Promoting the Quality of Medicines

Data Integrity in GXPs

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U.S. Pharmacopeial Convention

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USP U.S. Pharmacopeial Convention

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Outline

- What Is Data Integrity
- Why Is Data Integrity Important to Ensuring Medicines Quality
- Consequences of Data Integrity Issues and Why Organizations Fail to Comply
- Roadmap to Data Integrity Compliance
- Managing Data Integrity and the Data Life-Cycle
- Conclusion

What is Data Integrity?

USFDA: The completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate.

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

PIC/S: The extent to which all data are complete, consistent and accurate, throughout the data lifecycle.

WHO: The degree to which data are complete, consistent, accurate, trustworthy and reliable and that these characteristics of the data are maintained throughout the data life cycle.

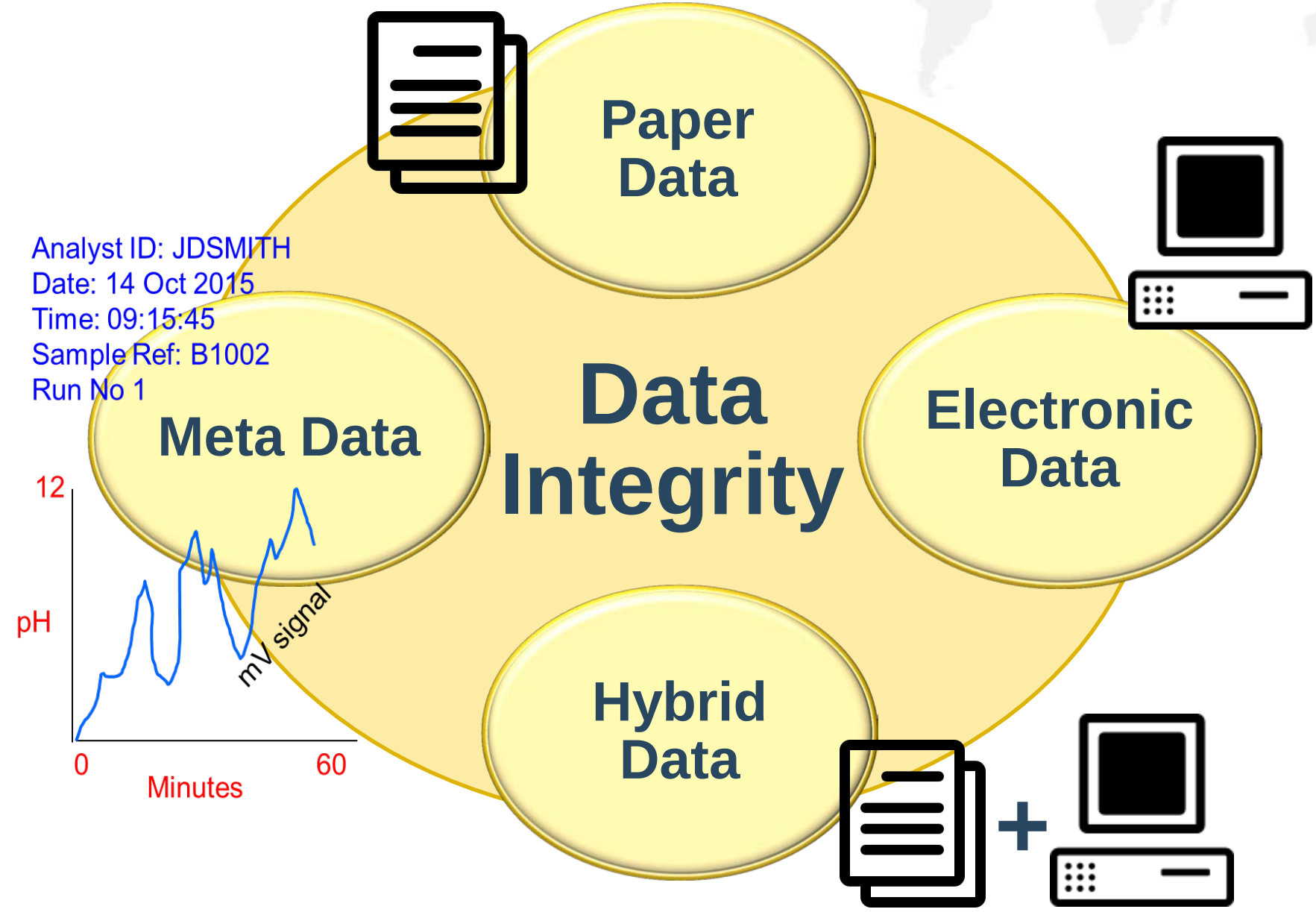
Data Integrity is **Not** a New Requirement

