# Data Integrity

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# Data Integrity

- **Introduction/Definitions**
- **Culture & Mindset**
- **Challenges**
- **FDA remarks/Examples**

# Introduction

## What is Data Integrity?

- 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

# Introduction

## Why is Data Integrity Important ?

- Reliability on the information used to ensure the quality of the drugs that consumers will take
- Data integrity problems break trust
- FDA/ Authorities rely on firm's to do the right thing when FDA/ Authorities are **not** present

# Introduction - Data and Data Type

## What is “Data”?

- Data can be defined as facts – information derived from raw data
- Data can exist in a variety of forms – as numbers or text on paper or as bits and bytes in electronic form

## This information can be contained in several formats:

- Paper Data
- Electronic Data
- Certified Copy
- Duplicate Data

# Data and Data Type

## What is “Raw Data”?

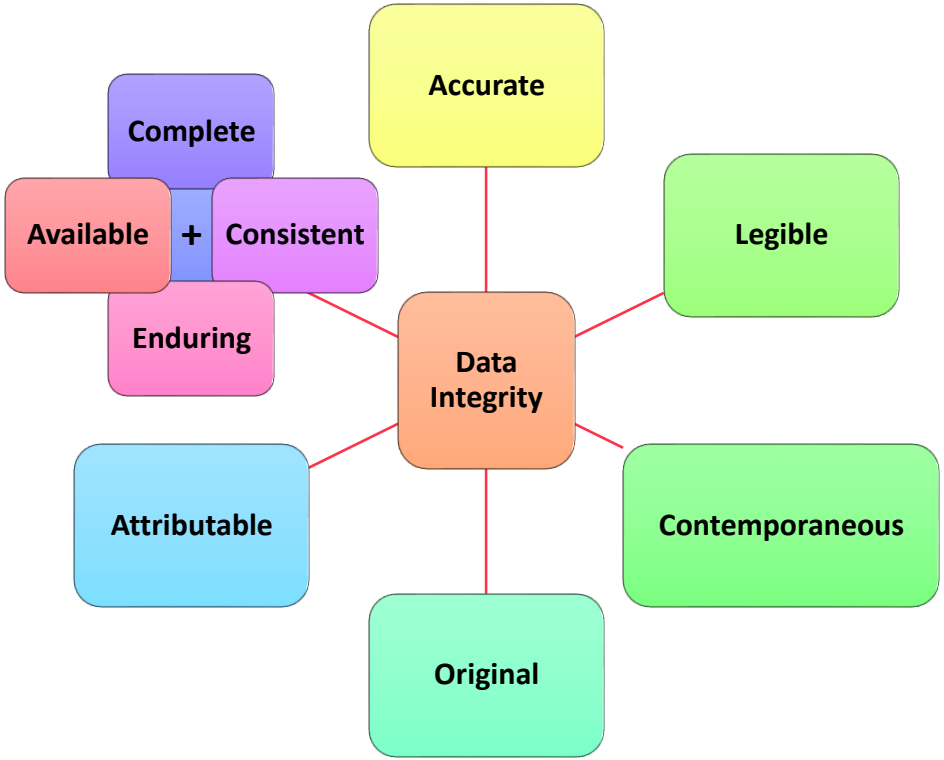
- Original records and documentation, retained in the format in which they were originally generated (i.e. paper or electronic), or as a ‘true copy’.
- Any work-sheet, record, note or exact copy that is the result of original observation and activity and which is necessary for the reconstruction and evaluation of a work project, process or study report, etc.
- Raw data must be accurately recorded by permanent means.
- Raw data may be hard/paper copy or electronic but must be known and defined in system procedures.

# Data and Data Type

## What is Metadata?

- Metadata is the contextual information required to understand data.
- A data value is by itself meaningless without additional information about the data.
- Metadata is often described as data about data.
- Metadata is structured information that describes, explains, or otherwise makes it easier to retrieve, use, or manage data.
- For example, the number “23” is meaningless without metadata, such as an indication of the unit “mg.”

