Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Good Documentation Practice
Sessions 3 & 4

Good Documentation Practice

Feedback from session 2

Workshop activity:

You discussed in groups

- What practical steps do you take to ensure Good Documentation Practice?
  - Decide on top 5 for group
- What is the biggest hurdle to ensuring Good Documentation Practice?
- 20 minute discussion

Quality Culture and Cultural Excellence

Good Documentation Practice

Quality Culture and Cultural Excellence

Workshop activity:

Discuss in groups

- What practical steps do you take in your companies?
- What more could you do?
- 15 minute discussion
- 15 minute feedback

Top 10 Most cited deficiency groups 2017 Jan to Jun

Ranking	Groups	Critical	Major	Others
1	Quality System	18	202	231
2	Documentation	7	113	223
3	Self Inspection	2	6	14
4	Qualification/Validation	1	133	102
5	Personnel	1	16	47
6	Sterility Assurance	0	101	59
7	Production	0	75	153
8	Premises/Equipment	0	41	144
9	Complaints/Recall	0	39	40
10	Computerised Systems	0	34	23

Note – Annex 13, Major deficiencies were identified under Release of Batches

Data integrity

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

International history

- Publicised data integrity failures date back to early 2000's

- 2013: increased focus on data integrity
  - Increasing failures identified
  - Change in regulatory approach.

Has this solved the problem?

No…….

In 2015:

- 35% EU ‘statements of non-compliance’ for Data Integrity
- Significant number of USFDA Warning Letters
- MHRA inspection findings*:
  - 121 Major, 218 Other deficiencies had references relevant to DI
  - 20 Major DI deficiencies in regulatory action cases
  - 10 Major DI deficiencies under compliance management.

Why is data integrity still an issue?

- Nothing new
  - Requirements in place for many years
  - No change in basic data expectations
    - **A**ttributable
    - **L**egible
    - **C**ontemporaneous
    - **O**riginal
    - **A**ccurate.

Think of it this way:

has it EVER been acceptable to have unreliable data?

