Australian Government
Department of Health
Therapeutic Goods Administration

Data Integrity: TGA Expectations

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PDA conference July 2015

TGA Health Safety Regulation

Presentation Overview

- What is Data Integrity?
- Global/Australian/US FDA Environments
- Data Integrity General Examples
- Basic Data Integrity Expectations
- ALCOA Principles
- TGA Licensed Manufacturers Expectations
- Conclusions

What is data integrity?

- The extent to which all data are complete, consistent and accurate throughout the data lifecycle

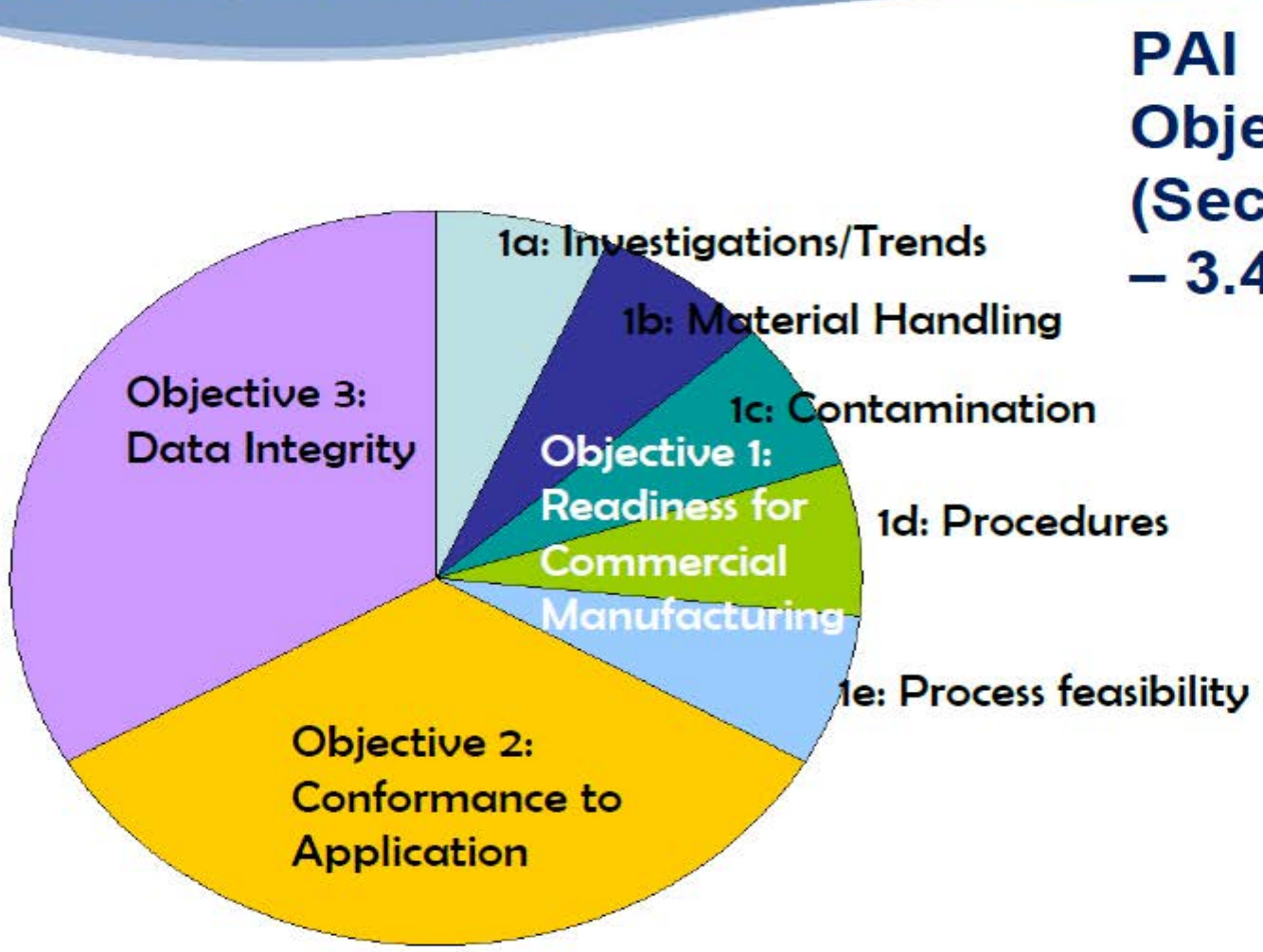
- From initial data generation and recording through processing (including transformation or migration), use, retention, archiving, retrieval and destruction.

