SHREE H. N. SHUKLA INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH

B.PHRAM

(SEMESTER –VII)

SUBJECT NAME: QUALITY ASSURANCE

SUBJECT CODE: BP706TT

UNIT 01: QUALITY ASSURANCE & QUALITY MANAGEMENT CONCEPT

Content

Quality Assurance and Quality Management concepts: Definition and concept of Quality control, Quality assurance and GMP

Total Quality Management (TQM): Definition, elements, philosophies

ICH Guidelines: purpose, participants, process of harmonization, Brief overview of QSEM, with special emphasis on Q-series guidelines, ICH stability testing guidelines

Quality by design (QbD): Definition, overview, elements of QbD program, tools

ISO 9000 & ISO14000: Overview, Benefits, Elements, steps for registration

NABL accreditation: Principles and procedures

Quality Assurance and Quality Management concepts

QUALITY

The totality of features and characteristics of a medicinal product and its ability to satisfy stated and/or implied needs.

QUALITY MANAGEMENT SYSTEM

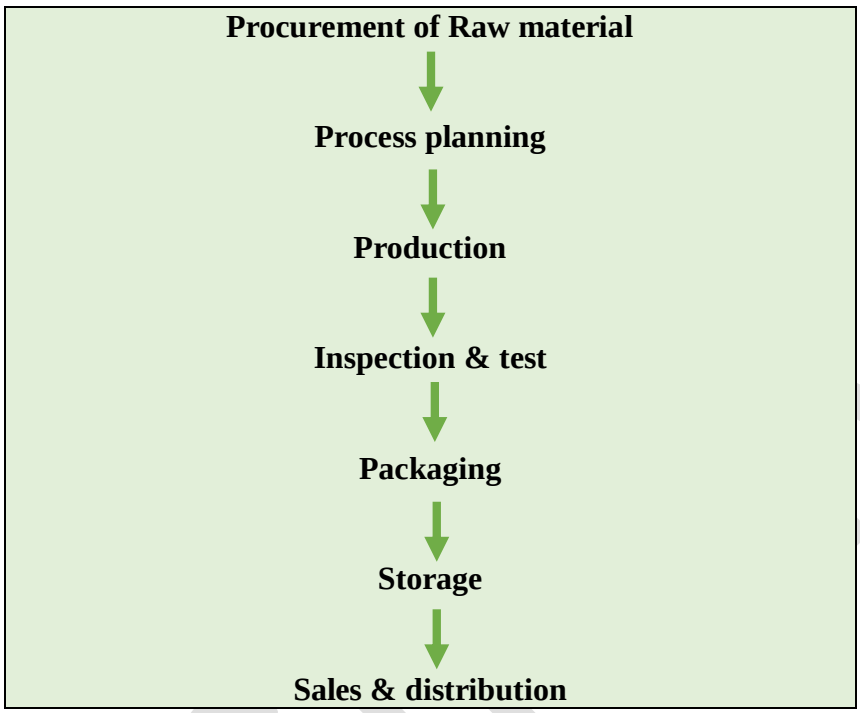
It is a management system to direct and control an organization with regard to quality – ISO 9000:2000.

The basic elements of quality managements are quality system and systemic actions. The quality system involves all phases from initial identification to final satisfaction of requirements and customers expectation. ISO:9000 state the following phases and activities:

- Marketing and market research
- Design, specification engineering & product development
- Procurement
- Process planning & development
- Production
- Inspection, testing and examination
- Packaging & storage
- Sales & distribution

The first thing that a manufacturer will like to know is what product should be manufactured? This may be found out by market research or survey.

Once the product is decided, the next thing is development of the product and its specification. The next step follow as under:



QUALITY MANAGEMENT IN THE DRUG INDUSTRY

In the drug industry at large, quality management is usually defined as the aspect of management function that determines and implements the "quality policy", i.e. the overall intention and direction of an organization regarding quality, as formally expressed and authorized by top management. The basic elements of quality management are:

- an appropriate infrastructure or "quality system", encompassing the organizational structure, procedures, processes and resources;
- systematic actions necessary to ensure adequate confidence that a product (or service) will satisfy given requirements for quality. The totality of these actions is termed "quality assurance".

Within an organization, quality assurance serves as a management tool. In contractual situations, quality assurance also serves to generate confidence in the supplier. The concepts of quality assurance, GMP and quality control are interrelated aspects of quality management. They are described here in order to emphasize their relationship and their fundamental importance to the production and control of pharmaceutical products.

QUALITY ASSURANCE

"Quality assurance" is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product.

It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use. Quality assurance therefore incorporates GMP and other factors, including those outside the scope of this guide such as product design and development.

QA is the heart and soul of quality control

QA = QC + GMP+GLP+GCP

The system of quality assurance appropriate to the manufacture of pharmaceutical products should ensure that:

a) pharmaceutical products are designed and developed in a way that takes account of the requirements of GMP and other associated codes such as those of good laboratory practice (GLP) and good clinical practice (GCP);

b) production and control operations are clearly specified in a written form and GMP requirements are adopted;

c) managerial responsibilities are clearly specified in job descriptions;

d) arrangements are made for the manufacture, supply and use of the correct starting and packaging materials;

e) all necessary controls on starting materials, intermediate products, and bulk products and other in-process controls, calibrations, and validations are carried out;

f) the finished product is correctly processed and checked, according to the defined procedures;

g) pharmaceutical products are not sold or supplied before the authorized persons have certified that each production batch has been produced and controlled in accordance with the requirements of the marketing authorization and any other regulations relevant to the production, control and release of pharmaceutical products;

h) Satisfactory arrangements exist to ensure, as far as possible, that the pharmaceutical products are stored by the manufacturer, distributed, and subsequently handled so that quality is maintained throughout their shelf-life.

i) there is a procedure for self-inspection and/or quality audit that regularly appraises the effectiveness and applicability of the quality assurance system;

j) deviations are reported, investigated and recorded;

k) there is a system for approving changes that may have an impact on product quality;

l) regular evaluations of the quality of pharmaceutical products should be conducted with the objective of verifying the consistency of the process and ensuring its continuous improvement.

The purpose of quality assurance in pharmaceutical supply system is to help ensure that each medicine reaching a patient is safe, effective and of appropriate quality.

To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of quality assurance incorporating GMP and quality control.

The quality of pharmaceutical products is ensured by the technical managerial activities of the quality system, which includes evaluating pharmaceutical product documentation, performing or reviewing quality control laboratory tests, and monitoring product performance.

All parts of quality assurance system should be adequately staffed with competent personnel and should have sufficient premises, equipment and facilities.

