Data integrity issues in pharmaceutical industry:

Common observations, challenges and mitigations strategies

ABSTRACT:

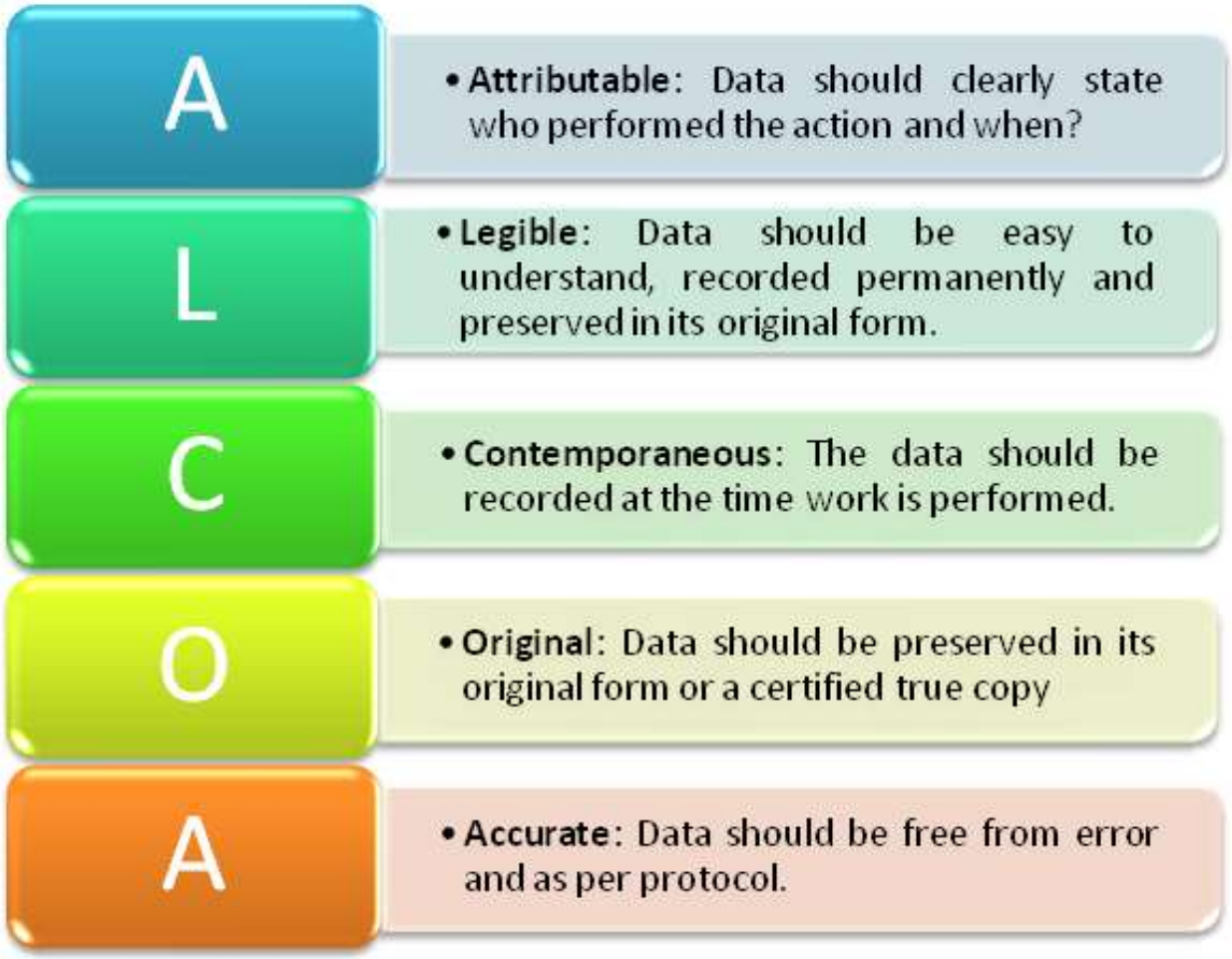
- The pharmaceutical industry's pledge to produce medicines that are secure, efficient, and meet quality requirements is reaffirmed by data integrity (DI). DI is also an essential instrument that regulatory bodies have at their disposal to safeguard public health. It appears from recent FDA Form-483 remarks and warning letters that the primary problem facing the pharmaceutical sector at the moment is DI. If DI standards are not met, there could be a large number of unvalidated results, which could lead to problems after the product is marketed and more frequent product recalls. A thorough strategy is required to address the root causes of DI issues.
- Data Integrity, which is data deemed Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, and Available (ALCOA-plus), has been the focus of the pharmaceutical industry in recent years. With the growing use of computerized systems and rising prevalence of outsourcing manufacturing processes, ensuring data integrity is becoming more challenging in an increasingly complex pharmaceutical manufacturing industry. To address this issue, multiple legislation and guidance documents such as 'Data Integrity and Compliance with CGMP Guidance for Industry' from the US Food and Drug Administration (FDA), 'GxP' Data Integrity Guidance and Definitions from the UK Medicines & Healthcare products Regulatory Agency (MHRA), and 'Guidance on Good Data and Record Management Practices' from the World Health Organization (WHO), have been published in recent years. However, with rising data integrity issues observed by FDA, WHO, MHRA and other pharmaceutical inspectors even after these guidance documents have been published, their overall effectiveness is yet to be determined.

WHAT IS DATA INTEGRITY :

- Data Integrity ,as defined by ISO/IEC2382:2015,Pertains to maintaining accuracy and consistency regardless of changes made.
- Data integrity (DI) reaffirms the pharmaceutical industry's commitment to manufacture drugs that are safe, effective and fulfil quality standards. At the same time, DI is a crucial tool for regulatory authorities to use in protecting public health.
- For pharmaceutical companies , DI is of utmost importance ,driving crucial aspects such as drug development,clinical trials,manufacturing and regulatory compliance.
- According to FDA the DI is the completeness,consistency and accuracy of data.