# Data Integrity - ALCOA



# Alcoa +

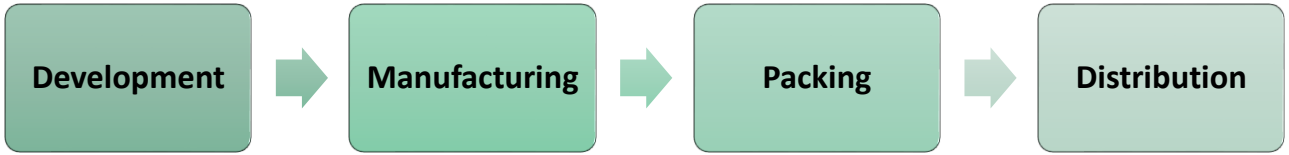
- Attributable
  - Traceable to a unique individual
- Legible
  - Data must be recorded permanently and be readable
- Contemporaneous
  - Activities must be recorded at the time they occur
- Original
  - First capture of data (not transcribed data), must review the original record, must retain the original or certified copy* of the original record
- Accurate:
  - records must be accurate, which is achieved thru the Quality Management System

# Alcoa +

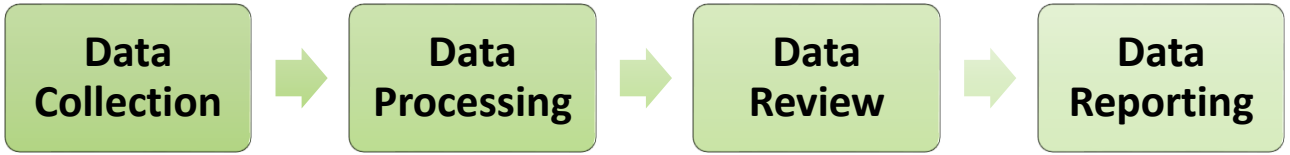
- Complete
  - All data including any repeat or re-analysis
- Consistent
  - All elements and sequence of events are dates in expected sequence
- Enduring
  - Data is recorded in proper records or electronic media
- Available
  - Data is available for review, audit or inspection