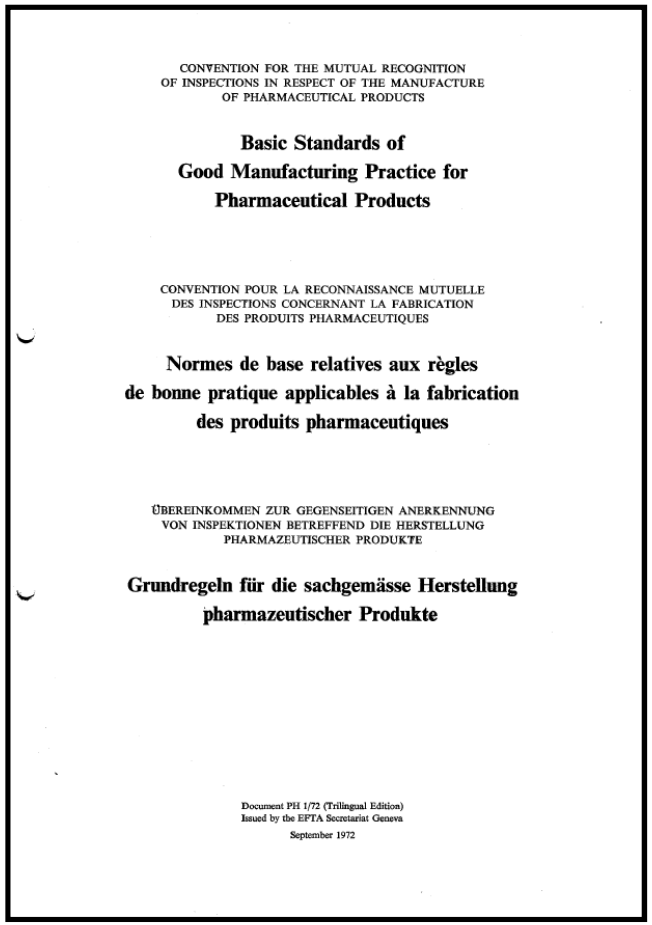
Existing PIC/S GMP requirements

	Basic Requirements for Medicinal Products (Part I): Chapter 4 (June 2011) Chapter 6 (October 2014)	Basic Requirements for Active Substances used as Starting Materials (Part II): Chapter 6 / Chapter 5 (Sept 2014)	Annex 11 (Computerized Systems) (June 2011)
Attributable	[4.20], [4.21, c & i], [4.29, e]	[6.14], [6.18], [6.52]	[2], [12.4], [15]
Legible	[4.1], [4.2], [4.7], [4.8], [4.9], [4.10]	[5.43] [6.11], [6.14], [6.15], [6.50]	[7.1], [9], [10], [17]
Contemporaneous	[4.8]	[6.14]	[12.4], [14]
Original	[4.9], [4.27], [Paragraph "Record"]	[6.14], [6.15], [6.16]	[8.2], [9]
Accurate	[4.1], [6.17]	[5.40], [5.45], [6.6]	[Paragraph "Principles"], [5], [6], [10], [11]

Historical expectations

PIC/S GMP Guide 1972:

- '[copies of master documents]….which avoids transcription error….'
- records enabling recreation of batch history
- 'all records shall be legibly written….and traceable'
- 'dated signature of the persons who performed each activity'



CONVENTION FOR THE MUTUAL RECOGNITION
OF INSPECTIONS IN RESPECT OF THE MANUFACTURE
OF PHARMACEUTICAL PRODUCTS

Basic Standards of Good Manufacturing Practice for Pharmaceutical Products

CONVENTION POUR LA RECONNAISSANCE MUTUELLE
DES INSPECTIONS CONCERNANT LA FABRICATION
DES PRODUITS PHARMACEUTIQUES

Normes de base relatives aux règles de bonne pratique applicables à la fabrication des produits pharmaceutiques

ÜBEREINKOMMEN ZUR GEGENSEITIGEN ANERKENNUNG
VON INSPEKTIONEN BETREFFEND DIE HERSTELLUNG
PHARMAZEUTISCHER PRODUKTE

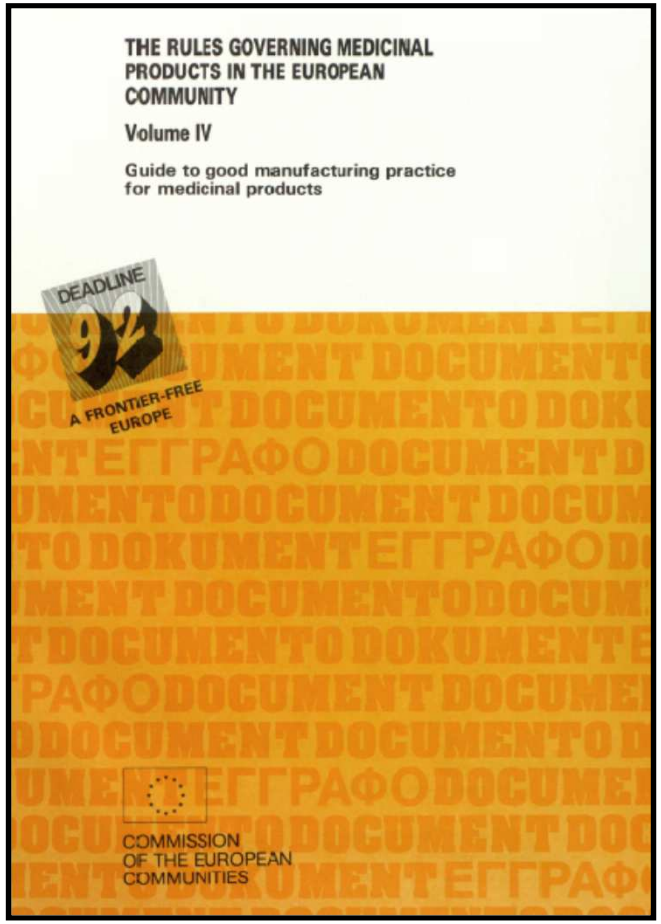
Grundregeln für die sachgemässe Herstellung pharmazeutischer Produkte

Document PH 1/72 (Trilingual Edition)
Issued by the EFTA Secretariat Geneva
September 1972

