REGULATION PART ONE

WHY REGULATION?

Need minimum standards and consistency in the industrial landscape

Quality, Integrity, Reliability

In Schools and Universities, formal (legal) regulatory frameworks don't normally apply, not so in industry. Most industrial research, development and manufacturing operations in the life sciences are required to carry out their work subject to a regulatory environment

Defective products can pose significant risks to human health

GxP

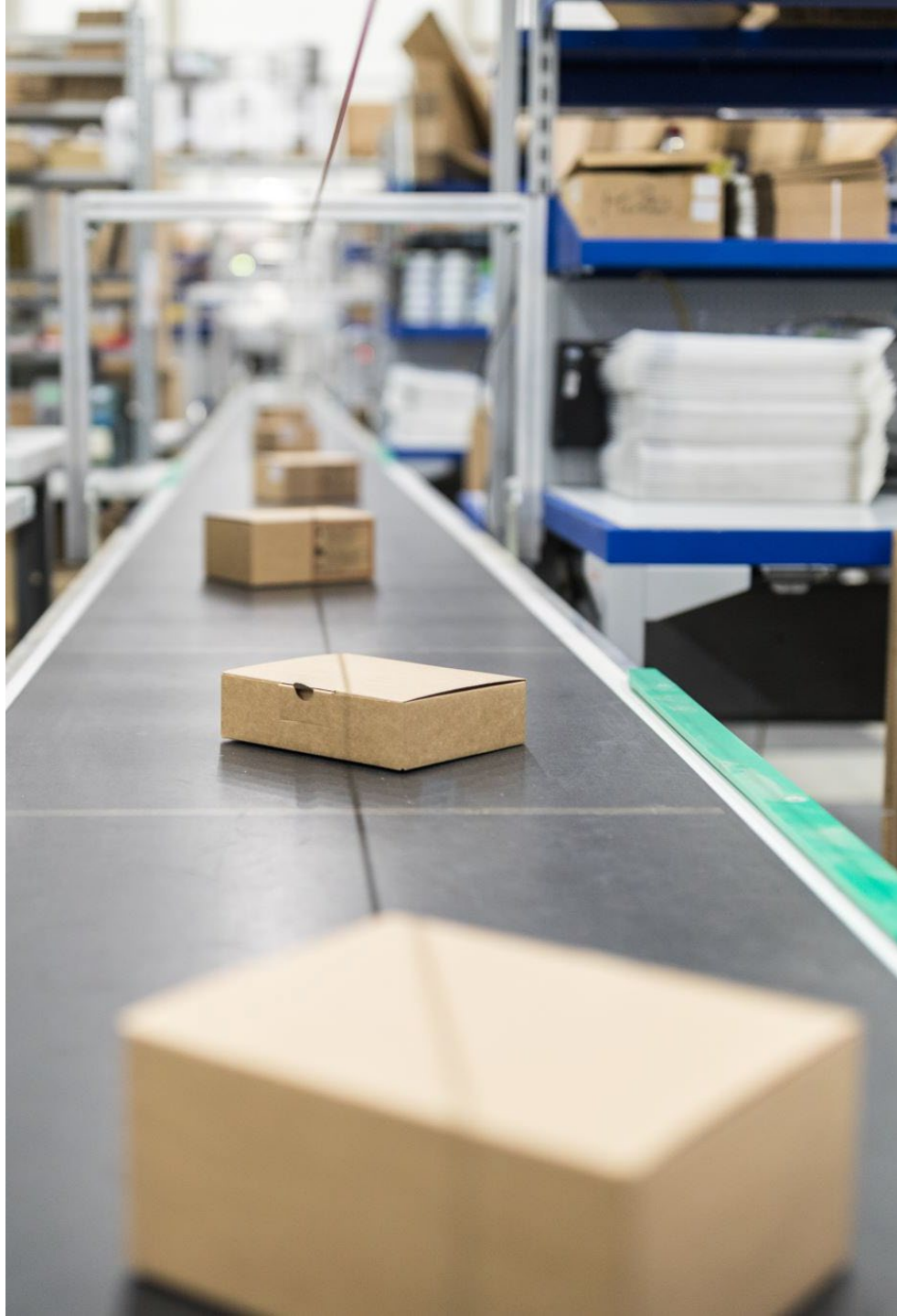
Good practice protocols ensuring that food, medical devices, drugs and other products are safe to use and effective.