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	The totality of features and characteristics of a medicinal product and its ability to satisfy stated and/or implied needs is known as	**Quality**
2	For quality, management system should comply with standards	**ISO 9000:2000**
3	What are the basic elements of quality management?	**Quality system and Systemic actions**
4	What is the first phase for quality management of all products?	**Market research**
5	How many phases are there for quality management system?	**8**
6	The aspect of management function that determines and implements the "quality policy" is known as	**Quality Policy**
7	The concepts of quality assurance, GMP and quality control are interrelated aspects of	**Quality management**
8	The totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use is known as	**Quality Assurance**
9	Wide-ranging concept covering all matters that individually or collectively influence the quality of a product is known as	**Quality Assurance**

10	Which procedure should be applied for effectiveness and applicability of the quality assurance system?	**Self-inspection and/or quality audit**
11	If any change is observed with quality of any product _____are reported, investigated and recorded.	**Deviation**

GOOD MANUFACTURING PRACTICE (GMP)

Good manufacturing practice is that part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

GMP are aimed primarily at diminishing the risks inherent in any pharmaceutical production. Such risks are essentially of two types: cross contamination (in particular of unexpected contaminants) and mix-ups (confusion) caused by, for example, false labels being put on containers. Under GMP:

- all manufacturing processes are clearly defined, systematically reviewed in the light of experience, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications;
- qualification and validation are performed;
- all necessary resources are provided, including:
  - appropriately qualified and trained personnel;
  - adequate premises and space;
  - suitable equipment and services;
  - appropriate materials, containers and labels;
  - approved procedures and instructions;
  - suitable storage and transport;
  - adequate personnel, laboratories and equipment for in-process controls;
- instructions and procedures are written in clear and unambiguous language, specifically applicable to the facilities provided;
- operators are trained to carry out procedures correctly;
- records are made (manually and/or by recording instruments) during manufacture to show that all the steps required by the defined procedures and instructions have in fact been taken and that the quantity and quality of the product are as expected; any significant deviations are fully recorded and investigated;
- records covering manufacture and distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form;
- the proper storage and distribution of the products minimizes any risk to their quality;
- a system is available to recall any batch of product from sale or supply;

- complaints about marketed products are examined, the causes of quality defects investigated, and appropriate measures taken in respect of the defective products to prevent recurrence.

QUALITY CONTROL

That part of GMP which is concerned with sampling, specifications and testing.

Quality Control (QC) is part of quality management focused on fulfilling quality requirements ISO 9000:2000.

QC is examining "control" materials of known substances along with patient samples to monitor the accuracy and precision of the complete examination (analytic) process.

The goal of QC is to detect errors and correct them before patients' results are reported.

The guidelines on quality control require that a manufacturer of drugs/pharmaceutical products should have a quality control department and it should be independent from production and other departments. It should be headed by a person with appropriate qualifications and experience.

Revised Schedule M has this element under the title "Quality Control System". These guidelines covers following criteria:

- Facilities
- Personnel
- Equipment
- Sampling
- Testing
- Documentation
- Assessment of finished product and its release
- Monitoring of procedures
- Retention of reference samples

QUALITY RELATIONSHIPS

❖ Difference between QA & QC

QC	QA
• QC is that part of GMP which is concerned with sampling, specifications, testing and within the organization, documentation, and release procedures which ensure that the necessary and relevant tests are carried out	• QA is the sum total of organized arrangements made with the object of ensuring that product will be of the Quality required by their intended use.
• Operational laboratory techniques and activities used to fulfill the requirement of Quality	• All those planned or systematic actions necessary to provide adequate confidence that a product will satisfy the requirements for quality
• QC is lab based	• QA is company based
• Q.C. is one compartment of multi compartment Q.A. system.	• Q.A. approves test
• Q.C. must provide authentic testing on batch of product by passing or failing it	• Q.A. team must establish
• Q.C. is interested in what is happening today.	• Q.A. is interested in what happened yesterday

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	Part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.	**Good manufacturing practive**
2	Which are the two risks in pharmaceutical company?	**Cross-contamination & Mix ups**
3	Which records are to be kept in pharmaceutical industry?	**Manufacturinng, Distribution & Testinng**
4	Which step will be taken when any issue or complain is given to the company after sale or supply?	**Recall**
5	It is the part of GMP which is concerned with sampling, specifications and testing	**Quality control**

6	_____ is a part of quality management focused on fulfilling quality requirements ISO 9000:2000.	**Quality Control (QC)**
7	Examining "control" materials of known substances along with patient samples to monitor the accuracy and precision of the complete examination (analytic) process is known as	**Quality Control (QC)**
8	Which department in pharmaceutical industry should be independent from production and other departments?	**QC Department**
9	Quality Control de[artment is independet from _____ department?	**Production**
10	In which department all tests of pharmaceutical products is carried out ?	**Quality control**
11	Operational laboratory techniques and activities used to fulfill the requirement of Quality is known as	**QC**
12	All those planned or systematic actions necessary to provide adequate confidence that a product will satisfy the requirements for quality	**Quality Assurance**

Total Quality Management (TQM):

Total Quality Management (**TQM**) is a management strategy aimed at embedding awareness of quality in all organizational processes. TQM has been widely used in manufacturing, education, government, and service industries.

Total Quality provides an umbrella under which everyone in the organization can create customer satisfaction. TQ is a people focused management system that aims at continual increase in customer satisfaction at continually lower real costs.

TQM = A process for managing quality; it must be a continuous way of life; a philosophy of continuous improvement in everything we do.

Definition:

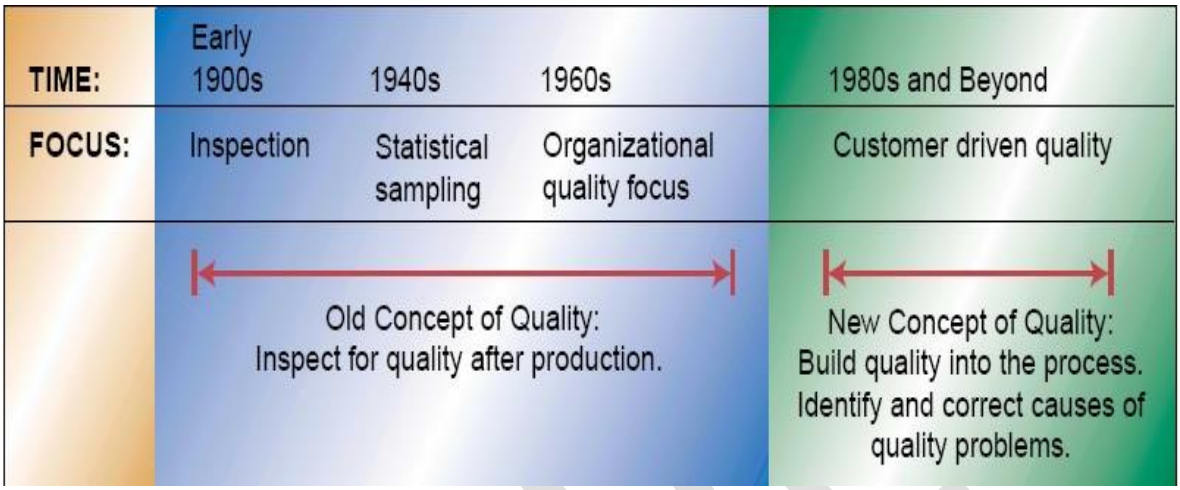
As defined by ISO:

"TQM is a management approach for an organization, centered on quality, based on the participation of all its members and aiming at long-term success through customer satisfaction, and benefits to all members of the organization and to society."

TQM (Total Quality Management) is the management of total quality. It's a part of Quality Management System, where Quality-by-design, Quality-by-time are the different techniques to achieve it.

TQM requires that the company maintain this quality standard in all aspects of its business. This requires ensuring that things are done right the first time and that defects and waste are eliminated from operations.

Traditionally, management includes the following activities: planning, organizing, leading, and controlling.



TQM IN PHARMACEUTICAL INDUSTRIES:

Total Quality Management is a managerial approach used by pharmaceutical manufacturers in ensuring pharmaceutical products meets the required quality with regard to their uses.

It is a potentially beneficial approach to manufacturing pharmaceutical products, as it ensures they exceed customers' expectations in relation to quality standards, efficiency and also effectiveness.

Pharmaceutical manufacturers play a key role in the system of health care and for that case, they are heavily regulated by the relevant authorities since; any slight mistakes in pharmaceuticals manufacturing can have fatal consequences.

In this case, pharmaceutical manufacturers need to maintain and improve continuously on their products through Total Quality management system process implementation.