*ALCOA principles first coined by **US FDA in 1980s***

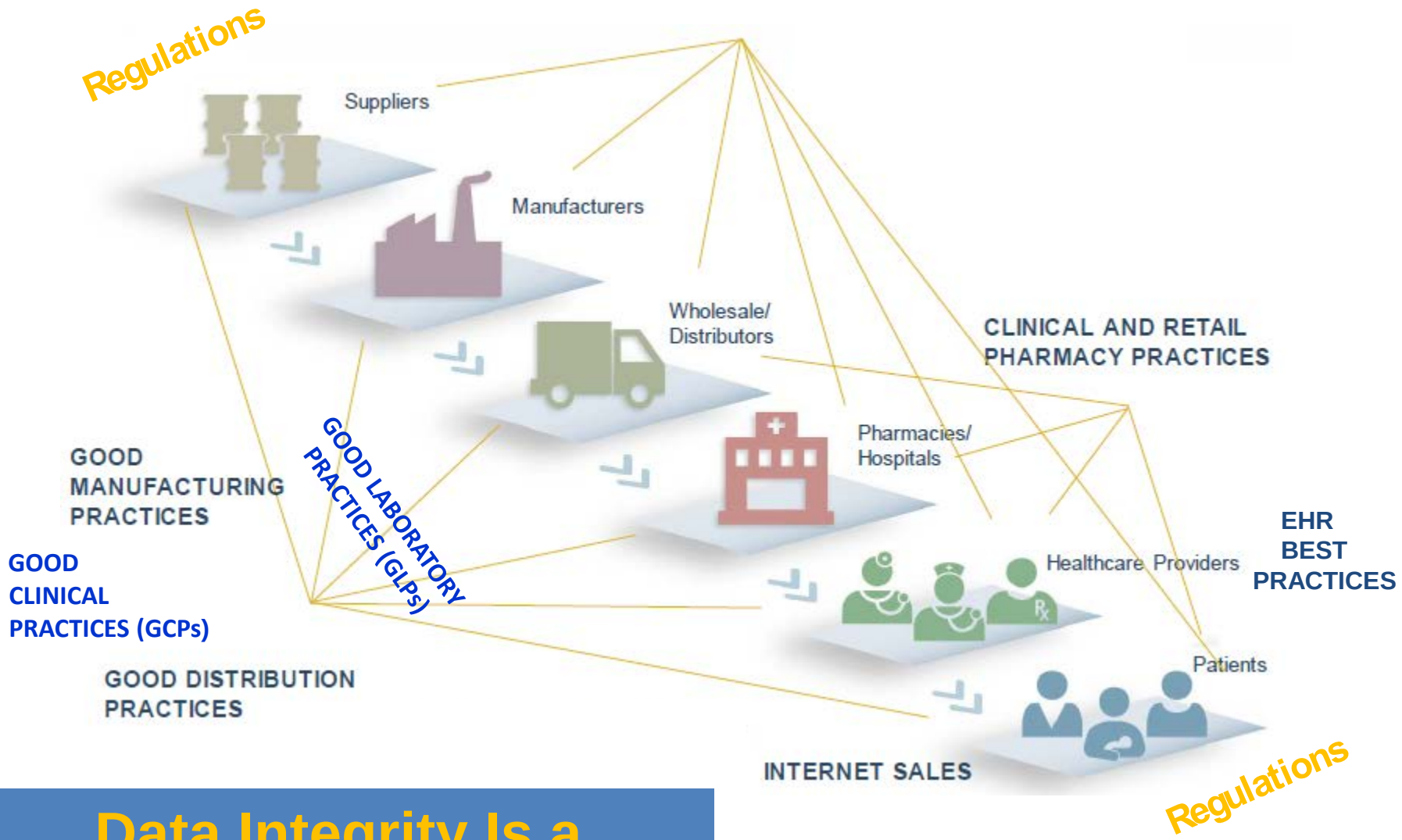
Attributable	[15.3] [15.7] [15.9] [15.27, d&e] [15.30 c&d] [15.43 g&h]
Legible	[15.2] [15.4] [15.6] [15.10]
Contemporaneous	[15.8]
Original	[15.3] [15.5]
Accurate	[15.2] [15.3] [15.4] [15.9] [15.11] [15.12] [17.11] [17.16]

WHO TRS 986, 2014; GMPs for pharmaceutical products, Main principles Annex 2

Types of Data



Data Integrity in Medicines Supply Chain



Data Integrity Is a Quality Assurance Issue!

What is data fraud?

Data Fraud

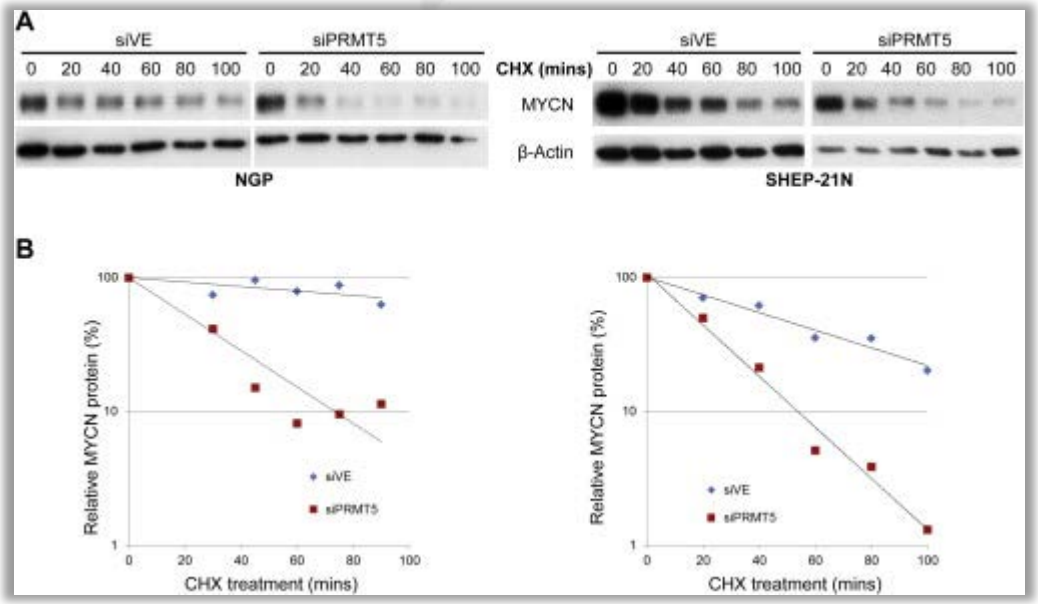
Changing the date/time stamp in the testing equipment used for IPC measurements