The ‘x’ defines different approaches:
GMP – Good Manufacturing Practice
GLP – Good Laboratory Practice
GDP – Good Distribution Practice

Internationally recognised.
Managed by national and international regulators:
USA – Food and Drug Administration
Europe – European Medicines Agency
UK – Medicines and Healthcare Products Regulatory Agency

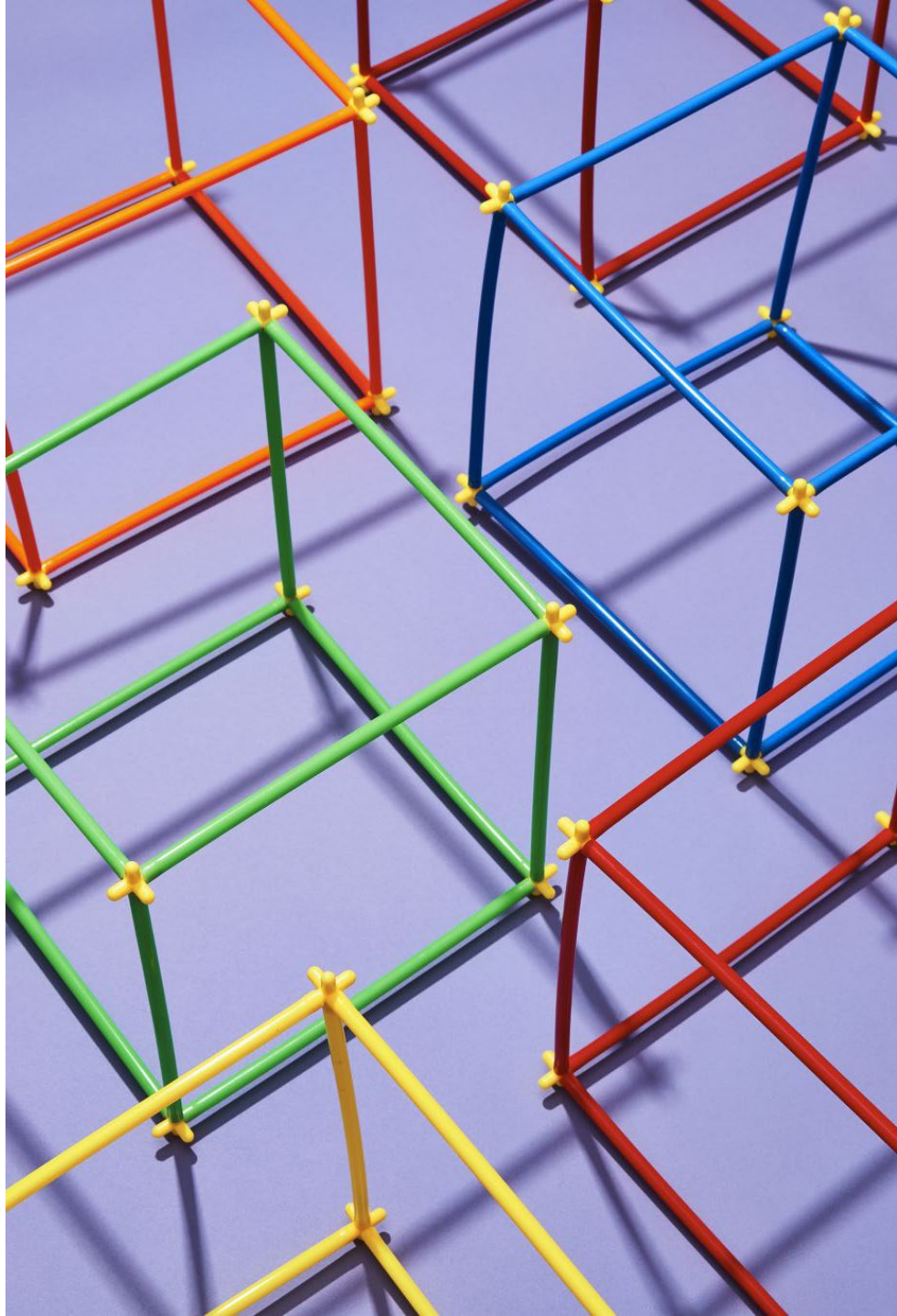
GxP Essentials

- Consistency of product manufacture
- Technology development
- Testing of product designs
- Calibration and testing of lab equipment – when does it become ‘obsolete’?
- Documentation of processes
- Storage and transportation of products
- Training of employees
- Recording of all processes