(MHRA Guidance March 2015)

Why so much interest now?- Global Environment

Manufacturer 1 **Overwriting of electronic raw data until acceptable results were achieved** **OOS not initiated** **Falsification of data to support regulatory filings** **Stand alone GC systems without adequate controls**	**Manufacturer 4** **Chromatographic software was not validated to ensure re-writing, deletion of data prohibited**
Manufacturer 2 Falsification of batch records (re-writing clean records) Non-contemporaneous recording of lab data Recording of sample weights on scraps of paper Missing raw data	Manufacturer 5 IPQC performed without batch record present Unexplained 'trial' samples run before analysis Deletion of HPLC data -lack of data security Missing stability samples
Manufacturer 3 Unofficial testing of samples (trial samples) OOS results not investigated Retesting completed but not justified No restriction/protection of electronic data	Manufacturer 6 Lack of records demonstrating who performed analysis Raw data not recorded contemporaneously nor by the performing analyst Failed injections of QC standards (SS) deleted, repeated and inserted into the analytical sequence without explanation.

US FDA



www.fda.gov.downloads/drugs/developmentapprovalprocess/smallbusinessassistance/UCM407991.pdf

Australian Environment: Inspection report

- **DEFINITIONS**

- **Critical Deficiency**
- A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. **Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data**.

Data Integrity: General Examples

Need to know the difference between falsification and poor/bad GMP/practice

- Human errors
  - data entered by mistake
  - ignorance (not being aware of regulatory requirements or poor training)
  - Wilfully (falsification or fraud with the intent to deceive)

- Selection of good or passing results to the exclusion or poor or failing results

- Unauthorised changes to data post acquisition

Ref: “Data Integrity”
pharmauptoday@gmail.com

Data Integrity: General Examples

- Errors during transmission from one computer to another
- Changes due to software bugs or malware of which the user is unaware
- Hardware malfunctions
- Technology changes making an older item obsolete – old records may become unreadable or inaccessible

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Basic Data Integrity expectations – *Manufacturing Principles*

- **PIC/S Guide PE009-8:**
  - Chapter 4
  - Annex 11
- **Australian Code GMP human blood, blood components, human tissues and human cellular therapy products**
  - Sections 400 – 415
- **ISO 13485**
  - Sections 4.2.3, 4.2.4

Basic Data Integrity expectations

- Regulator responses
  - MHRA notifications to industry: December 2013 & March 2015
  - FDA
  - Health Canada
- Influencing factors:
  - Organisational culture, risk awareness and leadership
  - QMS design of systems to comply with DI principles
    - "ALCOA" principles
  - Company processes for data review and system monitoring

A – Attributable

- Clearly indicates who recorded the data or performed the activity
- Signed / dated
- Who wrote it / when

L – Legible

- It must be possible to read or interpret the data after it is recorded
- Permanent
- No unexplained hieroglyphics
- Properly corrected if necessary

C – Contemporaneous

- Data must be recorded at the time it was generated
- Close proximity to occurrence

O – Original

- Data must be preserved in its unaltered state
- If not, why not
- Certified copies

A – Accurate

- Data must correctly reflect the action / observation made
- Data checked where necessary
- Modifications explained if not self-evident

ALCOA Principles

TGA Licensed Manufacturers Expectations

- Manufacturers should:
  - Understand their **vulnerabilities** to DI issues
    - Not just about your site –

      Contractors (outsourced activities)

  - Assess risks relating to data integrity- QRM Approach

TGA Licensed Manufacturers Expectations

- Manufacturers should:
  - Design systems to prevent DI issues
    - Ensure the data is authentic and retrievable
  - Train staff and encourage correct behaviours and practices
    - Open communication
    - Encourage feedback
  - System for ongoing DI review

Conclusions

- GMP requirements already include provisions for DI- inspection report definitions, PIC/S Guide to GMP for medicinal products

- Existing systems should be able to ensure data integrity, traceability and reliability-Understand your **vulnerabilities** to DI issues
  - The inability of a manufacturer to detect and prevent poor data integrity practices = lack of quality system effectiveness

- QRM approach to prevent, detect and control potential risks

Conclusions continued

- Where data is generated and used to make manufacturing and quality decisions, ensure it is trustworthy and reliable
- Increased regulator focus on DI
- Remember it's the responsibility of the manufacturer to prevent and detect data integrity **vulnerabilities**

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