Introduction to GxP Quality Management Systems (QMS)

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Objectives

- **Review History and purpose of Quality Management (QM)**
- **The Founders of Modern Quality Systems**
- **Compliance and Quality Management**
- **GxP Regulations, Guidance & Standards**
- **Quality Management Systems & Essential Elements of Quality**
- **Corrective and Preventive Actions**
- **Document Control**
- **Summary**

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HISTORY

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A Brief History of Quality Management

Origins of GxP laws & regulations

- **United States (US) and Europe - similar events occurred in US & Europe and elsewhere leading to the establishment of laws to ensure public safety**

- **US - Establishment of laws to ensure GxP manufacturers (i.e., manufactures of Pharmaceuticals and medical devices) bring safe and effective products to market, and ensure safe and effective patient care**

- **US - Establishment of regulatory requirement (as required by law, i.e., codified regulations) which define expectations for which entities operating within GxP regulated environments must comply**

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A Brief History of Quality Management

USA - Origins of GxP laws & regulations

- Medicines in the 19th Century USA were unregulated and there was no requirement that medicines be proven safe and/or effective
- Deaths and injury often occurred as neither the purity of medicinal products or potency of products was required to be demonstrated (e.g., many medicinal products in the 19th century contained opium)

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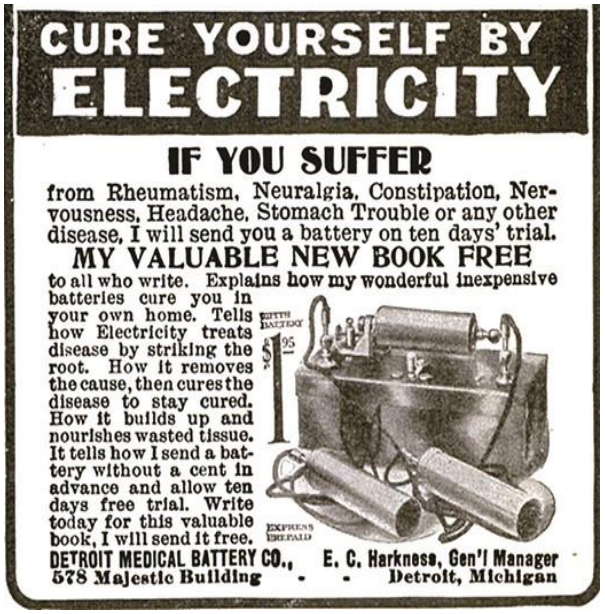
A Brief History of Quality Management

Examples of 19th Century Unregulated Medicinal Products



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A Brief History of Quality Management

Origins of GxP laws & regulations (cont…)

US Pure Food & Drug Act of 1906 –

- This law was ultimately proven unenforceable which led to…

US Food Drug and Cosmetic Act 1938

- The FD&C created the United States Food and Drug Administratin (FDA) an enforcement agency
- Required that drugs be proven safe but not necessarily effective.

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A Brief History of Quality Management

EUROPE - Origins of GxP laws & regulations

- **Europe -** The EU legal framework for human medicines sets standards to ensure a high level of public health protection and the quality, safety and efficacy of authorised medicines. It is based on the principle that a medicinal product requires a marketing authorisation by the competent authorities before being placed on the market.
- **50 years of pharmaceutical legislation -** Much of the impetus behind the adoption of the legal framework stemmed from the determination to prevent a recurrence of the thalidomide disaster of the late 1950s, when thousands of babies were born with limb deformities as a result of their mothers taking a medicinal product during pregnancy.

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A Brief History of Quality Management

EUROPE - Origins of GxP laws & regulations

- **Europe –** Enforcement of European law is through either
  - **European Commission through the centralised procedure, or by**
  - **National competent authorities through a mutual recognition, decentralised or national procedure**
- **Centralized enforcement** is through European Medicines Agency (EMA)
- **National competent authorities (within Europe) or** in case of disagreement additional assessment by the European Medicines Agency

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THE FOUNDERS OF MODERN QUALITY SYSTEMS

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A Brief History of Quality Management

General Concepts of Quality Management are well established and apply to multiple industries

Innovator	Date	Cycle
Walter A.Shewhart	**1920s**	Statistical Process Control
W. Edwards Deming	**1940s**	Continual Improvement
Joseph M. Juran	**1950s**	Quality Toolbox
Philip B. Crosby	**1970s**	Quality by Requirement
Robert W. Galvin	**1980s**	Micro Scale Error Reduction

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COMPLIANCE AND QUALITY MANAGEMENT

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QMS Overview

Origins of GxP laws & regulations

- **Law –** A rule that is passed by a government (legislated) which offers a minimum level of acceptable standards that must be met

- **Regulation –** a rule, policy and process that exists to implement and ensure compliance to an existing law (i.e., enforcement)

- **Industry Standards & Guidelines –** sets of principles and criteria aligned with regulatory requirements and laws, utilized to ensure compliance from a standardized platform which can be applied within applicable GxP environments (e.g., ISO standards, ICH Guidance, WHO Guidance)

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COMPLIANCE AND QUALITY MANAGEMENT

- GxP is a general abbreviation which refers to government regulated environments, to include but not limited to:
  - ✓ Good Manufacturing Practice (GMP)
  - ✓ Good Clinical Practice (GCP)
  - ✓ Good Laboratory Practice (GLP)

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GxP COMPLIANCE AND QUALITY MANAGEMENT

Total Quality management (TQM) includes the design of efficient monitoring tools and procedures for data collection and processing, as well as the collection of information that is essential to decision making, which ensures GxP reporting is accurate, reliable, and timely.

