Analytical BA/BE Case Study

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Disclaimer

- This presentation reflects the views of the author. It should not be construed to represent FDA's views or policies.

Learning Objectives

- Justifying rejection of an analytical run
- Highlighting the importance of complete and contemporaneous documentation during an analytical BA/BE study
- Maintaining analytical run data and audit trails

* BA/BE – Bioavailability/Bioequivalence

Outline

- Analytical BA/BE Case Studies (1, 2 and 3)
- Questions/Discussions Relevant to Each Case Study

Case Study 1: Rejection of Analytical Run

Case Study 1:

- During method validation, one precision and accuracy (P&A) run was excluded from global P&A statistical analyses.
- Method validation report stated that the P&A run did not meet acceptance criteria since both HQC samples failed .
- This incident was documented and assessed as an assignable cause, but the assignable cause was not specified in the incident report.

Case Study 1: Continued

- During inspection, the firm management said they suspected that there were sample processing errors.
- Method validation SOP specifies that P&A batches, which do not meet acceptance criteria without an assignable cause should be included in global P&A calculations.

Examples of Assignable Cause

- Malfunction of HPLC or Spectrometric apparatus – can be mechanical or electrical in nature (pump stopped, leakage, power failure).
- Computer network issue – data not saved.
- Sample preparation error – if the nature of the error is known along with contemporaneous documentation.

Pause for Discussion: Case Study 1

Case Study 2: Complete and Contemporaneous Documentation

Case Study 2

- During an inspection, a firm could not provide quality control (QC) samples preparation documentation used in long-term stability studies for method validation experiments.
- As a result, long-term stability experiments could not be reconstructed.

Case Study 2 – Continued

- In another inspection, set of subject samples was classified as run failure. That set was reprocessed and reanalyzed.
- The firm stated that there was a suspected sample processing error.
- The firm could not provide supporting evidence for this incident to justify the reprocessing.

Pause for Discussion: Case Study 2

Case Study 3: Best Practices for Retaining Analytical Study Data

Case Study 3

During an inspection, following issues were observed while checking the audit trails of an analytical run:

- Changes to peak integration parameters was not uniformly applied
- Results table was overwritten; each version of the results table was not saved.
- Sample type was changed from ‘quality control’ to ‘unknown’ after analysis was completed.

Results Table – Sample Type	N/A	run03.wif, sample 35) was changed from “Quality Control” to “Unknown”

Pause for Discussion: Case Study 3

Summary

- 2018 Bioanalytical Method Validation Guidance should be viewed as recommendations while conducting an analytical BA/BE study.
- Any unexpected incidents, deviations from protocol or SOP, repeat analysis etc. should be supported by contemporaneous documentation.
- Rejecting a run or a sample should be justified and substantiated by proper documentation.
- Original and re-integrated results data should be maintained and supported by SOPs, protocols or other written documents.

Resources

Regulations

- Regulation Part 320 – Bioavailability and Bioequivalence Requirements

Related Guidance

- Bioanalytical Method Validation (BMV) Guidance for Industry
- Handling and Retention of Bioavailability BA and Bioequivalence BE Testing Samples
- FDA Guidance on Part 11, Electronic Records; Electronic Signatures
- Good Laboratory Practice for Nonclinical Laboratory Studies
- Regulatory Education for Industry: Regulated Bioanalysis Workshop: Requirements and Expectations

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Thank You!

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