Data Integrity (DI): Status, Challenges & prevention to overcome DI issue in pharmaceutical Industry

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Introduction

The goal of data integrity (DI) is to prevent unauthorised modifications to the necessary information by guaranteeing that data records are accurate, complete, intact, and kept in their original context. (1)

Inadequate data integrity can have serious repercussions, such as data being rejected for marketing purposes and the need for extra research.

In the event that Clinical trial management is not done in this manner., there are also ethical concerns with subjecting participants for experimental drugs. Critical concerns in managing clinical trial data include data quality and integrity. (2) Clinical trial researchers must take into account all challenges related to maintaining data integrity and have tried and true processes in place throughout the investigation. (3)

The pharmaceutical quality management system, which depends on product quality to ensure that the medications produced are of the intended quality, includes data integrity as a key component.

The product quality is data dependent. Data integrity strives to prevent information fabrication by providing the confidence that they are exact, intact, true, and well-preserved in its original form, along with electronic and paper records. (4)

The degree of comprehensive, consistent, accurate, trustworthy, and dependable throughout lifetime of data is known as data integrity.(5)A data must be continuously checked for completeness and accuracy throughout.(6)

In last 40 years, data monitoring committees' techniques have changed. Decisions about early termination are guided by statistical techniques that have been established. [7]

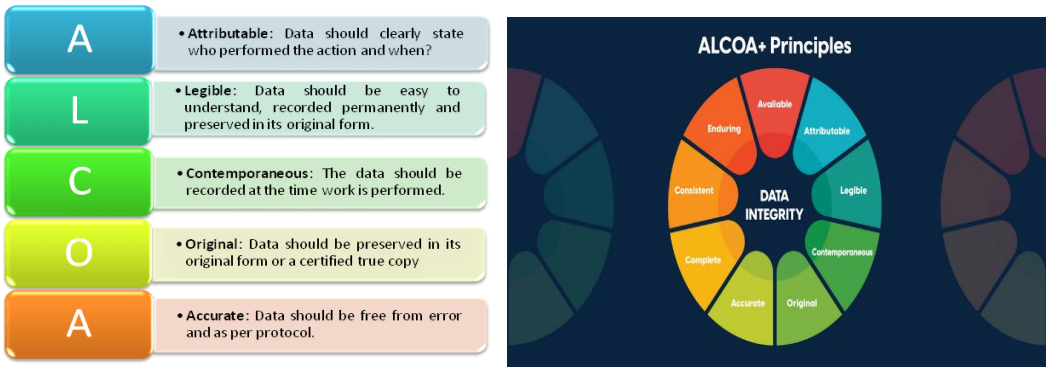


Figure 1: depicting data integrity principles i.e, ALCOA and ALCOA plus [9][10]

GUIDELINES FOR DATA INTEGRITY

Year	Guidance document
March 2015	MHRA:GMP data integrity definition & guidance for industry
Sept 2015	WHO (draft): Good data & record management practices
April 2016	FDA(draft): data integrity & compliance with CGMP
June 2016	WHO: Good data & record management practices
July 2016	MHRA (draft): GxP data integrity definition & guidance for industry
July 2016	PIC/s: good practices for data management & integrity n regulated GMP/GDP environment(draft 2)
Aug 2016	EMA: Question & Answer: Good manufacturing practices- Data integrity
March 2018	MHRA: GxP data integrity guidance & definition(revision 1)
November 2018	PIC/S: Good practice for data management & integrity in Regulated GMP/GDP environment (Draft3)
December 2018	FDA: Data integrity & compliance wih drug CGMP Questions & Answers

Fig 2 GxP relates to Good practices guidelines & regulation.