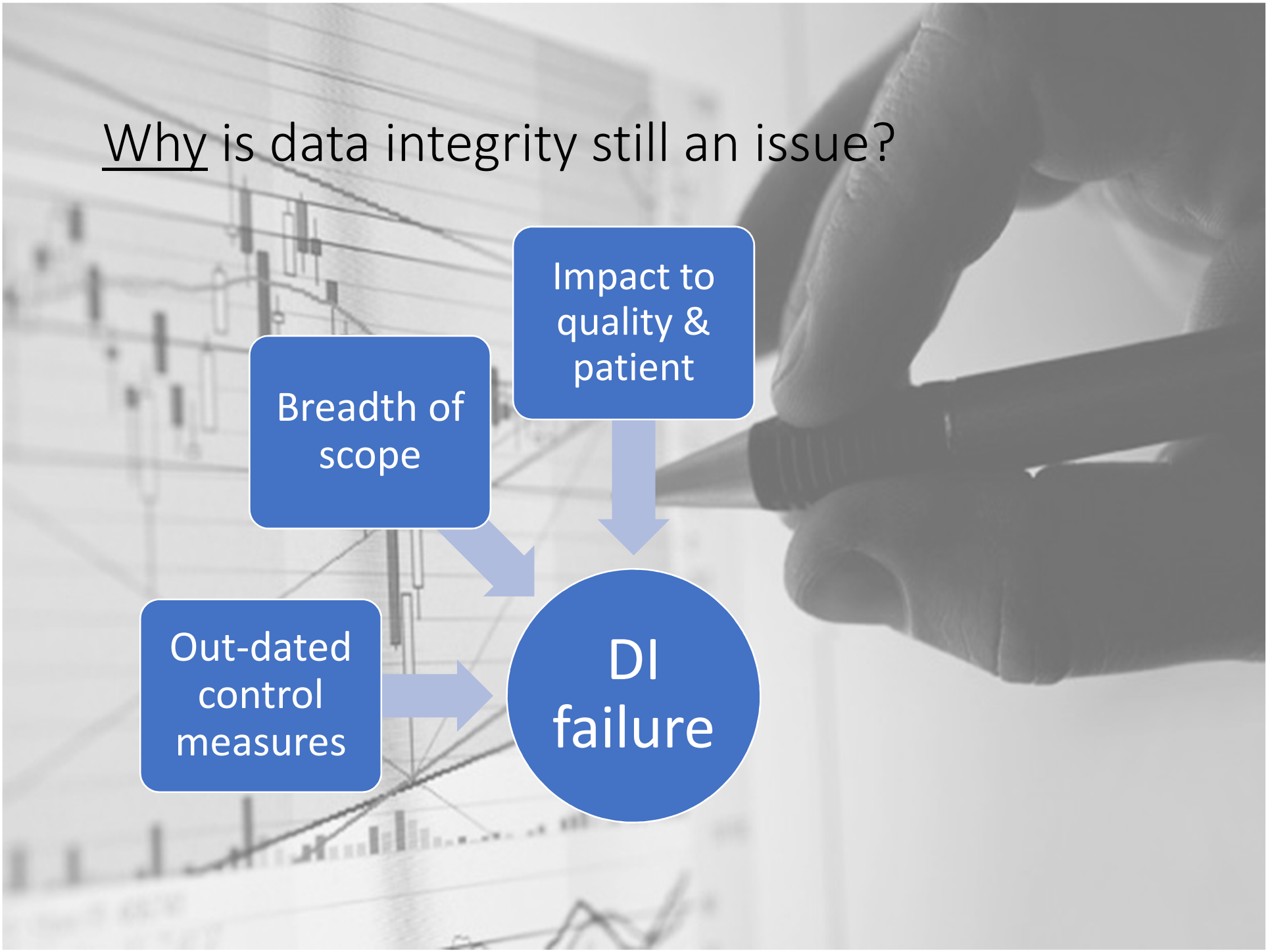
Historical expectations

EU GMP January 1989:

- "…entries made in clear indelible handwriting…."
- "[alterations]…signed and dated….permit reading of original….reason recorded"
- " …records completed at the time each action taken..."
- "…accuracy of records should be checked…"
- "…name of persons carrying out activities…".