Unintentional

Falsification

Data Fraud

Trial injections were performed and deleted, prior to testing "official" samples

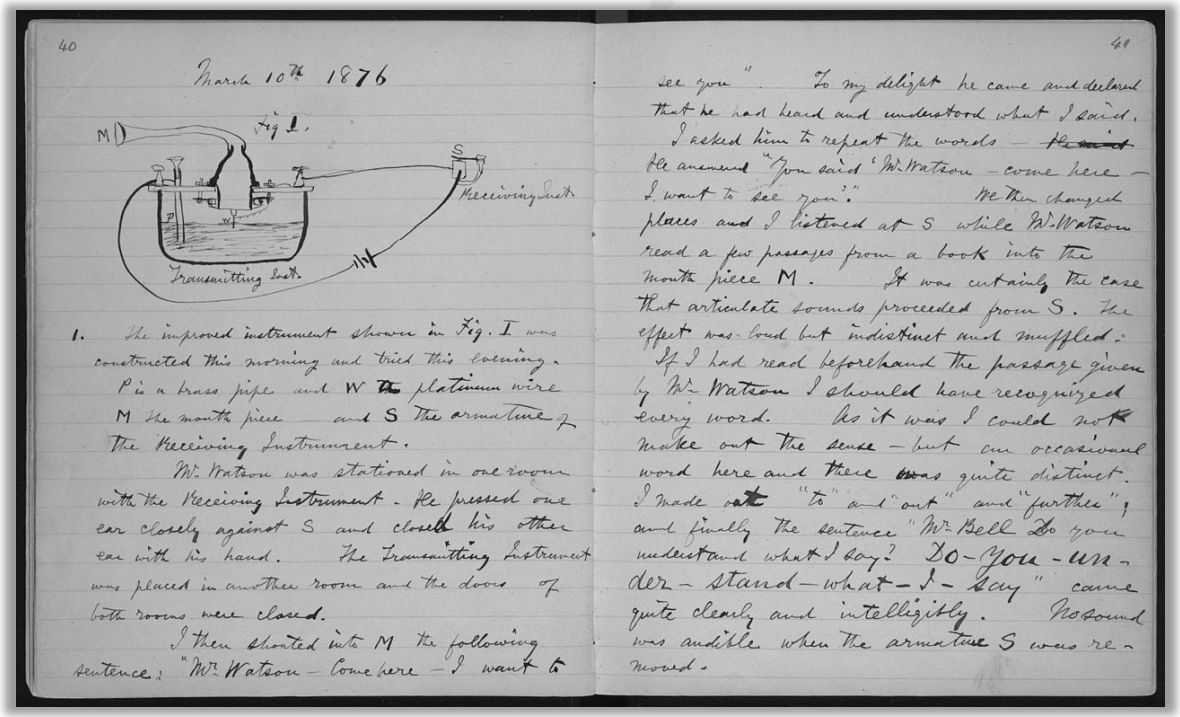


Unintentional

Falsification

Data Fraud

Laboratory notebook was lost



40

March 10th 1876

Fig 1.

M

S

Receiving Instr.

P

W

Transmitting Instr.

1. The improved instrument shown in Fig. I was constructed this morning and tried this evening. P is a brass pipe and W the platinum wire M the mouth piece — and S the armature of the Receiving Instrument.

Mr. Watson was stationed in one room with the Receiving Instrument - He pressed one ear closely against S and closed his other ear with his hand. The transmitting Instrument was placed in another room and the doors of both rooms were closed.

I then shouted into M the following sentence: "Mr. Watson — Come here — I want to

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see you". To my delight he came and declared that he had heard and understood what I said.

I asked him to repeat the words — He said He answered "You said 'Mr. Watson — come here — I want to see you'."

We then changed places and I listened at S while Mr. Watson read a few passages from a book into the mouth piece M. It was certainly the case that articulate sounds proceeded from S. The effect was loud but indistinct and muffled.

If I had read beforehand the passage given by Mr. Watson I should have recognized every word. As it was I could not make out the sense — but an occasional word here and there was quite distinct. I made out "to" and "out" and "further", and finally the sentence "Mr. Bell do you understand what I say? DO-YOU-UNDER-STAND-WHAT-I-SAY" came quite clearly and intelligibly. No sound was audible when the armature S was removed.

