Data Integrity
An EU Perspective

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Connecting a World of Pharmaceutical Knowledge

Medicines and Healthcare Products Regulatory Agency

Agenda

1. A foundation of good data
2. A Global Problem
3. Types of data fraud
4. Impact of falsification
5. Overall learning points

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MHRA – A foundation of good data

We **protect and improve** the health of millions of people every day through the effective regulation of medicines and medical devices, **underpinned by science and research**

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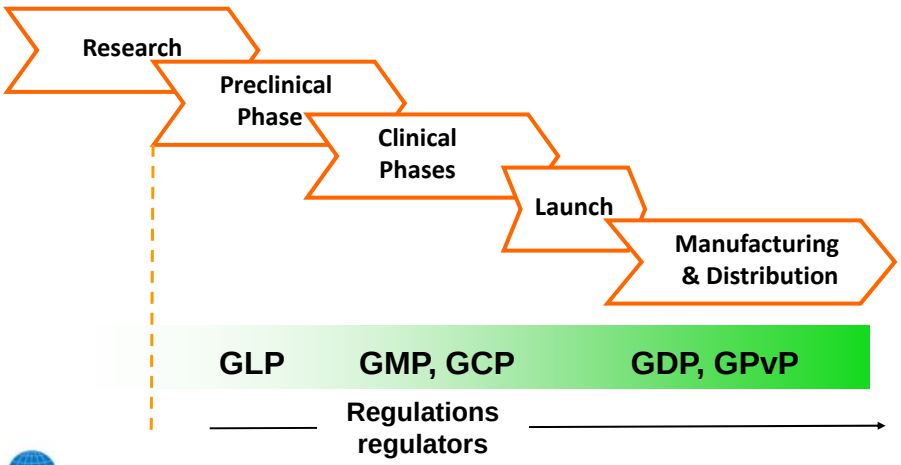
Good data across the product lifecycle



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THE NEW INDIAN EXPRESS

"Wockhardt plunges as UK MHRA regulator withdraws certification"

Wednesday November 13, 2013

"Ranbaxy Laboratories shares fall 32pct after another FDA ban, co pleads ignorance"

Monday September 16 2013

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chemistryworld

Court convicts ex-Aptuit researcher over drug data

March 2013

PharmaTimes

MHRA successfully prosecutes on preclinical data manipulation

March 2013

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The international view

- 2013: increased international regulatory focus on data integrity
  - Global problem
  - Future change in inspection approach?
- EU Compilation of Procedures revision to include 'falsification in the context of GMP/GDP'.

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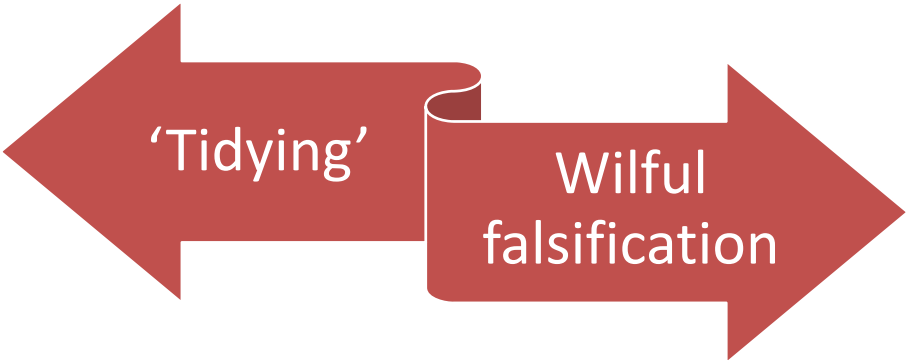
Types of data fraud



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Some 'tidying' doesn't really matter…?

- 'Tidying' often includes changes from original
- Undeclared duplication compromises integrity of all data presented
- Risk mitigating info becomes less reliable.

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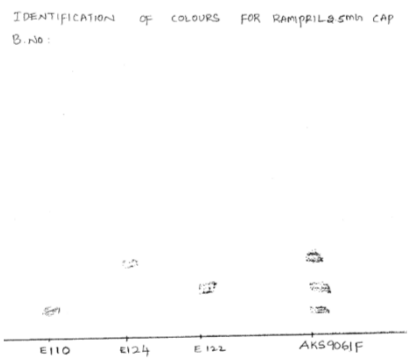
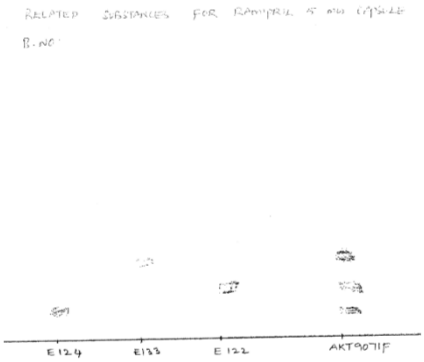
Wilful falsification

Analysis of lot A



Analysis of lot B



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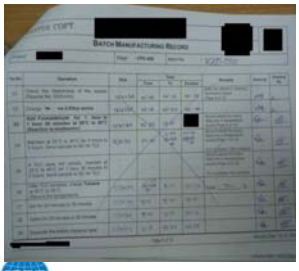
Falsification - desire to please?

- Poor quality original documentation being disposed
- Documents presented during the inspection had differing information compared to the documents found in the incineration area



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Falsification – no deviations / results ignored

- No deviations ever raised for EU supplied products.
- No OOS for water microbiology results
- Warehouse temperatures:
  - Temperatures noted during plant tour were out limits
  - The daily result had not been recorded for that day.
  - Later review of records showed the temperature had been recorded within acceptable limits

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Falsification - product stability data

- Falsification of data reported in the annual Product Quality Reviews (PQRs).
  - PQRs were supplied to the EU Qualified Persons as evidence of the absence of adverse trends,
  - Claim could not be substantiated when checks on site showed that data for key time points were absent

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Falsification

- Quality Assurance personnel signed multiple documents when they were not on site
- Lack of traceability of materials - the site could not produce manufacturing documents (batch records) for product shipments or reconcile quantities manufactured versus sold

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Impact on Industry

Company A; growth during 2012

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Impact on Industry

Company A; share price during 2013

Most Important Impact?

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Reputational Damage from data falsification

- We live in the 'Communications Age'
- Financial implications
  - User perception, brand loyalty
  - Patient confidence
  - Concerns re: future business.

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Falsification in the context of EU GMP

- Changes are being made to the definition of 'Critical' deficiency in EU GMP :

  *Any **wilful** mis-statement, misrepresentation, manipulation, adulteration, rewriting, hiding, replacing of quality related documents, materials, activities or buildings **in order to give** an item the appearance of GMP compliance when this is **not** the case*

  EU Compilation of Community Procedures

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Regulatory Actions

- Serious findings will result in a statement of GMP non-compliance:
  - Stop supply from affected sites
  - Recall of products in the supply chain
  - Possible removal of site from the Marketing Authorisation
- Re-inspections to verify corrective / preventive actions implemented
- Regular updates on the action plan
- Increased inspection frequency
- Actions may also be taken against EU import sites

Presenting false/misleading information is a criminal offence in the UK!

Overall learning points:

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- Where fraud is uncovered it will be extremely difficult for the organisation to recover and to supply to the EU
- Leads to move from "compliance" to "forensic" inspections
- Globalisation of products supply also means globalisation of regulatory coverage:
  - Joint inspections and reliance on the work of other Agencies
  - Partner countries will be notified!
- Be open and honest with the inspector and Agency:
  - **MHRA will work with you**

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THANK YOU FOR YOUR ATTENTION

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