Basic Approaches of TQM

- A committed and involved management to provide long-term top - to - bottom organizational support.
- A focus on the customer, both internally and externally.
- Effective involvement and utilization of the entire work force.
- Continuous improvement of the business and production process.
- Establish performance measures for the processes.

Major Elements of the TQM Approach

There are 8 elements of quality management for pharmaceutical companies.

1. **Customer Focus:**

"Striving to exceed customer expectations" should be the primary focus of a quality management system, according to ISO.

Organizations achieve success when they earn customer confidence and use every customer interaction to create value. Understanding the customers' needs in the present and future is a necessity for success.

Pharmaceutical companies are facing extraordinary pressure to adapt to changing market conditions, including the shifting role of the patient in healthcare.

Establishing a strong focus on the customer has clear benefits for quality driven organizations in any industry, especially in pharma where customer expectations are changing rapidly.

2. **Total Involvement of Employees:**

Every employee at a pharma organi zation has an impact on the company's ability to deliver a quality product, from research scientists to janitorial staff.

All employees are involved in the quality production process, and so they should as well take part in the innovation and improvement of quality.

Employees are ultimately responsible for quality, and continuous improvement could not be achieved unless leadership provides workers with the resources needed--including training, development, and recognition.

3. **Process-Centered Approach:**

A process-based approach is a core principle of ISO quality management systems with increased impact on pharmaceutical QMS. According to ISO, "consistent and predictable results are achieved more effectively and efficiently when activities are understood and managed as interrelated processes.

A process-centered approach involves the development of clear SOPs for every role and responsibility in the organization, but it also requires pharma organizations to shift their focus to the entire product lifecycle.

4. **Integrated Systems:**

Transparency throughout the product lifecycle is necessary to TQM. An organization can only optimize products and performance by understanding how a system produces results.

Transparency of information can be supported by a comprehensive QMS software which complies with cGMP and ICQ10.

Based on ISO guidance and cGMP, an integrated pharma system must support:

- Quality policy
- Personnel
- Development and implementation

- Production
- Documents
- Facilities and equipment
- Self-inspection
- Management responsibilities
- Evaluation of suppliers and purchasing
- Supplier production and analysis
- Risk analysis
- Monitoring and control
- Complaints and recalls (CAPA)
- Measurement, analysis, and improvement

5. Strategic and Systematic Approach:

Leadership is integral to a strategic and systemic approach to quality-driven organizations. In a pharma company, the leadership team is tasked with creating a culture of quality and inspiring excellent performance.

A strategic approach to pharma leadership allows a company to become more forward-thinking. Instead of focusing on immediate objectives, management review efforts are driven by a clear roadmap for clinical development. Decisions are made based on accurate documentation for risk management and clear quality objectives.

A QMS plays a core role in helping pharma companies take a systemic approach to achieving both short-term and long-term quality objectives by providing transparency, ease-of-access to information, and improving communication. An eQMS can support strategic leadership with:

- Coordination of processes across the organization
- Support for real-time collaboration and communication
- Training and education to help every member of the organization improve quality

6. Constant Improvement:

The mission for quality is an endless process in which individuals are constantly attempting to improve on the product's features.

The pharmaceutical industry is under intense pressure to meet strict regulatory requirements and pricing pressures while evolving to meet changing customer expectations. A formalized approach to improvement can allow organizations to meet standards while capturing new opportunities consistently.

Efforts to improve in pharma should focus on developing greater internal efficiencies, meeting current and emerging customer requirements, and adapting to meet changing market conditions.

7. Fact-based Decision Making:

"Evidence-based decision making" is among the core principles of ISO, who writes "decisions based on the analysis and evaluation of data and information are more likely to produce desired results."

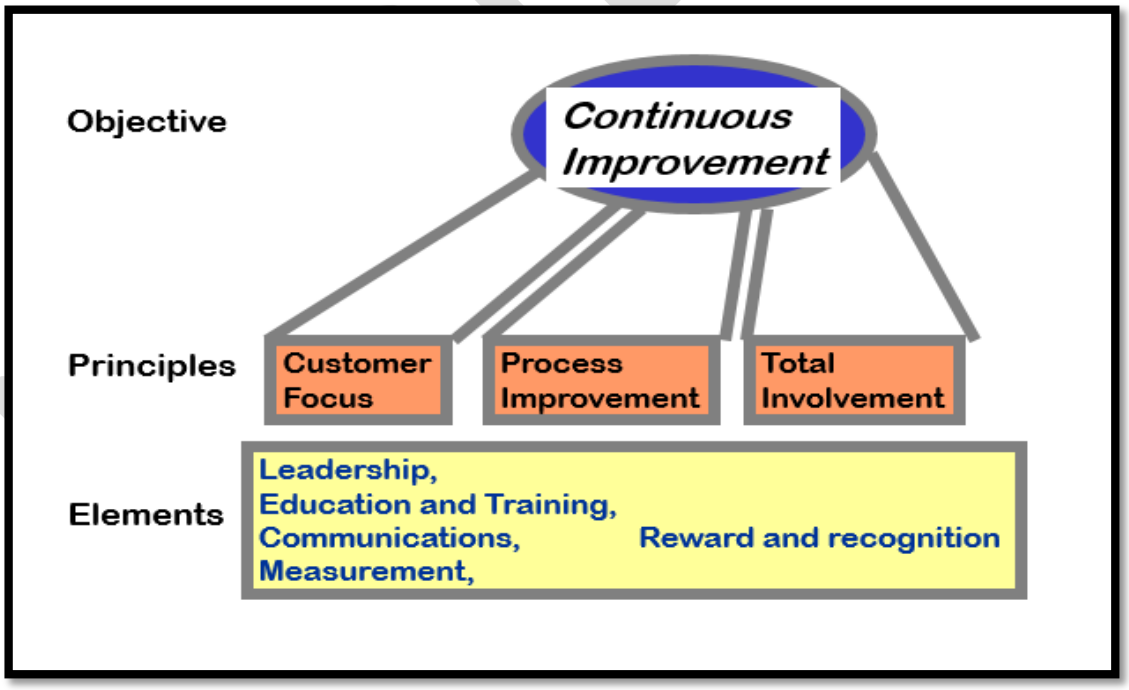
Pharmaceutical executives are now required to make decisions based on data throughout the product lifecycle.

Data can help leadership decide where change makes sense and when immediate changes are necessary to protect product quality.

8. Communications

Effective relationships and communication are important to achieving the alignment of people, processes and technology.

Systems for communication should support real-time, productive dialogue between leadership, quality, employees, and third-party organizations in the supply chain.



TQM Implementation in Pharmaceuticals

- TQM can be difficult to accomplish and maintain whether an organization is trying hard to retain its quality of products or be in line with regulations from the respective authorities. It can't be effectively accomplished without the significant and relevant resources like funds and workforce.

- TQM is a strategy through which managers, as well as employees, can be engaged in the constant process of quality improvement of products. It is a blend of value and managerial techniques focused on business expansion and reduction of losses because of inefficient practices.

Benefits of Total Quality Management

- TQM is the coordination of management efforts with the intention of improving on quality at all levels within the organization. Thus, the TQM approach has various benefits. It comes with monetary benefits which incorporate lowered costs of production, increased investment and sales profits, and also the power to increase product prices to the quality involved.

- Additional benefits may incorporate facilitated entry to worldwide markets, higher client maintenance levels, development of new innovations within a short period, and good company reputation.

- Just a few organizations implement the TQM approach on the grounds that a powerful program actualization is time-consuming and costly. In any case, organizations with the appropriate assets may gain upper hands in their enterprises by actualizing the TQM.

Cause of Failure in TQM Implementation

TQM has yielded tremendous monetary benefits in various pharmaceutical manufacturers, while struggles for quality fizzled and yielded peripheral outcomes in some different manufactures.