Unintentional

Falsification

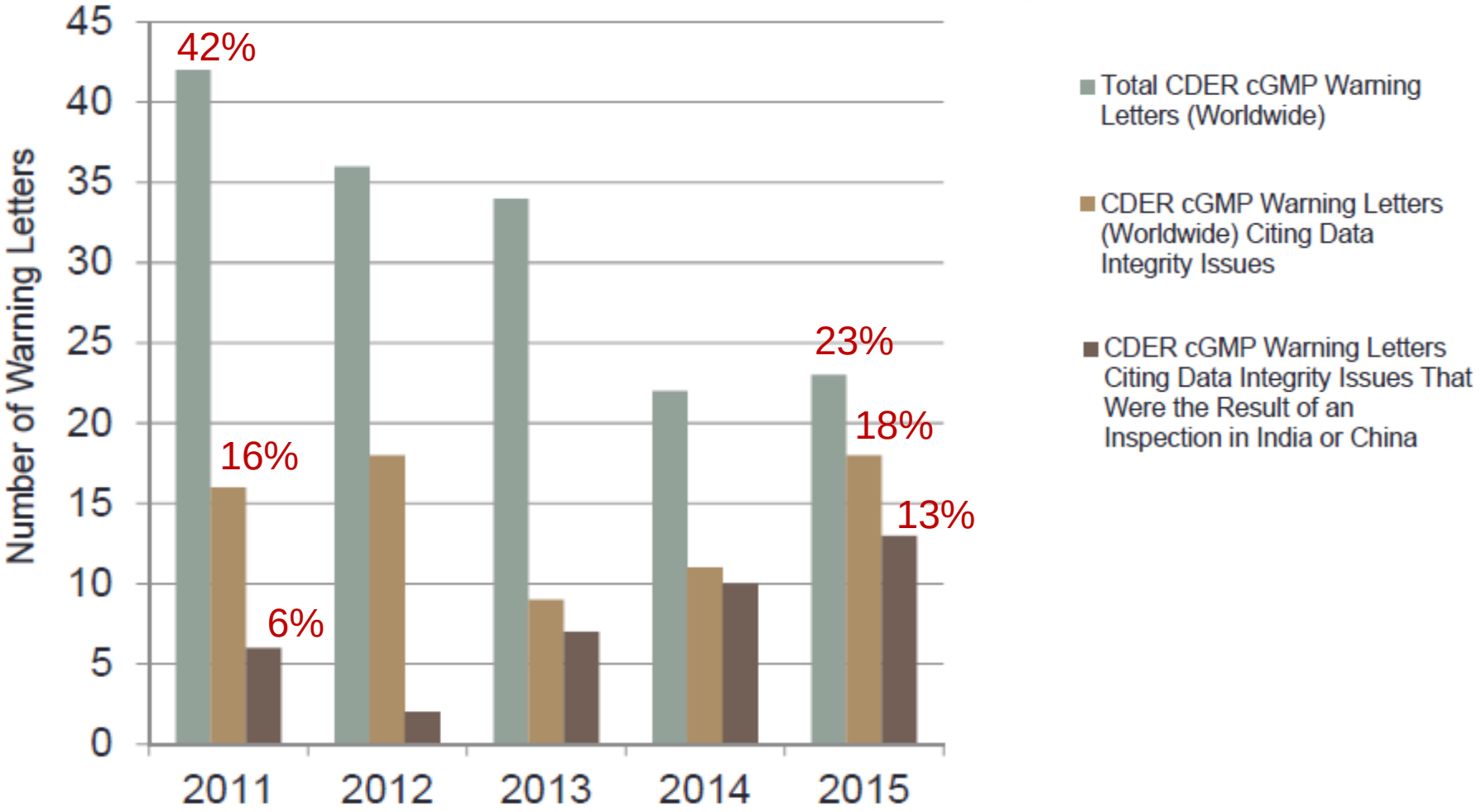
Data Fraud

Analytical balance not equipped with printer showing weighing date and time.

Unintentional

Falsification

Warning Letters Citing Data Integrity Issues



Source: https://www.pharmaceuticalonline.com/doc/ananalysis-of-fda-fy-drug-gmp-warning-letters-0001

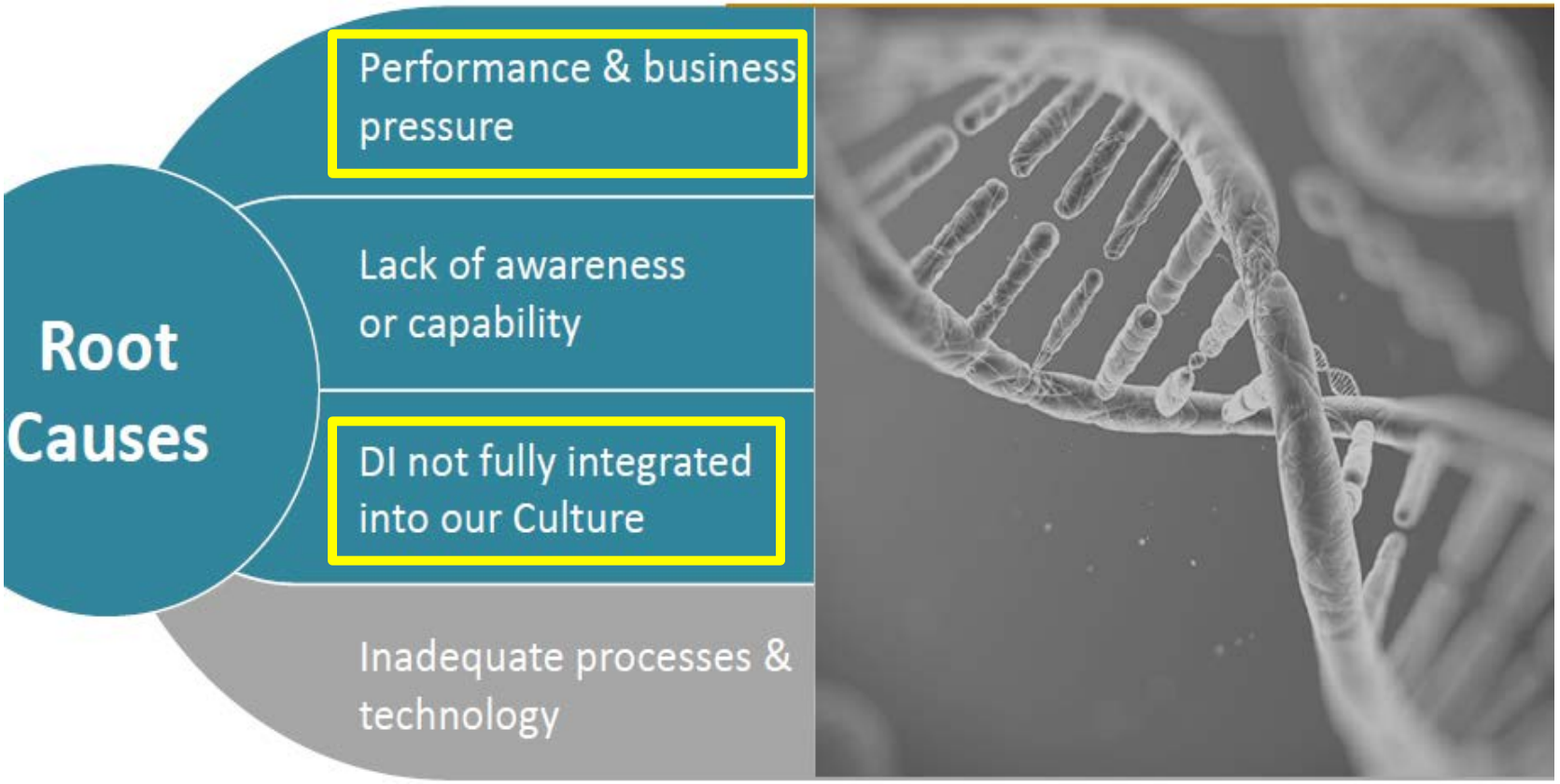
Cost of Data Integrity Issues

- Warning Letters, Consent Decrees, Notices of Concern, Loss of Regulatory Trust
- Import Embargos, Recalls and Seizure of Products
- Criminal Charges, Arrests and Court Trials
- Market share loss
- Drug shortage
- Patient Safety and Lives Can be Lost

