

Laboratory Data Integrity in FDA Warning Letters 2013

1. Test Results / (Raw) Data:

Your firm failed to ensure that laboratory records included complete data derived from all tests necessary to assure compliance with established specifications and standards.

Your firm discarded all raw data related to the OOS results including sample weights, sample solution preparations, and sample dilutions.

Out-of-specification or undesirable results were ignored and not investigated

Your firm did not retain documents associated with the sample weights, sample preparations and sample dilutions. You also acknowledged that without raw data it is difficult or impossible to definitively determine the root causes and the exact actions of the analyst when OOS results are encountered.

Your firm failed to ensure that laboratory records included complete data derived from all tests necessary to assure compliance with established specifications and standards.

Our review of ... found that your firm was testing samples unofficially, and not reporting all results obtained.

Your firm failed to maintain all the laboratory raw data used to support the release of finished product lots. During the inspection, the investigator requested the raw data from the finished product testing described in the certificates of analysis. However, your firm management stated that your firm does not maintain records of the raw data for each of the finished products ...

An FDA investigator identified the presence of torn raw data records in the waste area and asked one of your firm's QA Officers to remove these torn raw data records for the investigator's review. The FDA investigator asked three times if there were any more records found in the waste area, and the QA Officer responded to each question, "no, this is all of the records". The FDA investigator then re-visited the waste area and found that the raw data records had been removed and placed in a different holding bag. These records included raw data testing worksheets from ... stability protocol records.

2. Written (Control) Procedures:

Your firm did not retain any raw data related to sample weights and sample solution preparations for the ... assays In addition, you did not include those results in the calculation of the final assay values.

Your response acknowledged that a number of these trial injections involved sample testing. However, you provided no evidence that your firm retained laboratory records and raw data associated with these sample tests.

Your laboratory control records do not include data derived from all of the tests necessary to establish compliance with standards.

You are responsible not only for having controls to prevent omissions in data, but also for recording any changes made to existing data, which should include the date of change, identity of person who made the change, an explanation or reason for the change, and formal documentation as a deviation.

Our investigator also identified a backdated QC worksheet in the analytical report. ... Backdating documents is an unacceptable practice and raises doubt about the validity of your firm's records.

You analysed ...API lot ..., and then retested it ... using a new sample solution. You did not maintain any raw data associated with the initial test.

3. Computerised Systems / Laboratory Instruments

Your firm failed to establish and exercise adequate controls over computers to prevent unauthorized access or changes to electronic data.

For example, the computers that control your analytical laboratory instruments, including an HPLC, GCs, and an FTIR, lacked control mechanisms to prevent unauthorized access to, changes to, or omission of data files.

Your firm used ... different HPLC processing methods to process the data for these analyses. Your firm did not investigate or document all these tests, and discarded raw data related to sample weights and preparations, in disregard of the SOP requirements.

You stated in your response that you revised your investigation procedure and implemented ... audit trails for each laboratory instrument. Your QC managers will review the ... audit trail printouts to ensure identification and investigation of OOS results. We will verify the effectiveness of these corrective and preventive actions during our next inspection.

Our investigator requested to review the electronic analytical raw data to compare the values for ... assay and degradation products. However, your firm provided only the printed copies of the raw data because your firm did not have the software program available to view the electronic raw data.

Your quality control HPLC raw data files can be deleted from the hard drive using the common PC login used by all analysts.

Ensure that all electronic analytical raw data will be readily available for review during the next inspection.

Your firm failed to exercise appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records, or other records.

During our inspection, your analyst admitted that he also deleted other uninvestigated failing and/or OOS electronic data from the laboratory database ... prior to our inspection. Your QC Senior Manager also acknowledged this laboratory-wide electronic data deletion practice.

Your firm's ... HPLC instruments do not have restrictions in place to prevent any change or deletion of analytical raw data. Additionally, there is no audit trail in place to determine any previous deletion of raw data.

Unacceptable practices in the management of electronic data were also noted. The management of electronic data permitted unauthorized changes, as digital computer folders and files could be easily altered or deleted.

Your firm did not retain any raw data related to sample weights and sample solution preparations for the HPLC assays of ... that you conducted In addition, you did not include those results in the calculation of the final assay values. Instead, you repeated the analysis the next day using a new set of sample solutions, and reported the retest results on the certificates of analysis (COAs).

The FDA investigators identified the practice of performing "trial" sample analysis for High Performance Liquid Chromatography (HPLC) analyses prior to collecting the "official" analytical data for stability testing. These "trials" were performed on multiple products, and were not recorded in the equipment use log.

Include a review of all chronological records that clarify which equipment was used for the testing of the API batches. Finally, it should include a review of the audit trail from the software that describes surrounding events for each piece of extra data identified that represents a finished API batch.

This responsibility starts with designing computerized systems with appropriate security features and data audit trails, as well as many other elements that assure proper governance of your computerized systems.

4. Data Integrity Practices

... the practice of deleting critical analytical data and backdating records. This practice is a clear breach in your quality system that raises serious concerns regarding the integrity and reliability of the laboratory data used to release drug products.

You are responsible for the accuracy and integrity of the data generated by your firm. A firm must maintain all raw data generated during each test, including graphs, charts, and spectra from laboratory instrumentation. These records should be properly identified to demonstrate that each released batch was tested and met release specifications.

The above examples raise serious concerns regarding the integrity, reliability and accuracy of the data generated and available at your facility.

... explain the systemic actions that will be instituted to prevent these fundamental breaches of data integrity and management oversight in the future.

You failed to completely address how your firm will ensure the integrity and completeness of all analytical raw data.

The lack of reliability and accuracy of data generated by your firm's laboratory is a serious CGMP deficiency that raises concerns with all data generated by your firm.

Your inability to detect and prevent poor data integrity practices raises serious concerns about the lack of quality system effectiveness.

We expect your firm to extend your data integrity investigation to all relevant lots and data.

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