Following are reasons which can be behind a failed TQM implementation process:

- Concentrating solely on momentary financial related outcomes while turning a blind eye on the improvement of systems (Improvement on quality calls for a change of thought in the management of the basic systems).
- Managers' interference in teamwork,
- Unclear strategies and procedures,
- Failure to understand the TQM approach, and inadequate training as well as insufficient education resources

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	Management strategy aimed at embedding awareness of quality in all organizational processes is known as	**Total Quality Management (TQM)**

2	Total Quality provides an umbrella under which everyone in the organization can create	**Customer satisfaction**
3	A people focused management system that aims at continual increase in customer satisfaction at continually lower real costs is known as	**TQM**
4	TQM is a philosophy of	**Continuous improvement**
5	Management approach for an organization, centered on quality, based on the participation of all its members and aiming at long-term success through customer satisfaction, and benefits to all members of the organization and to society is known as.	**Total Quality Management**
6	Which are the different techniques of quality management system?	**Quality-by-design, Quality-by-time**
7	_____ ensures that things are done right the first time and that defects and waste are eliminated from operations.	**TQM**
8	Pharmaceutical manufacturers are heavily regulated by the relevant authorities because they play a key role in the system of	**Health care**
9	How many elements are there of quality management for pharmaceutical companies?	**8**
10	Organizations achieve success when they earn _____ confidence.	**Customer**
11	Pharmaceutical companies are facing extraordinary pressure due to	**Changing market**
12	Strong focus on the customer has more benefits for quality driven organizations like pharma industry. Why?	**Expectations chages rapidlly**
13	Which element is responsible for the innovation and improvement of quality in pharma company?	**Total involvement**
14	A process-centered approach involves the development of clear _____ for every role and responsibility in the organization.	**SOPs**
15	Transparency of information in pharma industry can be supported by a	**QMS software**
16	QMS software complies with	**cGMP and ICQ10**
17	What is the full form of cGMP	**Current Good Manufacturing Practice**
18	Decisions are made in pharma company is based on	**Documentation**
19	Which advance in QMS is helpful for real-time collaboration and communication in pharma company?	**eQMS**
20	What is the important to achieve the alignment of people, processes and technology?	**Effective relationship and communication**

21	TQM can't be effectively accomplished without the significant and relevant resources like	**Funds & workforce**
22	How manager contribute in TQM failure?	**By interference**
23	Failure to understand the TQM approach and inadequate training as well as insufficient education resources leads to	**TQM failure**

ICH

ICH is the "International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use".

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration.

ICH is a joint initiative involving both regulators and research-based industry representatives of the EU, Japan and the US in scientific and technical discussions of the testing procedures required to assess and ensure the safety, quality and efficacy of medicines.

❖ Purpose or Mission of ICH

- ✓ To make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration and the maintenance of such registrations;
- ✓ To maintain a forum for a constructive dialogue on scientific issues between regulatory authorities and the pharmaceutical industry on the harmonisation of the technical requirements for pharmaceutical products;
- ✓ To contribute to the protection of public health in the interest of patients from an international perspective;
- ✓ To monitor and update harmonised technical requirements leading to a greater mutual acceptance of research and development data;
- ✓ To avoid divergent future requirements through harmonisation of selected topics needed as a result of therapeutic advances and the development of new technologies for the production of medicinal products;
- ✓ To facilitate the adoption of new or improved technical research and development approaches which update or replace current practices;

- ✓ To encourage the implementation and integration of common standards through the dissemination of, the communication of information about and coordination of training on, harmonised guidelines and their use;

- ✓ And to develop policy for the ICH Medical Dictionary for Regulatory Activities Terminology (MedDRA) whilst ensuring the scientific and technical maintenance, development and dissemination of MedDRA as a standardised dictionary which facilitates the sharing of regulatory information internationally for medicinal products used by humans.

❖ History

The International Council for Harmonisation (ICH), formerly the International Conference on Harmonisation (ICH) held the inaugural Assembly meetings on 23 October 2015 establishing ICH as an international association, a legal entity under Swiss law.

The Need to Harmonise

The realisation that it was important to have an independent evaluation of medicinal products before they are allowed on the market was reached at different times in different regions.

For most countries, whether or not they had initiated product registration controls earlier, the 1960s and 1970s saw a rapid increase in laws, regulations and guidelines for reporting and evaluating the data on safety, quality and efficacy of new medicinal products.

The industry, at the time, was becoming more international and seeking new global markets; however the divergence in technical requirements from country to country was such that industry found it necessary to duplicate many time-consuming and expensive test procedures, in order to market new products, internationally.

The urgent need to rationalize and harmonize regulation was forced by concerns over rising costs of health care, a rapid increase of the cost of R & D and need to meet the public expectations that there should be a minimum of delay in making safe and efficacious new treatments available to patients in need.

Initiation of ICH

Harmonisation of regulatory requirements was pioneered by the EC, Europe, in the 1980s, as the EC, Europe moved towards the development of a single market for pharmaceuticals. The success achieved in Europe demonstrated that harmonisation was feasible.

At the same time there were discussions between Europe, Japan and the US on possibilities for harmonisation. It was, however, at the WHO Conference of Drug Regulatory Authorities (ICDRA), in Paris, in 1989, that specific plans for action began to materialise.

Soon afterwards, the authorities approached International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) to discuss a joint regulatory-industry initiative on international harmonisation, and ICH was conceived.

The Evolution of ICH

ICH's first decade saw significant progress in the development of ICH Guidelines on Safety, Quality and Efficacy and other multidisciplinary topics.

Second decade started towards facilitating the implementation of ICH Guidelines in ICH's own regions.

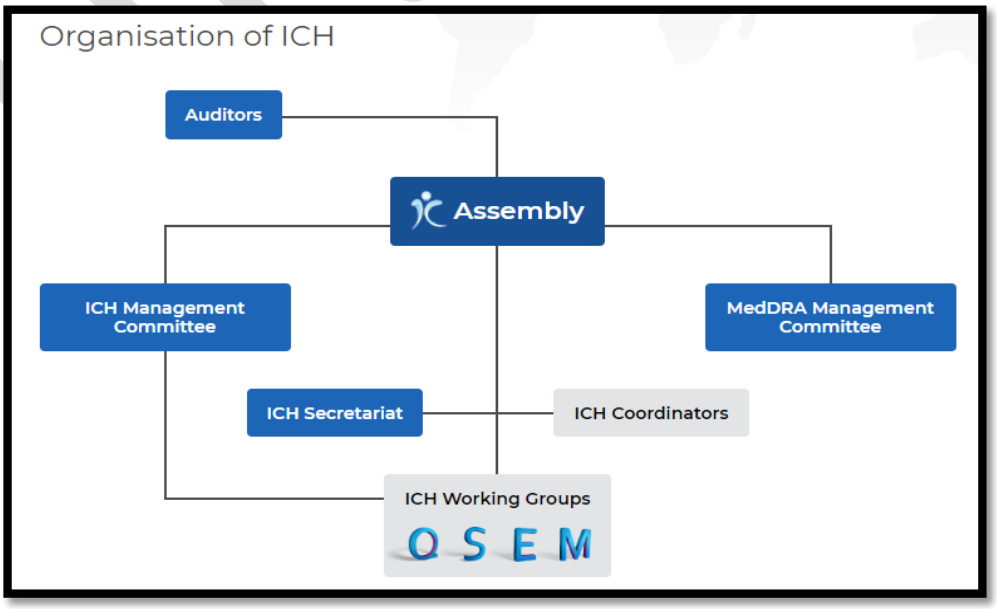
Now in its third decade of activity, ICH's attention is directed towards extending the benefits of harmonisation beyond the founding ICH regions. A significant step was taken in 2015 to facilitate this which saw ICH undergoing a series of organisational changes.