DATA INTEGRITY PRINCIPLES:

ALCOA Principle to maintain data integrity:



Attributable: All generated data must be traceable to the applicable instrument and the person who generated the data. The date and time of the collection or generation of data should also be recorded.

For example, A correction in the record should be initialed and dated to show when and who made the correction.

Legible: Data should be easy to understand, recorded permanently, and preserved in its original form. There should be no overwriting, All the corrections need to be clearly written with proper justification.

For example, when making corrections to a record, it should be struck using a single line, to ensure the data is legible.

Contemporaneous: Contemporaneous means data should be recorded at the time work is performed. Date and time entries should follow in chronological order. Data should never be backdated.

Original: Source data or Primary is a medium in which the data point is recorded for the first time. This could be an approved form or protocol or a dedicated notebook.

Accurate: To achieve accurate data, the data should be error-free, complete, truthful and it should reflect the observation made. If any correction is made to the data, it should record that who has made the corrected and when it is made.

WHAT IS DATA INTEGRITY :

USE OF DATA NTEGRITY IN PHARMACEUTICALS:

- These days, pharmaceuticals have started relying on computers and automated systems to a great extent ,whether in terms of manufacturing ,laboratory release testing or many other tasks involved.
- It is the responsibility of the pharmaceutical industry to ensure the efficacy ,quality and safety of drugs ,and at the same time safeguard public health
- All this led to the increased importance of data integrity in pharmaceuticals over the last few years.

21CFR Part-11 (Code of Federal Regulations):

- As we know, Now-A-Days, Pharmaceutical Industry adopting Machine (Computerized systems) for minimizing the Errors.
- The Code of Federal Regulations, Title 21 (21 CFR), contains the U.S. federal regulations for every product regulated by the Food and Drug Administration and Drug Enforcement Administration, including pharmaceuticals, veterinary products, medical devices, cosmetics, and foods.
- Part-11 of 21 CFR gives the detailed structure of Electronic signatures and Electronic record maintenance.
- As a part of this, implementing and adopting 21 CFR part-11 in their operating systems (Manufacturing, analysis, Accounts and Commercialization), one could reduce the errors of ALCOA and DI.

21CFR Part-11 (Code of Federal Regulations):

- Software should be chosen that does not allow for data modification without a permanent record and that creates records attributable to who did the work, when, and why.
- Once an appropriate software is chosen, it should be validated to the rigors of 21 CFR Part 11 and data integrity guidance to actively demonstrate complete compliance and secure data.

Recent FDA integrity observations in Review:

- In recent years, numerous warning letters have been issued from the FDA citing data integrity violations.
- Common findings violate principles of ALCOA+, 21 CFR Part 11, and the FDA's data integrity guidance document.
- Some of these findings include:

- Deletion or manipulation of data
- Aborted sample analysis without justification
- Destruction or loss of Manual data
- Failure to document work contemporaneously
- Uncontrolled documentation

Recent FDA integrity observations in Review:

- Implementing the Data Integrity and Part-11 of 21 CFR, the ALCOA can be followed as per regulatory Good Documentation Practices (GDP) and Good Manufacturing Practices (GMP) of ICH guidelines to overcome the issues generating in daily basis operations, analysis and Accounting.
- **Implementations of DI issues of common observations:-**

Deletion or manipulation of data:-

- 21 CFR, provides the record of every data in their audit trail report . By reviewing the audit trail report in periodical manner, one could trace the attributability of the data.
- Deletion of electronic records cannot be done by implementation of 21 CFR.

Recent FDA integrity observations in Review:

Aborted sample analysis without justification:-

- CAPA is provided by immediate revision of the Standard Operation Procedure (SOP) that every sample analysis aborting will be done by providing justification through following the implementation of Quality Management System (QMS).
- QMS controls this issue by Preliminary Investigation of the Incident.
- Recommendations are provided by the QMS Team and are addressed in the CAPA for future references.

Destruction/loss of Data of Manual data:-

- Proper Archival System of the documentations are provided for Manual forms.
- Each Manual forms are assigned with Unique Issuance code. This could help the Traceability of the data.

Recent FDA integrity observations in Review:

- Destruction of the Data can be done by approvals of QMS team by proper justification.
- Proper Obsoleting procedure for the Document shall be provided for future references .

Failure to document work contemporaneously:-

- Non-Contemporaneous work is the Major issue of the Data Integrity.
- The issue is happening as a result of delay in the manual recordings.
- This could be minimize by providing the Date and Time of the activity by adding the operator details through 21 CFR.
- Implementing 21 CFR and Part-11 to the activities, the work could be Contemporaneous.

Recent FDA integrity observations in Review:

Uncontrolled Documentation:-

- The Documents shall be issued with proper control number at the time of issuance.
- The issuance numbering system shall be addressed in the SOP.
- This could keep the Originality of the Document.

Conclusion:

Conclusion:-

- In order to overcome the Data Integrity issues, the documentation practices shall be done accordingly by following ALCOA principles.
- Proper Review system and authorization of the particular activity shall be authorized to the Trained personal.
- Implementation of 21 CFR helps us the Contemporaneous of the document and attributability of the document.
- Following Quality Management system (QMS) and Implementing periodical training the Personnel helps us to manage in minimizing the errors in regular work.
- Accountability and traceability of the stock records can be done by implementing software like Laboratory Information management system (LIMS) and System Applications & products in Data Processing (SAP) that are aligned with 21 CFR.