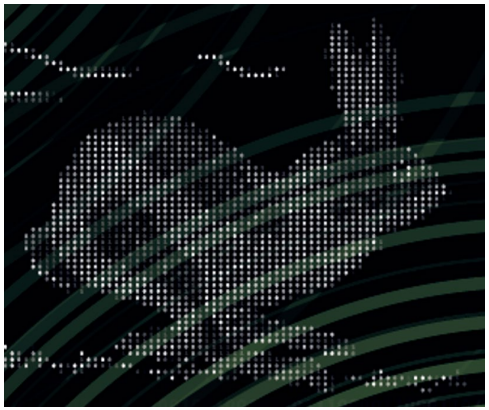
D4 Data and Ethics

Autumn 2022 – Lecture 2 - Part IV

Focus: Information security & cybersecurity | Author: Prof. Dr. Petra Maria Asprion | FHNW

Follow the white rabbit …..



The white rabbit and the metaphors referring to it stand for the fact that people start to investigate small doubts and discover a gigantic conspiracy.

Back in the 1980s computer programmers would sometimes leave a ‘back door’ in their code so if it got screwed up when they installed it at a business, they could get back in. These back doors were sometimes referred to as ‘white rabbits’. There is quite a famous reference to the practice in Jurassic Park (the book, not the movie).

On December 14, 2021, the Lodestone Forensic Investigations team responded to a client whose environment was affected by what appeared to be a new strain of ransomware: White Rabbit. Lodestone identified via open-source intelligence (OSINT) that White Rabbit was first publicly disclosed on Twitter on the same date by security researcher Michael Gillespie https://lodestone.com/insight/white-rabbit-ransomware-and-the-f5-backdoor).

If you have time, follow the "White Rabbit" phenomenon ... You will come across many interesting stories and also movies, etc. and last but not least ransomware , job offers, etc..

Agenda

Part I -- Intro: data & more	→ SD1
Part II -- From yesterday until today	→ SD2
Part III -- Organization Layer: Be informed!	→ SD3
Part IV -- Organization Layer: Be prepared -- GRCM	→ SD4
Coaching Session #2	→ SD5

→ SD = Slide Deck

GRC Today ---

Governance, **R**isk Management and **C**ompliance -- **GRC**

is the basis for a company to operate efficiently and sustainably!

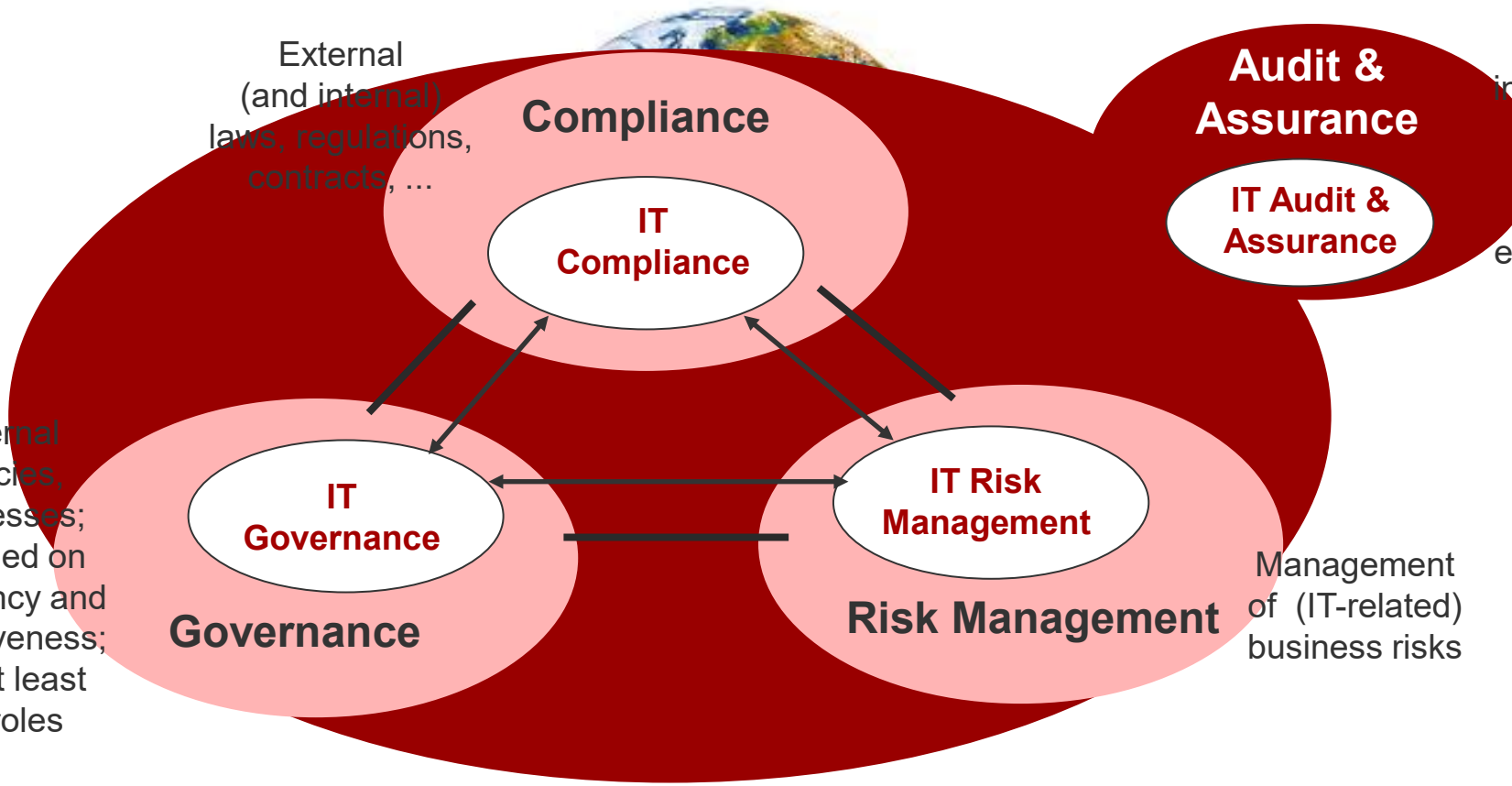
Today --

Government policies, stagnating R&D funding levels, laws and regulations which are constantly changing around the globe, these continue to affect how life sciences organizations operate.

GRC Management (GRCM) helps to be **Compliant** with relevant requirements and supports Risk Management

A short statement to explain GRCM …

Governance, Risks, Compliance Management -- it´s all related with each other …



Klotz, 2009, p. 11 (adapted)

Let's start with Compliance

in Life Sciences …

What is Compliance? In Short --

Conforming to a rule (law, regulation, policy, standard, directive..).
Companies work to be compliant with relevant rules.

To ensure high product **quality** and **services**
To ensure ethical behavior
To ensure patient **safety**

Doing business
Business integrity
Build **trust** & **reputation**

And for Life Sciences?

What is Compliance for Life Sciences? FDA --

FDA prioritizes **the safety of all staff**, as well as **compliance with applicable laws and regulations** including, but not limited to laboratory safety, use of animals, the environment, human subjects, and select agents and toxins.

To ensure compliance with safety and other regulatory requirements, **staff complete trainings on a regular basis relevant to their work duties or potential exposure to workplace hazards**.

In addition, FDA promotes laboratory quality and adherence to quality elements among FDA researchers and regulatory personnel to achieve robust and reproducible findings. FDA researchers are encouraged to publish original research findings in scientifically accepted, peer-reviewed scientific journals after appropriate review and clearance. Quality programs are imperative to ensure the highest scientific rigor that leads to data-based decisions.

