MHRA
Regulating Medicines and Medical Devices

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Medicines and Healthcare Products Regulatory Agency

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Data Integrity:
A new look at an old issue

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Objectives

- Outline basic data integrity expectations
- Impact of organisational culture on data governance
- How to build data integrity into the existing PQS
- Identifying data integrity weaknesses

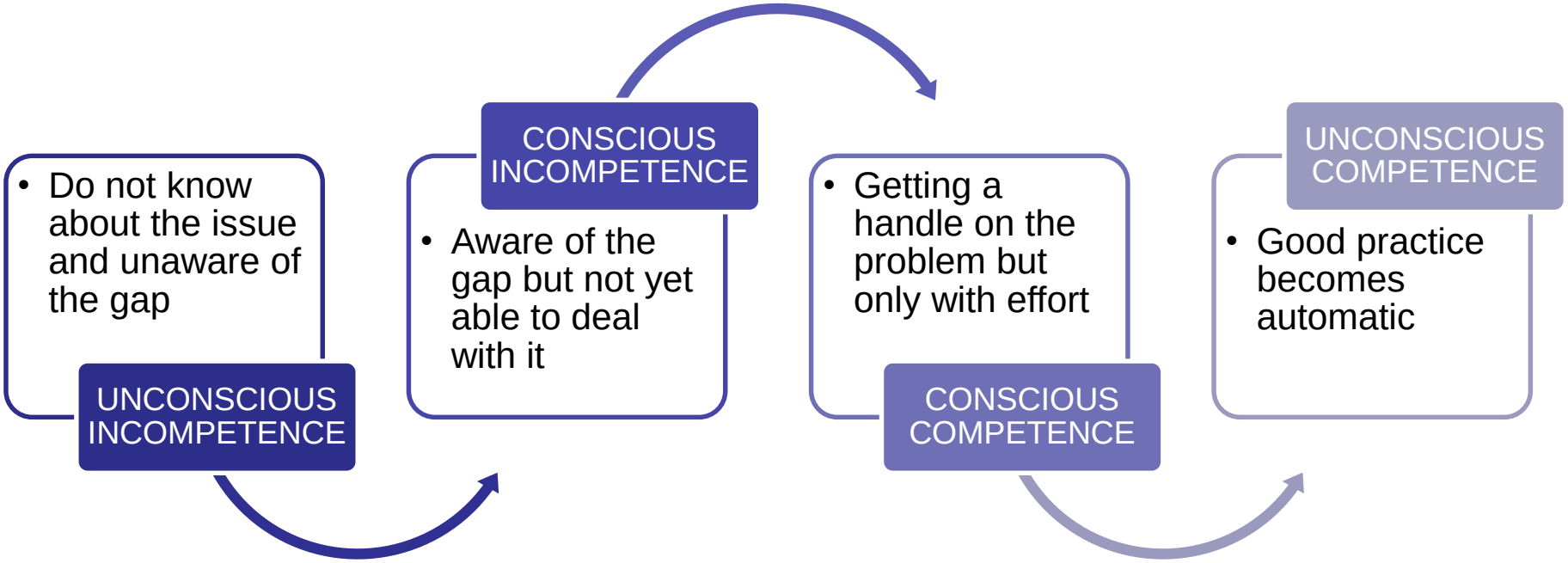
So….. what's data integrity?