# Data Integrity – Lifecycle approach

## Data Integrity involves the product lifecycle:



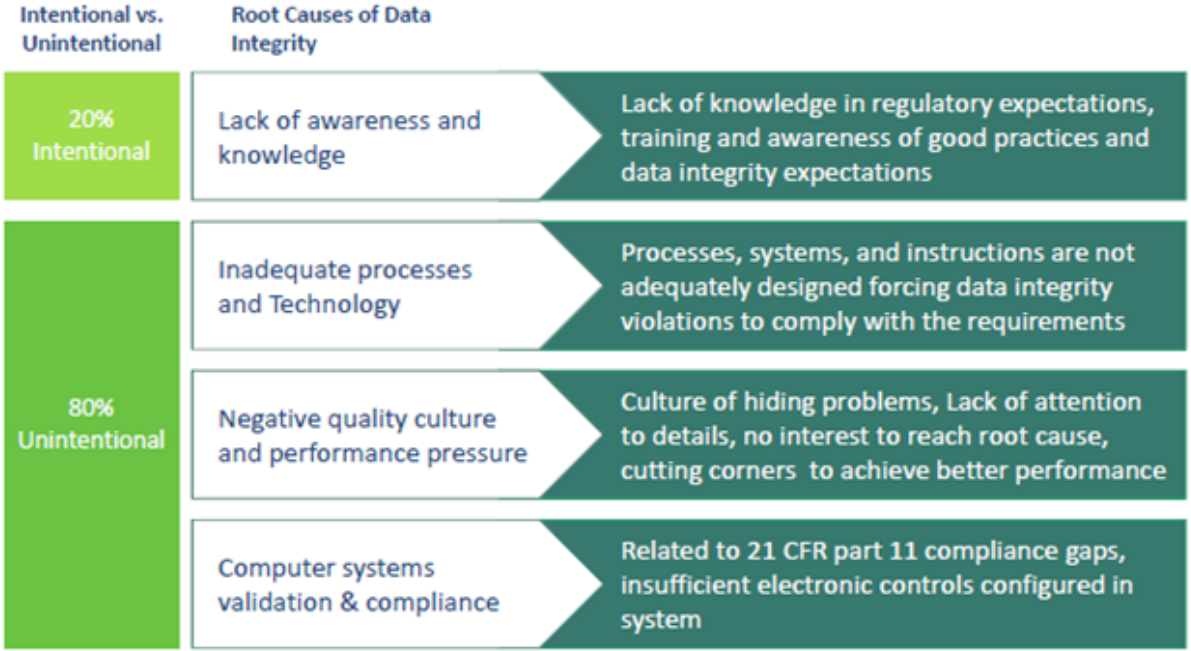

## Data Integrity involves the data lifecycle:



# What is needed???



# Data Integrity Issues



# Data Integrity – Culture & Awareness

## Change of Mindset

- Awareness
- Correct interpretation of regulations and cGMP requirements
- Gap Analysis and Remediation Plans for Equipments and Systems in QC and Production
- Training
  - adapt training to target audience
  - Provide real examples and case studies
  - Effective training to new entrants
  - Cultural training, mind-set corrections and molding of newly recruited staff from other organizations into Quality Culture of company

# Data Integrity – Culture & Awareness

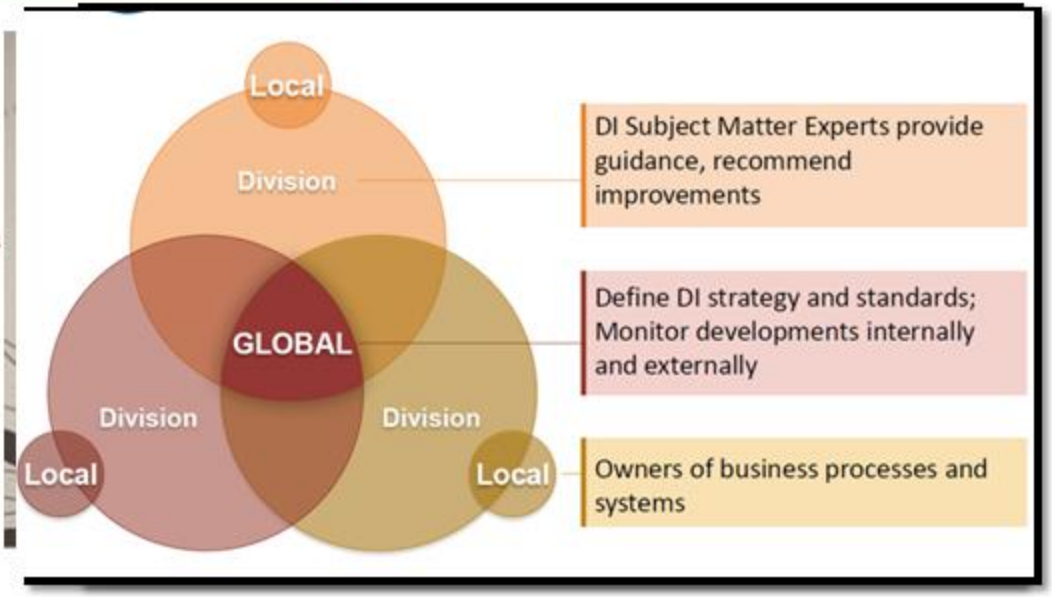
## Change of Mindset

- Shop floor visits
  - Verify what employees are doing
  - Try to understand why they are doing things
  - Were they trained to do it wrong?
  - Adherence to procedures and policies in place
- Site DI Champion
  - A knowledgeable person who can answer questions
  - Is present for the employees
  - Ensures the implementation of DI culture
- HR
  - Create a work environment that is transparent and open
  - Ensure people are telling the truth

# Four vital steps towards Data Integrity

*Novartis holistic approach to Data Integrity is driven by 4 work streams*

1. Education and Communication
2. Detection and Mitigation of Risks
3. Technology and IT Systems
4. Governance of DI



# FDA Comments

## Thomas Cosgrove- PINK SHEET

**Thomas Cosgrove, director of the Office of Manufacturing Quality in the Office of Compliance in FDA's Center for Drug Evaluation and Research, made these remarks at the Association for Affordable Medicines' Chemistry, Manufacturing and Controls Workshop on May 24 in Bethesda, Md.**