Picture FDA https://www.fda.gov/science-research/focus-areas-regulatory-science-report/safety-and-compliance

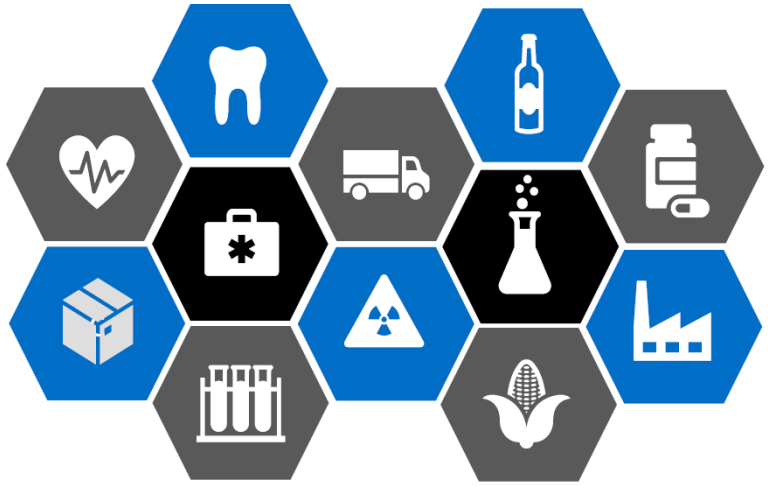
https://www.fda.gov/science-research/focus-areas-regulatory-science-report/safety-and-compliance

The focussed Industry …

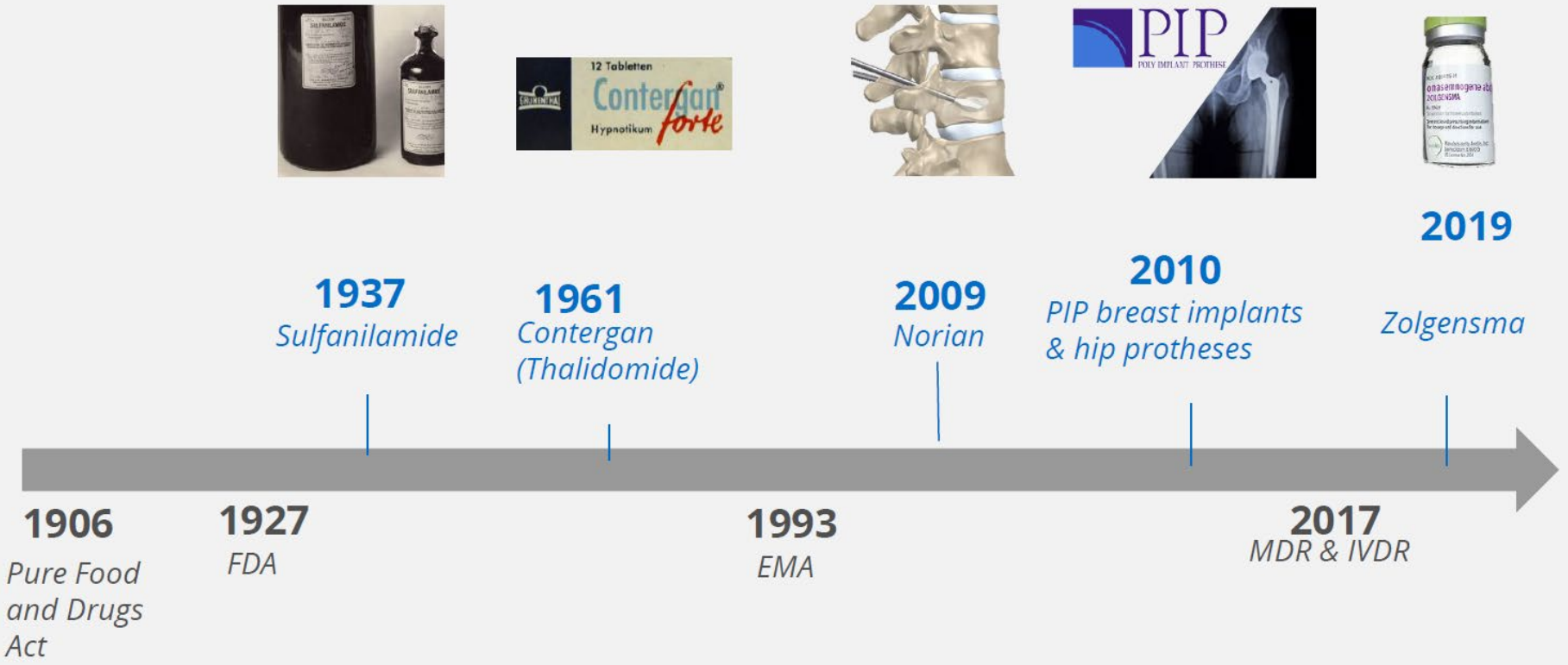
Pharma
Prescription, Biotech, Generics, OTC/Consumer
Supplier, Provider
Provider
Logistics

Medtech
Manufacturer
In-vitro Diagnostic Manufacturer
Supplier, Provider
Software manufacturer

Healthcare
Hospitals
Pharmacies
Medics
Insurance

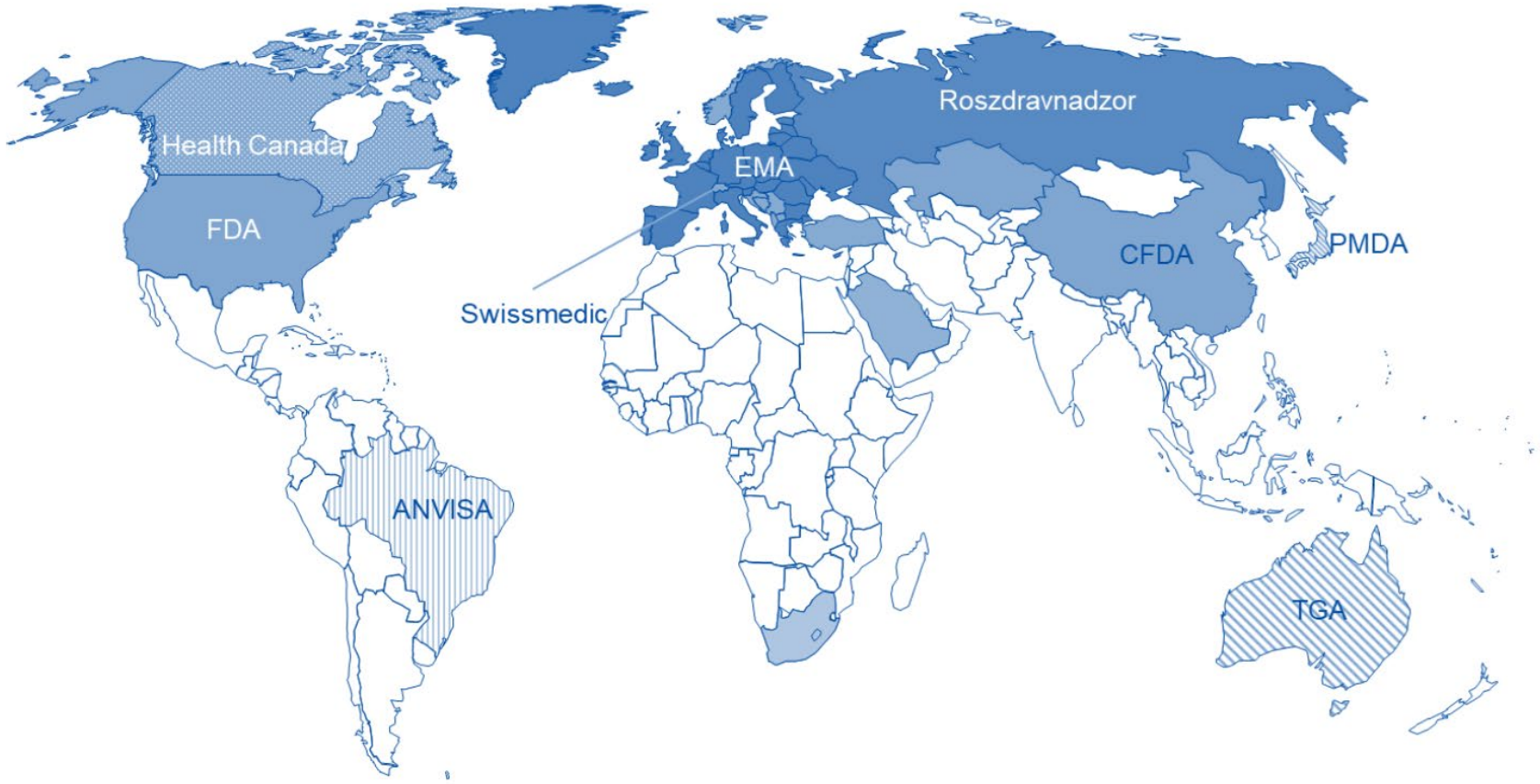


Why is Compliance in Life Science important?