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GxP COMPLIANCE AND QUALITY MANAGEMENT

Quality Assurance (QA) and Quality Control (QC):

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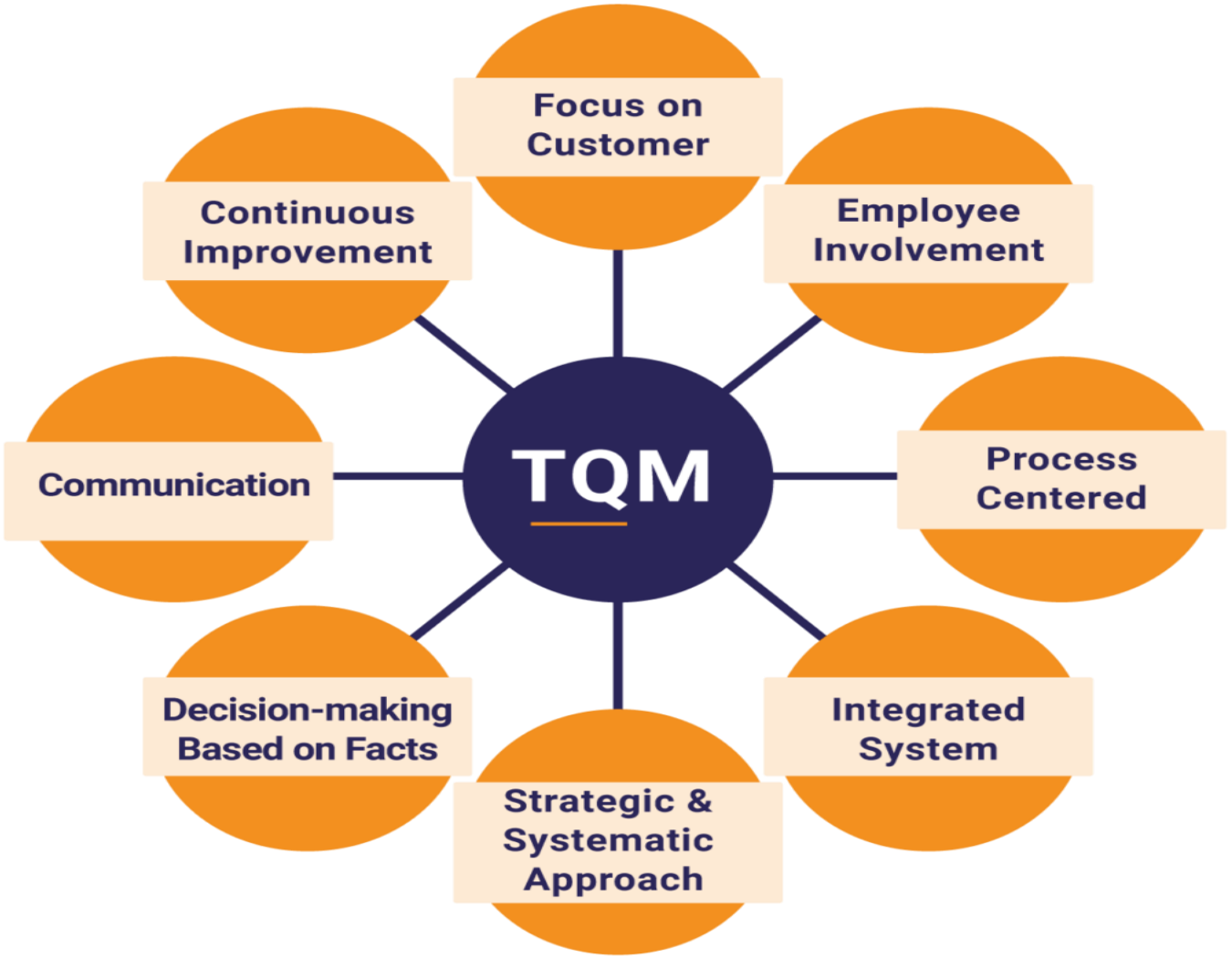
GxP COMPLIANCE AND QUALITY MANAGEMENT



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GxP Regulations, Guidance & Standards

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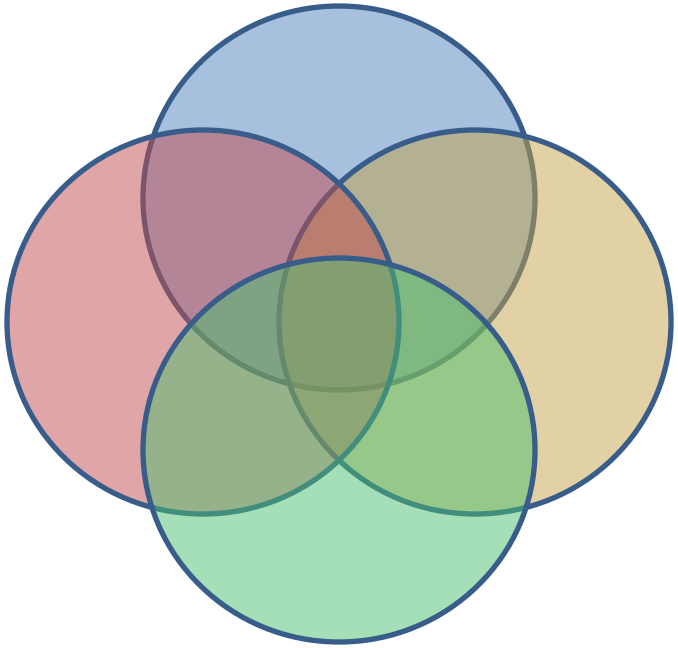
QMS is supported by a System of Mutual Accountability



Public Sector/Patient

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GMP

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GxP COMPLIANCE AND QUALITY MANAGEMENT

GMP Regulations, Guidance & Accreditations

- **US FDA – GMP (Requirements for Quality and Quality Systems)**
  - 21 CFR 210, (GMP Manufacturing, Process, Packing and Holding of Drugs)
  - 21 CFR 211 (GMP Practice for Finished Pharmaceuticals) &
  - 21 CFR 820 (Medical Device Quality Systems Regulation),
  - US FDA Biologics Guidance – Multiple guidance documents defining expectations for GMP process of Biologics
- **EMA - Three legal instruments lay down the principles and guidelines of GMP in the EU:**
  - Regulation No. 1252/2014 and Directive 2003/94/EC, applying to active substances and medicines for human use;
  - Directive 91/412/EEC applying to medicines for veterinary use.
  - Directive 2001/83/EC and Directive 2001/82/EC lay down related/common provisions.
  - The EU GMP guidelines provide interpretation of these principles and guidelines, supplemented by a series of annexes that modify or augment the detailed guidelines for certain types of product, or provide more specific guidance on a particular topic.
  - EMA Biologics Guidance - Multiple guidance documents defining expectations for GMP process of Biologics

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GxP COMPLIANCE AND QUALITY MANAGEMENT

GMP Regulations, Guidance & Accreditations (cont...)

- ICH "Q" Series Q1 to Q14 - provide a structured way to define product critical quality attributes, design space, the manufacturing process and the control strategy.

  - Q1 – Stability Testing
  - Q2 – Validation of Analytical Procedures
  - Q3 – Impurities in New Drug Substances
  - Q4 - Pharmacopoeia
  - Q5 – Biotechnology Products
  - Q6 – Specifications
  - Q7 – GMP for Active Pharmaceutical Ingredients
  - Q8 – Pharmaceutical Development
  - Q9 – Quality Risk Management
  - Q10 – Pharmaceutical Quality Systems
  - Q11 – Development and Manufacturing of Drug Substance
  - Q12 – Lifecycle Management
  - Q13 – Continuous Manufacturing of Drug Substance and Drug Products
  - Q 14 – Analytic Procedure Development

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GxP COMPLIANCE AND QUALITY MANAGEMENT

GMP Regulations, Guidance & Accreditations (cont...)