Documentation, Communication, Traceability and Accountability

- In order to verify that appropriate controls have been applied and to identify breaches in conformance, data and documentation must be traceable and accountable throughout the product journey
- Integrity of data – should be current, accurate, accessible and protected from tampering.
- GDocP – Good Documentation Practice! Underpins all GxP though it is not a formal standard



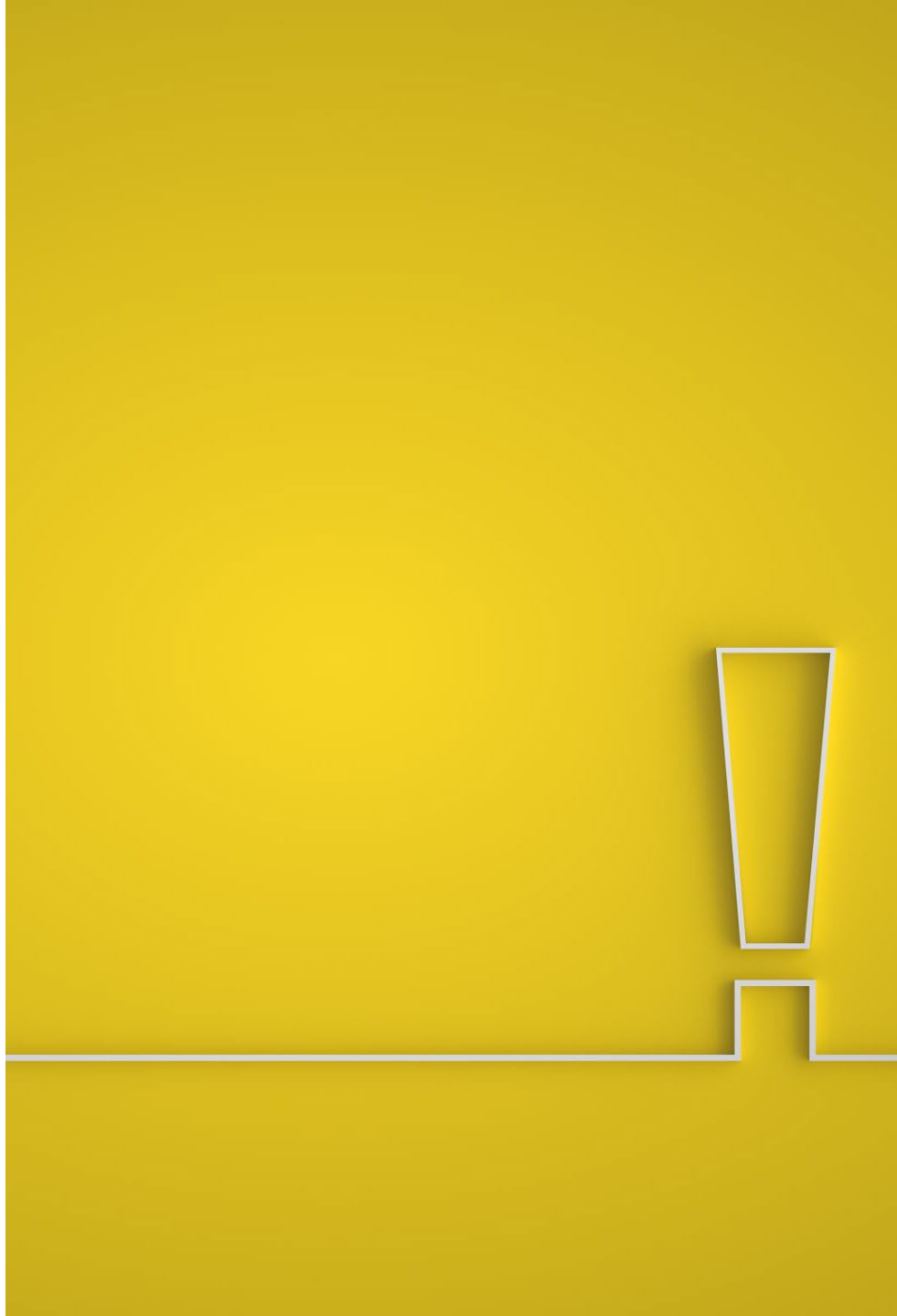
Documentation, Communication, Traceability and Accountability