Data Integrity provides trustworthiness/reliability regarding the data [8]. To guarantee the development of finest & accurate information, adequate and strong data management methods are essential. [11]

Regulatory Requirement

The larger category of data management includes assurance of data integrity, which is applicable to both paper records and electronic records. [12]

To clarify the need with regard to computerised health records, see 21 CFR Part 11. All electronic records created, amended, maintained, archived, retrieved, or communicated in accordance with any document requisite specified in Agency regulations are subject to Part 11. It also applies to electronic documents delivered to the agency in accordance with the Public Health Service Act and Federal Food, Drug, and Cosmetic Act. Computerized systems, a part of GMP-regulated activities must comply with GDP's Annex 11 regulation.

ALCOA is the term used by the Medicines and Healthcare Regulatory Agency (MHRA) and the US Food and Drug Administration (FDA) to describe what they require from electronic data. As the volume of data grows, internal consistency within the data becomes crucial. When data is appropriate for the activities and outcome for which it is intended, it is said to be of high quality. [13]

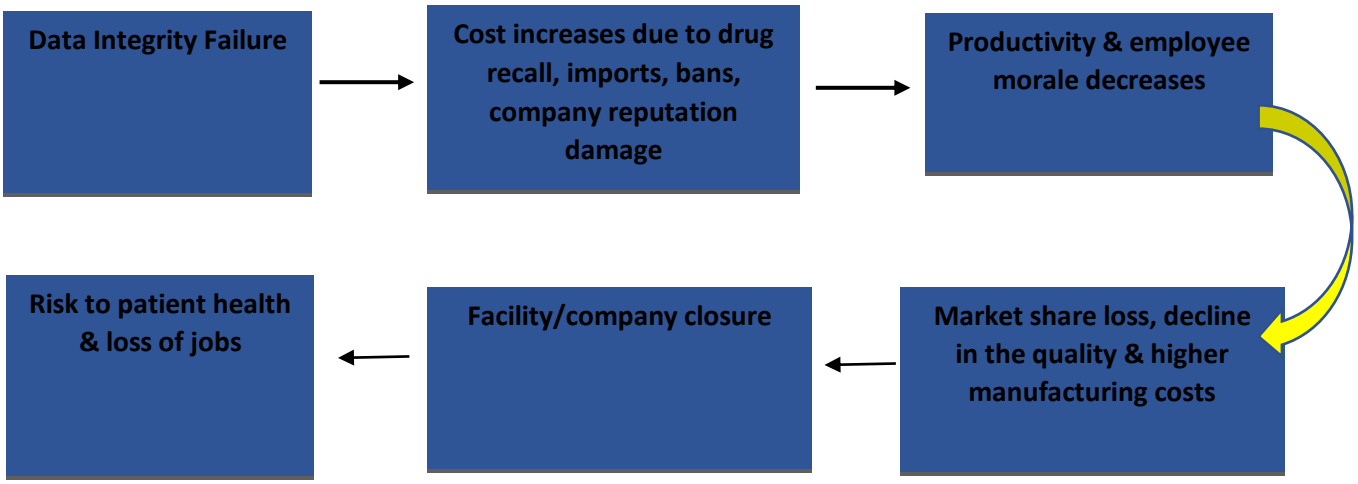


Fig 3: Chain showing data integrity breach & its consequences

Data Integrity violation[14]

A breach of data integrity is a failure by a company or organisation to ensure that its records and documents reflect reality and truth. This holds true for the whole drug development and discovery process.

- Research and development
- Quality control
- Quality assurance
- Manufacturing
- Clinical trials
- Inspection
- Post-inspection activities

Data integrity issues can arise through:

- errors caused by human
- Failure to manage data
- cyber threats & hacking
- hardware compromised
- physical damages to device. [15]

Related issues

- Data fabrication
- Data abandon
- Incorrect reporting of data
- Improper date of data
- irregular submission of data
- changing current data & considering it as modified data
- Replication of record