- **World Health Organization (WHO) Good Manufacturing Practice**
  - **WHO good manufacturing practices for biological products, Annex 2, TRS No 999** (Replacement of Annex 1 of WHO Technical Report Series, No. 822) - Guidelines published by WHO are intended to be scientific and advisory in nature. Each of the following sections constitutes guidance for national regulatory authorities (NRAs) and for manufacturers of biological products. If an NRA so desires, these WHO Guidelines may be adopted as definitive national requirements, or modifications may be justified and made by the NRA.
  - **WHO Prequalification Process** - mission of WHO prequalification is to work in close cooperation with national regulatory agencies and other partner organizations to make quality priority medical products available for those who urgently need them (Scoped for qualification of Immunization devices, In-vitro diagnostics, Vaccines, Medicines, Vector control and Inspection services)

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GCP

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GCP Regulations, Guidance & Accreditations

➢ US FDA – GCP

US FDA Compliance Program 7348.810 Sponsors and CROs - US FDA does not specifically define Quality Systems within regulations governing GCP; however, US FDA defines expectations for such systems in compliance program 7348.810 section (I) which states: *Although not required by regulations, many sponsors establish quality assurance departments, quality assurance units (QAUs) or similar entity to perform independent audits or data verifications and to critically review processes, procedures, and reports to determine their compliance with protocols and procedures. These quality assurance (QA) activities (e.g., independent audits, data verifications) may be conducted with or without the establishment of a QAU. All QAUs and/or auditing personnel should be independent of, and separate from, routine monitoring or quality control functions. The sponsor is ultimately responsible for the integrity of the study submitted to FDA.*

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GCP Regulations, Guidance & Accreditations

- **US FDA – GCP Regulations**
  - 21 CFR 50 (Protection of Human Subjects)
  - 21 CFR 54 (Financial Disclosures by Clinical Investigators)
  - 21 CFR 56 (Institutional Review Boards)
  - 21 CFR 312 (Investigational New Drug Application)
  - 21 CFR 314 (Applications for FDA Approval to Market a New Drug)
  - 21 CFR 812 (Investigational Device Exemptions)
  - 21 CFR 814 (Premarket Approval of Medical Devices)
  - US FDA GCP Guidance – Multiple guidance documents defining expectations for GCP process expectations

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GCP Regulations, Guidance & Accreditations

EMA GCP – Regulatory requirements and guidance are defined in the following documents:

- The protection of clinical trial subjects is consistent with the principles set out in the Declaration of Helsinki. This is a statement of ethical principles developed by the World Medical Association.
- Requirements for the conduct of clinical trials in the European Union (EU), including GCP and good manufacturing practice (GMP) and GCP or GMP inspections, are implemented in:
  - the 'Clinical Trial Directive' (Directive 2001/20/EC);
  - the 'GCP Directive' (Directive 2005/28/EC).
- Information concerning the activities in **EU Member States** can be found via the Heads of Medicines Agencies.
  - EMA GCP Guidance - Multiple guidance documents defining expectations for GMP process of Biologics

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GxP COMPLIANCE AND QUALITY MANAGEMENT

GCP Regulations, Guidance & Accreditations

- ICH "E" Serices Efficacy Guidellines E1 to E20 - Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics/ pharmacogenomics techniques to produce better targeted medicines.
- *NOTE: ICH E6 (R2) Section 5.0 defines requirements for Quality systems and oversight.*

- ❑ E1 – Clinical Safety for Drugs Used in Long-term Treatment
- ❑ E2 – Pharmacovigilance
- ❑ E3 – Clinical Study Reports
- ❑ E4 – Dose Response Studies
- ❑ E5 – Ethnic Factors
- ❑ E6 – Good Clinical Practice
- ❑ E7 – Clinical trials in Geriatric Populations
- ❑ E8 – General Considerations of Clinical trials
- ❑ E9 – Statistical Principals for Clinical trials
- ❑ E10 – Choice of Control Group in Clinical trials
- ❑ E11 – Clinical trials in Pediatric Population
- ❑ E12 – Clinical Evaluation by Therapy Category
- ❑ E13 – NO E13 TITLE
- ❑ E14 – Clinical Evaluation of QT
- ❑ E15 – Definitions in Pharmacogentics and Pharmacogenomics
- ❑ E16 – Qualification of Genomic Biomarkers
- ❑ E17 – Multiregional Clinical trials
- ❑ E18 – Genomic Sampling
- ❑ E19 – Safety Data Collection
- ❑ E20 – Adaptive Clinical Trials

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GxP COMPLIANCE AND QUALITY MANAGEMENT

GCP Regulations, Guidance & Accreditations

WHO requires Quality Systems under Principle 14 of this Handbook

WHO, Handbook for Good Clinical Practice Research, - Consolidated Guideline, and is organized as a reference and educational tool to facilitate understanding and implementation of GCP by:

- **describing the clinical research process as it relates to health and medical products, and identifying and explaining each of the activities that are common to most trials and the parties who are ordinarily responsible for carrying them out;**
- **linking each of these processes to one or more Principle(s) of GCP within this Handbook;**
- **explaining each GCP Principle and providing guidance on how each Principle is routinely applied and implemented;**
- **directing the reader to specific international guidelines or other references that provide more detailed advice on how to comply with GCP**