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

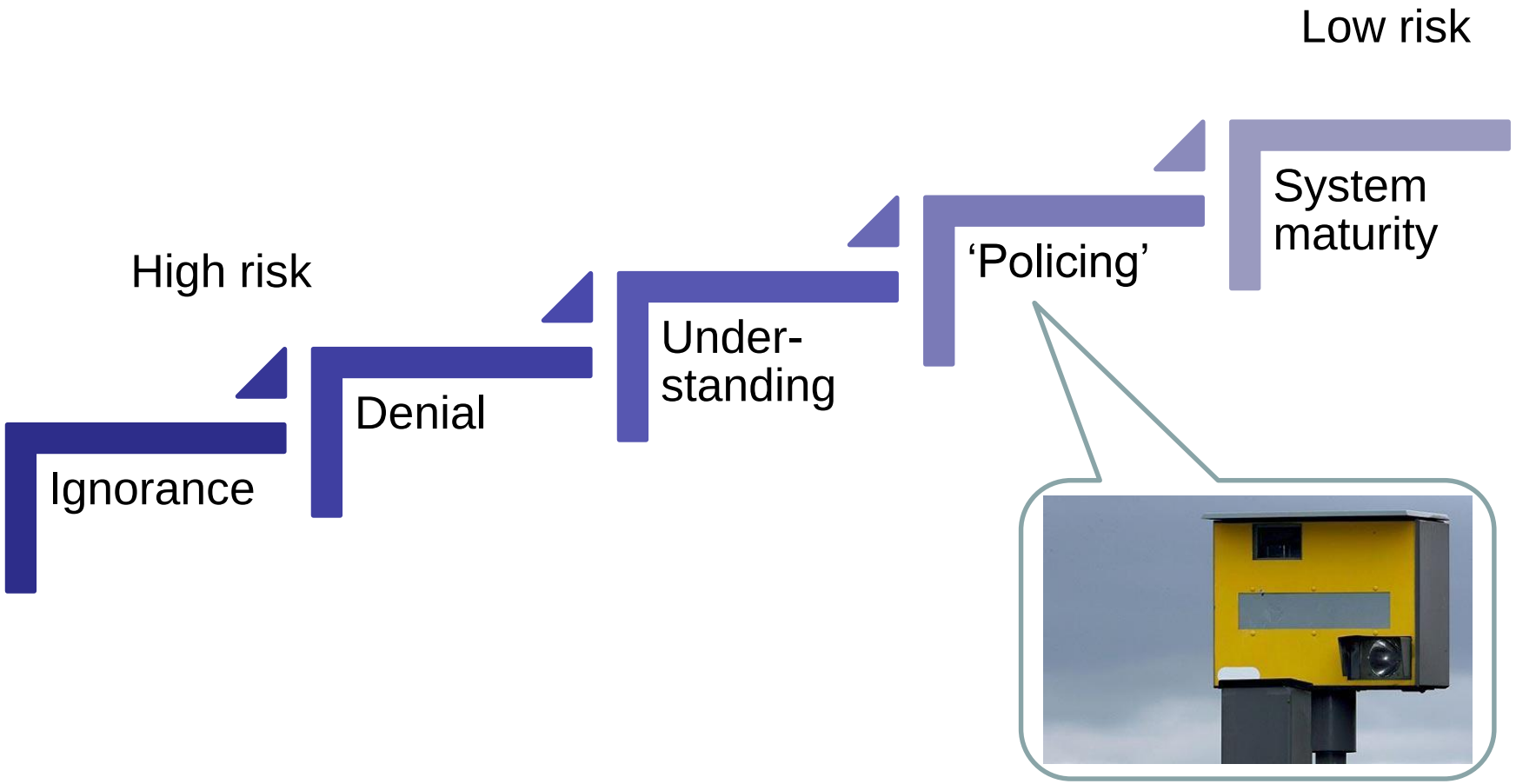
  * from initial data generation and recording, through processing (including transformation or migration), use, retention, archiving and retrieval.

Impact of organisational culture, risk awareness and leadership

Organisational culture and maturity



Data Integrity: Risk awareness



Data Lifecycle

- Does the company understand the data lifecycle concept?
  - All phases in the life of the data (including raw data), from initial generation and recording, through processing (including transformation or migration), use, retention, archiving and retrieval

- Important when reviewing DI risks as a whole.

System maturity

- Depth of understanding which does not just focus on the obvious
  - Not just about HPLC systems
- QRM approach to data integrity
  - On-going risk review
  - Awareness of residual risk
    - Is this managed to an acceptable level?
    - Legacy data residual risk – impact to quality system
  - What is their approach to mitigating these risks?
  - Do they understand the potential impact of these risks?.