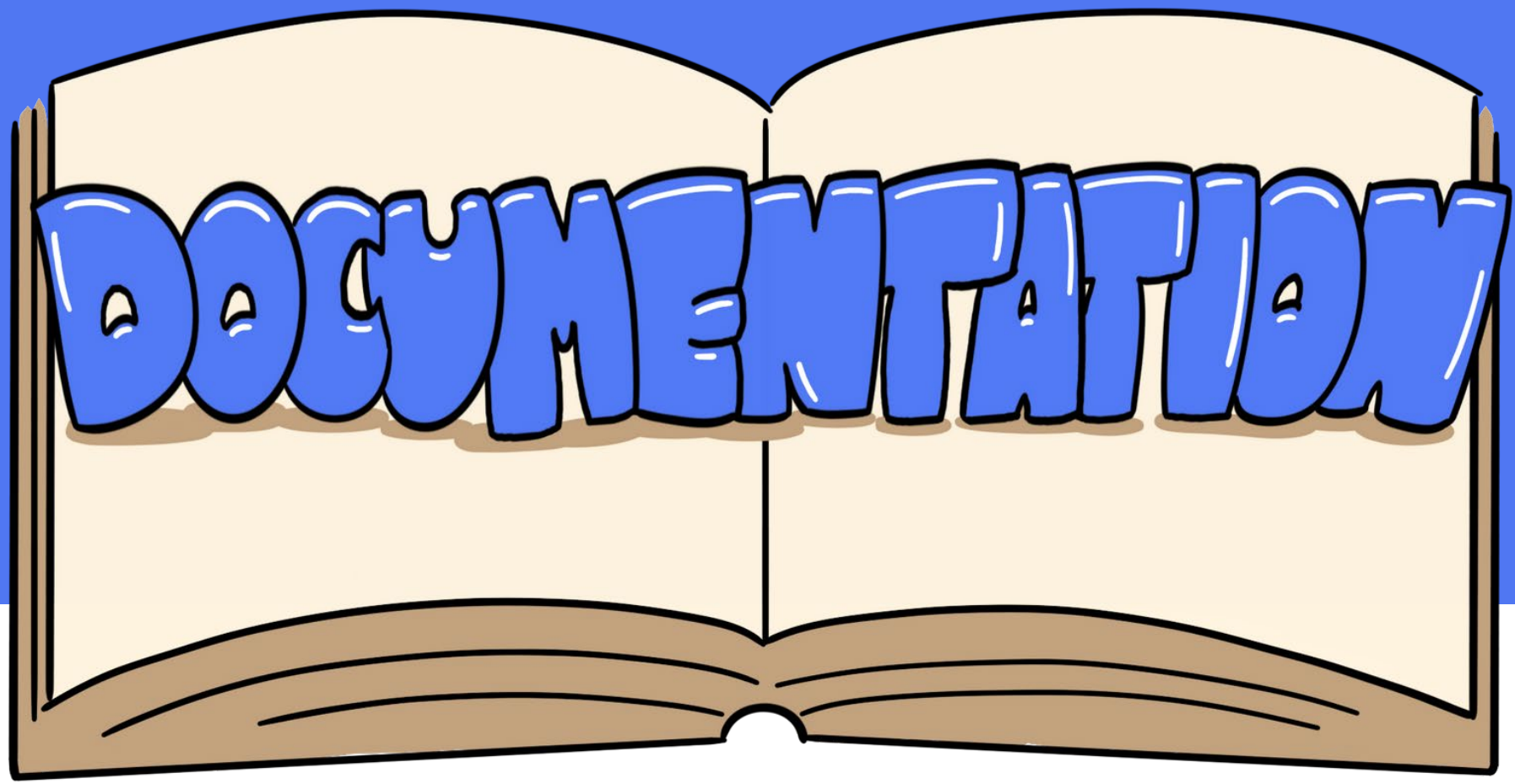
- Quality Management Systems (QMS) are used to qualify, record, and control GxP processes.

- QUESTION

- What do you think is the major cause of non-compliance with GxP?

- 1. Product Failure?
- 2. Lack of Documentation?
- 3. Fatalities?