Business

Patients

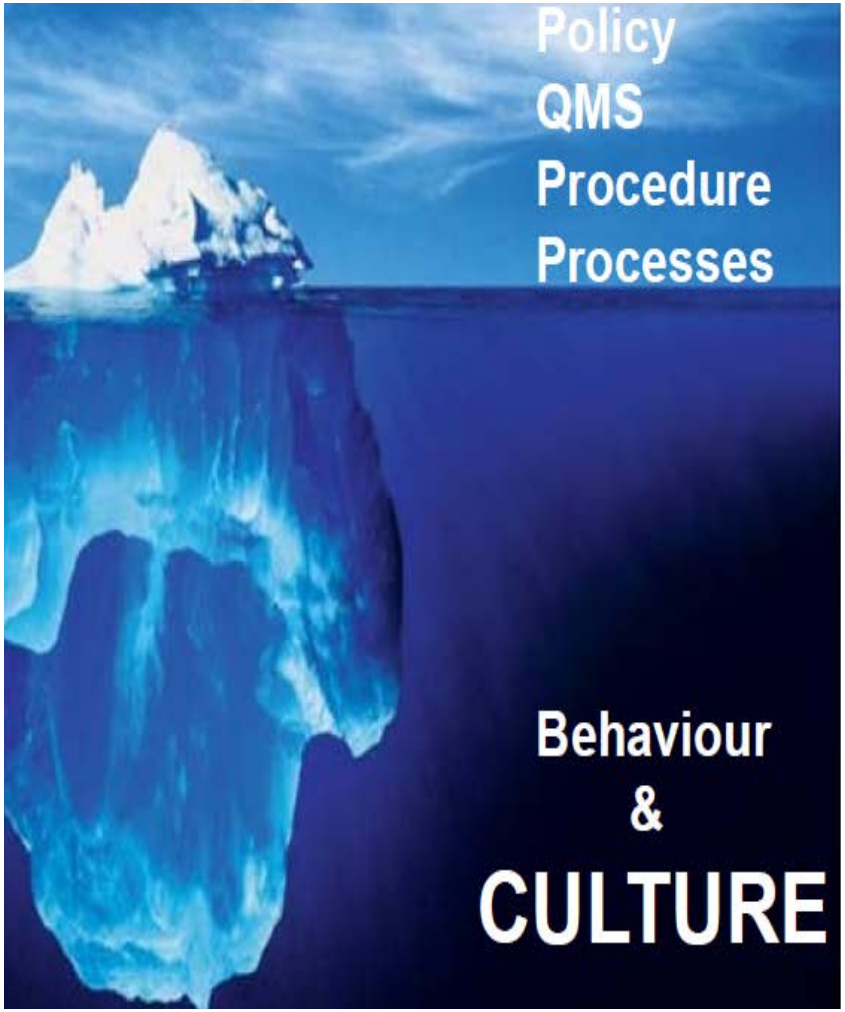
Why is it so hard for organizations to get Data Integrity right?!