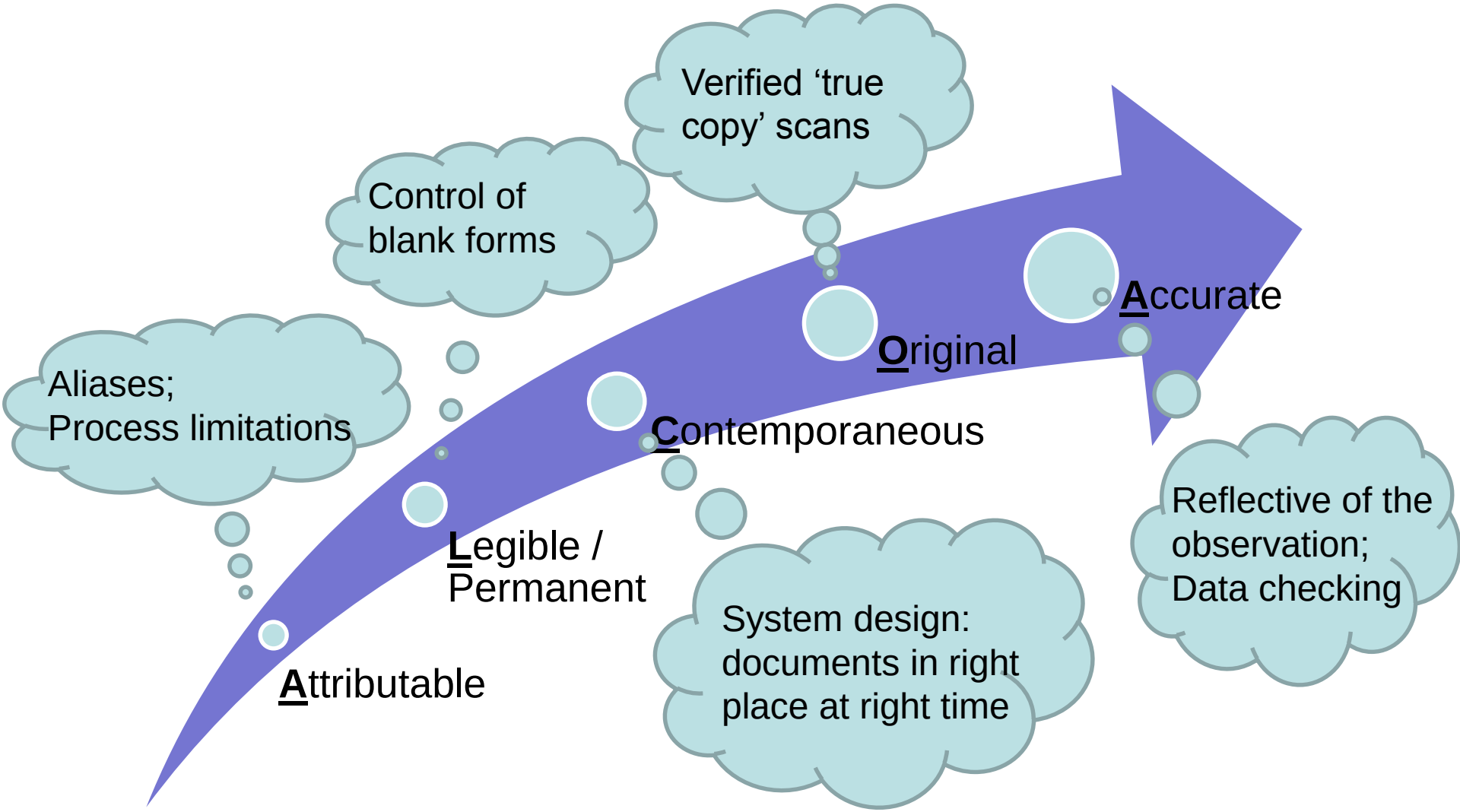
Encouraging the right behaviours at all levels in the organisation

