Compliance issues around Data Integrity; Data Management:

Typical Findings, How to Avoid them and How to Address Them

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Introduction

- **Typical data integrity finding from Regulatory audits**

- **How to avoid data integrity deficiencies**

- **How to address data integrity deficiencies**

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What is Data Integrity?

- Data integrity is the maintenance of, and the assurance of the accuracy and consistency of, **data over its entire life-cycle**, and is a critical aspect to the design, implementation and usage of any system which stores, processes, or retrieves data.

- The term is broad in scope and may have widely different meanings depending on the specific context – even under the same general umbrella of computing.

- Data integrity is **<u>not</u>** just about computer systems and electronic records but includes all records.

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What is Data Integrity?

- Data Integrity is a concept encompassing many things in the codes of Good Manufacturing Practice (GMP)

- Data Integrity is not just a specific code clause or set of code clauses

- The concept of Data Integrity is **not** new, but the concept has been given a name (under the banner Data Integrity) and it has had a focus in recent years and has been described in many guidelines

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When Did Data Integrity Enter The Code?

'Data integrity' as a phrase only has mention in one clause in the PIC/S Code for Good Manufacturing Practice for Medicinal Products; PE 009-13

PE 009-13 Annex 11

1. Risk Management

   Risk management should be applied throughout the lifecycle of the computerised system taking into account patient safety, **data integrity** and product quality. As part of a risk management system, decisions on the extent of validation and **data integrity** controls should be based on a justified and documented risk assessment of the computerised system.

When Did Data Integrity Enter The Code?

Records are data and the concept of integrity for records is not new

PE 009-13 Part I

GENERATION AND CONTROL OF DOCUMENTATION

4.1 … Appropriate controls should be in place to ensure the integrity of the record throughout the retention period.

What is Data Integrity?

Data integrity includes:

- Security of records

- Validation of systems

- Control of system configurations and policies

- Change control

- Backup

- Archiving

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What is Data Integrity?

Data integrity includes:

- Recording systems incidents (not only system failures and data errors)

- Training

- Service provider controls

- Entry checks

- Management supervition

- And much more …

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Typical data integrity finding from Regulatory audits

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Typical data integrity finding from Regulatory audits

- Failure to keep original records

  - Companies printed chromatograms but fail to control or even deleted the original electronic records

  - Original records from equipment outputs were not kept or controlled

  - Analysts were conducting runs that were not recorded or kept

  - Backups not being conducted

  - Failure to periodically check that archived data is readable

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Typical data integrity finding from Regulatory audits

- Failure to keep accurate records

  - The records of the stability trials held in controlled temperature cabinets did not match the actual number of items in the cabinet

  - Test specification sheets were marked as if the test had been conducted in house; however, the results were taken directly from the supplier's CoA

  - Original records of stock movements were discarded

  - Senior staff who were responsible for checking results failed to check original records and failed to check the audit trails

  - Critical software did not have audit trails

Typical data integrity finding from Regulatory audits

- Fraud

  – There have been many finding of fraud including

    - Falsification of stability data

    - Falsification of analytical results

    - Falsification of tests being done that were never preformed

    - Falsification of stock movements

US FDA

- FDA Warning Letter: 320-16-18; Shanghai Desano Chemical Pharmaceutical Co., Ltd. 6/16/16

- 1. Failure to have laboratory control records that include complete data derived from all tests conducted to ensure compliance with established specifications and standards.

  Your laboratory personnel conducted "unofficial" testing without appropriate documentation, justification, and investigation.

  The original, unofficial analyses were stored in a separate "Test" folder and were not part of the official quality control records. Our inspection found that your firm performed circa 8,400 of these **unofficial chromatographic analyses** between 2012 and 2014. According to your SOP-B-QC-022-01, Instrument Use Standard Operating Procedure, analysis of samples must be documented. The volume of data in these auxiliary "Test Folders" suggests that **performing unofficial analyses** is a common practice at your facility.

  Your quality unit must review all pertinent analytical data when making batch release decisions in order to determine batch quality.

  Your quality system does not adequately ensure the accuracy and integrity of data

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Example of Data Integrity Issues Found

- The FDA's inspection of the ██████ facility, which concluded on Jan. 11, 2014, identified significant CGMP violations. These included ██████ staff retesting raw materials, intermediate drug products, and finished API after those items failed analytical testing and specifications, in order to produce acceptable findings, and subsequently not reporting or investigating these failures.

  https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm382736.htm

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How to avoid data integrity deficiencies

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How to avoid data integrity deficiencies

- Understand what Data Integrity means

- Understanding original data and true copies

- Define which records are the primary records

- Data integrity is not just about technical fixes
  (it also involves procedures, management and people)

- Train staff in data integrity

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What is Data Integrity?

- **Data integrity** is the maintenance of, and the assurance of the accuracy and consistency of, **data** over its entire life-cycle, and is a critical aspect to the design, implementation and usage of any system which stores, processes, or retrieves **data**.

- For the purposes of this guidance, **data integrity** refers to the completeness, consistency, and accuracy of **data**. Complete, consistent, and accurate **data** should be **A**ttributable, **L**egible, **C**ontemporaneously recorded, **O**riginal or a true copy, and **A**ccurate (ALCOA).