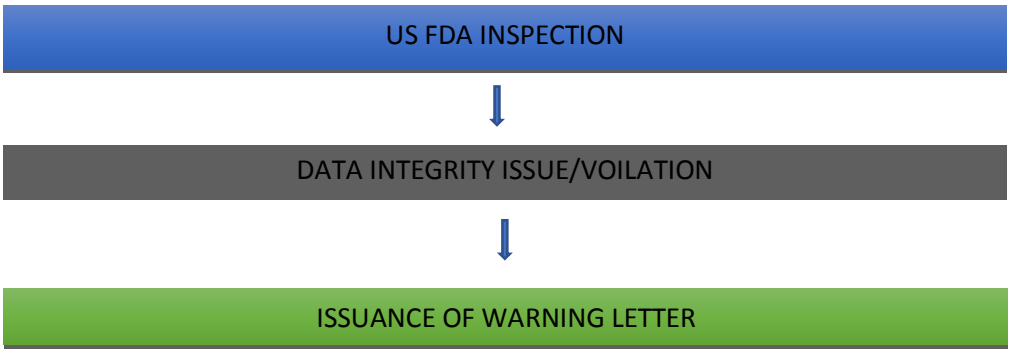


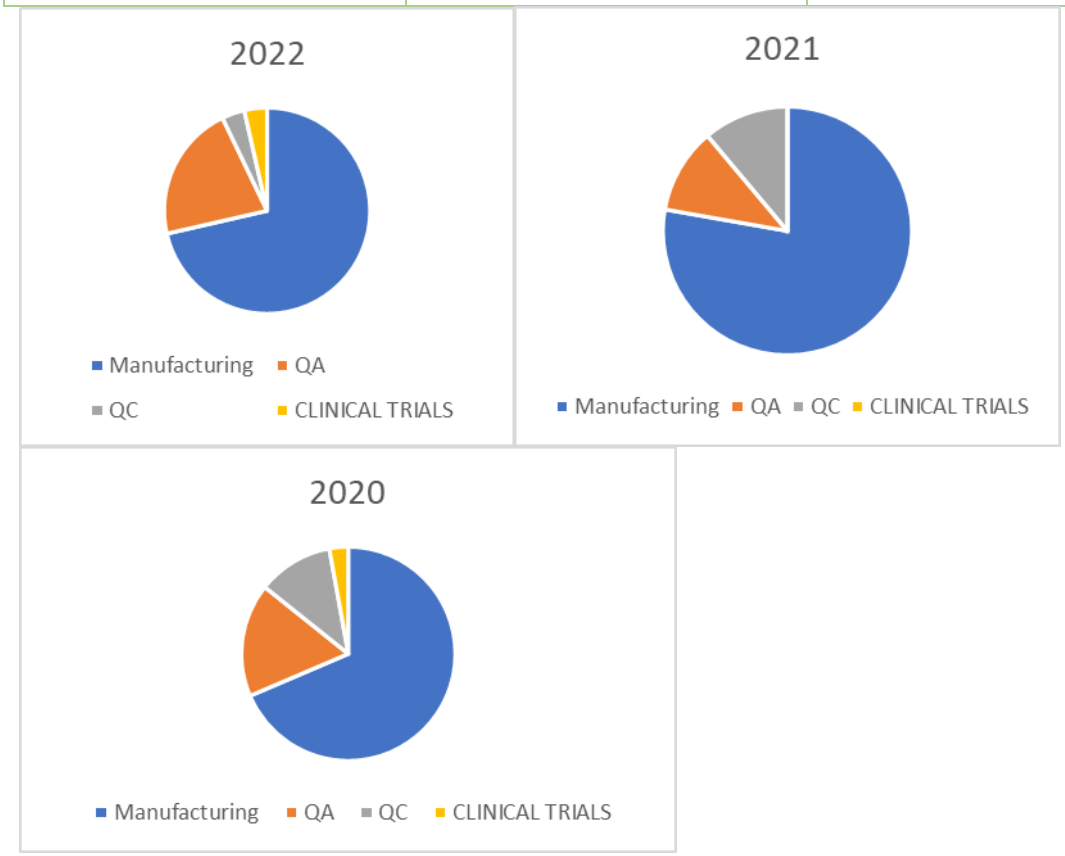
Fig 4: Data integrity identification & warning letter

2020-2022[16]