Encouraging the right behaviours

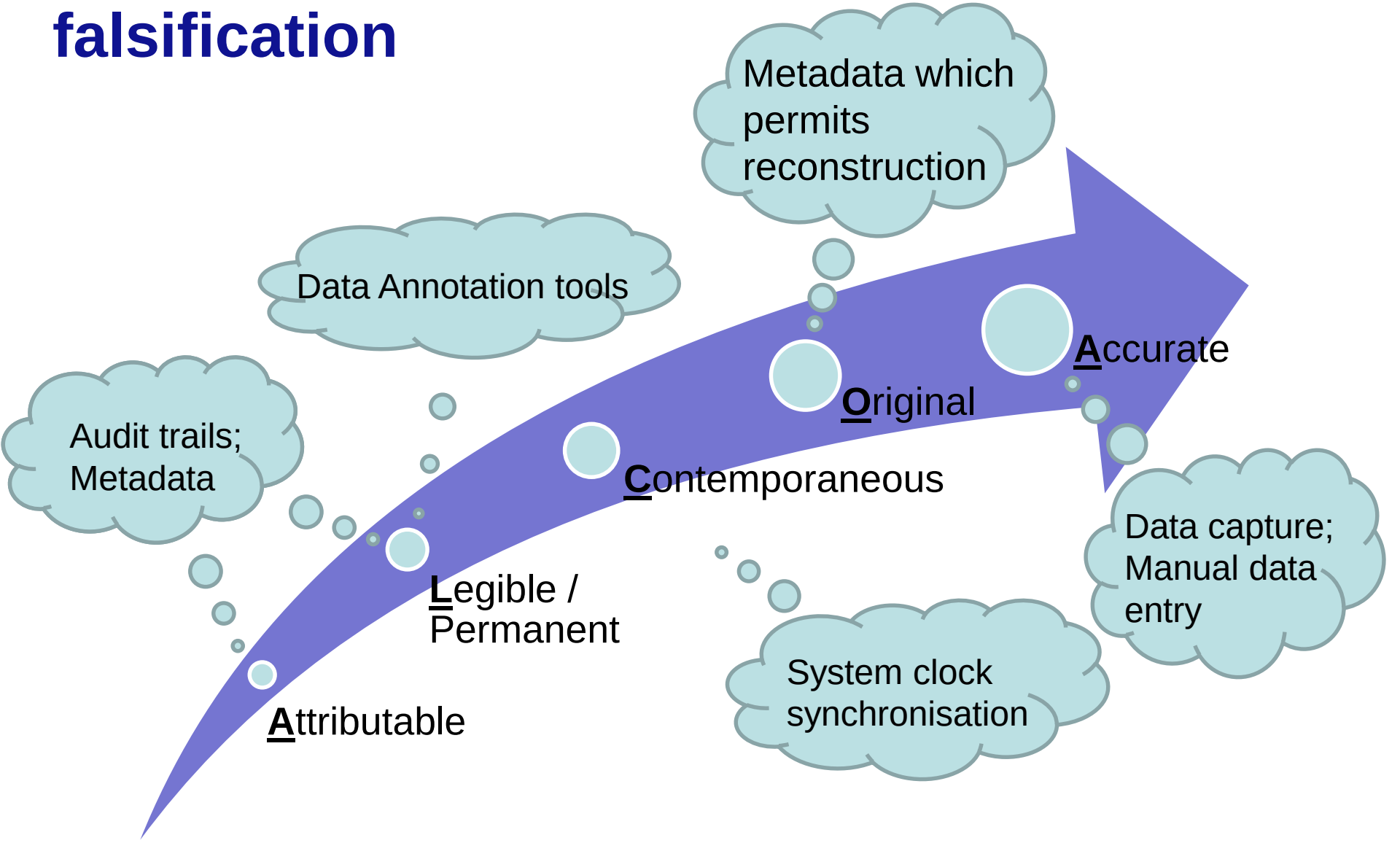
- Clear understanding of importance of data integrity at all levels
  - How do staff react to DI system weaknesses?
  - Is there evidence of non-contemporaneous recording?
- Internal reporting is encouraged
  - Can staff give their supervisor ‘bad news’ without fear?
- Senior management approach to data integrity which is not based on fear
  - ‘zero tolerance’ – what does that mean?.

