UNIT-1

Quality Control

- Quality control includes various techniques and activities of an organisation that are involved in monitoring and improving the business so that the products, processes or services meet the standard specifications.
- It aims to identify and eliminate the causes of sub-standard performance by removing or reducing the variation sources.
- Quality control also includes selecting and rating of suppliers to make sure that the purchased products meet the quality requirements.
- ISO 9000 defines quality control a " A part of quality management focused on fulfilling quality requirements. It is that part of GMP concerned with sampling, specification and testing, documentation and release procedures which ensures that the relevant and necessary tests are performed and the product is released only after ascertaining its quality.

Conformance Quality → It determines how much the product matches the set standards.

Responsibilities of QC

- Read blueprints and specifications.
- Monitor operations to ensure that they melt production standards.
- Reccomend adjustments to the production process.
- Inspect, test and measure materials.
- Measure products with calipers, gauges, micrometers.
- Operate electronic inspection of equipment and software.
- Inspect the environment around manufacturing of dosage forms.
- Testing of raw materials and packaging of materials.

Quality Assurance

The term quality assurance includes all the planned and systematic activities required for assuring that a product or service will meet the standards.

ISO 9000 defines it as " part of quality management focused on providing confidence that quality requirements will be fulfilled.

Responsibilities of QA

→ The QA department is responsible for ensuring that the quality policies are followed.

→ Identify and prepare the SOPs that are necessary.

→ Determine that the product meets all the applicable specifications and manufacturing is done according to the internal standard of GMP.

→ Plan and conduct internal quality audits.

→ Collect quality data.

GMP

- GMP is a part of quality management that ensures that the products are consistently manufactured and analysed as per the quality standards appropriate for use and as required by the market authorities, clinical trial authorities.
- GMP should be followed by the production department as well as by the quality control unit.
- GMP minimises the risks in pharmaceutical manufacturing and ensures quality, safety and efficacy of products.

GMP Provisions

1) Qualification and validation of the product is performed.
2) All instructions and procedures are given in clear and unmistakable language.
3) The personnel are trained to carry out all the manufacturing processes correctly.
4) During manufacturing, records are made to describe that the steps taken are as per the defined procedures and instructions.

5) Any significant deviations are recorded and investigated with their root cause.

6) All the complaints related to the marketed products are examined and required corrective steps are taken.

Total Quality Management

An integrated organisational effort to improve the product quality at every level is called TQM.

Elements

According to their function, the TQM elements can be categorised into:

1) Foundation: It involves ethics, integrity and trust.

2) Building Bricks: It involves training, teamwork and leadership.

3) Binding Mortar: It involves communication between all the elements of TQM.

4) Roof: It involves employee recognition in TQM department.

Philosophies

TQM focuses on determining the root causes of quality problems and overcoming them at the source. TQM is customer driven.

1) Quality Circle

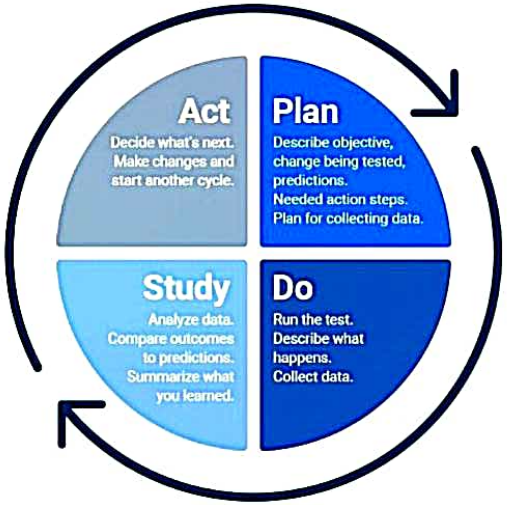
Quality circle, also known as quality teams, is defined as a small group of employees who voluntarily meet at regular intervals so that they can identify, analyse and solve problems related to their work environment and organisation.