2019: Zolgensma (Novartis) https://www.pharmaceutical-technology.com/analysis/manipulated-data-novartis-zolgensma/
2010: PIP scandal https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3676226/
1961: Contercan https://www.autentic.com/63/pid/8/Behind-Closed-Doors:-The-Contergan-Scandal.htm
1937: https://www.fda.gov/files/about%20fda/published/The-Sulfanilamide-Disaster.pdf

Global/National Regulatory Authorities



EU: also national authorities

Authorities and International Organisations

International Organisations

Pharmaceutical Inspection Convention Scheme – PIC/S
International association of 46 GMP-monitoring institutions. Goal: Development, Implementation and fostering of GMP Standards & Quality System.

International Medical Device Regulators Forum (IMDRF)
International forum of medical device regulation

International Society for Pharmaceutical Engineering (ISPE)
ISPE as international operating agency that represents the interests or Pharmacoepidemiology and Pharmacovigilance.

Council for Harmonisation
International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is responsible for the harmonization of human pharmaceuticals as basis for the pharmaceutical admission in Europe, the USA and Japan.

Authorities

Food & Drug Administration (FDA)
U. S. Food and Drug Administration monitors food and pharmaceuticals in the USA

Federal Institute for Drugs and Medical Drugs (Bfarm)
Bfarm is an agency under the Federal Ministry for Health in Germany

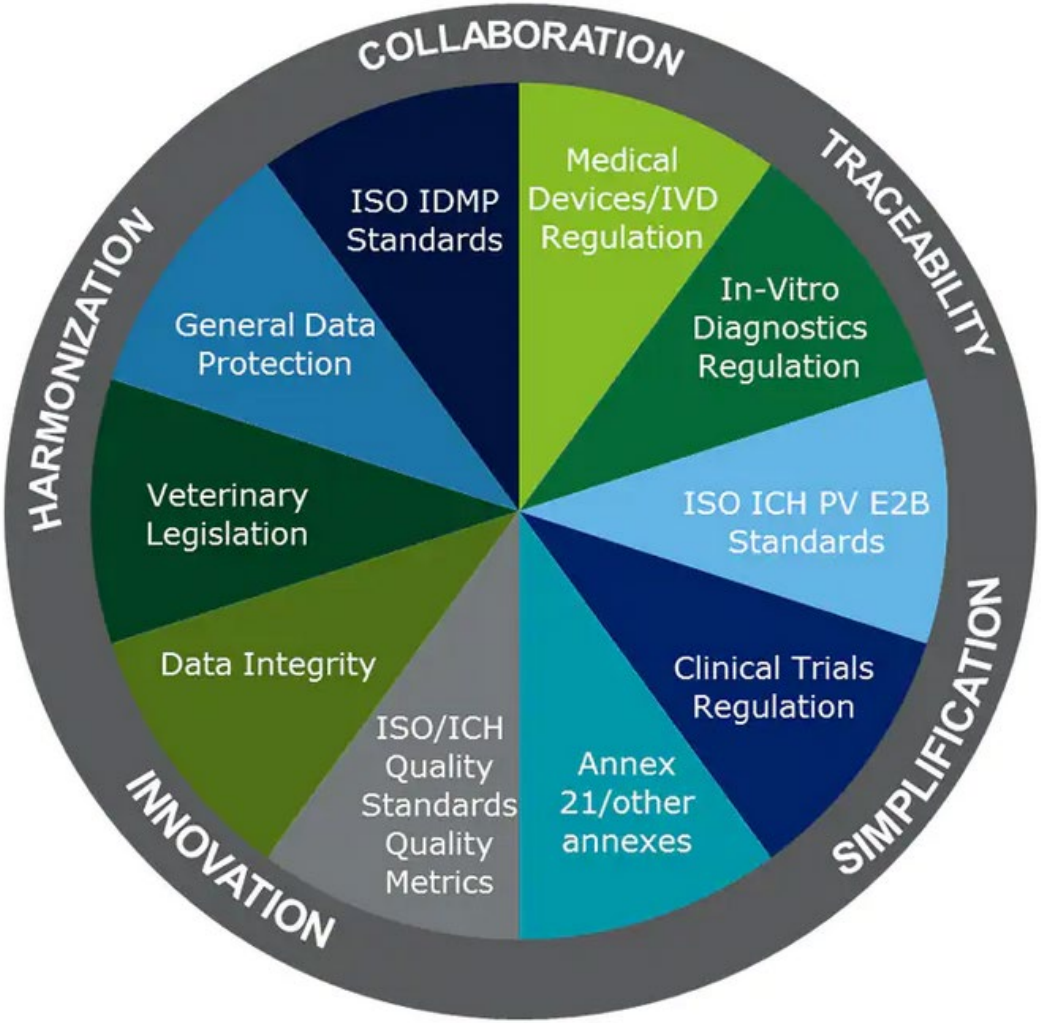
European Medicines Agency (EMA)
The European pharmaceutical agency, responsible for the testing and monitoring pharmaceuticals

Medicines & Healthcare Products Regulatory Agency (MHRA)
MHRA is the monitoring and admission authority of medicines in the UK

Swissmedic
Swissmedic is the swiss admission and control authority for medication.

World Health Organization (WHO)
Coordinating authority of the united states for the internation public healthcare.

Overview of EU regulatory changes



"Recent and ongoing European regulatory changes will impact every pharmaceutical, biotechnology or medical technology (medtech) company that currently sells or sponsors products in the European Union (EU). Companies can be well-equipped by taking a proactive approach to tracking and monitoring the regulatory developments and understanding their independent and combined impact on the business." (Deloitte, 2022)

Source: Deloitte (2022) https://www2.deloitte.com/global/en/pages/life-sciences-and-healthcare/articles/eu-regulatory-changes-impact-global-life-sciences-industry.html

Examples of regulated Products …

Over the counter

some herbal products

Prescription drugs

Vaccines

Personalized medicine

Medtech

Combination products

Note: The FDA is responsible for protecting public health by regulating **human drugs and biological products, animal drugs, medical devices, tobacco products, food (including animal food), cosmetics, and electronic products that emit radiation**

Have a Look: https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/importing-fda-regulated-products

Regulations, Guidelines & Procedures

Regulations

FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

swissmedic
Schweizerisches Heilmittelinstitut

acknowledged or required

Guidelines (GxP)