DOCUMENTATION

Good Manufacturing Practice (GMP)

- Guidance (UK) from HM Government at Good manufacturing practice and good distribution practice - GOV.UK (www.gov.uk)

Good Manufacturing Practice (GMP)

GMP Essentials:

Products shall be

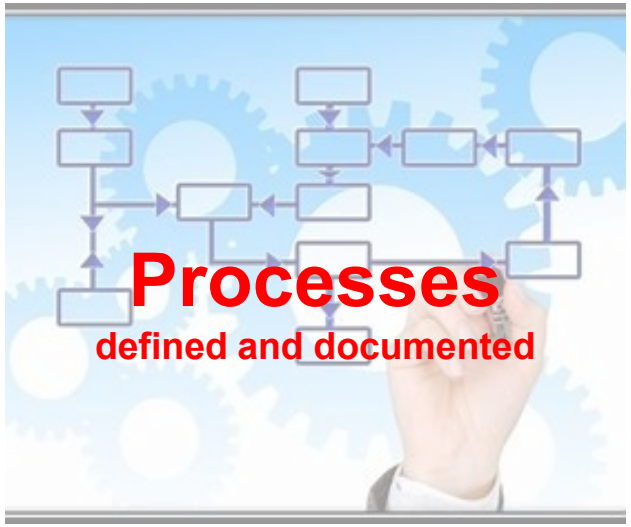
1. Of consistently high quality
2. Appropriate for use
3. Meet marketing or clinical trial authorization

Life Sciences – What is different about the LS manufacturing sector?

Failure of products constitutes a risk to human health.

Batch testing can be carried out to ensure Quality Control, but under GMP, manufacturers are required o ‘design in’ quality.


Procedure



Processes

defined and documented

Products

specifications
and repeatable
methodologies

Procedures

documented and recorded

Premises

designed and validated

People

trained and with clear
repsonsibilities

Good Manufacturing Practice (GMP)

- Standard Operating Procedures in place
- Manufacturing processes defined and recorded…and any changes documented
- Environment is controlled (preventing cross contamination)
- Quality defects investigated

- And don’t forget correct packaging and labelling!

Computerised Systems Validation

Validation of computer systems applies not only to GMP but GxP more generally

Intention is to create documentation so that a computerized/automated system will consistently make products meeting predetermined specifications

Much CSV follows the GAMP 5 guidelines, introduced by the International Society for Pharmaceutical Engineering (ISPE Homepage | ISPE | International Society for Pharmaceutical Engineering) which takes a risk-based approach

GOOD LABORATORY PRACTICE (GLP)

Principles underlying non-clinical laboratory studies for research.

Applies to

- Medicines
- Pesticides
- Cosmetics
- Veterinary Drugs
- Food and additives
- Industrial Chemicals

5.1 GOOD LABORATORY PRACTICE (GLP)

Again, founded in GDocP, Good Documentation Practice

Again, use of Quality Management Systems ensures that processes are reproducible and consistent

Again, controlled by International regulators…in the UK, this is MRHA. For details of compliance see:

Good laboratory practice (GLP) for safety tests on chemicals - GOV.UK (www.gov.uk)

Original UK regulations are at The Good Laboratory Practice Regulations 1999 (legislation.gov.uk)

OECD (Organisation for Economic Co-Operation and Development) are major players in GLP.

In addition to disseminating the principles of GLP, they also publish guidelines on the testing of chemicals which is required for GLP compliance. Check them out at OECD Test Guidelines for Chemicals – OECD

EXAMPLES OF STUDIES CARRIED OUT UNDER GLP INCLUDE:

- Physical-Chemical Testing
- Toxicity and Mutagenicity Studies
- Environmental Toxicity Studies on Aquatic and Terrestrial Organisms
- Bioaccumulation
- Determination of Pesticide Residues in Food
- Effects on Mesocosms and Natural Ecosystems

Mesocosm=any outdoor experimental system that examines the natural environment under controlled conditions

- Analytical and Clinical Chemistry Testing

Compliance is enforced through inspection and validation of submitted data.

Local regulators operate national Compliance Monitoring Programmes (CMP)to ensure verification

