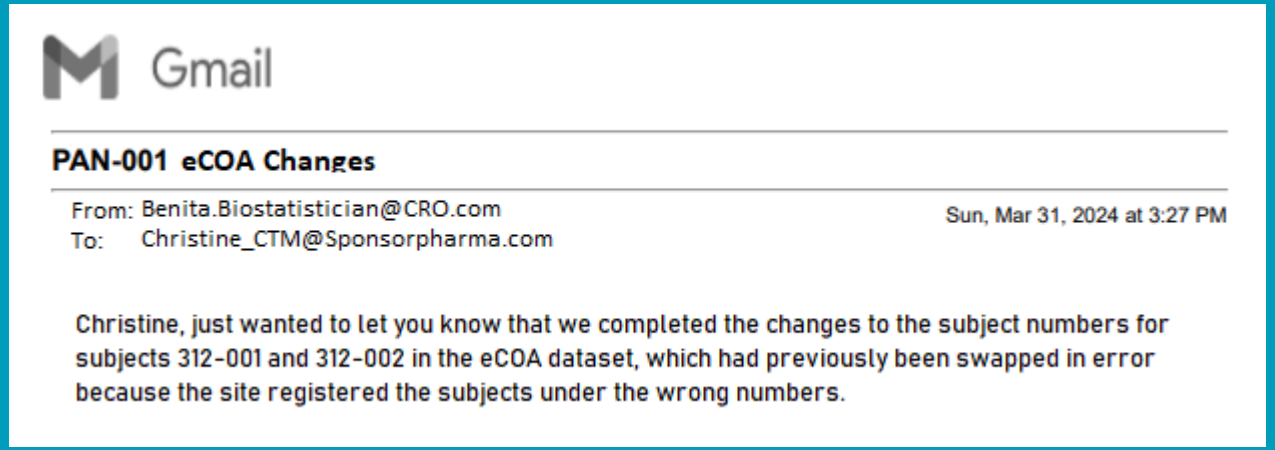
- Controls at each stage of the data life cycle should be commensurate with the criticality of the data and the risk of data corruption/loss
  - Computerized Systems
    - Build
    - Validation
    - Security
    - Change Control
    - User Management
    - Contingency
  - Data
    - Data capture
    - Metadata and audit trails
    - Data review
    - Data corrections
    - Data transfer
    - Data finalization (e.g., edit checks, reconciliation, coding, evaluability)

ICH Guideline for Good Clinical Practice E6 R3 (Draft), May 2023

Assessing Risk

- How critical are the records to subject safety or decision-making?
- How easy would it be for a bad actor to falsify a data source?
- Where data are being transcribed, transformed, or transferred, how easy would it be to introduce inaccuracies or to lose data?
- Given these factors, how strictly should **computer system validation** and the **data lifecycle** be controlled?

"Provide documentation that the biostatistician made back-end changes to site numbers for subjects 312-001 and 312-002 in the eCOA system and no other changes were made."



Gmail

PAN-001 eCOA Changes

From: Benita.Biostatistician@CRO.com
To: Christine_CTM@Sponsorpharma.com

Sun, Mar 31, 2024 at 3:27 PM

Christine, just wanted to let you know that we completed the changes to the subject numbers for subjects 312-001 and 312-002 in the eCOA dataset, which had previously been swapped in error because the site registered the subjects under the wrong numbers.

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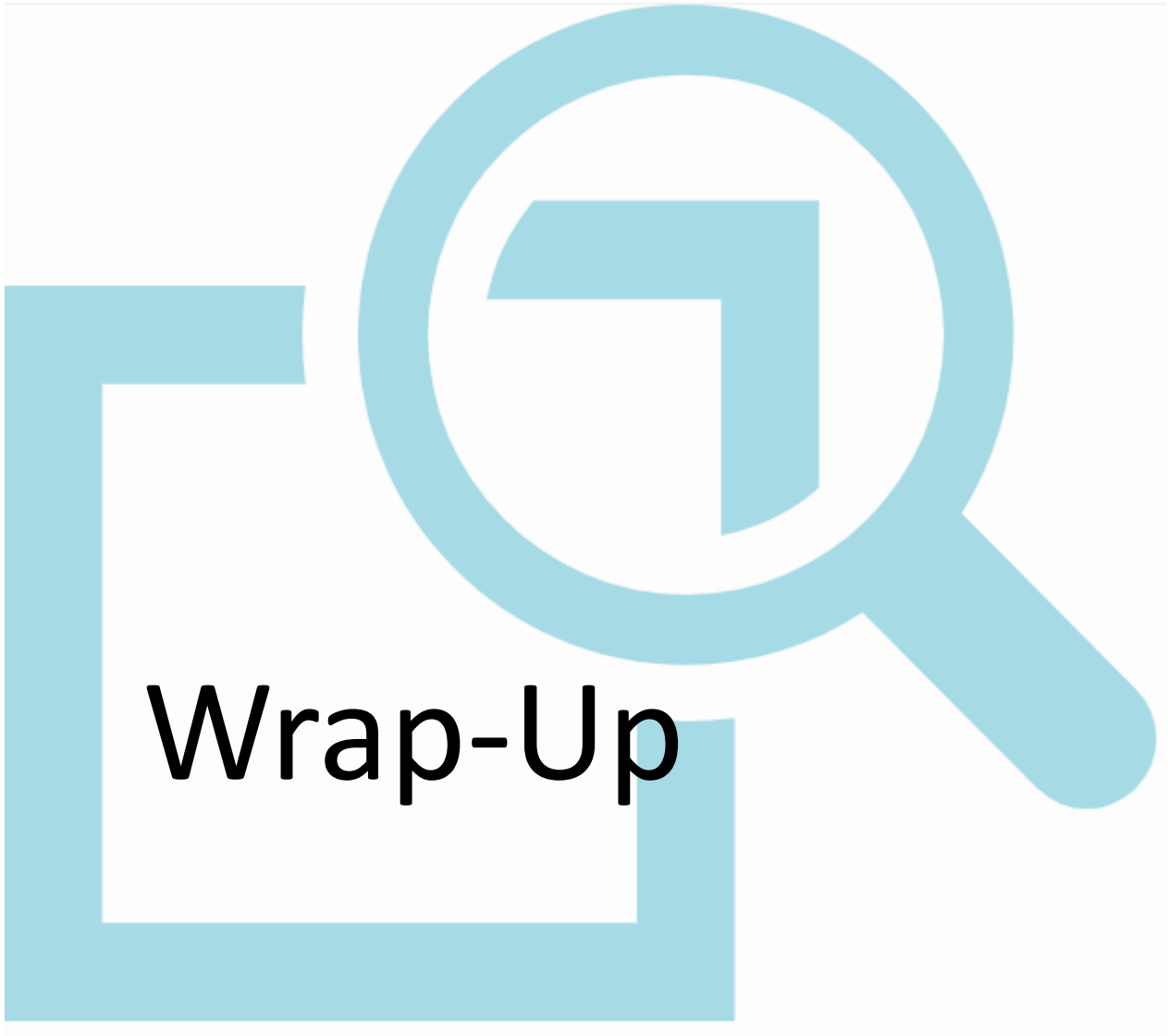

Wrap-Up

Objective

- By the end of this session, GCP QA personnel will be able to utilize five key concepts to promote understanding of data integrity with their study teams

Thank you!

dlacey@synclinical.com
https://readyroom.net