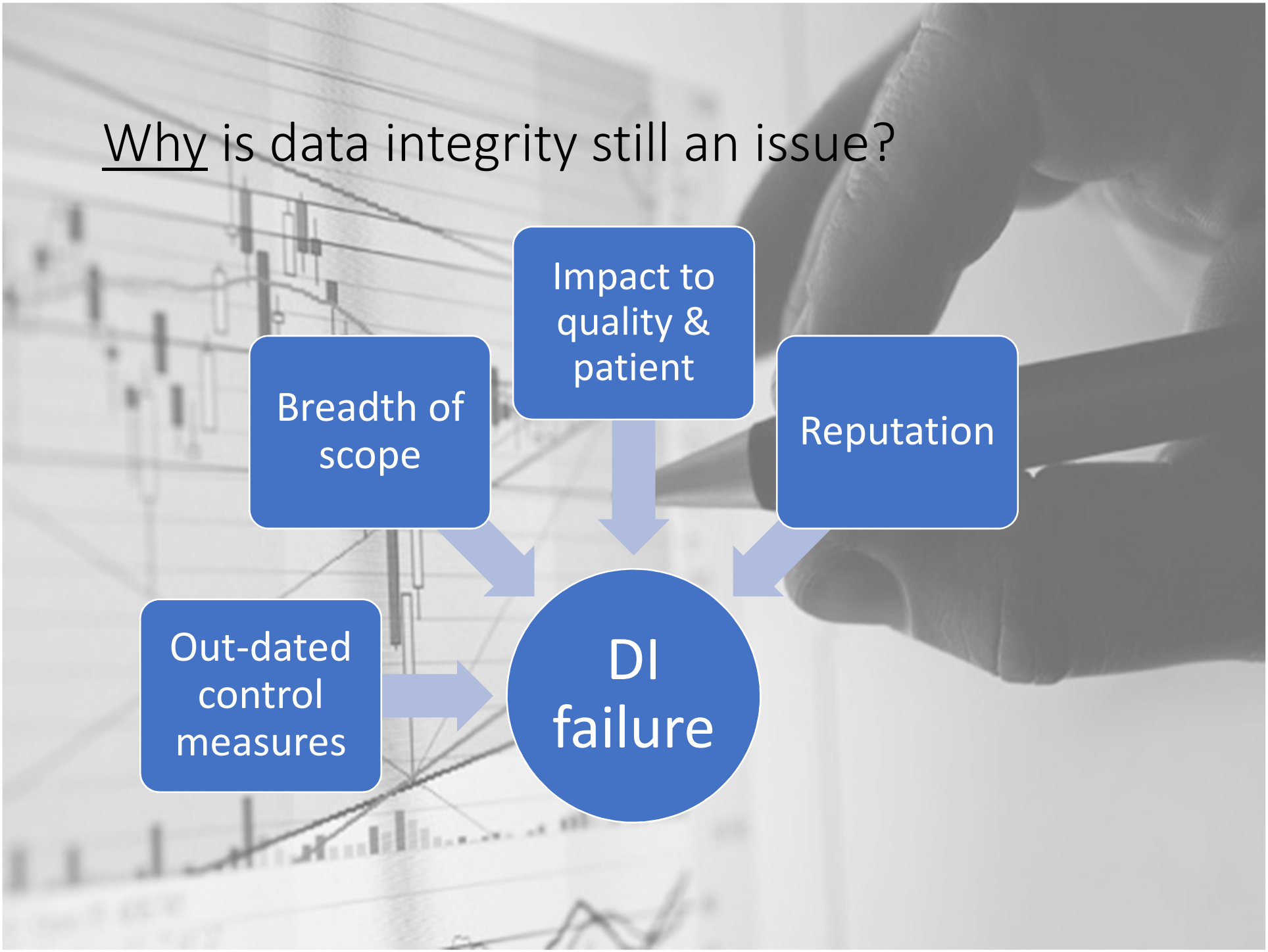
Why is data integrity still an issue?