Designing systems to comply with DI principles

Design *paper* systems which reduce opportunities for falsification



Design *electronic* systems which reduce opportunities for falsification



Data review and system monitoring

Data and system review

- Data Review
  - Paper
  - Electronic – source data (not the paper)
  - Non-contemporaneous is OK (unless verifying an observed value)
- Iterative data governance system review
  - QRM-type approach
  - Self inspection.

Applying DI principles to contractor management

Contractor management

- Data governance can’t be just about a single site
- Contractor-generated data can have significant impact
- Technical Agreements
  - What is the CA required to tell the CG?
  - Will they notify in a timely manner?
- Can the CG trust paper reports?
  - Audit scope - focus on data integrity
  - Paper can be reviewed off line.

What's next? Impact to inspections

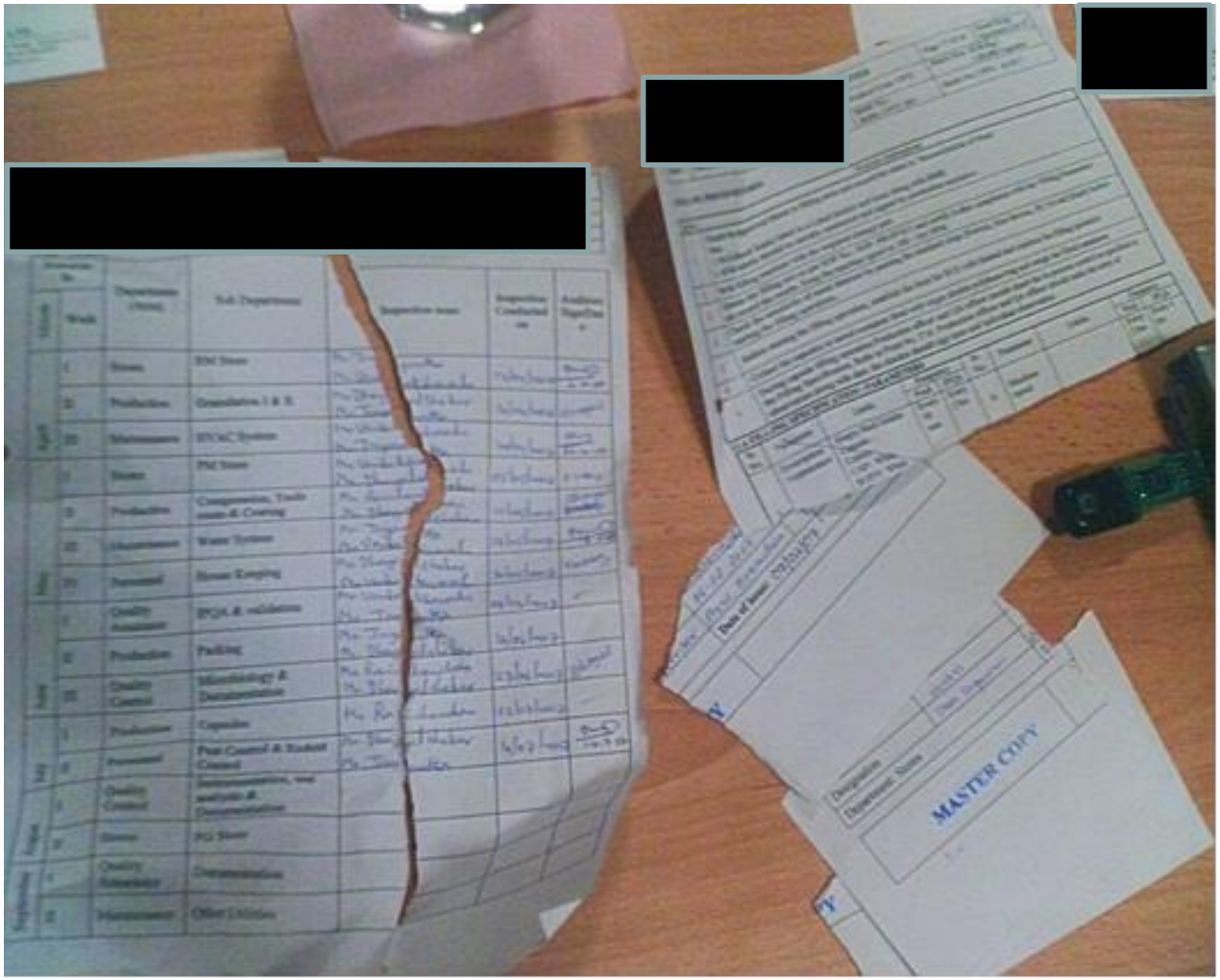
- Stakeholder information resources
  - MHRA GMP definitions & expectations for data integrity
- Impact on inspections
  - Part of routine scope
  - Verifying Data Governance throughout the PQS
  - Compliance report.