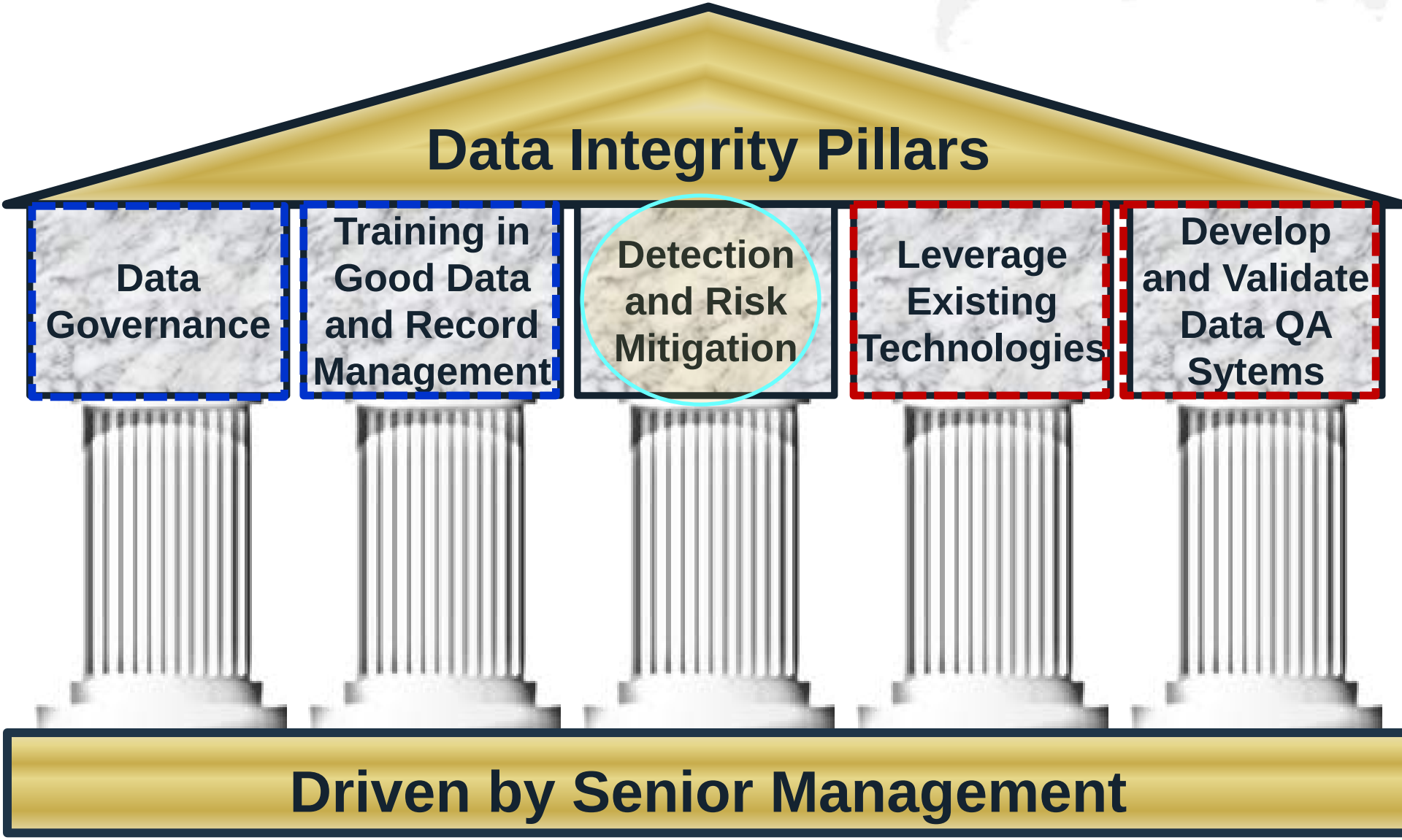
The Culture of Data Integrity

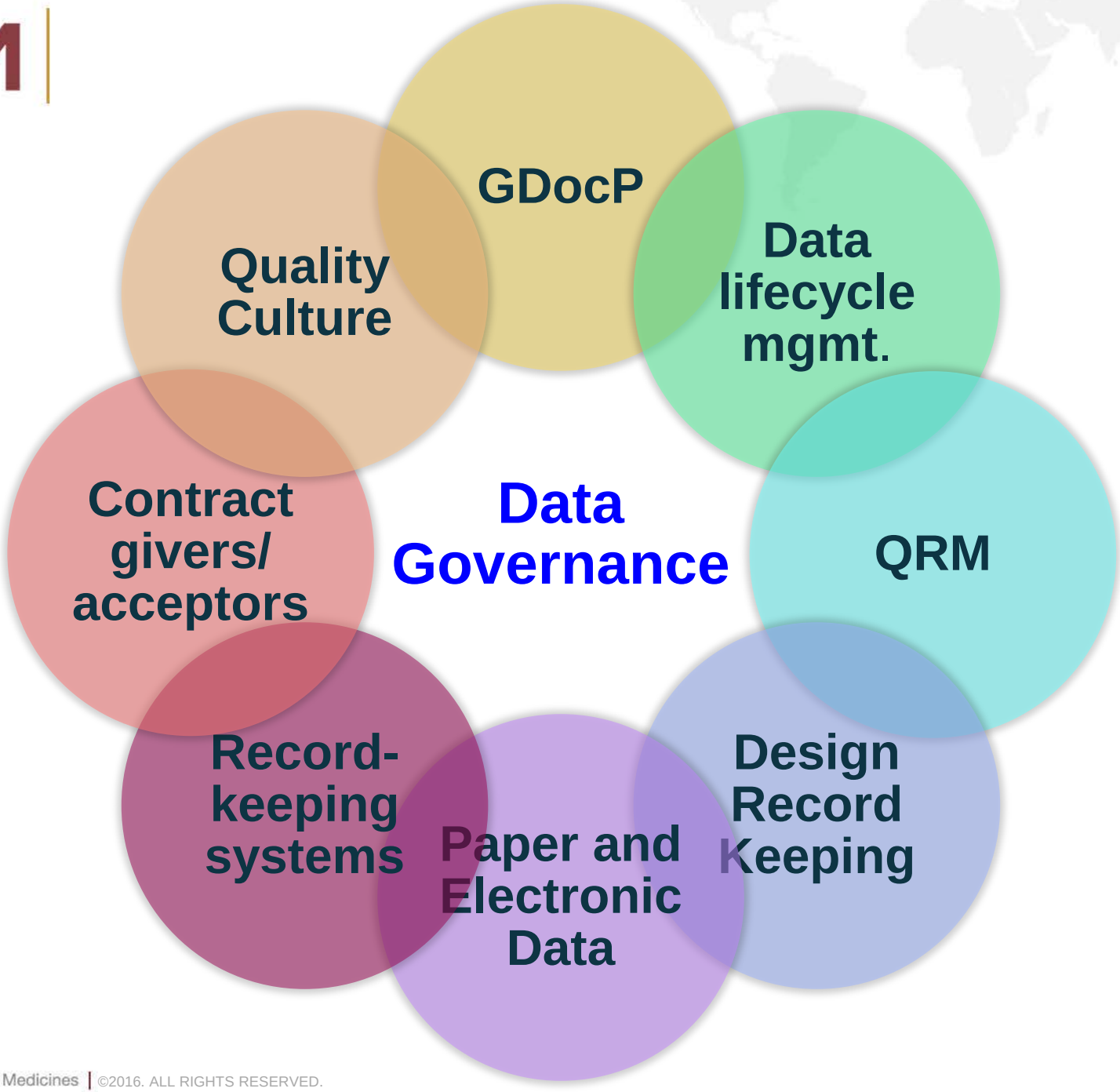
- You can fix policies
- You can fix systems
- You can fix procedures

- **Can** you **“Fix” people**?
  - How do you change behavior
  - How do you create **CULTURE?**