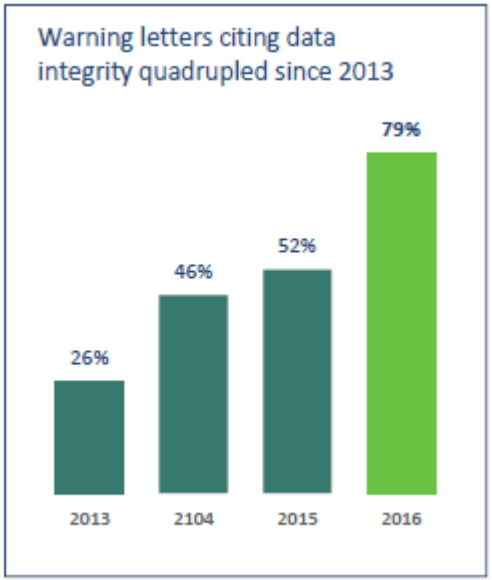
- A top FDA compliance official said that data integrity problems are not going away any time soon as many brand-name drugs are now going off patent and the pressure to be the first to file intensifies with an "enormous" amount of money at stake, harking back to the days of the generic drug scandal.

# FDA Comments cont.

- Data integrity problems have been a common theme in drug GMP warning letters and these problems are increasing.
- Of the 26 warning letters to active pharmaceutical ingredient firms in calendar year 2016, 16 (61%) focused on data integrity issues
- Data integrity problems surfaced in at least 13 (30%) of drug GMP warning letters in FY 2015 and in 17% the year before.

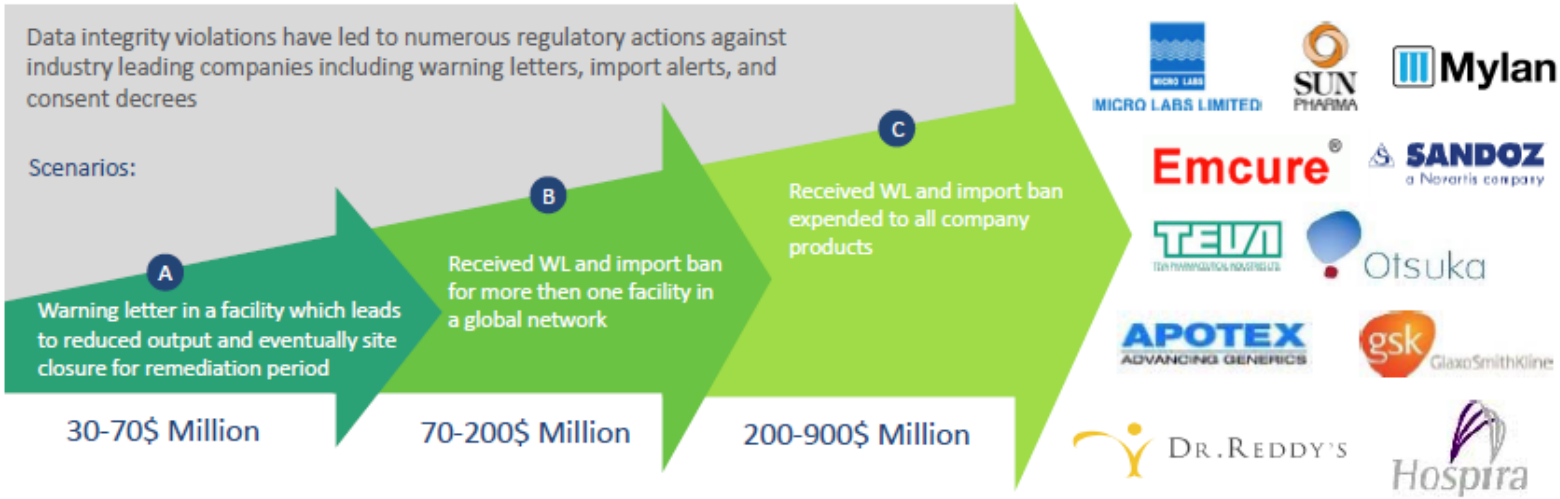
# Global Regulatory Focus on Data Integrity

In recent years regulators globally **increasingly observed CGMP violations involving data integrity** during inspections. The violations identified have raised regulators' concerns on the ability of companies to ensure the safety, efficacy, and quality of drugs.



# Business Impact of Poor Data Integrity

In recent years regulators globally increasingly observed CGMP violations involving data integrity during inspections. The violations identified have raised regulators' concerns on the ability of companies to ensure the safety, efficacy, and quality of drugs.

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# FDA Comments cont.