  - (U.S. Department of Health and Human Services Food and Drug Administration; Data Integrity and Compliance With CGMP Guidance for Industry DRAFT GUIDANCE, April 2016)

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Data Integrity Guidances

- FDA – Data Integrity & Compliance with cGMP (Draft April 2016)

- FDA Data Integrity and Compliance With Drug CGMP Questions and Answers Guidance for Industry (December 2018)

- TRS 996, Annex 5: Guidance on Good Data and Record Management Practices (May 2016)

- Medicines & Healthcare products Regulatory Agency (MHRA) 'GXP' Data March 2018

- PIC/S Good Practices for Data Management & Integrity in Regulated GMP/GDP Environments (Draft November 2018)

- European Medicines Agency, Question & Answers: Data Integrity (August 2016)

- GAMP Guide: Records & Data Integrity March 2017

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Data Integrity Guidance (cont.)

- PDA, Elements of a Code of Conduct for Data Integrity in the Pharmaceutical Industry

- WHO Expert Committee on Specifications for Pharmaceutical Preparations Fiftieth report Annex 5 Guidance on good data and record management practices

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Original Data

- The original record must be kept as evidence (whether it is hardcopy or electronic)

- Data must be traceable, accurate and complete

  - Data includes meta data (data about data)

  - Meta data includes audit trails

  - Inspectors will check for missing/deleted data, items out of sequence and/or modified records

    - i.e. failed runs must be connected to an out of specification report and electronic records must be retained and complete

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What is Original Data?

- As a rule of thumb,

  - original data is the first time that information is recorded on a durable recording device

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# Things that Lead to Data Integrity Issues

- **Opportunity** or the ability to manipulate data by those with access

    - Existing regulatory guidance, typically focus on the ability with controls such as written procedures and technical controls

- **Pressure** or incentive - the reason for amending, deleting or falsifying data

    - Existing regulatory guidance do not focus the influence of management behaviour (although there is some in the form of independence of QA & Production and sufficient resources)

- **Rationalisation** (how an individual can justify their actions)

    - Not a focus of existing guidance

The Company's Management Style Matters in Preserving Data Integrity

1. Does the company make systems and processes that take a lot of effort to follow and/or are very **complex** to understand and/or **hard to learn**?

2. Are middle level managers **conflicted between quality and time**/costs in which they are mostly rewarded for time/cost saving and punished only if found out for quality failures?

3. Are staff regularly put under **excessive time constraints**?

4. Does the company **leave systems open**, with poor or no locks and little or no checks and alternative easier unapproved paths or methods available?

5. Are staff left **unsupervised** for long periods (e.g. night shifts)?

6. Are staff **punished** for admitting mistakes or admitting that they do not know how to do something in the job role?

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People Follow the Laws of Physics

- In physics; the phase "path of least resistance", in very simple situations, is an approximation of the tendency to the least energy state.

- People, generally follow the path of least resistance.

- If company systems are excessively complex and/or difficult to learn, people will naturally look for an easier way.

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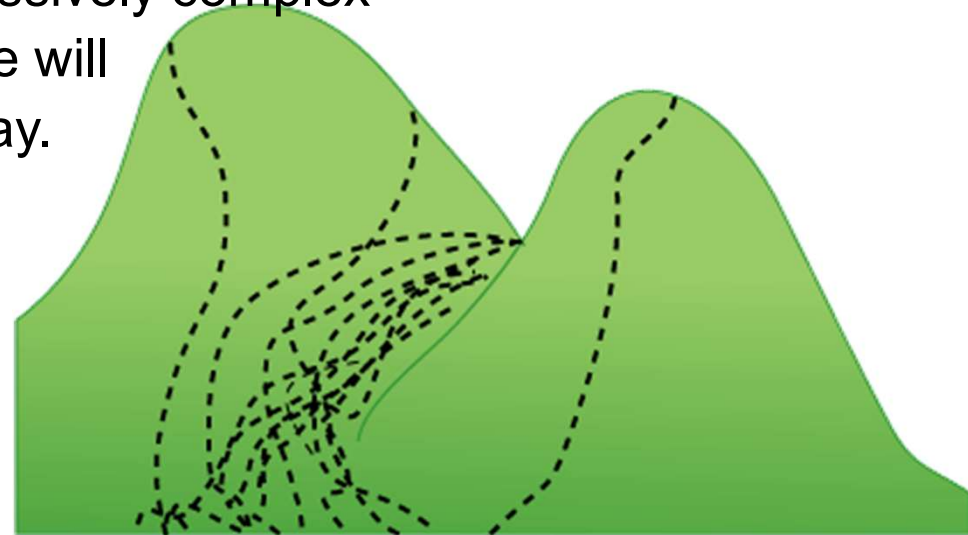
Summary

- Understand the meaning of data integrity

- Understand which records are original records and ensure that they are appropriately saved, stored and protected

- Sometimes people do the wrong thing because they believe it is the right thing to do for the company

- The style of management can affect the likelihood of failures of data integrity

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Thank You for Participating
Any Questions?

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