Roadmap to Data Integrity Compliance





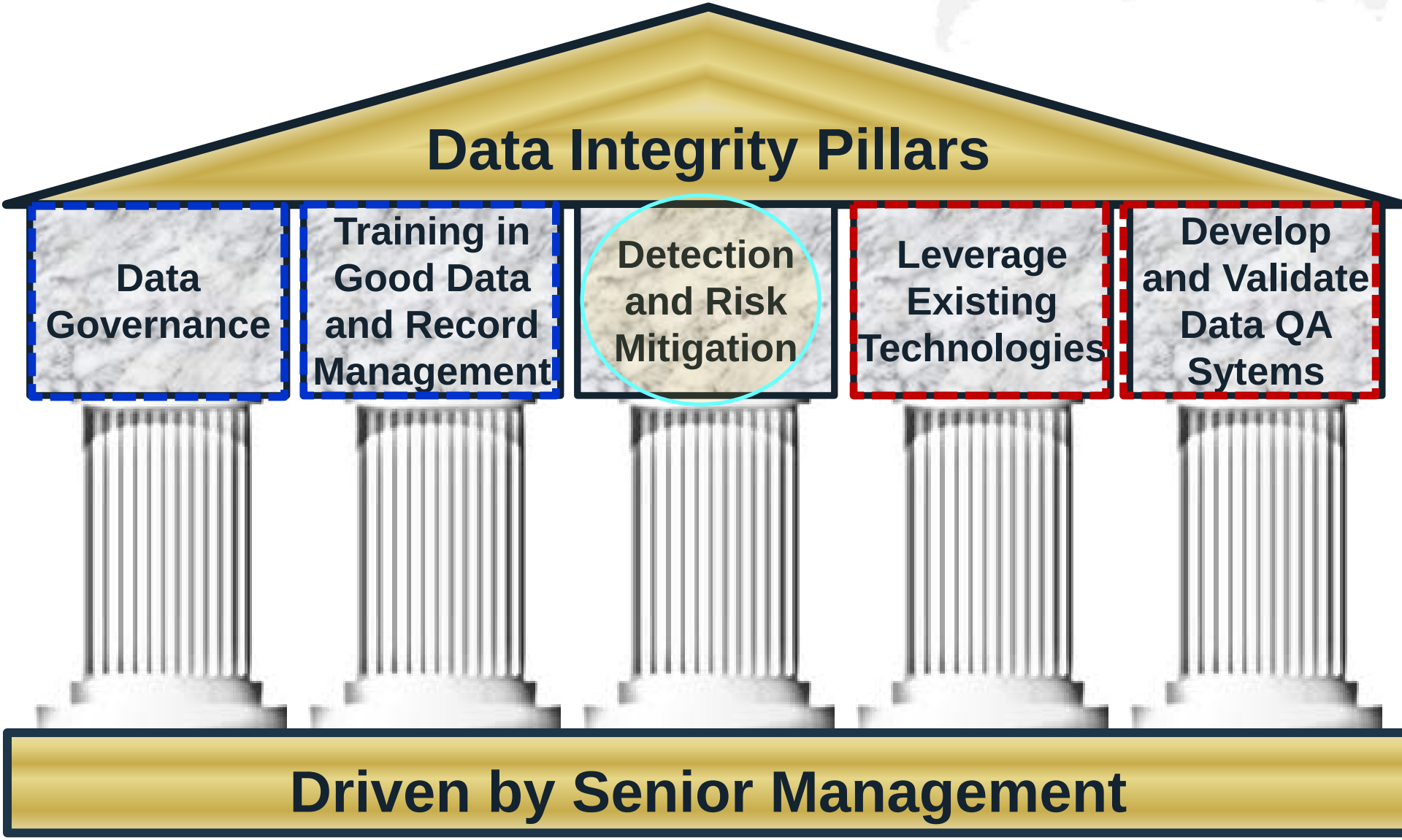

Training in Good Data & Record Management
All Personnel
New Hires
Referesher
Self-auditing


Detection and Risk Mitigation
Follow GDRP
Should be Risk-based
Two-person verification

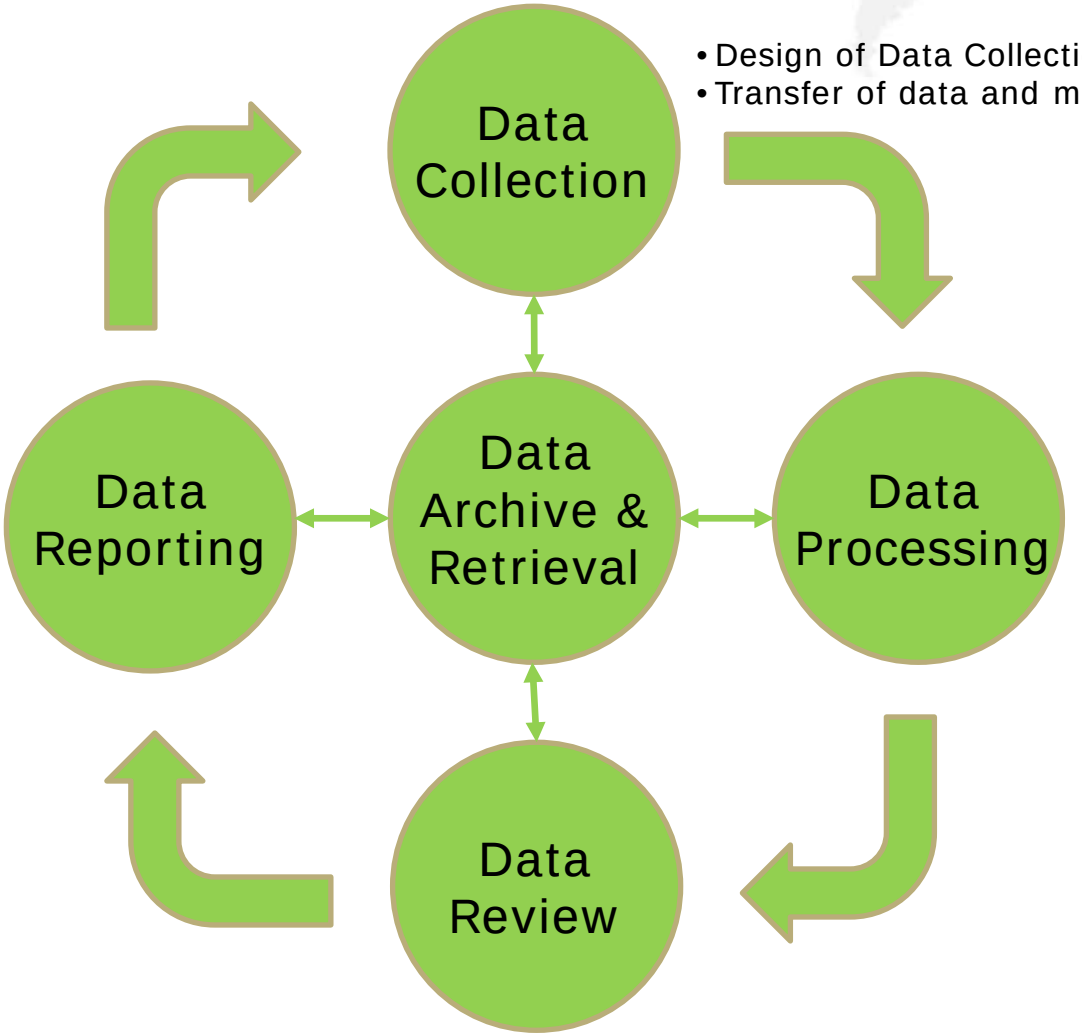
Leverage existing technologies; E.g. Implementing Process Analytical Technology (PAT) and other real-time measurements

Designing and validating systems to assure data quality and reliability

Roadmap to Data Integrity Compliance



Managing DI (Data Life-Cycle)



- Design of Data Collection
- Transfer of data and meta data

- Objective Processing
- Handling Failures

- Source electronic data
- Re-processing events
- Failures

- Objective Reporting
- Transparency in failures
- Tracking and Trending failures

Data Collection — **ALCOA** Principles

ALCOA principles first coined by US FDA in 1980s

A	**Attributable**
L	**Legible**
C	**Contemporaneous**
O	**Original**
A	**Accurate**