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GLP

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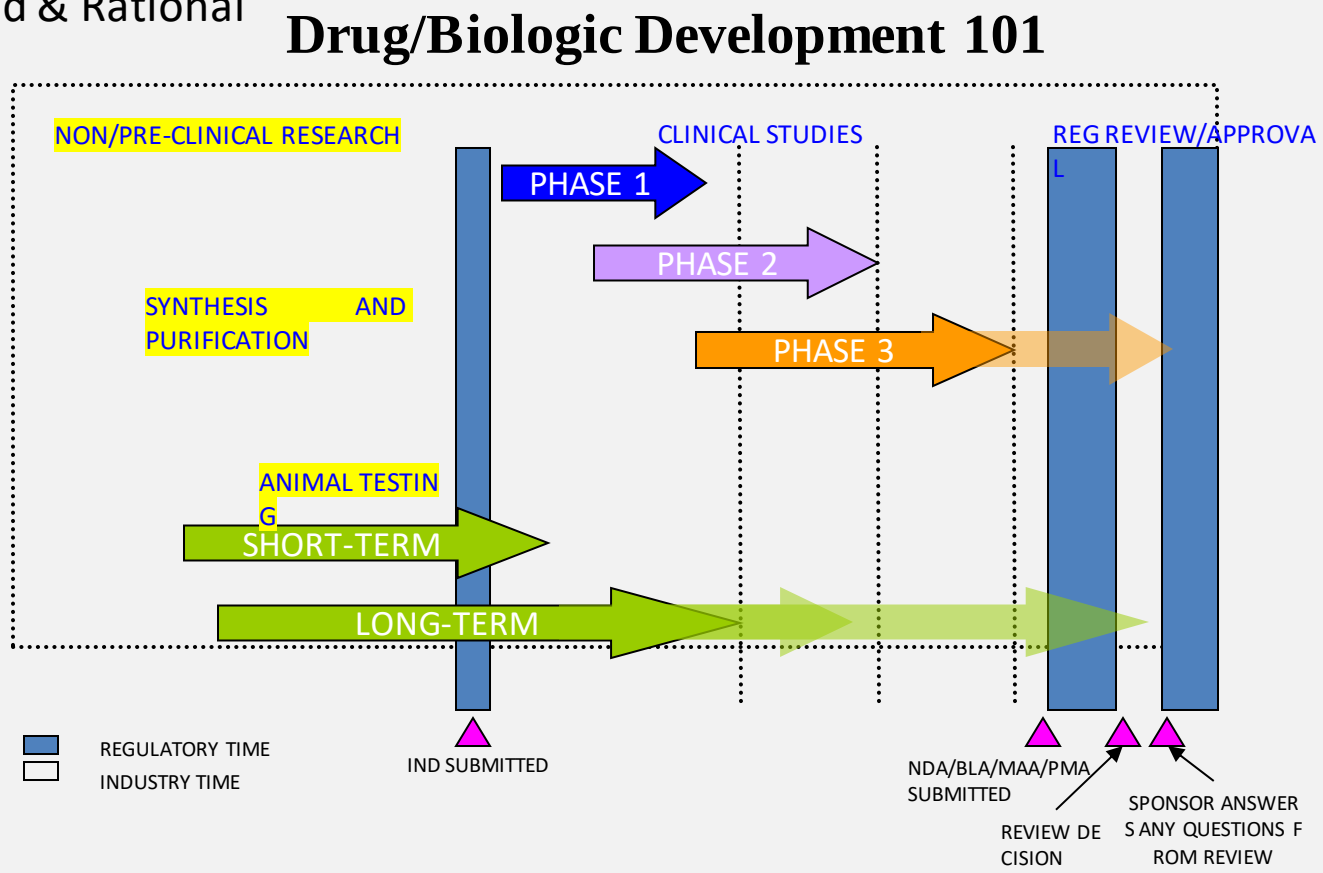
GLP & Non-clinical Development

Background & Rational



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GxP COMPLIANCE AND QUALITY MANAGEMENT

US FDA – GLP Regulations

- 21 CFR 58 (Good Laboratory Practice for Non-clinical Laboratory Studies)
- 21CFR58.35 - A testing facility shall have a ***quality assurance unit*** which shall be responsible for monitoring each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with the regulations in this part. For any given study, the quality assurance unit shall be entirely separate from and independent of the personnel engaged in the direction and conduct of that study.
- US FDA GLP Guidance – (Good Laboratory Practices Questions and Answers**)**

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GxP COMPLIANCE AND QUALITY MANAGEMENT

GCP Regulations, Guidance & Accreditations

EMA

- **EMA GLP** - The principles of Good Laboratory Practice (GLP) define a set of rules and criteria for a quality system concerned with the organisational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, reported and archived.
- Information about GLP can be found on the websites of the OECD and the European Commission.
- The GLP Directives are applicable:
  - Directive 2004/9/EC and
  - Directive 2004/10/EC.

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GCP Regulations, Guidance & Accreditations

OECD – GLP International Regulations

- The Principles of GLP define the responsibilities of test facility management, study director, study personnel and quality assurance personnel that are operating within a GLP system, and minimum standards concerning the suitability of facilities and equipment to perform studies, the need for standard operating procedures, documentation of raw data, study reports, the archiving of records, etc.
- Section 2.0 of OECD –
  - The ***test facility should have a documented Quality Assurance Programme*** to assure that studies performed are in compliance with these Principles of Good Laboratory Practice.
- OECD Principles of GLP – Guidance to OECD GLP Requirements

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GLP Regulations, Guidance & Accreditations

- ICH M3(R2) guidance - non-clinical safety studies for the conduct of human clinical trials and marketing authorisation for pharmaceuticals
- WHO GLP – Quality Practice for Regulated Non-Clinical Development
- WHO GLP – Chapter 2 requires QAU (Quality Assurance Unit – the group of persons with a set of defined duties, mostly of an audit and control nature) is part of this total quality assurance process. The QAU's mandated role is that of an independent witness of the whole preclinical research process and its organizational framework.

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GxP Electronic Systems

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GxP COMPLIANCE AND QUALITY MANAGEMENT

GxP Shared Requirements for Electronic Systems

- 21 CFR 11 Electronic Records and Signatures (Cross references GAMP),
- Annex 11 Computerized Systems,
- PIC/S 2007 Good Practices for Computerized Systems in GXP Environments,
- GAMP - A Risk-based Approach to Compliant GXP Computerized Systems.
- US FDA Guidance – General Principles on Software Validation
- US FDA Guidance – Computerized Systems Used in Clinical Investigations

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Quality Management Systems

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QMS SYSTEMS in GxP Environments

ISO 9001:2015 – Quality Management System Requirements

- Global accreditation defining general elements of QMS requirement meeting GxP expectations for QMS.
- The benefits of QMS implementation:
  - the ability to consistently provide products and services that meet customer and applicable statutory and regulatory requirements;
  - facilitating opportunities to enhance customer satisfaction;
  - addressing risks and opportunities associated with its context and objectives; d) the ability to demonstrate conformity to specified quality management system requirements

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QMS SYSTEMS in GxP Environments

ISO 9001:2015 – Quality Management System Requirements

The quality management principles are:

- customer focus;
- leadership;
- engagement of people;
- process approach;
- improvement;
- evidence-based decision making;
- relationship management

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Twelve (12) Essential Elements of Quality Systems

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Quality System Essentials

The twelve (12) Quality system essentials (QSE) are the building blocks of a total quality management system (TQMS) *Note: these general categories are conserved all GxP requirements*:

1. Organization
2. Customer/Patient focus
3. Facility and Safety
4. Personnel
5. Purchasing and Inventory
6. Equipment Maintenance/Control
7. Process Management
8. Documents Control & Records
9. Information Management
10. Nonconforming Event Management
11. QMS Assessments
12. Continual Improvement

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Quality System Essentials

1. Organization

Organizational structure should be defined to describe leadership responsibilities that are integral to the success in achieving and maintaining a systematic approach to quality and meeting regulatory, accreditation, customer, patient and internal requirements.