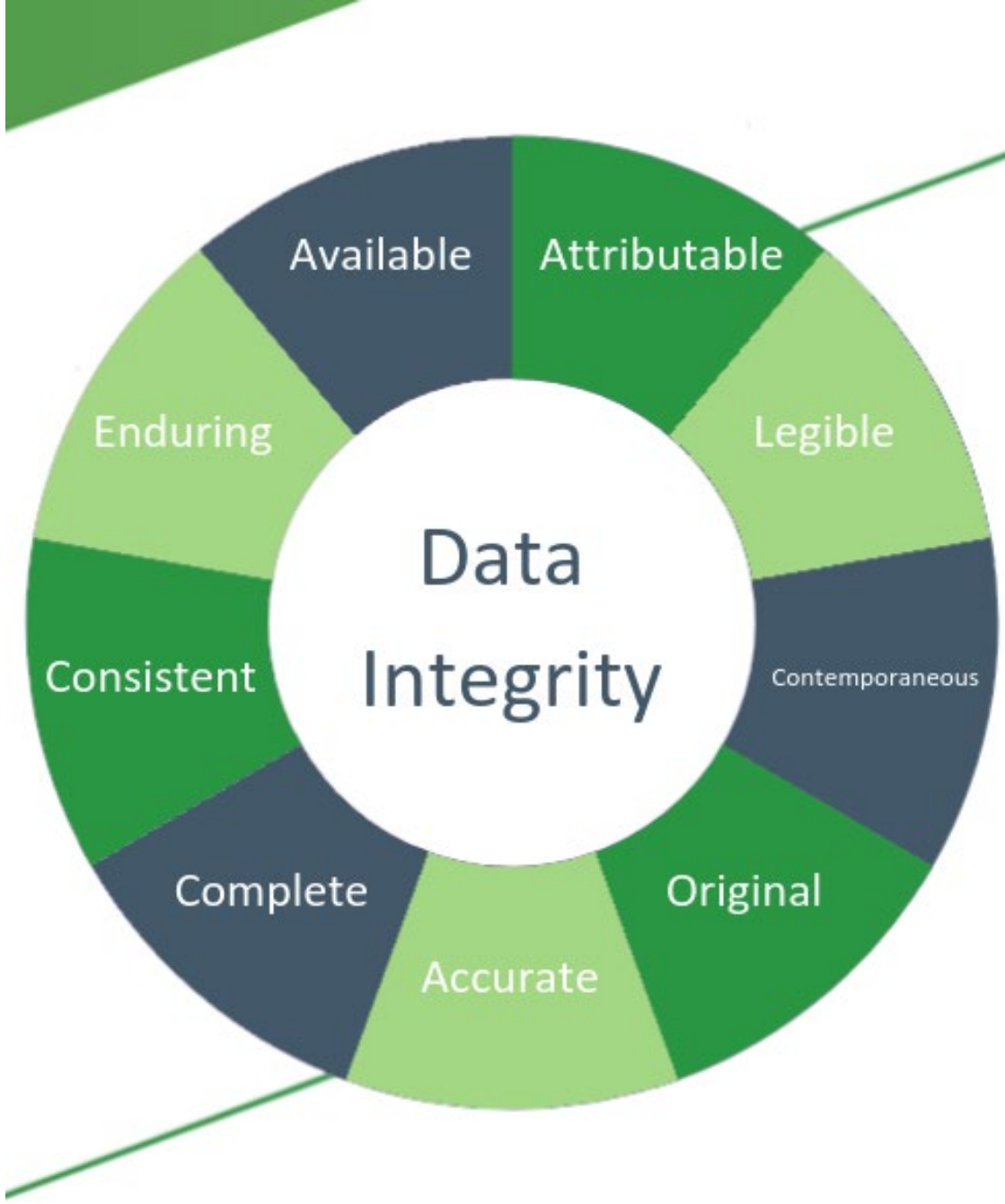
See OECD Principles of Good Laboratory Practice (GLP) and GLP Compliance Monitoring – OECD

MUTUAL ACCEPTANCE OF DATA (MAD)

Data collected in one OECD member state is accepted by others – intended to reduce duplication of effort

ALCOA:

ATTRIBUTABLE, LEGIBLE, CONTEMPORANEOUS, ORIGINAL AND ACCURATE



ALCOA was introduced by the FDA (Food and Drug Administration) but has been taken up by many organisations around the world.

Original ALCOA principles (shown on previous slide) have been supplemented by:

- Complete
- Enduring
- Consistent
- Available

Known as ALCOA+

ATTRIBUTABLE: Record details of whatever (device) and whoever collected the data…and the source…and the time.

LEGIBLE: Clarity is essential…and the data should be permanent

CONTEMPORANEOUS: If the data is recorded manually, it should be done at the time of the process…and if electronic it should be time-stamped

ORIGINAL: Students are notorious for writing down results on scraps of paper and then transferring to a lab-book or journal ‘later’. This breaches the ALCOA protocols

ACCURATE: Error-free records…and if anything is changed, the original data should not be lost. Accuracy checks and calibrations of equipment required (ties into GxP)

COMPLETE: Audit trails in recorded data to validate that nothing has been deleted, and to flag any changes made…also affects metadata

CONSISTENT: Data is chronological…and time-stamped

ENDURING: Data should be available long after it is recorded

AVAILABLE: Databases should be readable and searchable