2) Customer Focus

Organisations depend on their customer and therefore should understand their current and future needs, meet customer requirements and strive to exceed customer satisfaction.

3) Continuous Improvement

- Make continual improvement in products, processes and systems.
- Periodic assessments to identify areas of potential improvement.
- PDSA cycle for improvement:
  Plan - Do - study - Act
  or
  Check



Benchmarking → study of the business practices of other companies for comparisons.

4) Quality Tools

Employees have been assigned the job to identify and overcome quality problems. They should be provided proper training and should be made aware of how to evaluate quality by using various quality control tools, how to interpret findings and how to rectify problems.

7 tools of quality control

1) Cause-and-effect diagrams : identify cause
2) Flowcharts
3) Checklists
4) Control Charts
5) Scatter diagrams
6) Pareto Analysis
7) Histograms

Advantages of TQM

- increase productivity
- enhances market image
- eliminates defects and waste
- Reduces costs and better cost management
- increases profitability
- improves customer focus and satisfaction.
- builds trust in market and customers.
- enhances shareholder and stakeholder value.

Disadvantages

- Initial introduction costs: training workers, etc.
- Benefits may not be seen for several years.
- It is a long term process.

ICH Guidelines

ICH → International Council on Harmonisation

ICH is a joint initiative in which regulatory bodies and research-based industry involve in scientific and technical discussions regarding the testing and evaluation of medicines to ensure their safety, quality and efficacy.

Purpose

The year 1990 marked the establishment of ICH by the joint efforts of USA, Japan and Europe.

ICH serves the following purposes;

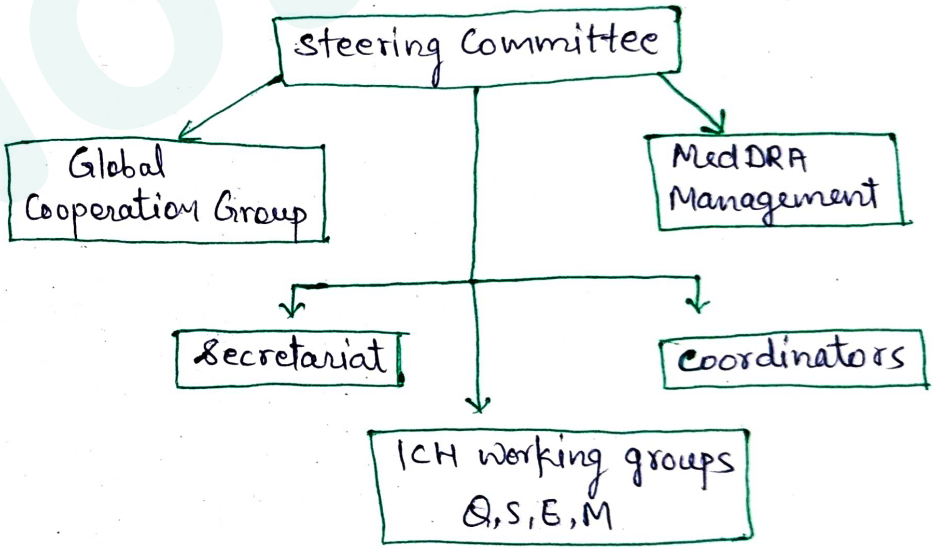
1) It promotes and protects public health from an international perspective.
2) guides on clinical trials in humans.
3) ensures safety, efficacy and quality of medicines
4) reduces animal testing without compromising the safety and effectiveness.
5) improves efficiency of global drug development.

Participants

Six official members of ICH :

i) EFPIA
ii) EU
iii) MHLW
iv) JPMA
v) PhRMA
vi) FDA

Organisation structure of ICH



Process of Harmonisation

ICH steering committee is responsible for ICH administration.

The ICH Harmonisation process follows under:

1) Formal ICH Procedure

New topic for harmonisation of ICH.

Concept paper and a business plan required.

concept paper → proposal with a short summary of something.

Business plan → It outlines or covers the costs and benefits of harmonising the topic proposed by concept paper.

