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Implementation and Management of Data Integrity

Data integrity is the assurance that data records are accurate, complete, intact and maintained within their original context, including their relationship to other data records. This definition applies to data recorded in electronic and paper formats or a hybrid of both. To assure the quality of raw materials, in process materials and finished goods, laboratory data integrity is assuming greater importance in current Good Manufacturing Practices (cGMP) for US Food and Drug Administration (FDA)-regulated industry.

In recent years, FDA has increasingly observed violations involving data integrity during cGMP inspections. This is troubling because ensuring data integrity is an important component of industry's responsibility to ensure the safety, efficacy, and quality of drugs, biologics and medical devices. These data integrity-related cGMP violations have led to numerous regulatory actions, including warning letters, import alerts, and consent decrees.

Data integrity and security infractions are on the upswing when it comes to regulatory citations. The reason behind this is quite simple: if the integrity of laboratory data is compromised, batches of finished goods may not comply with regulatory authorization terms and, consequently, will not be released for sale.

Most companies have experienced being audited and, where necessary, "defending" the work carried out in their analytical laboratories during audits.

Historically, laboratories provide information about the validation of their methods and procedures, the qualification and suitability of their analytical equipment, and information about training of their laboratory staff as justification for the validity of the analytical results.

FDA warning letters have highlighted the increasing focus on data integrity in the laboratory. Data integrity is a subject that many laboratories currently have significant concerns about. To add to those concerns, even the term "data integrity" can have widely differing meanings or interpretation, and there are currently few definitive reference sources available on the subject.

The acronym ALCOA has been widely associated with data integrity by FDA and was first used by Stan Woollen when he worked for the agency to help him remember compliance terms relevant to data quality. The good automated manufacturing practice (GAMP) guide

"A Risk-Based Approach to GxP Complaint Laboratory Computerized Systems" includes an appendix (Appendix 3) on data integrity. The terms used in the appendix are sometimes referred to as "ALCOA +" because they incorporate additional terms based on the European Medicines Agency's concept paper on electronic data in clinical trials. The terms associated with ALCOA + are described as Attributable, Legible, Contemporaneous, Original, Accurate, complete, consistent, enduring, and available (see Table I).

Table 1.

Attributable - Who performed an action and when? If a record is changed, who did it and why? Link to the source data.

Legible - Data must be recorded permanently in a durable medium and be readable.

Contemporaneous - Data should be recorded at the time the work is performed and date / time stamps should follow in order.

Original - Is the information the original record or a certified true copy?

Accurate - No errors or editing performed without documented amendments.

Why is data integrity important? Without it, it undermines the safety and efficacy and/or assurance of quality of the drugs that consumers will take. Data integrity problems break trust. Consumers rely largely on trust that the firm will do the right thing when no one is watching.

FDA expects data be reliable and accurate. cGMP regulations and guidance allow for flexible and risk-based strategies to prevent and detect data integrity issues. Firms should implement meaningful and effective strategies to manage their data integrity risks based upon their process understanding and knowledge management of technologies and business models.

Table 2.

Common Issues with Data Integrity:

Common Passwords : Not possible to identify who creates or changes the data/records when analysts share passwords.

User Privileges : No defined or segregated user levels for modifications of methods/sequences and integration.

Processing Methods : Integration process not controlled and/or no defined procedure of Integration. Regulatory bodies are more concerned over the re-integration of chromatograms.

Audit Trails : Audit trail functionality turned off within the system. As a result, impossible to trace who/when modified the data and why.

Incomplete Data : Most common data integrity issue. Record not complete.

Computer System Control : No adequate control over data and unauthorized access to modify, delete or not save electronic files; which lead to files that may not be original, accurate or complete.

Alteration of raw, original data and records (e.g., the use of correction fluid).

Multiple analyses of assay with the same sample without adequate justification.

Manipulation of a poorly defined analytical procedure and associated data analysis in order to obtain passing results.

Backdating stability test results to meet the required commitments.

Creating acceptable test results without performing the test.

Using test results from previous batches to substitute testing for another batch.

Laboratory best practices for meeting regulatory and compendial requirements are changing to meet FDA's emerging expectations for data integrity. What are some things that regulators look for regarding data integrity?

- Demonstrating the integrity and security of laboratory data, records, results and information is paramount for a successful audit or inspection for any Good Pharmaceutical Practices (GxP)-regulated laboratory.
- Analytical instrumentation used within GxP analytical laboratories is computerized either via firmware inside the instrument or via software installed on a workstation situated next to the instrument.
- All analytical instruments must be qualified and computerized systems validated.

In conclusion, the integrity of data generated by any regulated laboratory is a prime factor in determining the credibility of that laboratory. The finding of a single instance where data integrity is compromised casts a shadow over the whole of the data generated. Remember that inspections and audits can only sample, finding one instance of falsification raises the question of how many more instances of non-compliances exist?

Ensuring data integrity is of major importance to analytical scientists, managers and quality assurance of any organization, as the consequences of getting it wrong are very costly and it will take a long time to rebuild regulatory trust.

ABOUT THE AUTHOR:

Danielle DeLucy has been in the industry for 15 years serving in numerous Quality Management Roles, such as the Director of Product Quality, the oversight of Sterility Assurance practices and provided QA oversight of numerous filling and packaging operations. Danielle began her QA career as a Quality Control Pharmaceutical Microbiologist at a contract laboratory where she performed various tests for their clients. In the years after, she has held positions in the Quality management arena while increasing her responsibility. She has helped to lead many Regulatory Health Inspections and was instrumental in the coaching process of her peers prior to any inspection. Currently, Danielle assists companies who are faced with warning letters, consent decrees and those wishing to improve compliance establish more robust quality systems so that the company can succeed.