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Quality System Essentials

Well defined organizational structure ensures:

- A *top-down* commitment to quality (e.g., Implementation of a Quality Policy and Quality manual)
- Roles and responsibilities of line management and personnel are clearly defined
- QMS is effectively implemented and maintained, and exhibits continuous quality improvement
- Proactive planning of resource requirements to include facility, personnel, capital and material resources
- Development and definition of quality goals and utilization of tools for tracking achievements (e.g., use of quality metrics)
- Requires routine quality reports for management review
- Defines requirements for routine communications to internal and external stakeholders/customers to ensure QMS driven activities and issues are readily communicated

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2. Customer focus

The customers/patients are at highest risk for negative impact related to poorly implemented QMS, therefore, customer satisfaction must be ensured by:

- By clearly identifying the customer/patient and their expectations, and the need to design efficient work-flow to meet expectations.
- By ensuring the customer/patient can provide feedback by implementation of methods to seek customer/patient input to conform that expectations are met and that the organization can identify opportunities for improvement.

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3. Facility and Safety

- The organization should plan and implement process to ensure the work environment is both ergonomically designed and safe for personnel, i.e., physical environment, maintenance and safety programs should be clearly defined & effectively implemented.

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4. Personnel

Personnel are the most important resource.

Management of personnel includes:

- Development of job descriptions to clearly define personnel qualifications and responsibilities.
- Development of proper on-boarding training to Introduce new staff to the organization
- Implement effective initial and continuous training programs (Personnel should be trained and assess upon hiring; at 6 months from hiring and annually thereafter)
- Reviews of staff performance and routinely assess competence
- Provide for and encourage continuing education and professional development
- Development, maintenance and storage of personnel files

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5. Vendors, Purchasing and Inventory

- The organization must implement procedures to identify, qualify and manage vendors and suppliers for which GxP driven scope of work is transferred
- Critical vendors and suppliers should be qualified by audit prior to use to ensure efficient and cost- effective operations and to identify potential risks to availability of reagents, supplies and services.

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6. Equipment

- Implement process for selection and installation of equipment, equipment maintenance and calibration,
- Documentation of equipment related problems and record maintenance to ensure that equipment performs as expected for intended use.
- Ensure proper management of the equipment to ensure accurate, reliable, and timely testing/analysis.

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7. Process management

- Describes processes directly and indirectly related to GxP workflow to optimize both effectiveness and cost
- Process should be continually evaluated to ensure customer expectations, and regulatory/accreditation requirements are met
- Basically, evaluate quality systems to ensure effectiveness and efficiency

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8. Documents and records

Describes the creation, management and retention of the policy, process and procedure documents for the quality system essentials and path of workflow (i.e., establish a document control system)

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9. Information Management

- An organizational structure to ensure management of information throughout the information lifecycle regardless of source or format (data, paper documents, electronic doczments, audio, video, etc.)

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Quality System Essentials

Basic requirements related to Information Management

- ***Electronic systems must be validated and in a continuous state of validation***
- Planning for information needs
- Maintaining confidentiality of information
- Security for data access
- Integrity of data transfers or transmissions
- Provision of information availability during downtime

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10. Nonconforming event/product Management

The facility must define and implement processes to support:

- ✓ Detection and documentation of nonconformances/noncompliance,
- ✓ Manage products and services that do not meet specified requirements,
- ✓ Routine review of quality trends (e.g., in lab use of levey-Jennings plots in laboratory environments)
- ✓ Classifying nonconformances for analysis, and a process for corrective and/or preventive measures.

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11. Assessment

The GxP organization must implement a process to conduct routine and thorough interim self-inspections/audits and document any corrective/preventive measures implemented to address deficiencies

- Describes the use of external and internal monitoring and assessments to verify that GxP processes meet requirements and to determine how well those processed are functioning
- Ensure written evidence (e.g., audit reports) of self-inspection findings with records of corrective/preventive actions

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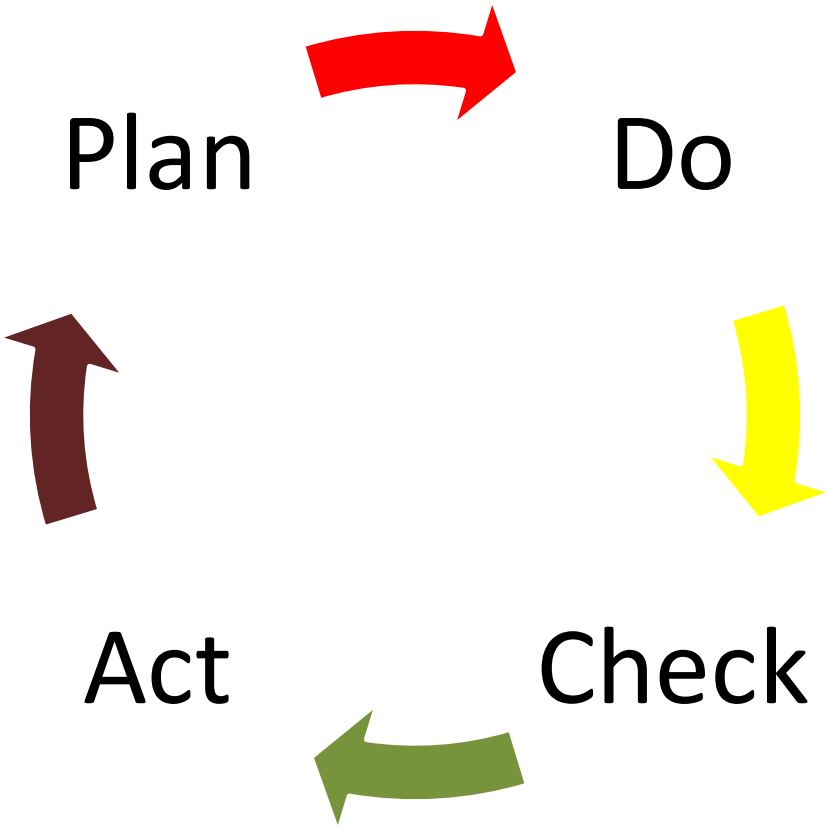
Quality Management Approach



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12. Continual Improvement

Continual improvement is the core of quality management and requires:

- Organizational and management commitment to quality
- Effective Planning,
- Infrastructure development,
- Dedicated leadership,
- Organization wide participation,
- Sustained engagement.