ICH
harmonisation for better health

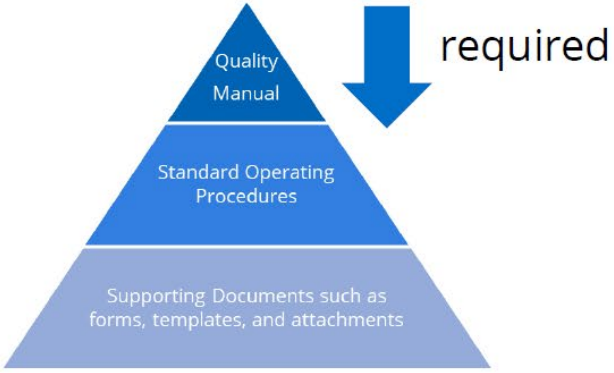
ISPE

World Health Organization

ISO

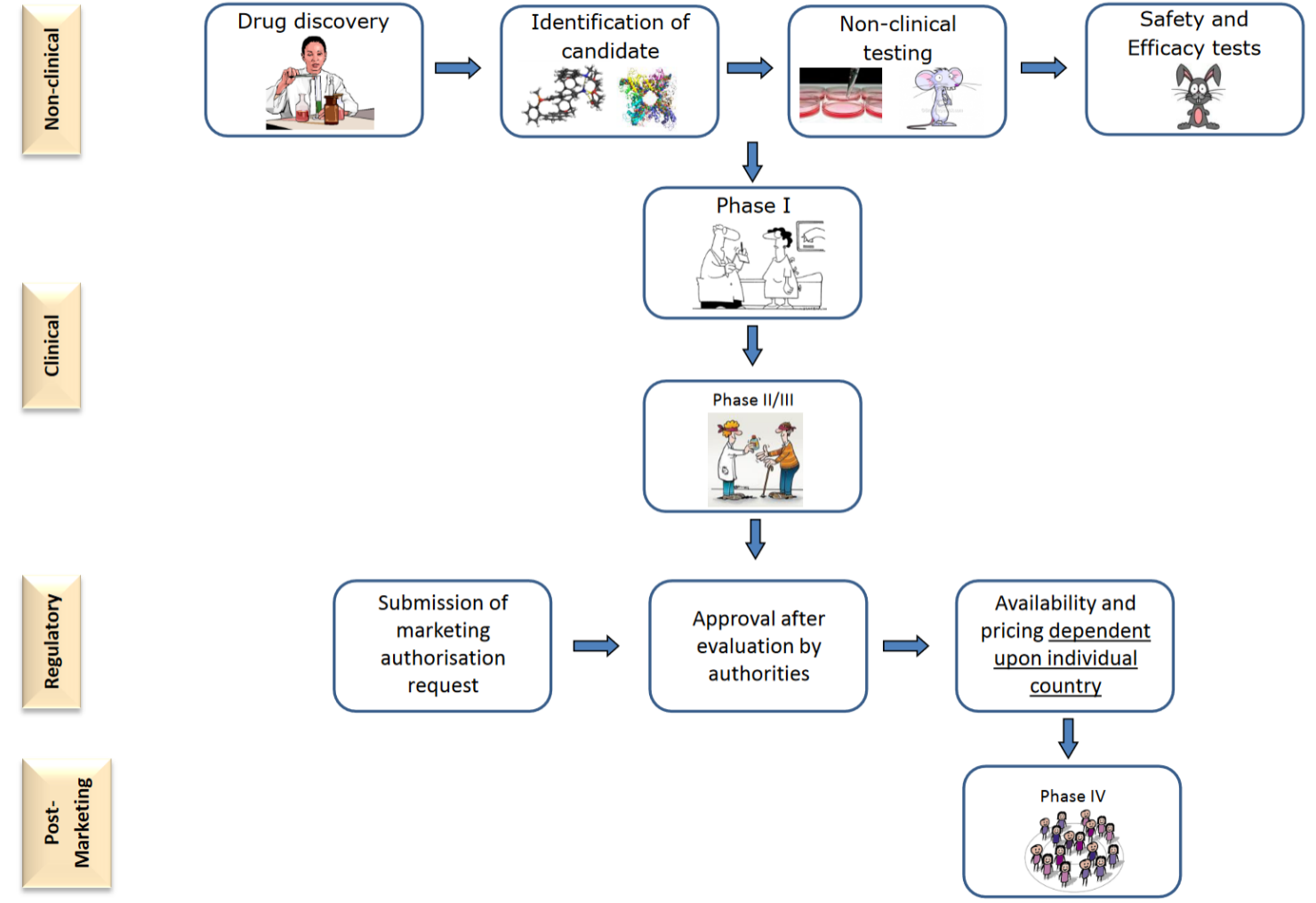
PIC/S

Companies Procedures



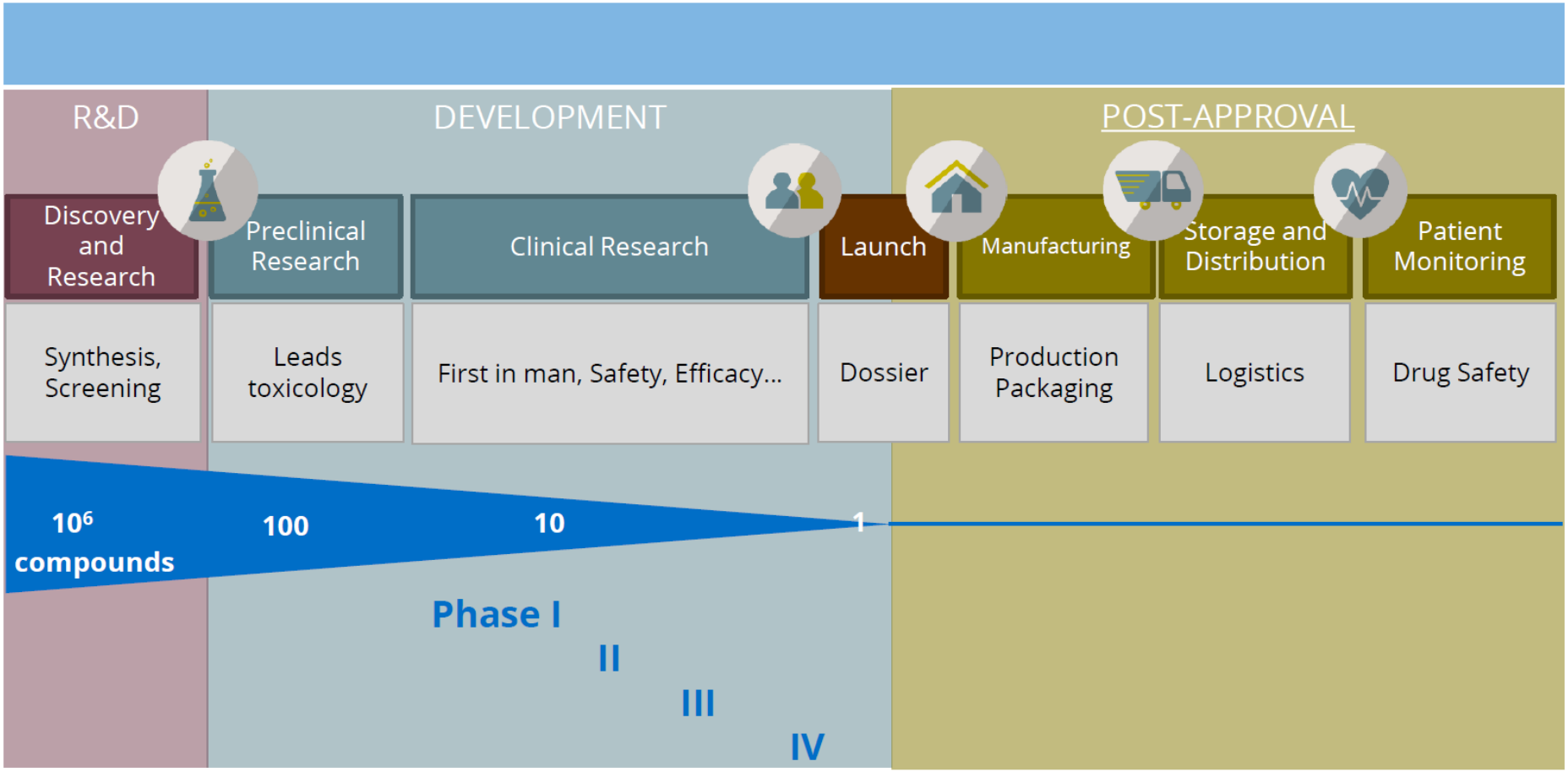
required

Overview of medicines development

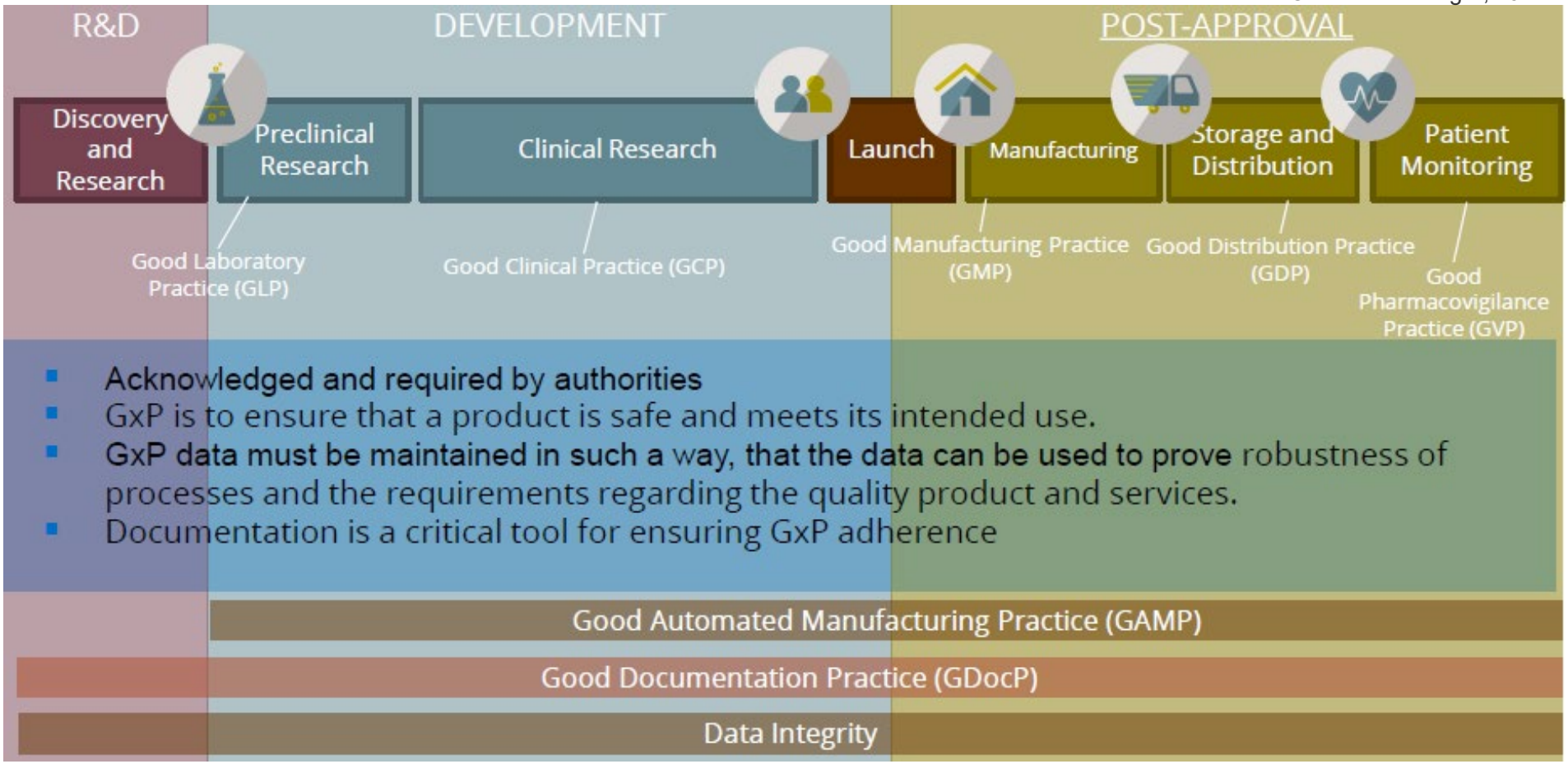


Source: EMA (2022) „How are medicines evaluated at the EMA" https://www.ema.europa.eu/en/documents/presentation/presentation-how-are-medicines-evaluated-ema-nathalie-bere_en.pdf

The regulated lifecycle of a medicine – an overview



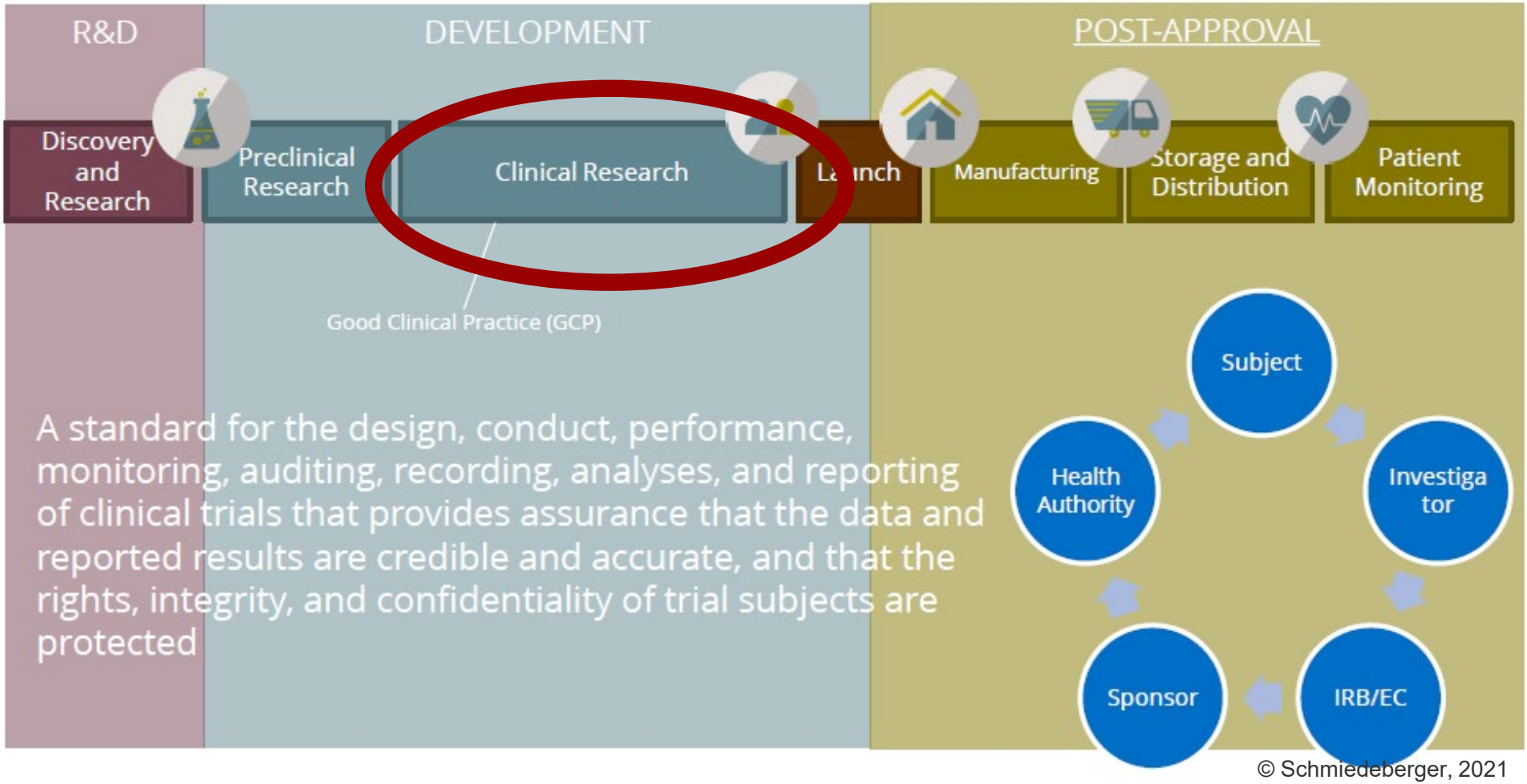
GxP* – An established standardized good practices



* GxP -- is a general abbreviation for the "good practice" quality guidelines and regulations. The "x" stands for the various fields, including the pharmaceutical and food industries, for example good agricultural practice, or GAP.

In the pharmaceutical industry, the 'x' denotes the following areas: Manufacturing, Distribution, Laboratory, Clinical facilities related, and Documentation

Example I: Good Clinical Practices (GCP)



Have a Look: https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice

Good Clinical Practices – Why is the protection of the study participants extremely important?

Nuremberg Code

Declaration of Helsinki

International Committee for Harmonization (ICH)

WHO GCP

* see details next page

*

International Committee for Harmonization (ICH)

ICH harmonisation for better health

Four main focus Areas

Pharmaceutical Quality System

Electronic submission standards (ESTRI, eCTD)

Medical Dictionary for Regulatory Activities (MedDRA)