Data Collection — **ALCOA+** Principles

EMA 2010 GCPs guidelines on electronic data for clinical records

ALCOA+	*Emphasis on attributes of being:*
E	**Enduring**
C	**Complete**
A	**Available**
C	**Consistent**

Data Collection – Manipulation

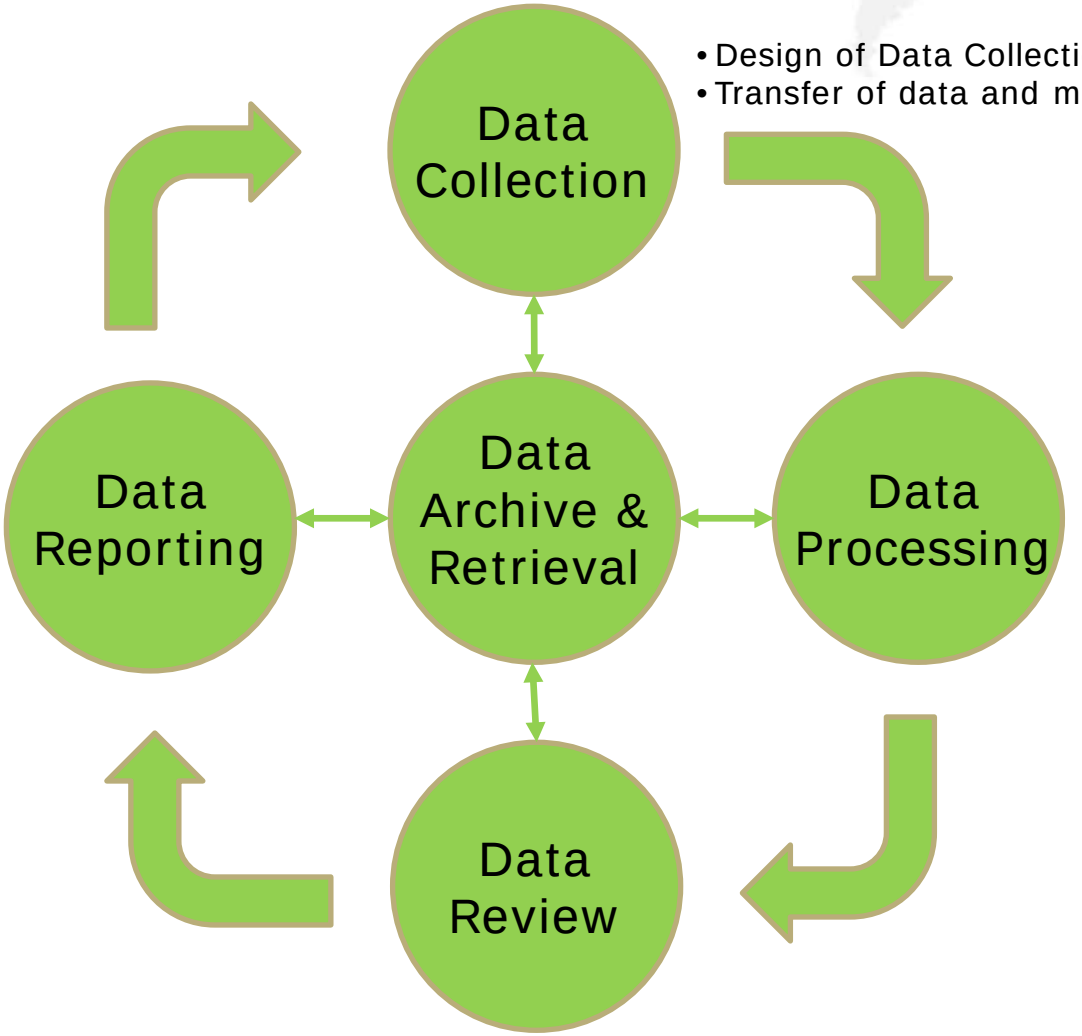
- Regulators expect human errors
- Corrections are accepted by regulators, provided they follow appropriate procedures and controls
- Allow for corrections in
  - Paper based processes
  - Hybrid systems
  - Electronic systems


Data Processing
• Objective
• Validated method or tool
• Follow approved procedure

Data Review and Reporting

- Review of the original paper, printouts, notebooks and electronic records
- Check where data may have been stored, including locations where voided, deleted, invalid or rejected data may have been stored (Don’t forget metadata!)
- Statistically evaluate DI performance of all data – i.e. atypical, suspected, rejected, in addition to reported data

Managing DI (Data Life-Cycle)



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Data Storage: Archiving & Retrieval

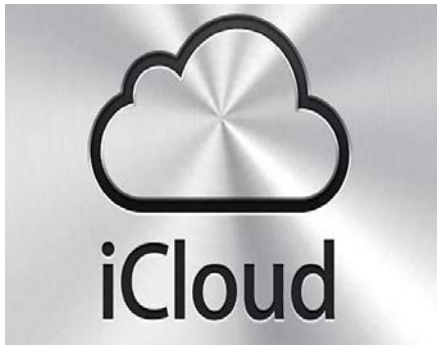
- Don’t forget metadata
- Verify retrieval process
- Consider media lifespan
- Use validated systems

Data Storage

- Paper Record

- Electronic:
  - Offline

  - Online – Local or Cloud-based



Data Deletion (**Intentional/non-fraudulent**)

- SOP required
- When – periodically every quarter, every year, etc.
- What data – need to be precise and accurate
- Verification process required
  - *Was correct data deleted?*
  - *Was other data impacted or deleted?*

Data Deletion (**Unintentional**)

- SOP required **for recovery and restoration**

- Data restoration testing required
  - Multiple software
  - Multiple versions
  - Hardware changes

- Can you rebuild the data?
  - Take nto account upgrade and compatibility challenges

Data Integrity Summary

References

US FDA Data Integrity and Compliance With CGMP Guidance for Industry; Draft guidance April 2016
https://www.fda.gov/downloads/drugs/guidances/ucm495891.pdf

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PIC/S Good Practices for Data Management and Integrity in Regulated GMP/GDP environments: Draft PIC/S guidance August 2016
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http://apps.who.int/medicinedocs/documents/s21467en/s21467en.pdf

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Thank You

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Questions

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