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	Who bring together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration?	**ICH**
2	Which countries took joint initiative for ICH?	**EU, Japan & US**
3	Which two things have been come together to discuss scientific and technical aspects of drug registration?	**Regulatory authorities and Pharmaceutical industry**
4	Which requirements have been harmonized by ICH for drug registration?	**Scientific and technical**
5	What is protected in the interest of patients by ICH?	**Public health**
6	To encourage the implementation and integration of common standards through	**Communication of information**
7	Which section involves ICH Medical Dictionary for Regulatory Activities Terminology?	**MedDRA**
8	In ICH MedDRA is for	**Medical Dictionary**
9	When the name of ICH has been changed?	**23 October 2015**
10	ICH as an international association, a legal entity under _____ law.	**Swiss**
11	In which years there was a rapid increase in in laws, regulations and guidelines for reporting and evaluating the data on safety, quality and efficacy of new medicinal products?	**1960s and 1970s**
12	What was disadvantages when there was a the divergence in technical requirements from country to country?	**Time-consuming and expensive test procedures**
13	The urgent need to rationalize and harmonize regulation was forced by concerns over	**Rising costs of health care & R & D**

14	In which year, Harmonisation of regulatory requirements was pioneered by the EC, Europe?	**1980s**
15	Which countries were involved in the discussion on possibilities for harmonisation?	**Europe, Japan and the US**
16	In which year specific plans for action on harmonization began to materialise?	**1989**
17	In which city, plans for action on harmonization began to materialise?	**Paris**
18	Who is approached by authorities to discuss a joint regulatory-industry initiative on international harmonisation?	**IFPMA**
19	What is the full form of IFPMA?	**International Federation of Pharmaceutical Manufacturers and Associations**
20	Which step had been taken for harmonization of technical requirement for registartion of medicinal product for human use in ICH's first decade?	**Development of ICH Guidelines**
21	Which topics are coverd in ICH guidelines?	**Safety, Quality and Efficacy and other Multidisciplinary**
22	How many topics are covered in ICH guidelines?	**4**
23	Which step had been taken for harmonization of technical requirement for registartion of medicinal product for human use in ICH's second decade?	**Implementation of ICH Guidelines**
24	Which step had been taken for harmonization of technical requirement for registartion of medicinal product for human use in ICH's third decade?	**Extended the benefits of harmonisation beyond ICH regions**
25		

❖ Organization of ICH:



- **ASSEMBLY**

  The ICH Assembly brings together all Members and Observers of the ICH Association as the overarching governing body of ICH. It adopts decisions in particular on matters such as on the Articles of Association, admission of new Members & Observers and adoption of ICH Guidelines.

  The ICH Assembly meets biannually and its agendas as well as reports are made available on the ICH website summarising the main decisions taken at each meeting

- **AUDITORS**

  The Auditors are appointed for a period of two years and may be re-appointed. The responsibility of the Auditors is to audit the financial statements of the Association upon conclusion of each Fiscal Year. They should ensure that the accounting of the Association complies with Swiss law and generally accepted Swiss accounting principles.

- **MANAGEMENT COMMITTEE**

  The ICH Management Committee (MC) is the body that oversees operational aspects of ICH on behalf of all Members, including administrative and financial matters and oversight of the Working Groups (WGs).

  The MC is responsible for submitting recommendations or proposals to the Assembly in preparation of Assembly discussions.

  To date, the ICH MC is composed of 14 Regulatory and Industry Members and 2 Standing Observers. The ICH MC has permanent representatives from the six Founding Members (Europe, United States, Japan), Standing Regulatory Members (Health Canada, Canada; Swissmedic, Switzerland) as well as Standing Observers (IFPMA; WHO).

  In addition, since June 2018 and as per the ICH Articles of Association, the following MC Elected Representatives have been nominated to join the MC and will serve until the next election in June 2021: ANVISA, Brazil; BIO; HSA, Singapore, IGBA; MFDS, Republic of Korea and NMPA, China.

- **MedDRA MANAGEMENT COMMITTEE**

  The MedDRA Management Committee (MC) has responsibility for direction of MedDRA, an ICH standardised dictionary of medical terminology. The MedDRA MC is composed of the EC, Europe; EFPIA; MHLW/PMDA, Japan; JPMA; FDA, United States; PhRMA; MHRA UK; Health Canada, Canada; and WHO (as Observer).

- **SECRETARIAT**

  The ICH Secretariat is responsible for day-to-day management of ICH, coordinating ICH activities as well as providing support to the Assembly, the ICH Management Committee and its Working Groups.

The ICH Secretariat also provides support for the ICH MedDRA Management Committee. The Secretariat is located in Geneva, Switzerland.

- **COORDINATORS**

Fundamental to the smooth running of ICH has been the designation of an ICH Coordinator per ICH Member to act as the main contact point with the ICH Secretariat.

Coordinators ensure proper distribution of ICH documents to the appropriate persons from their organisation and are responsible for the follow up on actions within their respective organisation within assigned deadlines.

They also assist communication between the ICH Management Committee and/or Assembly and the ICH Working Groups as needed.

- **WORKING GROUPS**

An ICH Working Group (WG) is established for each technical topic selected for harmonisation.

There are several different types of ICH working group:

- EWG: Expert Working Group is charged with developing a harmonised guideline that meets the objectives in the Concept Paper and Business Plan.
- IWG: Implementation Working Group is tasked with developing Q&As to facilitate implementation of existing guidelines.
- Informal Working Group: Is formed prior to any official ICH harmonisation activity with the objectives of developing/finalising a Concept Paper, as well as developing a Business Plan.
- Discussion Group: Is a group established to discuss specific scientific considerations or views i.e. Gene Therapy Discussion Group (GTDG), and ICH & Women Discussion Group.

ICH Members and Observers appoint experts to participate in the WGs in line with the applicable procedures in the Assembly Rules of Procedure and EWG/IWG Standard Operating Procedures. A Rapporteur from one of the Members is designated by the Assembly to lead the scientific discussions of the WG.

The Management Committee oversees the work of the WGs on an ongoing basis, while the Assembly receives reports on each WG's progress at the time of its biannual face-to-face meetings.

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	How many committees are there in ICH organization?	7

2	Which committee brings together all Members and Observers of the ICH Association as the overarching governing body of ICH?	**ICH Assembly**
3	Who adopts decisions in particular on matters such as on the Articles of Association, admission of new Members & Observers and adoption of ICH Guidelines?	**ICH Assembly**
4	How many times in a year meeting of ICH Assembly is held?	**2 times**
5	What are made available on the ICH website after each meeting of ICH Assembly?	**Agendas of meeting as well as reports**
6	For how much period the Auditors are appointed?	**2 years**
7	Whose responsibility is to audit the financial statements of the Association upon conclusion of each Fiscal Year?	**ICH Auditors**
8	Accounting of the ICH Association complies with _____ law.	**Swiss**
9	Who ensures that the accounting of the Association complies with Swiss law and generally accepted Swiss accounting principles?	**Auditors**
10	The body that oversees operational aspects of ICH on behalf of all Members, including administrative and financial matters and oversight of the Working Groups (WGs)	**ICH Management Committee (MC)**
11	Who is responsible for submitting recommendations or proposals to the Assembly in preparation of Assembly discussions?	**Management Committee**
12	What is the composition of ICH MC?	**14 Regulatory and Industry Members and 2 Standing Observers**
13	How many Regulatory and Industry members are involved in ICH MC?	**14**
14	How many Standing Observers are involved in ICH MC?	**2**
15	ICH MC has permanent representatives from _____ Founding Members of ICH MC?	**Six**
16	From which countries ICH MC has permanent representatives?	**Europe, United States, Japan, Canada, Switzerland &**
17	Since when ANVISA, Brazil; BIO; HSA, Singapore, IGBA; MFDS, Republic of Korea and NMPA, China have been nominated to join the MC?	**June 2018**
18	When next election will be conducted to elect representative of Management Committee?	**2021**
19	Which countries are involved in MedDRA Management Committee?	**Europe, JapanUS, UK, Canada and WHO**
20	Who is responsible for day-to-day management of ICH?	**ICH Secretariat**
21	Who is responsible for coordinating ICH activities as well as providing support to the Assembly, the ICH Management Committee and its Working Groups?	**ICH Secretariat**