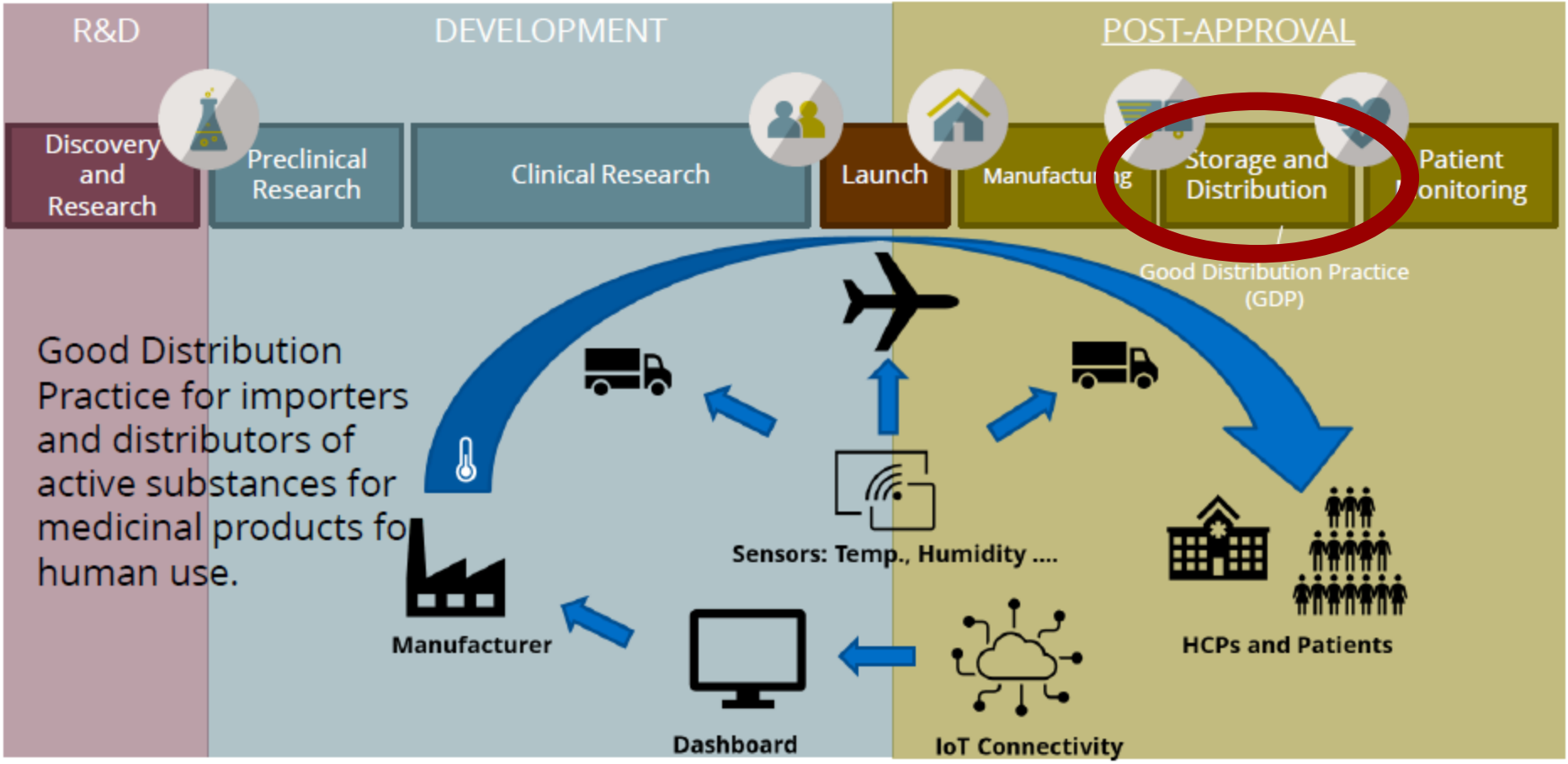
Updated regularly

Quality	▪ 54 guidelines
Safety	▪ 20 guidelines
Efficacy	▪ 37 guidelines
Multidisciplinary	▪ 25 guidelines

Source: https://www.ich.org/

Habe a look on the guidelines overview: https://www.ich.org/page/ich-guidelines

Example II: Good Distribution Practice (GDP)



Have a look: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/compliance/good-distribution-practice

Distribution Risks: Falsified, illegal and stolen medicines

Definition?

medicine which is deliberately and fraudulently mislabeled with respect to identity and/or source WHO

Facts?

Falsified medicines industry much bigger than illicit drug trade combined

No active pharmaceutical ingredient

Wrong pharmaceutical ingredient

Wrong doses of correct ingredient

Harmful chemicals

with fake packaging

Impacts?

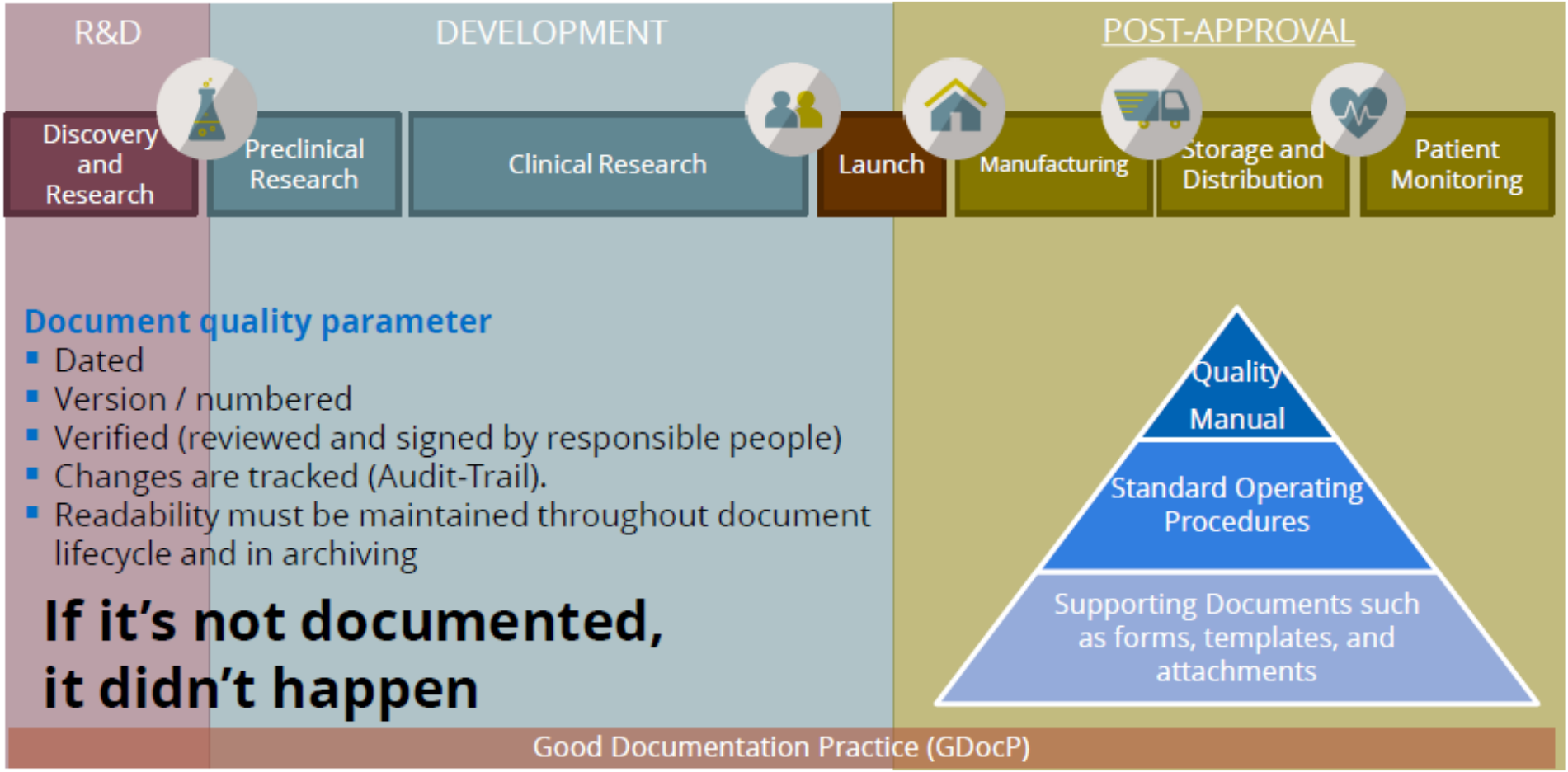
Harmful to patients

- Side effects
- Serious health issues

Building of disease resistance (e.g., malaria, HIV)

Have a Look: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/falsified-medicines-overview

