THE OHIO STATE UNIVERSITY

CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE

ALCOA-C and Documentation

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If it's not documented, it didn't happen!

but conversely

You should document not only what was done but also what was not done.

Objectives

- Identify what is specified in the Regulatory documents
- Ability to implement ALCOA-C to clinical research studies
- Discuss Quality by Design methods to improve documentation

ICH GCP – E6 (R2)

ICH E6 4.9.0 -The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be *attributable, legible, contemporaneous, original, accurate, and complete.* Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).

ICH GCP – E6 (R2)

ICH E6 1.51 source data

All *information* in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

Includes: medical history, results (exam, test & lab), demographics (DOB, gender, weight,), patient ID, study number, drug dispensing information, informed consent, IRB approval, visit dates, concomitant medications & intercurrent illnesses.

ICH GCP – E6 (R2)

ICH E6 1.52 source documents

Original documents, data and records - describes the various types of documents which collectively form the source document.

Includes: hospital records, clinical and office charts, laboratory reports, subjects' diaries or evaluation checklists, pharmacy dispensing records, data recorded from automated instruments, diagnostic or surgical reports.

Copies or transcriptions must be "certified" after verification as being accurate copies.

Photocopies of completed case report forms are not valid source documents.

FDA Requirements

21 CFR 58.130(e)

e) All data generated during the conduct of a nonclinical laboratory study, except those that are generated by automated data collection systems, shall be recorded directly, promptly, and legibly in ink. All data entries shall be dated on the date of entry and signed or initialed by the person entering the data. Any change in entries shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of the change. In automated data collection systems, the individual responsible for direct data input shall be identified at the time of data input. Any change in automated data entries shall be made so as not to obscure the original entry, shall indicate the reason for change, shall be dated, and the responsible individual shall be identified.

FDA – Standards of Good Documentation

ALCOA-C

- ***A*** – Attributable
- ***l*** – Legible
- ***c*** – Contemporaneous
- ***O*** – Original
- ***A*** – Accurate
- ***c*** – Complete

A is for Attributable

Definition: produced by or originating in the time, period, place, etc.

Who is recording the information?

What role or responsibilities do they have?

Are they properly trained to perform the recording?

Other pertinent logs

- Delegation of responsibility
- Training logs
- AE logs
- SAE logs
- Medication logs
- Consent Version logs
  - Final credits at the end of the movie!

L is for Legibility

Definition: ability of being read or deciphered, especially with ease; easily readable.

Are you able to clearly understand what has been recorded or does one have to guess?

Interpretation errors when unable to decipher what was written

If not legible, the author can make an original note that indicates the location of a later “typed” rendering of what was written

On source documents provided places to record easily if you can (QbD)

e is for Contemporaneous

Definition: occurring in the same period of time

Was the information recorded at the time of the event?

When was the information obtained?

Scene of the accident

best to ask questions immediately – best time for memory

Fresh in your mind; and others for questions

EHR's – be sure to include date obtained

O is for Original

Definition: arising or proceeding independently of anything else

Has the information been copied from another source?
Source Documents

could be a post-it, paper towel, etc.

electronic records

A is for Accurate

Definition: free from error; careful or meticulous; consistent with a standard

Once documented, has the information been reviewed?

e is for Complete

Definition: Having all parts or elements; lacking nothing; whole; entire; full

Importance of source documents – can include reminder notes

wait 15 minutes before taking BP

ICH GCP – E6

ICH E(6) 2.10 All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification. ADDENDUM This principle applies to all records referenced in this guideline, irrespective of the type of media used.

Why are these so important?

Validation of results

Reproducibility

Standard of care vs research: ensure that each study subject was treated exactly the same – demonstrates a controlled value

Can be your saving grace – Oral insulin study example

ICH GCP – E6 (R2)

ICH E6 5.18.7 Monitoring Plan - The sponsor should develop a monitoring plan that is tailored to the specific human subject protection and data integrity risks of the trial. The plan should describe the monitoring strategy, the monitoring responsibilities of all the parties involved, the various monitoring methods to be used, and the rationale for their use. The plan should also emphasize the monitoring of critical data and processes. Particular attention should be given to those aspects that are not routine clinical practice and that require additional training. The monitoring plan should reference the applicable policies and procedures.

Notes to File Not Always the Answer

Inadequate or inaccurate records represent the second most common inspection finding behind failure to adhere to the protocol, however

1. Notes to file: when, why, purpose
2. Generally created when there is an absence of good documentation
3. Often asked for when should actually be documented somewhere else
4. If information is documented elsewhere, a note to file should not be written

Essential Documents

If documentation logs are kept elsewhere, include a statement regarding where the documents are kept:

temperature logs for equipment

Updated personnel CV's and license documents

Use of shadow charts – notes on where information filed electronically

(hit by the bus concept)

Use of QbD for Source Documentation

(QbD = Quality by Design)

Collection of pertinent data points

Are the end points being collected?

Document the safety of the subject – safety labs?

Proof that inclusion and exclusion were completed correctly and timely

EHR – Where, what, when, who

Electronic Health Records

- Make sure you have subject permission (ICF or Record Release)
- Document who obtained the records and when
- When sharing EHR w/ sponsor be sure to de-identify properly as well as document what was sent, to whom and when

Electronic Data Sets: Part 11 compliance

System can demonstrate the tenets of ALCOA-C

- Must be able to show a data trail for all changes
  - Data Queries and corrections
- Be sure your system is Part 11 compliance, not just capable of being compliant
- CRC should maintain their own data trail of changes to the data base, queries address and changes made

References

- 21 CFR 58 - https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=58.130
- https://conductscience.com/portfolio/alcoa-c/
- https://www.fda.gov/media/93884/download

THANK YOU

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Objectives - JTF Competencies

- 4.3 Evaluate the design, conduct and documentation of clinical studies as required for compliance with Good Clinical Practice Guidelines
- 5.6 Identify and explain the specific procedural, documentation and oversight requirements of principal investigators, sponsors, CROs and regulatory authorities that relate to the conduct of a clinical study
- 6.3 Describe best practices and resources required for standardizing data collection, capture, management, analysis, and reporting