Continual improvement is an outcome of an active and dedicated **GxP** quality management system.

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OVERVIEW - CORRECTIVE & PREVENTIVE ACTIONS (CAPA)

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Differences between correction, corrective action and preventive action

Correction

Put fire out
(at the time)

Corrective Action

What caused fire and how to prevent recurrence
(after event)

Preventive Action

Stop fire from happening
(before event)

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CAPA

Definitions

- Corrective Action - Planned action taken to eliminate the cause(s) of an existing nonconformity, defect , or other undesirable situation in order to prevent recurrence.
- Preventive Action – Planned action taken to eliminate the causes of a potential nonconformity, defect, or other undesirable situation in order to prevent occurrence.
- Effectiveness Verification - The means by which effectiveness of corrective and/or preventive action i mplementation is verified by a documented and systemic process.
- Root Cause - is the basic cause of any undesirable condition or problem, which when eliminated or mi tigated will prevent or significantly reduce the effect of the condition or problem.
- Root Cause Analysis (RCA) - Is a structured approach utilized in the identification of the basic factor(s) that attribute to an issue(s) of non-compliance within a system (i.e., root cause(s)).

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CAPA

Root cause analysis (RCA)

RCA is required to identify the basic cause(s) of any undesirable condition within a quality system. There are several techniques which may be utilized to assist an auditee in identifying root cause; two common and effective methods are:

- Five (5) Whys Technique - a question-asking method used to explore the cause/effect relationships underlying a particular problem. This method is effective in evaluating root cause relating to a single or less complex issue. Ultimately, the goal of applying the *5 Whys* method is to determine a root cause of a defect or problem.

- Fishbone Analysis (Ishikawa Diagram) or Cause and Effect Analysis - This method of RCA is useful in evaluating more complex/multi-factorial issues which have led to issues of non- compliance. The fishbone diagram identifies many possible causes of an effect or problem. It can be used to structure a brainstorming session as it allows a team of individuals to sort ideas into functional categories.

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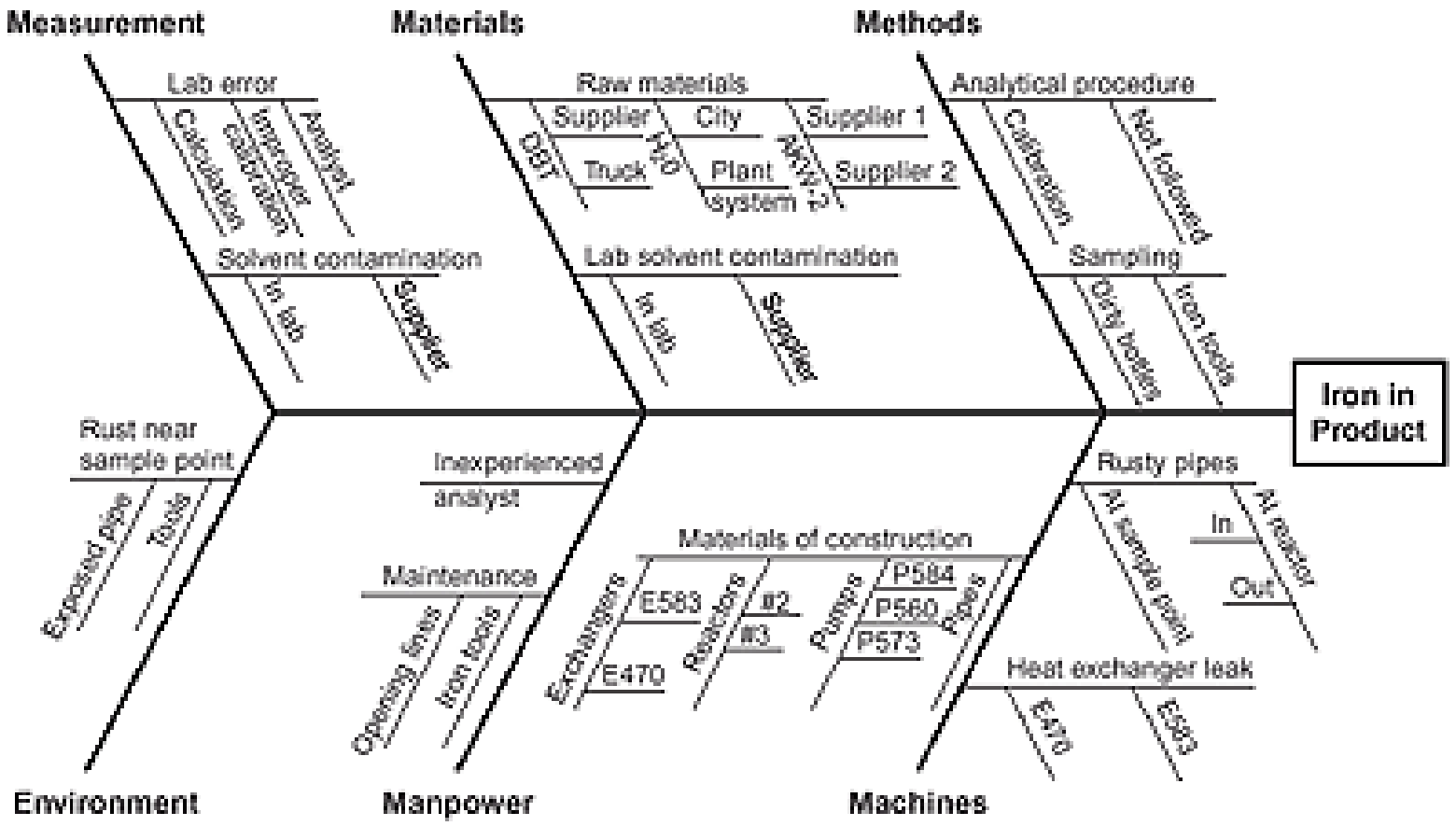
Fishbone Diagram



Ref: https://www.template.net/design-templates/print/sample-fishbone-diagram-template

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CAPA

Identification of RC and CAPA Implementation

- **Once RC is defined, the auditee proceeds to describe how corrective and/or preventive measures will be defined and applied to address the audit observation(s):**
  - Observations may require both corrective and preventive action
  - Observations may only require preventive measures (e.g., due to elapsed time of noncompliance it is too late to correct data or gather missing data)
  - Observations may only require corrective measures (e.g., isolated observations)

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CAPA

- **CAPA Management and Tracking**
- Quality Assurance/Compliance units should develop and implement a CAPA tracking system.
- This process should be overseen by organizations QA department responsible for audit management and non-compliance escalations and ensures that the CAPA and its status (e.g., open or closed) can be determined at any point to satisfy both organization management and/or regulatory agency requirements.