2) Q4A Procedure

It is needed when a clarification of an ICH guideline is required.

Concept paper required. Business plan is some cases may be required.

3) Revision Procedure

This procedure in two cases:

i) Content of an existing ICH guideline is out of date or no longer required.

ii) New information to be added to an existing ICH guideline.

Concept paper required for this procedure.

4) Maintenance Procedure

If a change to be made to either a guideline with a maintenance procedure or M2 recommendations.

Concept paper required for maintenance of guidelines and not for M2 recommendations.

Overview of QSEM

ICH guidelines are mainly categorised into four types.

1) Q- Quality guidelines
2) S- Safety guidelines
3) E- Efficacy guidelines
4) M- Multidisciplinary guidelines

Q-series Guidelines

1) Q1 [Q1A-Q1F] : Guidelines for stability
2) Q2 : Validation for analytical procedure
3) Q3 [Q3A-Q3D] : Impurities
4) Q4 [Q4A-Q4B] : Pharmacopoeias
5) Q5 [Q5A-Q5E] : Quality of biotechnology Products.
6) Q6 [Q6A-Q6B] : Specifications
7) Q7 : GMP for APIs.
8) Q8 : Pharmaceutical development
9) Q9 : Quality Risk Management
10) Q10 : Pharmaceutical quality systems
11) Q11 : Development and manufacture of drug substances.

ICH Stability Testing Guidelines

Types of stability :

i) Chemical
ii) Physical
iii) Microbial
iv) Therapeutic
v) Toxicology

Principle of guidelines

1. Purpose of stability testing is to provide evidence how quality varies with time under influence of temperature, humidity, light.
2. Establish Re-test period for drug substances.
   Re-test → the period after which samples of the drug ~~samples~~ substances should be examined to ensure it still in compliance with specification and thus suitable for manufacturing.
3. Establish shelf life for drug product.
4. Recommends storage conditions.
5. Give test condition based on analysis of effects of climate conditions in the three regions of the Europe, Japan, USA.

6. Divided world into four different climatic zones → I-IV

(i) Temperate : 21°C / 45 % RH

(ii) Subtropical and Mediterranean 25°C / 60 % RH

(iii) Hot and Dry : 30°C / 35 % RH

(iv)(a) Hot and humid : 30°C / 65 % RH

(iv) (b) Hot and very humid : 30 VC / 75 % RH

Stability Testing Protocol

- stability testing is the systematic approach towards drug development process.
- The protocol for stability protocol (testing) is a pre-requisite for starting stability testing and is necessarily a written document that describes the key components of a regulated and well-controlled stability study.
- A well designed stability protocol should contain the following information:
  - → number of batches
  - → containers and closures
  - → orientation of storage of containers
  - → Sampling time points
  - → Test storage conditions
  - → Test parameters
  - → Test methodology
  - → Acceptance criteria

Quality by Design

A systematic approach for development of pharmaceutical products that begins with pre-defined objectives and empasises product and process understanding and process control, based on sound science and quality risk management.

Overview

labelled use safety and efficacy
→ Define quality target product profile
→ Design formulation and process
→ Identify critical material attributes and critical process parameters.
→ Control materials and process.

Key elements of QbD

In QbD approach to product development, an applicant identifies the desired characteristics of quality from the patient's viewpoint and translates them into the drug product.

QbD consists of the following elements:

1) Quality Target Product Profile (QTPP)

A prospective summary of the quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account safety and efficacy of the drug product.

2) Identifying the quality attributes

A physical, chemical, biological or microbiological property or characteristics that should be within an appropriate limit, range, or distribution to ensure the desired product quality.

3) Quality Risk Management

Risk management is a strategic safety program designed to reduce product risk by using one or more inventions / tools.

4) Determination of Critical Process Parameters

Any measurable input or output of a process step that needs to be controlled to achieve the desired product quality and process consistency is stated as a critical process parameter.

5) Design space

Multidimensional combination and interaction of input variables and process parameters established to provide quality assurance.