22	Who provides support for the ICH MedDRA Management Committee.	**ICH Secretariat**
23	In which city ICH Secretariat is located?	**Geneva, Switzerland**
24	Who to act as the main contact point with the ICH Secretariat?	**ICH Coordinator**
25	Who ensure proper distribution of ICH documents to the appropriate persons from their organisation and are responsible for the follow up on actions within their respective organisation within assigned deadlines?	**Coordinators**
26	Who assist communication between the ICH Management Committee and/or Assembly and the ICH Working Groups as needed?	**Coordinators**
27	Coordinators assist communication between the	**ICH MC, Assembly and ICH WGs**
28	_____ is established for each technical topic selected for harmonisation.	**ICH Working Group (WG)**
29	Which type of Working Group is charged with developing a harmonised guideline that meets the objectives in the Concept Paper and Business Plan?	**Expert Working Group**
30	Which type of Working Group is tasked with developing Q&As to facilitate implementation of existing guidelines.	**Implementation Working Group**
31	Which type of Working Group is formed prior to any official ICH harmonisation activity with the objectives of developing/finalising a Concept Paper, as well as developing a Business Plan.	**Informal Working Group**
32	_____ is a group among all Working Groups established to discuss specific scientific considerations or views.	**Discussion Group**
33	Give the examples of Dıscussion Working Groups.	**Gene Therapy Discussion Group (GTDG), and ICH & Women Discussion Group.**
34	Give the full form of GTDC.	**Gene Therapy Discussion Group**
35	What is the full form of EWG?	**Expert Working Group**
36	What is the full form of IWG?	**Implementation Working Group**
37	Who appoint experts to participate in the WGs in line with the applicable procedures in the Assembly Rules of Procedure and EWG/IWG Standard Operating Procedures?	**ICH Members and Observers**
38	Who are appointed by ICH Members and Observers to participate in the WGs in line with the applicable procedures	**Experts**

	in the Assembly Rules of Procedure and EWG/IWG Standard Operating Procedures?	
39	Who degignate a Rapporteur from one of the Members of WGs to lead the scientific discussions of the WG?	**Assembly**
40	A _____ from one of the Members of WGs is designated by the Assembly to lead the scientific discussions of the WG	**Rapporteur**
41	Who oversees the work of the WGs on an ongoing basis?	**Management Committee**
42	Management Committee oversees the work of the _____ on an ongoing basis	**WGs**
43	Who receives reports on each WG's progress at the time of its biannual face-to-face meetings?	**Assembly**
44	When Assembly receives reports from WGs?	**on each WG's progress**

♣ ICH Guidelines:

The ICH topics are divided into the four categories as below.

1. Quality Guidelines
2. Saftey Guidelines
3. Efficacy Guidelines
4. Multidisciplinary Guidelines

1) Quality Guidelines:

Harmonisation achievements in the Quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.

Q1A – Q1F	Stability
Q2	Analytical Validation
QA3 – Q3D	Impurities
Q4A – Q4B	Pharmacopoeias
Q5A – Q5E	Quality of Biotechnological produts
Q6A – Q6B	Specifications
Q7	Good Manufacturing Practice
Q8	Pharmaceutical development
Q9	Quality Risk Management
Q10	Pharmaceutical Quality System
Q11	Development and Manufacture of Drug Substances
Q12	Lifecycle management

Q13	Continuous Manufacturig of Drug Substances and Drug Products
Q14	Analytical Procedure Development

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	How many categories are there for ICH guidelines?	**4**
2	How ICH guidelines are shortly described?	**QSEM**
3	Q1A – Q1F series is for _____ guidelines.	**Stability**
4	Which are the stability guidelines?	**Q1A – Q1F**
5	Q2 is for _____ guidelines.	**Analytical Validation**
6	In which section Analytical Validation guidelines are given?	**Q2**
7	QA3 – Q3D guidelines are stands for	**Impurities**
8	In which section "Impurities" guidelines are given?	**QA3 – Q3D**
9	In which section pharmacopoeial harmonization guidelines are given?	**Q4A – Q4B**
10	Q4A – Q4B guidelines are stands for	**Pharmacopoeia**
11	Guidelines of Quality of Biotechnological produts are involved in section	**Q5A – Q5E**
12	Q5A – Q5E guidelines are for	**Quality of Biotechnological produts**
13	Guidelines related Specifications are involved in section	**Q6A – Q6B**
14	Q6A – Q6B guidelines are for	**Specifications**
15	In which section "Good Manufacturing Practice" guidelines are given?	**Q7**
16	Q7 includes the guidelines about	**Good Manufacturing Practice**
17	In which section "Pharmaceutical development" guidelines are given?	**Q8**
18	Q8 includes the guidelines about	**Pharmaceutical development**
19	In which section "Quality Risk Management" guidelines are given?	**Q9**
20	Q9 guidelines stands for	**Quality Risk Management**
21	In which section "Pharmaceutical Quality System" guidelines are given?	**Q10**
22	Which topic is covered in Q10 guidelines?	**Pharmaceutical Quality System**
23	In which section "Development and Manufacture of Drug Substances" guidelines are given?	**Q11**

24	Which topic is covered in Q11 guidelines?	**Development and Manufacture of Drug Substances**
25	In which section "Lifecycle management" guidelines are given?	**Q12**
26	Which topic is covered in Q12 guidelines?	**Lifecycle management**
27	In which section "Continuous Manufacturig of Drug Substances and Drug Products" guidelines are given?	**Q13**
28	Which topic is covered in Q13 guidelines?	**Continuous Manufacturig of Drug Substances and Drug Products**
29	In which section "Analytical Procedure Development" guidelines are given?	**Q14**
30	Which topic is covered in Q14 guidelines?	**Analytical Procedure Development**

❖ Q1A – Q1F Stability Guidelines

1) Q1A(R2) STABILITY TESTING OF NEW DRUG SUBSTANCES AND PRODUCTS

Objectives: The following guideline is a revised version of the ICH Q1A guideline and defines the stability data package for a new drug substance or drug product that is sufficient for a registration application within the three regions of the EC, Japan, and the United States.

General Principles:

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light.

The choice of test conditions defined in this guideline is based on an analysis of the effects of climatic conditions in the three regions of the EC, Japan and the United States.

GUIDELINES

1. Drug Substance

- **Stress Testing:**

  Stress testing of the drug substance can help identify the likely degradation products, which can in turn help establish the degradation pathways and the intrinsic stability of the molecule and validate the stability indicating power of the analytical procedures used.

  Stress testing is likely to be carried out on a single batch of the drug substance. It should include the effect of temperatures (in 10°C increments (e.g., 50°C, 60°C, etc.) above that

for accelerated testing), humidity (e.g., 75% RH or greater) where appropriate, oxidation, and photolysis on the drug substance.

In case of solution or suspension, the testing should also evaluate the susceptibility of the drug substance to hydrolysis across a wide range of pH values.