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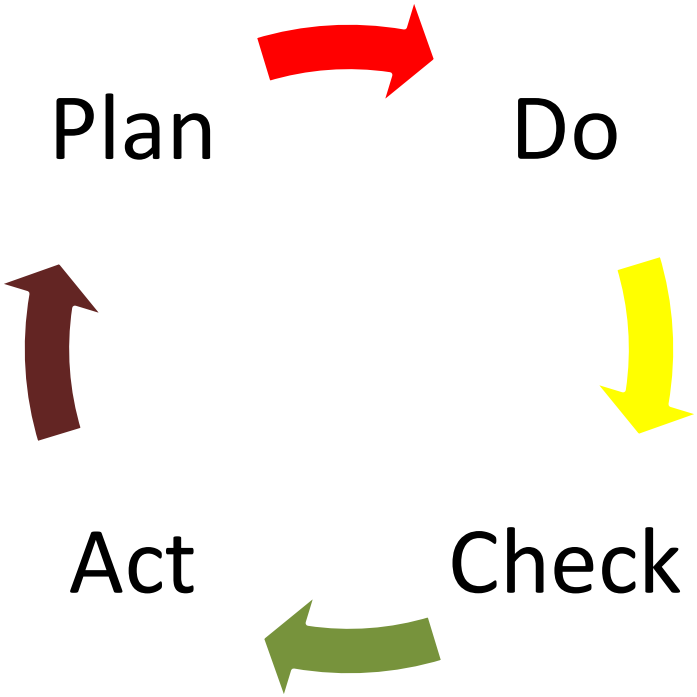
Audit cycle / CAPA Cycle (CAPA is a sub-cycle of the report)



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DOCUMENT CONTROL

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Controlled Documents System

Document Control

Represents document management for the purpose of enforcing controlled processes and practices for the creation, review, modification, issuance, distribution and accessibility of documents and is managed within QMS (i.e., Quality Systems)

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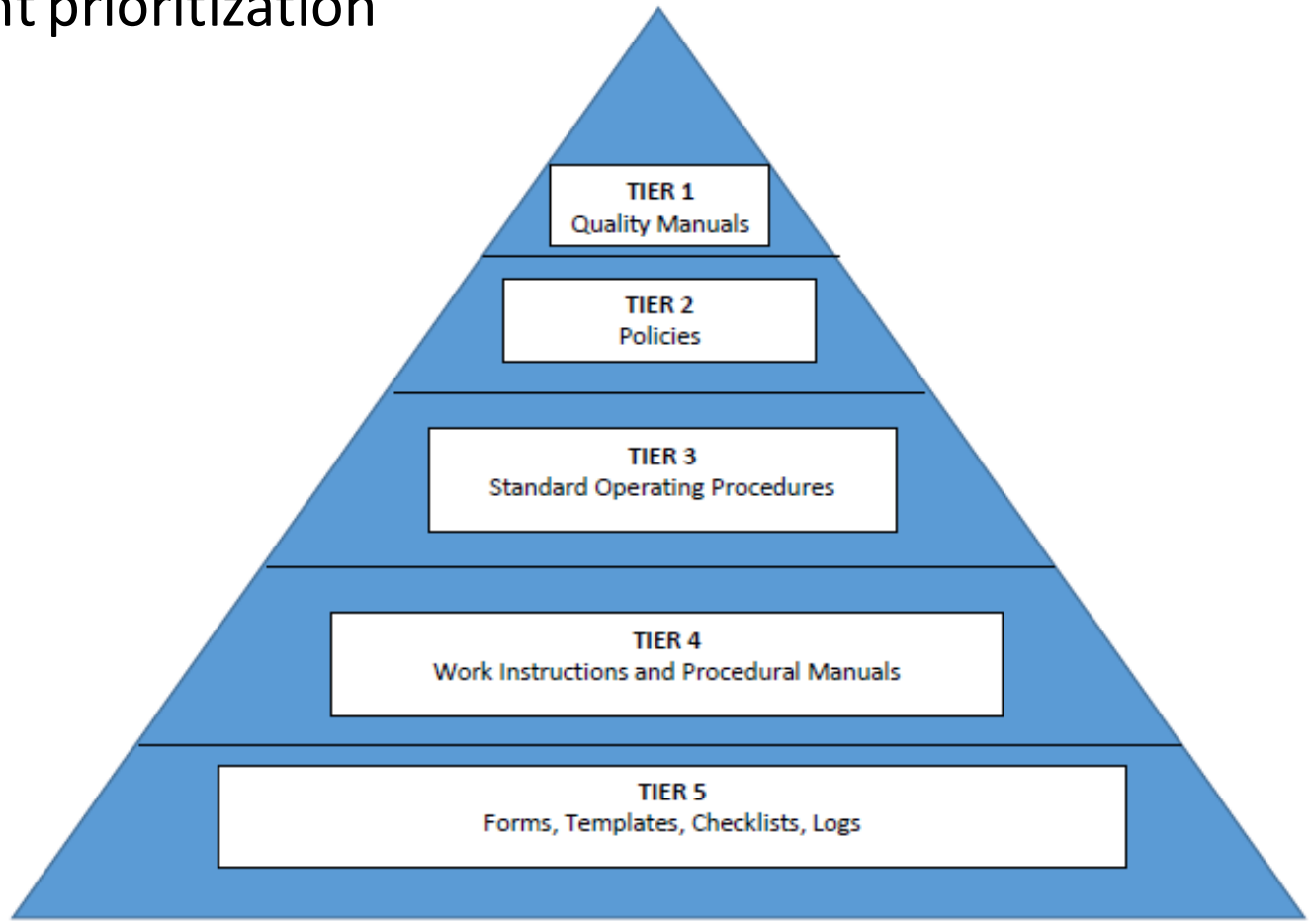
Controlled Documents System

A system of tiers or hierarchy should be defined to support Controlled Document prioritization



