Good Documentation Practices
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Announcements

• Slides from March Meeting.

• Topics for future QUIBITs?
  • GMP Facility Design Considerations.
  • ISO 17025
What does this figure mean?
Do you agree?
GDP in Regulations and Standards

- FDA
  - GLP
  - GMP
- USDA
  - Animal Biologics
- ISO 13485: Medical Devices
• **21CFR§58.130  Conduct of a nonclinical laboratory study.**
  
  • **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.
USDA Animal Biologics

• 9CFR§116.1

• (1) Records shall be made concurrently with the performance of successive steps in the development and preparation of biological products, including new products under development. Such records shall include the date and where critical, the time that each essential step was taken, the identity and quantity of ingredients added or removed at each step, and any gain or loss of product from the beginning to the end of product preparation.

• (2) Records shall be legible and indelible; shall be as detailed as necessary for a clear understanding of each step by one experienced in the preparation of biological products; and shall be verified by initials or signature of the person immediately responsible for the action taken.
ISO 13485: 2016 Medical Devices

• 4.2.5
  • “Records shall remain legible, readily identifiable and retrievable. Changes to a record shall remain identifiable.”
Guidance Document to help answer questions about regulations

Data Integrity and Compliance With Drug CGMP Questions and Answers Guidance for Industry
What is “data integrity”? 

• *Data integrity* refers to the completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate *(ALCOA).*
FDA’s Questions

• When considering how to meet many of the GDP regulatory and standard requirements, it may be useful to ask the following questions:
  • Are controls in place to ensure that data is complete?
  • Are activities documented at the time of performance?
  • Are activities attributable to a specific individual?
  • Can only authorized individuals make changes to records?
  • Is there a record of changes to data?
  • Are records reviewed for accuracy, completeness, and compliance with established standards?
  • Are data maintained securely from data creation through disposition after the record’s retention period?
Question for the group

• Does your current program include a Documentation/Data Integrity SOP?
ALCOA +
Title 21 -- Food and Drugs
Chapter I -- Food and Drug Administration
Department of Health and Human Services
Subchapter A -- General
Part 58 -- Good Laboratory Practice for Nonclinical Laboratory Studies
Subpart G -- Protocol for and Conduct of a Nonclinical Laboratory Study

Sec. 58.130 Conduct of a nonclinical laboratory study.
(a) The nonclinical laboratory study shall be conducted in accordance with the protocol.
(b) The test systems shall be monitored in conformity with the protocol.
(c) Specimens shall be identified by test system, study, nature, and date of collection. This information shall be located on the specimen container or shall accompany the specimen in a manner that precludes error in the recording and storage of data.
(d) Records of gross findings for a specimen from postmortem observations should be available to a pathologist when examining that specimen histopathologically.
(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.

ALCOA +

• Attributable — Who did what?
• Legible — Must be readable
• Contemporaneous — Written when performed
• Original — Not photocopied
• Accurate — Actual data. Avoid guesses etc....
• +
  • Complete — No blanks or missing details
  • Consistent — Same practices (e.g., date format)
  • Enduring — Designed to last throughout retention period (no acid based tape)
  • Available — Can be readily retrieved
• Traceable — Can you match your documents to events?
At your Chikalthana site, our investigators observed poor documentation practices during in-process testing. Specifically, an operator performed the in-process tablet (b)(4) testing for the (b)(4) mg tablet batch #(b)(4) without the batch record or a manufacturing form to document the results contemporaneously. The FDA investigator was informed that the pre-test and post-test weight values are documented in the batch record located in a separate manufacturing room rather than in the same room where the actual weights are measured. Moreover, your operator stated that he records the two weights with (b)(4) significant figures into the batch record from memory. Your investigation into this issue is inadequate because it did not consider other in-process tests or whether the operator(s) have been involved in the same poor documentation practices for others batches. Your response does not indicate whether this poor documentation practice is an isolated case or is a matter of widespread behavior in this facility.
FDA Warning Letter Snippets

Your employees did not complete batch production and control records immediately after activities were performed. When QA reviewers noticed missing entries in the batch records, they made a list of all the missing items on separate, uncontrolled pieces of paper that were provided to the production manager. Data were later entered into CGMP documents after operations had already ended as though they had been entered at the time of the operation.

For example, on November 17, 2014, we saw eight production records for (b)(4) and (b)(4) that had blank entries for weights of material used for production, checked-by signatures, accessories used, in-house batch numbers, quantity added, and product labeling for material dried specimens. The yield report sheet and batch summary sheet were also incomplete.
SLIDR

• When errors occur, they must be corrected and corrected properly.

• Use the following:
  • Single Line
  • Initials
  • Date
  • Reason

• Footnotes can be used as well.


Samples were tested on 23Aug2017 using HPLC
Additional Notes

• For decimals, add a 0.
  • E.g., 0.3mm not .3mm.

• For time use standard format in workplace.
  • E.g., 1352hrs, 1:52pm.

• Use standardized date:
  • 7/6/17, 6/7/17, 20170706, 06Jul2017.

• Ink color may be specified.

• Pencils are prohibited.

• White-out is prohibited.

• Ditto marks prohibited: “ ” or lining down.
Additional Notes

• Copy must have “Copy” stamp.
• Pagination must be in place.
• Data must be controlled.
  • Should you allow data to leave the premises?
  • How will you (and how fast can you) retrieve it during an audit?
• Don’t double document if you can.
• Ink used shouldn’t smear.
• Avoid slang.
  • “Assay was jacked up.”
• Sticky notes…..prohibited.
Example...

• How many errors can you find?
Things to Ponder?

• What if your initials are NA?
• What if you need to write in cold wet areas?
• What if your pen runs out of ink halfway through writing a word?
• What if you are generating data at midnight?
• What if you are working in an anaerobe chamber/glove box?
• What if your data is eaten by an animal?
• What if you spill soda on your document?
• What is the value of your data?