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TECHNOLOGY GROUP

WHITE PAPER:

Best Practices for Conducting Data Integrity Assessments

In order to ensure the safety, efficacy and quality of human and veterinary drugs, biological products, and medical devices, the FDA has stepped up its regulatory focus on data integrity significantly over the last several years. From the moment data is generated, and extending through to the end of its life cycle, the FDA considers data integrity to be critical to the manufacture of high quality and safe medications and devices. The FDA's expectation is that all data involved in the production of FDA regulated products is both reliable and accurate.

Compliance violations involving data integrity have led to numerous regulatory actions (e.g., warning letters, import alerts, and consent decrees) by the FDA in recent years. FDA enforcement actions can result in significant consequences including facility shutdown, import and/or distribution bans, remediation costs, delayed/denied drug approvals, damaged reputation and recalls. In addition, data integrity violations can result in loss of trust by the FDA, leading to more frequent and in-depth inspections in the future.

As remediation of FDA data integrity warning letters tends to be significantly more expensive than finding and correcting the issues internally, it is wise to have an effective Quality Management System (QMS) in place to identify and correct data integrity deficiencies without the need for intervention by the FDA. Given the FDA's focus on data integrity, data integrity assessments should be included in your organization's QMS as part of GMP audit programs. In this white paper, we will discuss best practice recommendations for data integrity assessments that help to ensure compliance with FDA regulations.

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Data Integrity 101

Data integrity should be an important consideration in the design, implementation and use of any system that stores, retrieves or processes data in the production of regulated products. Whether recorded in paper or electronic format, data records should be accurate, complete and maintained within their original context. Organizations should also take steps to protect original data from accidental or intentional modification, falsification or deletion.

In its latest guidance on data integrity released in December of 2018, the FDA identifies a number of characteristics that are important to ensuring data integrity: "For the purposes of this guidance, *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)."

ATTRIBUTABLE	LEGIBLE	CONTEMPORANEOUS	ORIGINAL	ACCURATE
This refers to the fact that a reviewer must be able to determine who collected the data, when it was collected, from which instrument it was collected, and who made any data modifications or manipulations. Note that the use of shared passwords in a LIMS or other informatics system makes it impossible for a reviewer to attribute the data to a specific person.	Data must be legible/ readable. Electronic data must have the capability to be made readable by humans.	Data must be recorded at the time it is created, not transcribed at a later date. Data is not transcribed from scrap paper to "official" documents such as laboratory notebooks or batch records.	Data must be recorded in the file or format in which it was originally generated (original paper record from a manual observation or electronic raw data file from a computerized system), preserving the accuracy, completeness, content and meaning of the record. The paper printout from an instrument would not be considered official, original GMP data, as it is lacking the necessary complete information – audit trail, metadata, system configuration, etc.	Recorded data needs to be accurate and 2nd person verified when appropriate. Data that is recorded in multiple locations should be in agreement.

Best Practices for Conducting Data Integrity Assessments

Data integrity assessments/audits can be conducted by internal staff in the Quality unit, or by an independent third party. When outsourcing to an external consultant, it is important to verify that auditors have appropriate training for data integrity evaluations.

An effective data integrity assessment will contain the following activities:

Operational Review

The assessment team should spend time reviewing relevant documentation and familiarizing themselves with your organization's environment, processes, systems and procedures prior to any actual on-site assessment activities.

Kick-Off Meeting

The assessment team and key stakeholders in your organization should meet to effectively kick-off the project. This meeting will serve to introduce the assessment team and key stakeholders in your organization, confirm project direction, finalize project scope and approach, and establish effective coordination with any other initiatives as needed.

Project Plan

Following the kick-off meeting, a formalized project plan should be created containing all agreed-upon, relevant details that are necessary to conduct the assessment.

Data Integrity Assessment

The assessment team reviews all aspects of your organizations records and data recording practices, with a focus on completeness, consistency, and accuracy of regulated data collected, maintained, stored, analyzed, and/or reported by computer systems. This includes the accuracy and reliability of data submitted in drug and biologic marketing authorization applications.

The following items should be evaluated during the assessment:

- **Data origination**
- **Data traceability**
- **Data backup, archive, restore and recovery processes**
- **Data review and approval**
- **Electronic signatures**
- **Audit trails**
- **User access/roles/permissions**
- **Instrument integration**
- **Documentation related to system(s) operation**
- **Quality culture**

The FDA lists a series of threshold questions in their December 2018 guidance document[1] on data integrity that are helpful to ask when conducting the assessment:

- **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?**

The level of risk associated with a process or system should be a key consideration when deciding whether to implement/modify technical or procedural controls.