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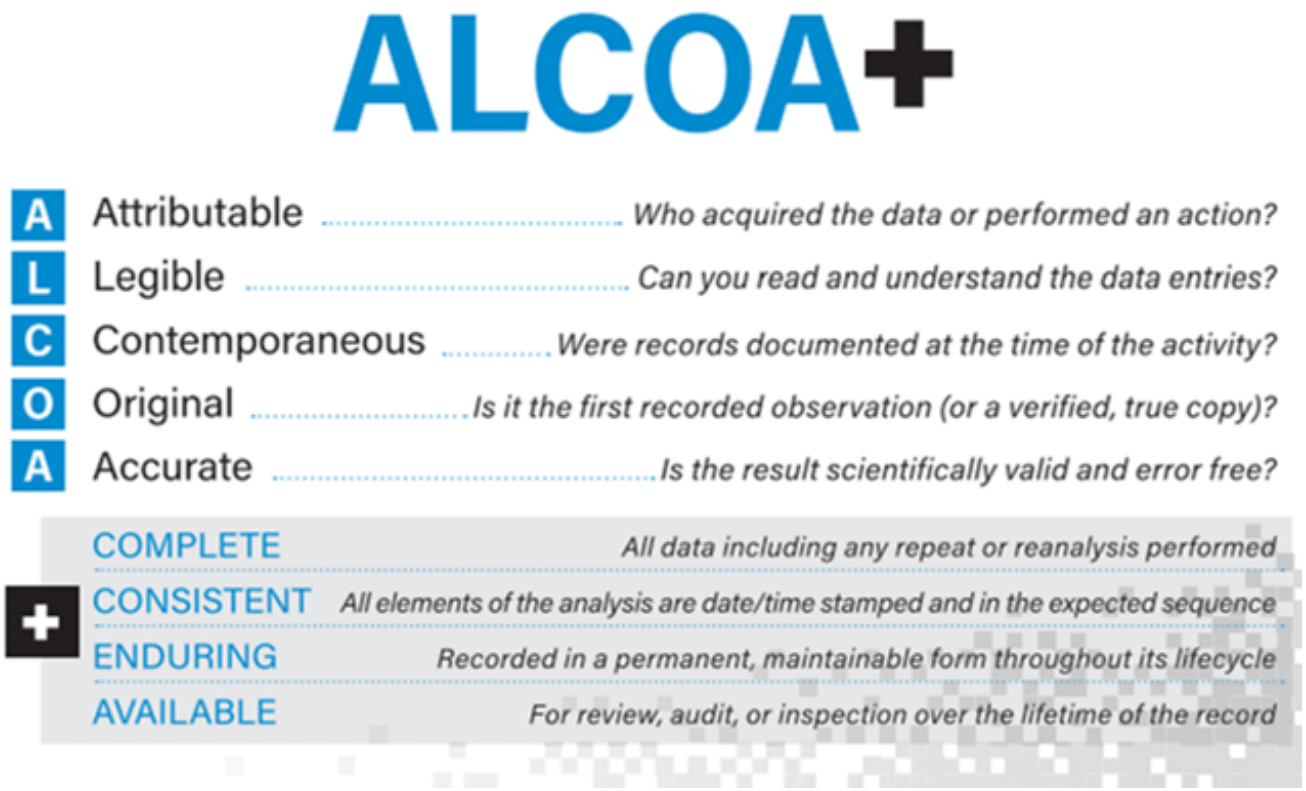
GCP COMPLIANCE AND DOCUMENTATION

ALCOA (+C)



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SUMMARY

Successful implementation of a quality management systems requires a detailed understanding of regulatory requirements (GxP), top-down executive management support, planning, management commitment, an understanding

of the benefits, engaging staff at all levels, setting realistic time

frames, and looking for ways to continually improve.

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QUESTIONS

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A Brief History of Quality Management

WALTER A. SHEWHART

The father of statistical Quality who successfully brought together the disciplines of statistics, engineering, and economics and became known as the father of modern quality control.

https://asq.org/about-asq/honorary-members/shewhart

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A Brief History of Quality Management

W. EDWARDS DEMING

Recognized for his role as adviser, consultant, author, and teacher to some of the most influential businessmen, corporations, and scientific pioneers of quality control, is the most widely known proponent of statistical quality control. He has been described as a national folk hero in Japan, where he was influential in the spectacular rise of Japanese industry after World War II; as a curmudgeon; as the high prophet of quality control; as an imperious old man; and as founder of the third wave of the Industrial Revolution.

https://asq.org/about-asq/honorary-members/deming

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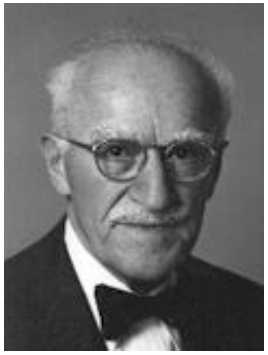
A Brief History of Quality Management



JOSEPH M. JURAN

*"It is most important that **top management** be quality-minded. In the absence of sincere manifestation of interest at the top, little will happen below."*
— Joseph M. Juran

Juran emphasized the need for top management involvement, the Pareto principle, the need for widespread training in quality, the definition of quality as fitness for use, the project-by-project approach to quality improvement. These are the ideas for which Juran was best known, and they are still widely used today.

https://asq.org/about-asq/honorary-members/juran

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A Brief History of Quality Management

PHILIP CROSBY

The Guru of Quality Management

Philip B. Crosby was a legend in the discipline of quality. A noted quality professional, consultant, and author, he is widely recognized for promoting the concept of "zero defects" and for defining quality as conformance to requirements.

https://asq.org/about-asq/honorary-members/crosby

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A Brief History of Quality Management

Robert W. Galvin

The 'inventor' of the Six Sigma process which is a method that provides organizations tools to improve the capability of their business processes. Defined by an increase in performance and decrease in process variation helps lead to defect reduction and improvement in profits, employee morale, and quality of products or services.

https://asq.org/quality-resources/six-sigma

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Acknowledgement

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ICH E11(R1) Clinical Investigation of Medicinal Products in Pediatric Population https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E11/Step4/E11_Guideline.pdf

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US FDA Guidance – Computerized Systems Used in Clinical Investigations http://www.fda.gov/OHRMS/DOCKETS/98fr/04d-0440-gdl0002.PDF

PIC/S Guidance- Good Practices for Computerized Systems in Regulated GXP Environments https://www.picscheme.org/

CLINIQAL Inc https://www.clinicalquality.com

CRSC https://www.4crsc.com

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- CLSI. Quality management system: A model for laboratory services; approved guidelines https://clsi.org/standards/products/quality-management-systems/documents/qms01/

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Merci!
Gracias!
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