Impact to quality and patient

- Important daily decisions regarding safety, efficacy and quality of medicines are based on data
- Unreliable data is a significant barrier to providing safe and effective medicines
  - “Precision guesswork”
- Safety / efficacy risks from substandard or falsified medicines.

Why is data integrity still an issue?



DI failure vs defect: reputational impact

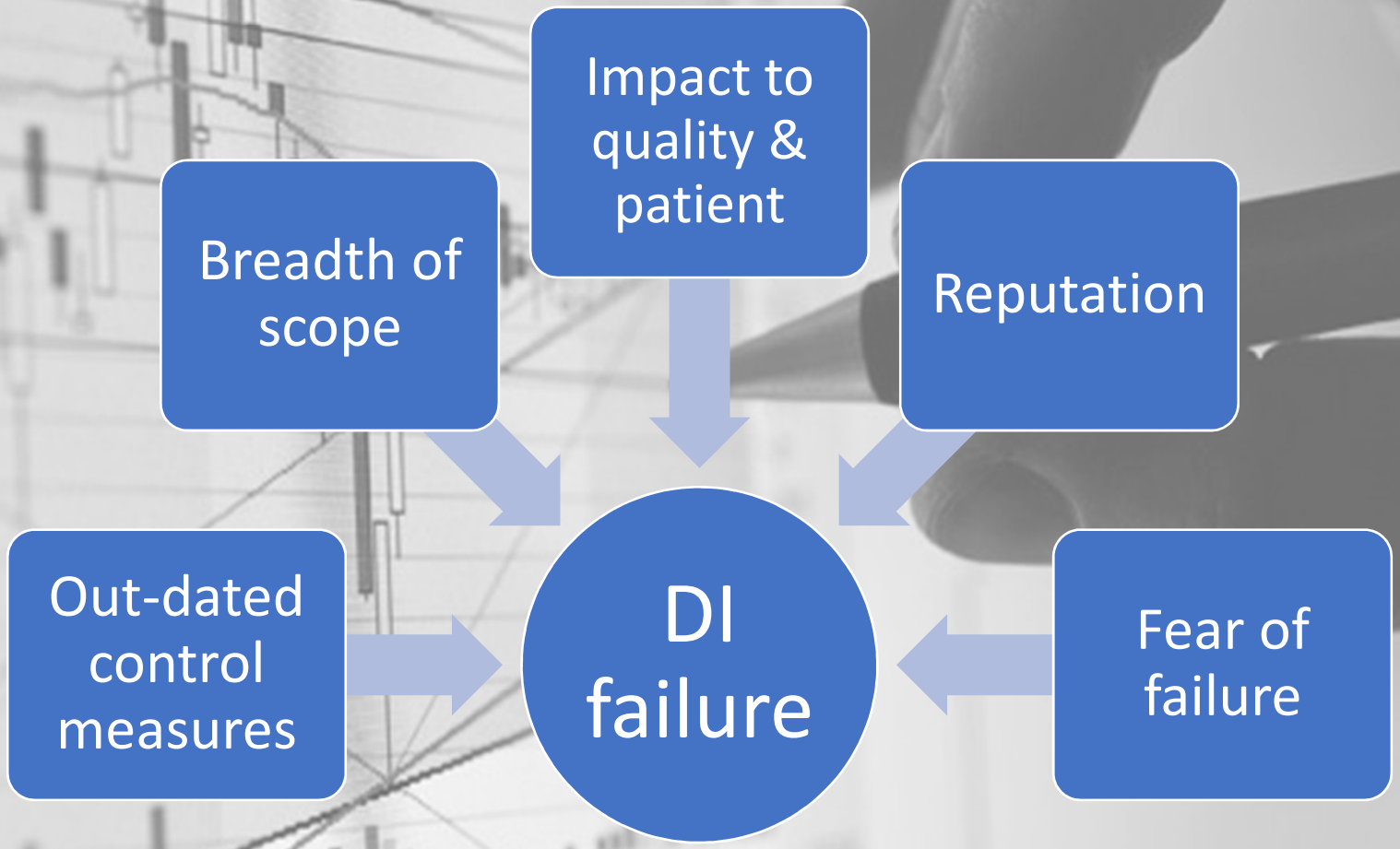
Alleged falsification of emissions data

- €26bn (~20%) loss in share value
- 4.8% global reduction in 2015 sales; first drop in 11 years
- (General Motors increased 8%)
- €1bn cut in investment

Software fault: engine stops and all electrics fail while vehicle in motion

- 59,000 cars recalled in 40 markets
- Transient impact to share price (-3%)
- Share price continues upward trend.