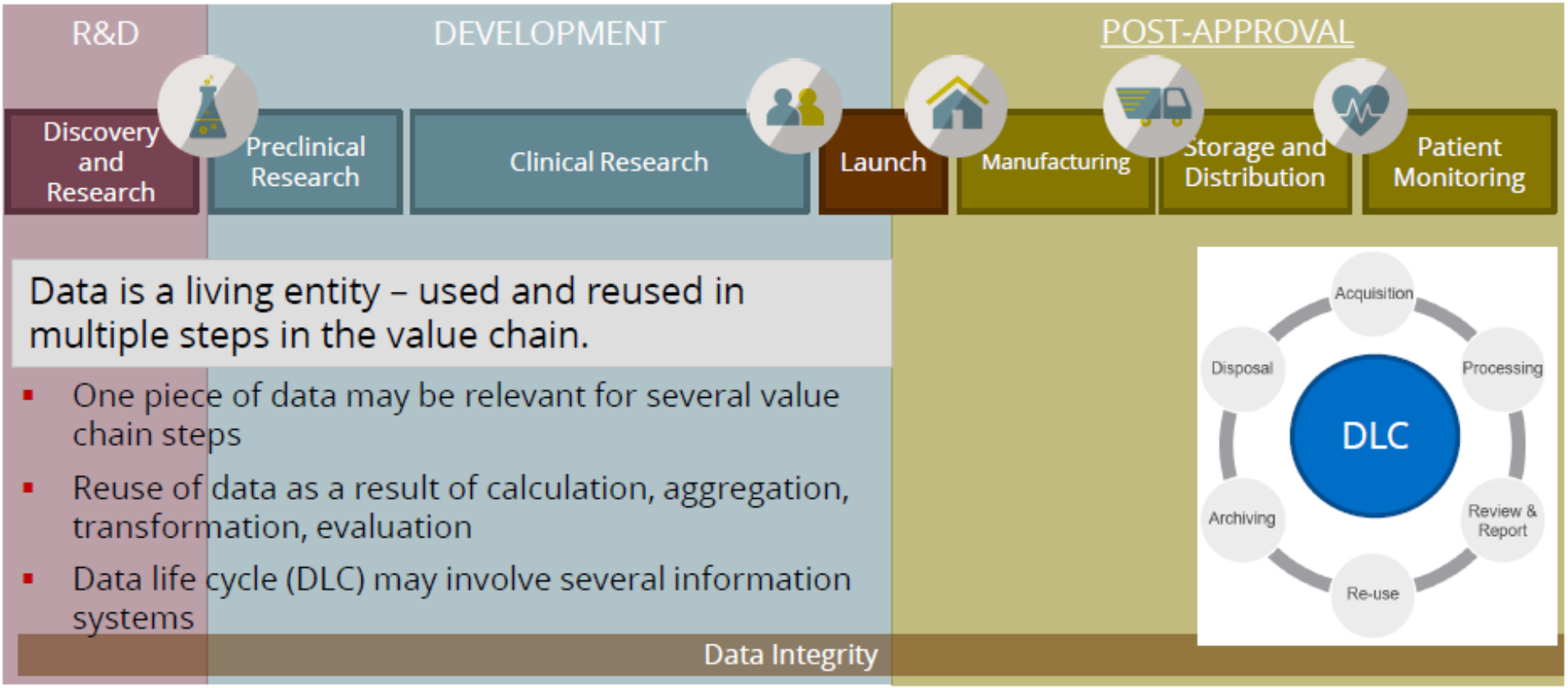
Example III: Good Documentation Practice (GDocP)



Have a Look: https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/guidance-good-manufacturing-practice-good-distribution-practice-questions-answers

GDocP requires: Data Integrity

Generating, transforming, maintaining and assuring the **accuracy**, **completeness** and **consistency** of data over its entire life cycle in compliance with applicable regulations.



Have a Look: https://www.chromatographyonline.com/view/data-integrity-focus-part-viii-what-good-documentation-practice-gdocp

Examples of data integrity problems

Technology

Inadequate or misconfigured IT systems

Missing functionality in infrastructure and applications

Weak technical security controls

Organization & Personnel

- Inadequate business processes
- Weak organizational security controls
- Time pressure on workforce
- Inadequate incentive systems, fear to fail
- Lack of understanding GxP regulations
- Lack of training on IT systems and business processes

Conclusion.
Why should you care about data integrity?

The regulators care about data integrity
- Increasing amount of findings in audits/inspections
- Release of guides on data integrity (FDA, MHRA, WHO, PIC/S)
- Sanctions (Recall, Import ban, ...)

Integrity facilitates evidence-based business decision making

Good data management practice is a good foundation to manage data-centered business requirements such as digital transformation and implementation of data privacy (e.g. GDPR)

Revelation of data integrity problems has reputational impacts on business

Ensuring data integrity reduces data ownership costs through the data lifecycle

Integrity is the foundation of business excellence and patient safety. Integrity builds trust.

Add-on

Computerized System Validation

Computer system validation (CSV) is a documented process that is required by regulatory agencies around the world to verify that a computerized system does exactly what it is designed to do in a consistent and reproducible manner. (https://www.complianceonline.com/dictionary/computer_system_validation.html).

What is a Computerized System?

A system that includes software, hardware, application software, operating system software, supporting documentation, e.g. automated laboratory systems, control systems, manufacturing, clinical, or compliance monitoring database systems, etc.

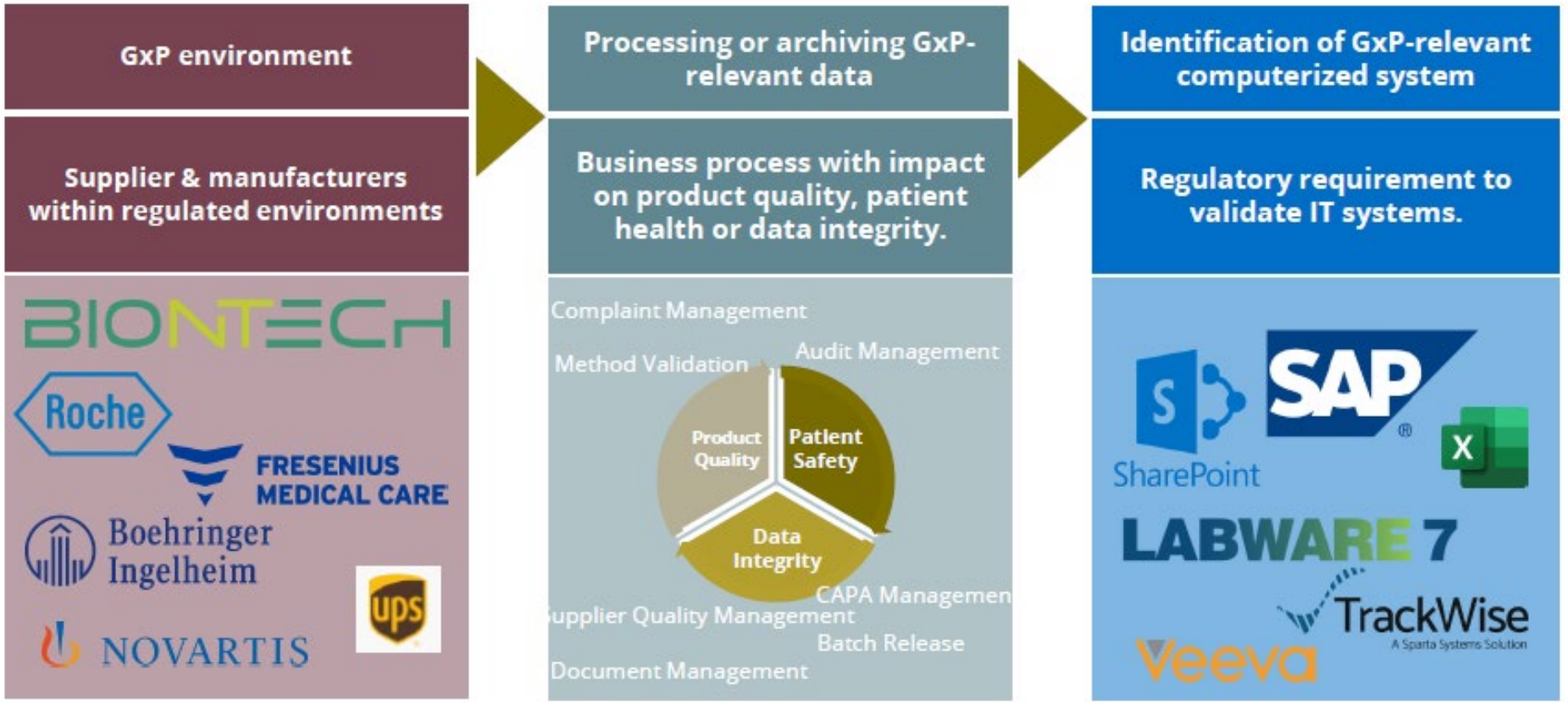
Source. https://www.igi-global.com/dictionary/practical-approach-computerized-system-validation/5177

What is Validation?