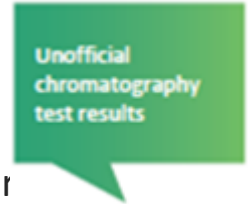
Cosgrove said that FDA investigators are seeing a lot of these data integrity problems in their inspections:

- Testing into compliance;
- Cherry picking data;
- Reusing data;
- Batch records that don't match test results; and
- Audit trails and back-ups going on and off.

# FDA Comments cont.

Cosgrove said that two recent warning letters reflect these data integrity trends. One was FDA's warning letter in March 2015 to Hospira Inc. after the company was found deleting or altering raw data files.

- FDA said that Hospira's high performance liquid chromatography software did not have sufficient controls to prevent the deletion or alteration of raw data files.
- Trial injections of stability samples were saved in the test folder and official samples wer analyzed after trial injection.
- In another case, a warning letter was sent to Tai HengIndustry in Shanghai, China, after personnel were found changing the time clock on their high-performance liquid chromatography equipment rather than investigating and correcting issues underlying the out-of-specification results obtained in batch release testing.



# FDA Comments cont.

Recently, the agency has come to rely more on Form 483 reports to combat data integrity failures. This was the tool the agency used in the Semler Research Center Private Ltd. data integrity fraud case.

- FDA gave Semler a Form 483 report of inspectional observations in April 2016 when it found that the company's clinical and bioanalytical studies were not acceptable as a result of data integrity concerns.
- Semler is a contract research organization that conducts bioequivalence and bioavailability studies for a number of pharmaceutical companies. FDA found evidence that the firm substituted samples and data from one patient group for another.

# FDA Comments cont.

- Cosgrove said that it is in a firm's best interests to have robust quality systems and to catch problems before FDA investigators walk in the door. "Even if you have done as good a job as possible in hiring and have the most morally upstanding folks on the planet, there are going to be folks within your company who are going to cut corners.

➢ **Your job is to try to prevent that. It is your job to ferret that out!**

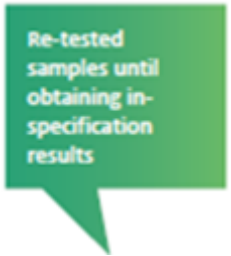
➢ **You need to prevent that and protect your patients!**

# Data Integrity – Examples

- The receipt of incoming material was documented by an employee who was not physically present on site at the time of entering the data to the system.
- A general username and password was set. Two identical users attached to the user list of equipment, which means that it was not possible to identify who entered data into the system.
- Different dates recorded on same Batch Manufacturing Record.

# Data Integrity – Examples

- Analytical results were tested until acceptable results were obtained… without appropriate documentation, justification and investigation
- OOS results were not included in the official laboratory test data sheet.
- Sample ID was not assigned to the specific batch tests thus, the traceability and/or integrity of the test performed was in question.



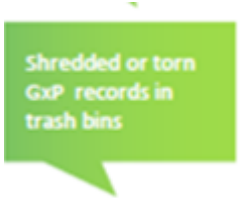
# Data Integrity – Examples

- Laboratory records do not include complete data derived from all tests…
- There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.
- Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.
- Procedures for the preparation of master production and control records are not followed

# Data Integrity - Examples

## Examples of significant issues

- No raw data to support records
- Creating inaccurate and incomplete records
- Test results for one batch used to release other batches
- Backdating
- Fabricating data
- Discarding data

# **Data Integrity –** Top Ten Data Integrity Traps - FDA Recommendations

1) **Quality Culture**: Leadership emphasis; Message credibility; Peer involvement ; Employee ownership
2) **Personnel**: All employees need to be trained in the concept of data integrity
3) **Batch Records**: Review records; Confirm ; Look for corrections; verify suitable document control
4) **Document Control**: Controlled documents are a key component of data integrity
5) **Electronic Data Systems**: Systems should be validated; segregation of duties; Maintain audit trails.
6) **Analytical Documentation**: review the data in the documents against the electronic data.
7) **Laboratory Controls**: sure that all procedures are clearly spelled out and understood
8) **Laboratory Equipment**: make sure that all procedures are clearly spelled out and understood
9) **Materials management**: Storage and distribution operations need to be strictly controlled
10) **The Manufacturing Floor**: walking the floor to just get a feel for what's going on

# Thank You.