Why is data integrity still an issue?

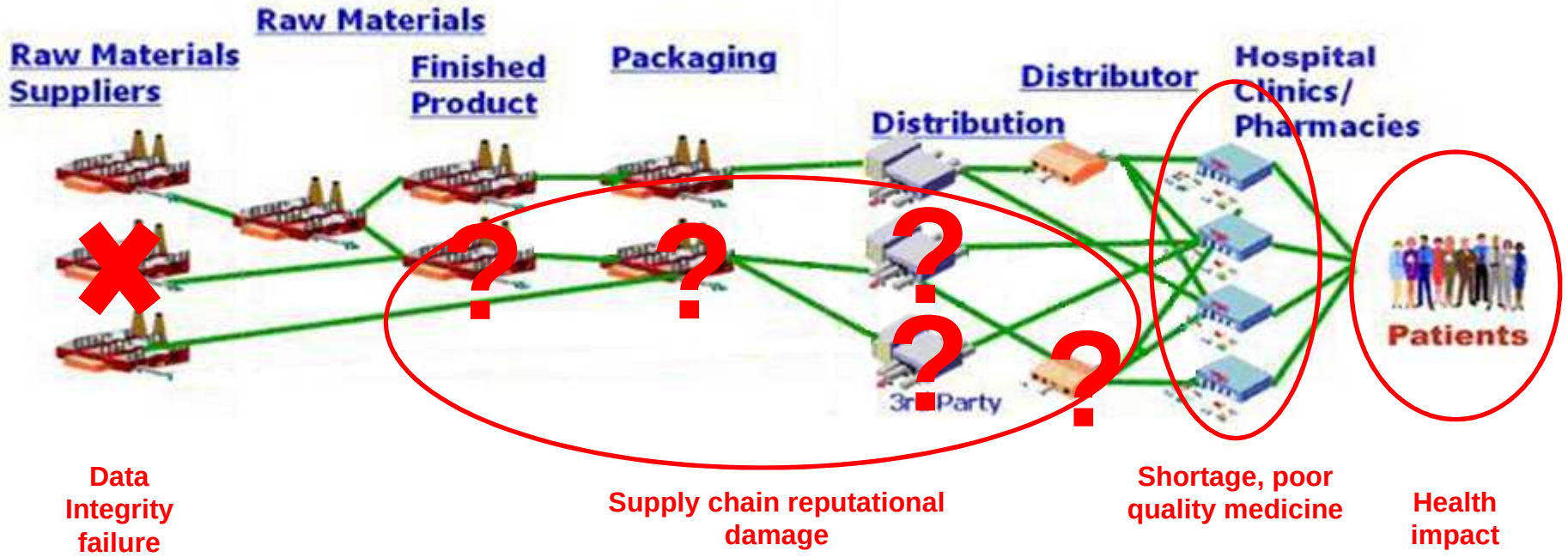


DI failure: Fear of failure

- Causes the wrong behaviour
  - Panic
  - Disproportionate management action: ‘zero tolerance’
- Complexity of proposed remediation
  - Aspirations vs action
- Quality Risk Management approach
  - Risk identification, mitigation and communication
  - Balanced with other GMP priorities
  - Perfection is a barrier to progress.

Data Integrity in the Global Supply Chain

Supply chain:
Influence of others around me



Supply chain: data integrity considerations

- Global supply chain requires a global approach to data governance
  - Interaction between contract giver and acceptor
  - Verifying equivalence of data management systems
  - Challenges of remote data verification.

Supply chain: can we trust summary reports?

- Audit / self inspection scope - focus on data integrity
  - Summary documents can be reviewed off line
  - Capacity vs output
  - Where contracts permit, perform horizontal checks
    - Across batches, across products
- What is the company's approach:
  - Data lifecycle and risk management
  - Data governance.

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