Examining degradation products under stress conditions is useful in establishing degradation pathways and developing and validating suitable analytical procedures.

- **Selection of Batches:**
  Data from formal stability studies should be provided on at least three primary batches of the drug substance.

- **Container Closure System:**
  The stability studies should be conducted on the drug substance packaged in a container closure system that is the same as or simulates the packaging proposed for storage and distribution.

- **Specification**
  Stability studies should include testing of those attributes of the drug substance that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy.

  The testing should cover, as appropriate, the physical, chemical, biological, and microbiological attributes. Validated stability-indicating analytical procedures should be applied.

- **Testing Frequency**
  For long term studies, frequency of testing should be sufficient to establish the stability profile of the drug substance.

  For drug substances with a proposed re-test period of at least 12 months, the frequency of testing at the long term storage condition should normally be every 3 months over the first year, every 6 months over the second year, and annually thereafter through the proposed re-test period.

  At the accelerated storage condition, a minimum of three time points, including the initial and final time points (e.g., 0, 3, and 6 months), from a 6-month study is recommended.

  When testing at the intermediate storage condition is called for as a result of significant change at the accelerated storage condition, a minimum of four time points, including the initial and final time points (e.g., 0, 6, 9, 12 months), from a 12-month study is recommended.

- **Storage Conditions**
  A. General Case:

Study	Storage condition	Minimum time period covered by data at submission
Long term	25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH	12 months
Intermediate	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

B. Drug substances intended for storage in a refrigerator

Study	Storage condition	Minimum time period covered by data at submission
Long term	5°C ± 3°C	12 months
Intermediate	25°C ± 2°C/60% RH ± 5% RH	6 months

C. Drug substances intended for storage in a freezer

Study	Storage condition	Minimum time period covered by data at submission
Long term	- 20°C ± 5°C	12 months

- **Stability Commitment**

  When available long term stability data on primary batches do not cover the proposed re-test period granted at the time of approval, a commitment should be made to continue the stability studies post approval in order to firmly establish the re-test period.

  The stability protocol used for studies on commitment batches should be the same as that for the primary batches, unless otherwise scientifically justified.

- **Evaluation**

  The purpose of the stability study is to establish, based on testing a minimum of three batches of the drug substance and evaluating the stability information (including, as appropriate, results of the physical, chemical, biological, and microbiological tests), a re-test period applicable to all future batches of the drug substance manufactured under similar circumstances.

  The degree of variability of individual batches affects the confidence that a future production batch will remain within specification throughout the assigned re-test period.

- **Statements/Labeling**

A storage statement should be established for the labeling in accordance with relevant national/regional requirements. The statement should be based on the stability evaluation of the drug substance.

2. Drug Product

- **General**

  The design of the formal stability studies for the drug product should be based on knowledge of the behavior and properties of the drug substance and from stability studies on the drug substance and on experience gained from clinical formulation studies.

- **Photostability Testing**

  Photostability testing should be conducted on at least one primary batch of the drug product if appropriate.

- **Selection of Batches**

  Data from stability studies should be provided on at least three primary batches of the drug product. The primary batches should be of the same formulation and packaged in the same container closure system as proposed for marketing.

  Two of the three batches should be at least pilot scale batches and the third one can be smaller, if justified. Where possible, batches of the drug product should be manufactured by using different batches of the drug substance.

  Stability studies should be performed on each individual strength and container size of the drug product.

- **Container Closure System**

  Stability testing should be conducted on the dosage form packaged in the container closure system proposed for marketing (including, as appropriate, any secondary packaging and container label).

- **Specification**

  Stability studies should include testing of those attributes of the drug product that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy.

  The testing should cover, as appropriate, the physical, chemical, biological, and microbiological attributes, preservative content (e.g., antioxidant, antimicrobial preservative), and functionality tests (e.g., for a dose delivery system).

  A single primary stability batch of the drug product should be tested for antimicrobial preservative effectiveness (in addition to preservative content) at the proposed shelf life for verification purposes.

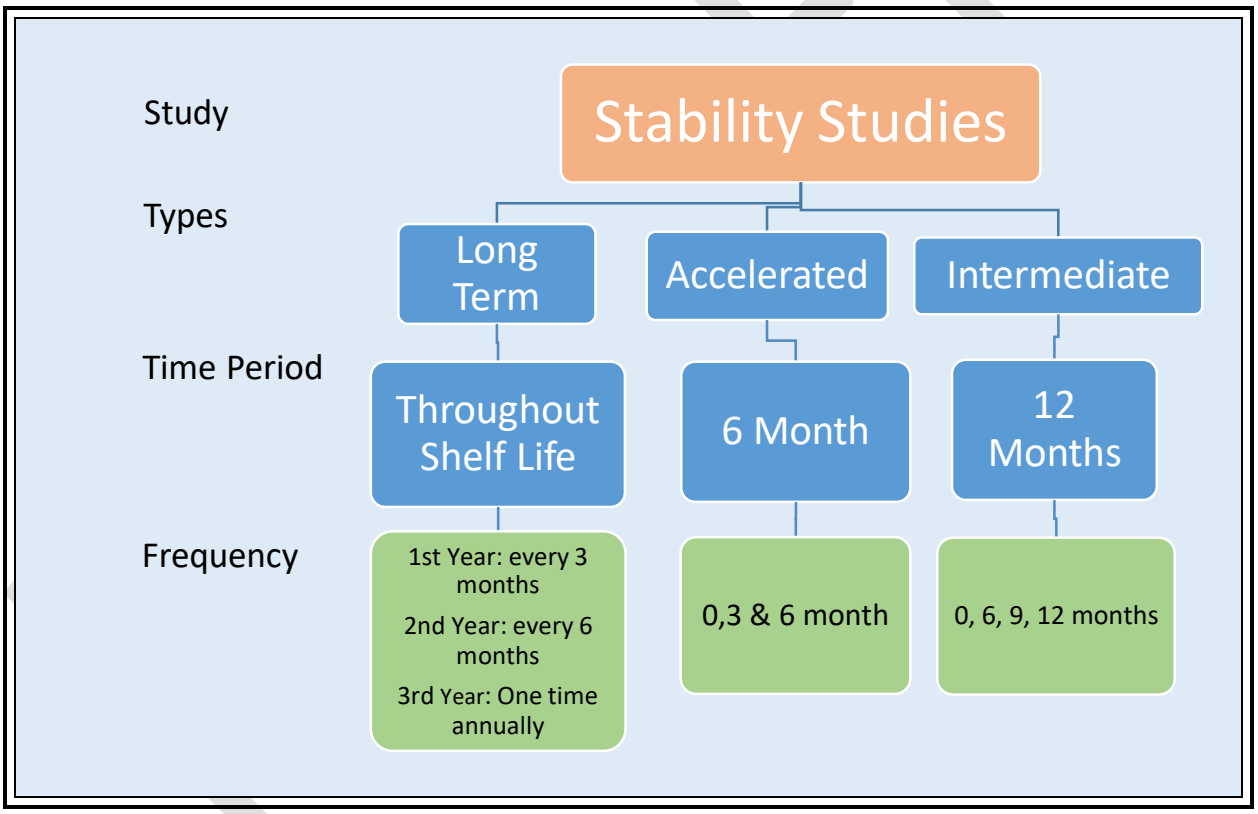
- **Testing Frequency**

  For long term studies, frequency of testing should be sufficient to establish the stability profile of the drug product.

  For products with a proposed shelf life of at least 12 months, the frequency of testing at the long term storage condition should normally be every 3 months over the first year, every 6 months over the second year, and annually thereafter through the proposed shelf life.