6) Control strategy

A planned set of controls derived from current product and process understanding that assures process performance and product quality.

* You can remember the headings only if that is enough for you.

Tools

The tools of QbD include the following:

1) Prior knowledge
2) Design of experiments
3) Process analytical technology
4) Risk management Methodology.

ISO 9000

- ISO refers to International Organisation for standardisation.
- ISO 9000 is a set of international standards on quality management and quality assurance.
- It has been developed to help the companies in effectively documenting the quality system elements to be implemented so that an efficient quality system can be maintained. They are not specific to any one industry and can be applied to any big or small organisations.

Overview

- ISO 9000 helps a company to satisfy its customers, meet regulatory requirements and achieve constant improvement.
- ISO 9000 is widely recognised in the world. It aims to implant a quality management system in an organisation for increasing productivity.

Benefits

Benefits that an organisation acquires by obtaining the ISO certification are:

1) The organisation gains customer's confidence.
2) ISO 9000 requires a well-documented software production process that contributes to repeatable and higher quality of the developed software.
3) ISO 9000 makes the development process focused, efficient and cost effective.
4) ISO certification recognises the weaknesses of an organisation and recommends corrective measures.
5) ISO 9000 sets the basic framework for developing an optimal process and TQM.

Elements

1) Management Responsibility
2) Quality System
3) Contract Review
4) Design Control
5) Document control
6) Purchasing
7) Handling of purchaser supplied product
8) Product Identification and traceability
9) Process control
10) Inspection and testing
11) Inspection, Measuring and Test Equipment
12) Inspection and Test status
13) Control of non-conforming product
14) Corrective action
15) Handling, storage, packaging, delivery
16) Quality Records
17) Internal Quality Audits
18) Training
19) Servicing
20) Statistical Techniques.

Steps for registration

1) Selecting the type of registration (ISO certificⁿ).
2) Selecting an ISO Certification Body.
3) Creating an application / contract
4) Quality documents review
5) Making an action plan
6) Initial certification audit
7) Completing the ISO certification
8) Surveillance Audits

ISO 14000

ISO 14000 is a series of international environmental management standards, guides and technical reports.

Standards in the ISO 14000 series are:

1) ISO 14004 → general guidelines on principles systems and support techniques.
2) ISO 14006 → guidelines for incorporating ecodesign.
3) ISO 14015 → Environmental Assessment of sites and organisations
4) ISO 14020 → Environmental labels and declarations.

5) ISO 14031 → environmental performance evaluation
6) ISO 14040 → Life cycle assessment
7) ISO 14050 → Vocablury
8) ISO 14064 → Greenhouse gases
9) ISO 19011 → guidelines for auditing management systems.

Benefits

- Cost savings
- enhanced customes satisfaction
- Access to global markets
- Increased productivity
- negative impacts on environment are reduced.

Elements

Six key elements:

1) Environmental policy
2) Planning
3) Implementation
4) study and correct
5) Management Review
6) Continuous improvement.

Steps for registration

1) Selecting certification body
2) Complete Questionnaire and establish contract
3) Document Review
4) First stage assessment
5) Certification assessment
6) Award Certification
7) Surveillance visit
8) Renewal Assessment

NABL Accreditation

National Accreditation Board for Testing and Calibration Laboratories.

"Accreditation is the formal recognition, authorisation and resistration of a laboratory that has demonstrated its capability, competence and credibility to perform the tasks it claims to be able to do."

NABL is an autonomous body under the Department of Science and Technology, GoI, and registered under the Societies Act.
NABL has been authorised by the Government of India as the accreditation body for testing and calibration laboratories.
It aims to provide third-party assessment of quality and technical competence.

Procedures

1) Application for NABL Accreditation
2) Acknowledgement of application
3) Review by Lead Assessor
4) Pre-Assessment
5) Assessment
6) Scrutiny of Assessment Report
7) Accreditation Committee
8) Issuing of Acreditation Committee