Identifying data integrity weaknesses

DI Requirements – Data Generation & Review

- Traceability
  - Raw data to summary reports
- Verify raw data and metadata
  - What to check?
- Does documentation support stated activities?

Data Generation & Review - Deficiencies



Data Generation & Review - Deficiencies

Excel spreadsheet used to calculate assay:

Date:	28/04/2010	Sample:	T=10
Product Code	FLS 001		Top
Sample Weight	0.9976 g	A	
pH	~~4.23~~		
Date:	28/04/2010	Sample:	T=10
Product Code	FLS 001		Bottom
Sample Weight	2.5599 g	B	
pH	~~4.23~~		

Corresponding Lab book entries for sample weights:

T=10	2.5813 g	A
M=10	2.5911 g	
B=10	2.5405 g	B

Data Generation & Review - Deficiencies

Nine-month stability results for Product A were reported in the product quality review

- No raw data (in either hard copy or electronic format) could be located to verify the authenticity of these results

Data Generation & Review - Deficiencies

Not all of the tests which were performed on HPLC ‘x’ were recorded in the log book

Not all of the batch numbers of Product A that were tested between 06th and 07th September 2013 on HPLC ‘y’ were recorded in the log book.

Data Generation & Review - Deficiencies

- On viewing the electronic data the missing results (REP 3 & 4) had been run at ~17:21 and ~17:25
- The results had been disregarded
- The HPLC ‘passed’ the Performance Qualification (PQ) RSD requirement using the amended data set
- The HPLC would have failed the PQ RSD requirement using the original results.

DI Requirements – Computerised Systems

- Is the system configured for GxP compliance?
  - If software has configuration for GxP compliance, these should be activated
- Are the audit trails and meta data backed up?
  - Sites often back up method / analysis files, but not the audit trail.
  - Ask to see the audit trail in the backup copy.
  - A specification of which files are backed up should be defined and validated.
- Where is data hosted?
  - Who owns the data – it may not be you!
  - Public vs Private

DI Requirements – User Access

- System access
  - Individual log-ins

- User / group permissions
  - Appropriate to an individuals role
  - No IT department?
    - Dual account
    - Independence of roles
    - QMS visibility

User Access - Deficiencies

The Laboratory System Administrators are within the Quality Control team and as such have inappropriate administrative access to all of the Laboratory software.

Data Integrity
- Take home messages

- Data Governance is about maintaining data integrity throughout the lifecycle
  - Risk based challenge of its effectiveness
  - Risk based priorities with other GMP requirements
  - Awareness and education
- Culture: led from the top; empowered from below
- Embedding within PQS: ALCOA principles
- Data integrity weaknesses – approaches to assessment

Data Integrity
- Take home messages

- Not just about fraud, not limited to labs and IT

- Keep calm and carry on!

Final thought….

Has your company / supply chain had any Data Integrity events?

How would you know?

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