Establishing documented evidence which provides a **high degree of assurance** that a specific process will **consistently** produce a product -- **meeting** its **pre-determined specifications** and **quality attributes!**

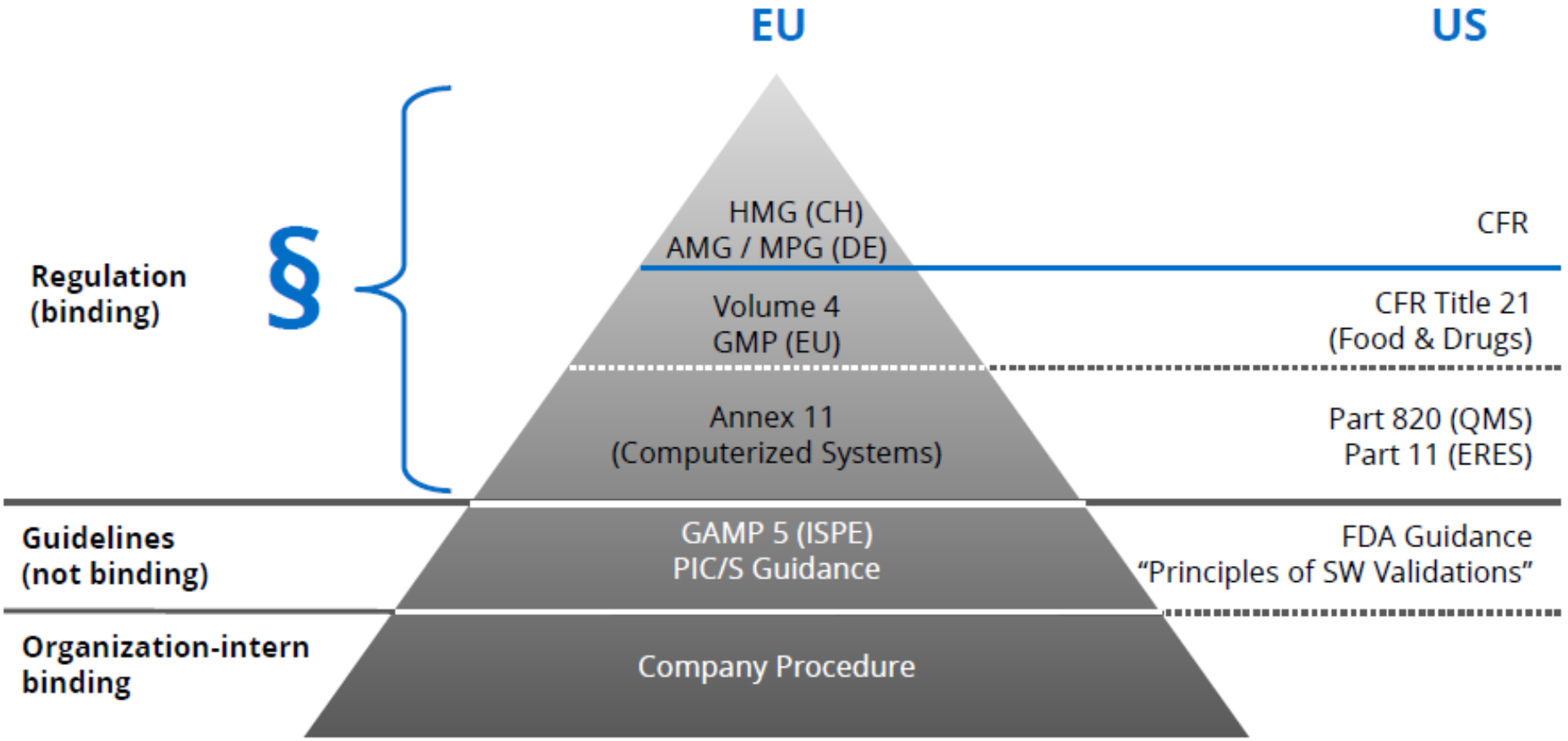
Source. https://www.igi-global.com/dictionary/practical-approach-computerized-system-validation/5177

When & Why is Computerized System Validation needed?



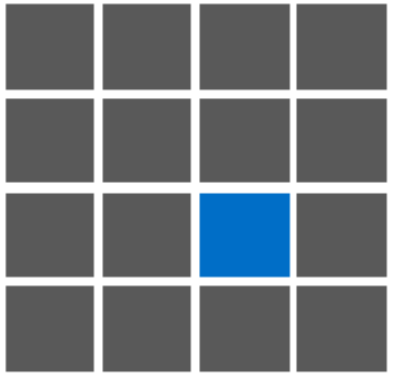
Have a Look: EMA (2022) EMA clarifies Computer Validation and Data Integrity responsibilities in Clinical Trials
https://www.gmp-compliance.org/gmp-news/ema-clarifies-computer-validation-and-data-integrity-responsibilities-in-clinical-trials

Regulatory Requirements for computerized Systems

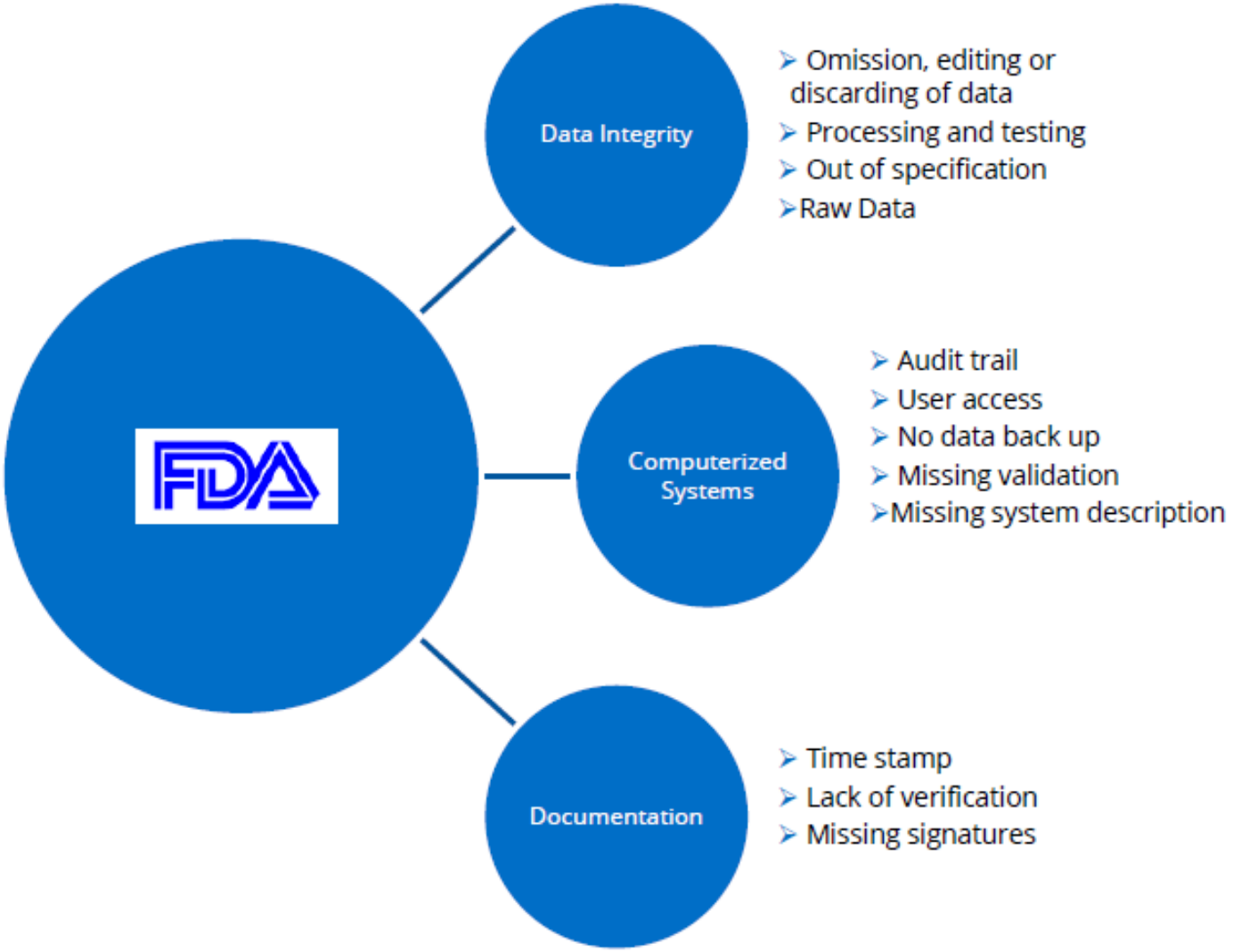


Monitoring Streams …

System Audit	**Process** Audit	**Procedure** Audit	**Product** Audit
All processes of the system	One individual (part) process	One concrete procedure	Relevant basic elements for achieving product specification
In all organisational fields	In the responsible organizational fields	In the responsible organizational field	In the responsible organizational fields
Individual samples (products, orders)	Individual samples (products, orders)	Individual samples (products, orders)	One concrete product



Frequent Findings …



What have we discussed so far?

Governance, Risk Management and Compliance Management as precondition for secure data and to comply with regulations

Definition of Compliance

Life Science - The focussed Industry …

Regulations in Life Science

GxP

Data integrity

and as add-on …

Monitoring Streams and Frequent Findings …

Computerized System Validation – the “documented evidence”