Fig 5: data showing warning letters issued in past 3 years

YEAR	CATEGORY	WARNING LETTER ISSUED
2022	Manufacturing	20
	QA	6
	QC	1
	CLINICAL TRIALS	1

2021	Manufacturing	7
	QA	1
	QC	1
	CLINICAL TRIALS	0
2020	Manufacturing	24
	QA	6
	QC	4
	CLINICAL TRIALS	1



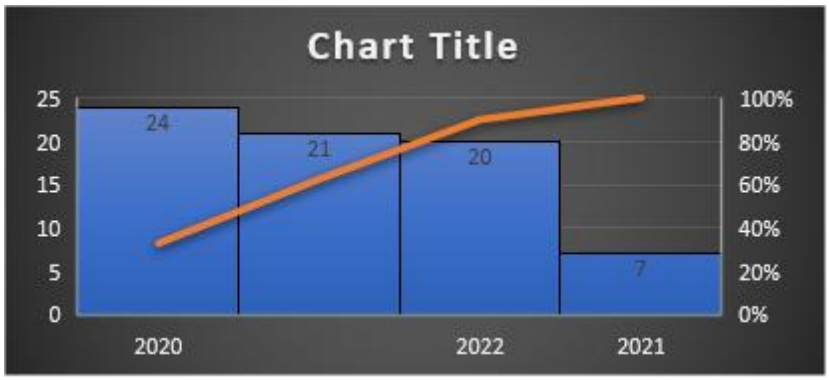


Fig 6: Models showing percentage & rate of occurrence of data integrity in different discipline.

Risk-based approach to data integrity

1. Awareness: The relevance of the integrity of the data and the effects that users at all levels may have on the data when given the appropriate authorizations for their work functions must be understood by all employees.

   The business can gain this understanding with a relatively brief, straightforward training session.

2. Standardization: To establish a shared understanding of terminology and concepts, the regulatory guidance that is currently accessible, such as MHRA should serve as the foundation for the standardisation stage .

3. The interpretation of internal regulations, terms, idea and the risk levels related to the data should be included in this process, but not exclusively.

4. Analysis of Gap : The risk associated with each process or system and the data it creates or modifies will be evaluated using analysis of gap of the processes and systems that follow, with a focus on the existing controls for data integrity and their compliance with requirements.

   Before assigning criticalities to the various data elements and associated controls, risk assessment, thresholds for mitigating action should be established. Generally, any such risk-based strategy should be founded on accepted criteria, such as Quality Risk Management and ICH Q9. [17]

Summary of the observations raising question about data integrity

- ✓ Replacing pages of documentation
- ✓ Data Falsification
- ✓ No OOS/OOT
- ✓ Lack of personnel
- ✓ Training records blank

Data integrity issues consequences

Issues with data integrity could send the organisation warning letters, import warnings, and penalties. Debarment and imprisonment may be the consequences for those who committed the wrongdoings.

Future potential for integrity protection

It is essential to take into account additional measures to minimise hazards as the pharmaceutical business grows more digitally mature and progresses toward industry. Individual logins are recommended, which is a substitute for identity sign even on common computing device so that record can be attributed and traced at the time of investigation.

Prospective approaches will take into account blockchain applications, that depend on numerous verifications of the data collected to guarantee data accountability, integrity, and privacy. [18]

Conclusion

Integrity of data is a aspect of fundamental of keeping, reliability and protection [19]. Data is now an asset thanks to the cloud, big data, and AI, which opens up many opportunities for process improvement, scientifically based methods, ongoing process verification, and more.

In "smart" manufacturing, where cutting-edge information and manufacturing technology add flexibility to physical processes, it is possible to transition from reactive to predictive and from stringent to adaptive process control.

In big data environment, where built-in data management tools automatically monitor compliance, current data integrity best practises and recommendations are applicable.

Manufacturing data analysis powered by AI technologies also enables continuous risk analysis and monitoring utilising advanced analytics to identify and separate questionable data. Without any overall structure or context, continuous data collection collects information from any manufacturing or production source. [20]

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