GAP Analysis

Once the data integrity assessment is complete, it is essential to perform a GAP Analysis on your organization's processes and systems with regards to their compliance with data integrity regulations.

Risk Assessment

Identified regulatory gaps should be accompanied by a determination of the risk, based on accepted standards, associated with each process or system and the data which is generated or modified by it. Identified gaps should then be prioritized based on risk.

Remediation Plan

Based on the risk assessment, a plan of action should be developed to remediate data integrity regulatory gaps. The level of risk associated with a process or system should be a key consideration when deciding whether to implement/modify technical or procedural controls. Once implemented, reviews of systems, controls and data should occur at a frequency consistent with the level of risk present, the type of system and regulatory requirements.

Data Integrity Assessment Deliverables

The data integrity assessment, along with any gaps identified and corresponding remediation activities, must be documented. Deliverables produced as a result of the assessment should include:

- **Finalized Project Plan** – Documentation of finalized assessment project team, project direction, project scope and approach, coordination with other initiatives, assessment activities.

- **On-site Assessment Notes** – Documentation of initial findings of on-site assessment to determine the completeness, consistency, and accuracy of regulated data collected, maintained, stored, analyzed, and/or reported by your organization's computer and paper systems.

- **Data Integrity Assessment Final Report** – Documentation of full findings from on-site assessment, data integrity gaps and risks identified, and the plan of action to remediate the data integrity gaps and risks.

All of these deliverables should be provided by the assessment team to your organization's stakeholders for review and comment prior to being finalized.

Benefits of Data Integrity Assessment

A data integrity assessment performed by a qualified team of regulatory experts provides a number of important benefits for your organization:

- **Strengthens Your Organization's Data Integrity Focus** – Helps reinforce the fact that your organization is committed to data integrity compliance for all company employees.

- **Provides Peace of Mind** – You know that your data integrity issues have been identified and are being addressed.

- **Reduces Costs** – The cost of remediating data integrity issues identified by the FDA is generally much more significant than when the issues are proactively identified and corrected internally.

- **Stay Focused on Your Core Business** – Proactively identifying and correcting data integrity issues allows your organization to spend less time on compliance issues so you can stay focused on your core business.

Conclusion

Data integrity violations can be the result of many factors: employee errors, lack of awareness of regulatory requirements, poor procedures or not following procedures, insufficient training, intentional acts of falsification, software or system malfunction, poor system configuration, etc. It is therefore critical for companies to develop a quality culture mindset in their employees.

It is important to note that company executives and management are ultimately responsible for creating a quality culture that will support data integrity compliance. By taking assessment of the maturity of their quality culture and making intentional plans for improvement, senior management can generate significant business value by improving product quality and reducing their organization's compliance and financial risk.

As part of you organization's efforts to improve quality culture, data integrity assessments should be included in your QMS as part of GMP audit programs. Utilizing a quality external consultant with expertise in data integrity evaluations for your GMP audit is best practice, as an expert with fresh eyes will likely be able to locate any data integrity issues you missed.

While data integrity assessments can be conducted at any time, there are certain times that it is particularly convenient and/or called for. These include:

- **When implementing a new system that must be integrated into existing infrastructure**
- **When performing system upgrades, patches, enhancements**
- **When performing computer system validation activities**
- **After receiving FDA warning letter or 483 observations regarding data integrity issues**
- **When you identify or suspect data integrity issues**

Ultimately, data integrity is about more than just regulatory compliance. It's also about making sure that your data accurately represents what actually occurred in your organization's manufacturing and quality processes in order to ensure that patients receive safe and efficacious medicines.

About Astrix

Astrix Technology Group has an experienced team of expert informatics consultants that bring together technical, strategic, regulatory and content knowledge to provide the most effective solutions to problems faced by scientific organizations. Astrix provides experienced professionals knowledgeable about FDA regulations to conduct a thorough assessment of your laboratory informatics environment to identify data integrity risks. If you would like to have Astrix conduct a data integrity assessment in your laboratory, or if you would like to discuss your laboratory informatics strategy, please contact us at **www.astrixinc.com**.

[1]"Data Integrity and Compliance with Drug cGMP," U.S. Department of Health and Human Services Food and Drug Administration. December 2018. Available at: https://www.fda.gov/media/119267/download