  At the accelerated storage condition, a minimum of three time points, including the initial and final time points (e.g., 0, 3, and 6 months), from a 6-month study is recommended.

  When testing at the intermediate storage condition is called for as a result of significant change at the accelerated storage condition, a minimum of four time points, including the initial and final time points (e.g., 0, 6, 9, 12 months), from a 12-month study is recommended.



- **Storage Conditions**

  In general, a drug product should be evaluated under storage conditions (with appropriate tolerances) that test its thermal stability and, if applicable, its sensitivity to moisture or potential for solvent loss.

  Stability testing of the drug product after constitution or dilution, if applicable, should be conducted to provide information for the labeling on the preparation, storage condition, and in-use period of the constituted or diluted product.

A. General Case:

Study	Storage condition	Minimum time period covered by data at submission
Long term	25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH	12 months
Intermediate	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

B. Drug products packaged in impermeable containers

Sensitivity to moisture or potential for solvent loss is not a concern for drug products packaged in impermeable containers that provide a permanent barrier to passage of moisture or solvent.

Thus, stability studies for products stored in impermeable containers can be conducted under any controlled or ambient humidity condition.

C. Drug products packaged in semi-permeable containers

Aqueous-based products packaged in semi-permeable containers should be evaluated for potential water loss in addition to physical, chemical, biological, and microbiological stability.

Ultimately, it should be demonstrated that aqueous-based drug products stored in semi-permeable containers can withstand low relative humidity environments.

Other comparable approaches can be developed and reported for non-aqueous, solvent-based products.

Study	Storage condition	Minimum time period covered by data at submission
Long term	25°C ± 2°C/40% RH ± 5% RH or 30°C ± 2°C/35% RH ± 5% RH	12 months
Intermediate	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/not more than (NMT) 25% RH	6 months

D. Drug products intended for storage in a refrigerator

Study	Storage condition	Minimum time period covered by data at submission
Long term	5°C ± 3°C	12 months

Accelerated	25°C ± 2°C/60% RH ± 5% RH	6 months

E. Drug products intended for storage in a freezer

Study	Storage condition	Minimum time period covered by data at submission
Long term	- 20°C ± 5°C	12 months

- **Stability Commitment**

  When available long term stability data on primary batches do not cover the proposed shelf life granted at the time of approval, a commitment should be made to continue the stability studies post approval in order to firmly establish the shelf life.

  The stability protocol used for studies on commitment batches should be the same as that for the primary batches, unless otherwise scientifically justified.

- **Evaluation**

  A systematic approach should be adopted in the presentation and evaluation of the stability information, which should include, as appropriate, results from the physical, chemical, biological, and microbiological tests, including particular attributes of the dosage form (for example, dissolution rate for solid oral dosage forms).

- **Statements/Labeling**

  A storage statement should be established for the labeling in accordance with relevant national/regional requirements. The statement should be based on the stability evaluation of the drug product.

  Where applicable, specific instruction should be provided, particularly for drug products that cannot tolerate freezing.

  There should be a direct link between the label storage statement and the demonstrated stability of the drug product. An expiration date should be displayed on the container label.

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	Guidelines about Stability Testing of New Drug Substances And Products is given in _____ guidelines of Stability guidelines.	**Q1A(R2)**
2	Q1A(R2) is revised version of the _____ guidelines.	**ICH Q1A**
3	Revised version of ICH Q1A guidelines is	**Q1A(R2)**

4	Q1A(R2) is data package for stability guidelines that is sufficient for a registration application within the three regions. Which are those regions?	**EC, Japan, and the United States**
5	Which environmental factors affect the stability of drug substance and drug product?	**Temperature, humidity, and light**
6	Which characteristic of drug substance and drug product is mostly affected by temperature, humidity and light?	**Stability**
7	Test conditions like temperature and humidity of stability testing depends on climatic conditions of _____ countries.	**EC, Japan and the US**
8	What are the test factors of stress stability testing?	**Temperature & Humidity**
9	What can be identified about drug substance and product by stress testing?	**Degradation products**
10	What can be established about drug substance and product by stress testing?	**Degradation pathways**
11	On how many batches of drug substance stress testing is carried out at a time?	**Single Batch**
12	In which type of formulation the susceptibility of the drug substance to hydrolysis across a wide range of pH values should be evaluated?	**Solution or suspension**
13	How many batches' stability data of drug substance should be provided for registration?	**3**
14	The stability studies should be conducted on the drug substance packaged in a container closure system that is the same as or simulates the packaging proposed for storage and distribution. True or False?	**True**
15	Which type of attributes of drug substance and drug product to be tested for stability study?	**Physical, chemical, biological, and microbiological**
16	How many types of stability testing study are there?	**3**
17	Give the name of types of stability study.	**Long term, Accelerated and Intermeiate**
18	How many times in first year stability testing is carried out on drug substance or product in case of Long term stability testing?	**4 times (every 3 months)**
19	What is the duration of stability testing over the second year in case of long term stability study?	**Every 6 months**
20	What is the duration of stability testing over the third year in case of long term stability study?	**Once Annually**
21	How many minimum time points are there in accelerated stability studies?	**3**
22	What is the total time period for long term stability study in case of drug substance?	**Throughout retest period**
23	Which are the three time points in accelerated stability studies?	**0, 3 & 6 months**

24	What is the total time period for accelerated stability study?	**6 months**
25	How many minimum time points are there in intermediate stability studies?	**4**
26	Which are the four time points in intermediate stability studies?	**0, 6, 9, 12 months**
27	What is the total time period for intermediate stability study?	**12 months**
28	What is the storage condition for long term stability studies of drug substance and drug product in general case?	**25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH**
29	How much minimum time period is covered by long term stability data of drug substance and drug product at the time of submission in general case?	**12 months**
30	What is the storage condition for accelerated stability studies of drug substance and drug product in general case?	**40°C ± 2°C/75% RH ± 5% RH**
31	How much minimum time period is covered by accelerated stability data of drug substance and drug product at the time of submission in general case?	**6 months**
32	What is the storage condition for intermediate stability studies of drug substance and drug product in general case?	**30°C ± 2°C/65% RH ± 5% RH**
33	How much minimum time period is covered by intermediate stability data of drug substance and drug product at the time of submission in general case?	**6 months**
34	What is the storage condition for long term stability studies of drug substance and drug product intended for storage in a refrigerator?	**5°C ± 3°C**
35	How much minimum time period is covered at the time of submission about long term stability data of drug substance intended for storage in a refrigerator?	**12 months**
36	What is the storage condition for accelerated stability studies of drug substance and drug product intended for storage in a refrigerator?	**25°C ± 2°C/60% RH ± 5% RH**
37	How much minimum time period is covered at the time of submission about accelerated stability data of drug substance intended for storage in a refrigerator?	**6 months**
38	What is the storage condition for long term stability studies of drug substance and drug product intended for storage in a freezer?	**- 20°C ± 5°C**
39	How much minimum time period is covered at the time of submission about long term stability data of drug substance intended for storage in a freezer?	**12 months**
40	What should be made when available long term stability data on primary batches do not cover the proposed re-test period granted at the time of approval?	**Commitment**

41	A storage statement should be established for the labeling in accordance with relevant _____ requirements.	**national/regional**
42	Which type of 2 batches of drug product should be selected for stability testing?	**pilot scale batches**
43	Which type of 3rd batch of drug product can be selected for stability testing?	**Smaller than first 2**
44	Which batch of the drug product should be tested for antimicrobial preservative effectiveness at the proposed shelf life for verification purposes?	**Single primary stability batch**
45	What is the total time period for long term stability study in case of drug product?	**Throughout Shelflife**

2) Q1B Stability Testing: Photostability Testing of New Drug Substances and Products

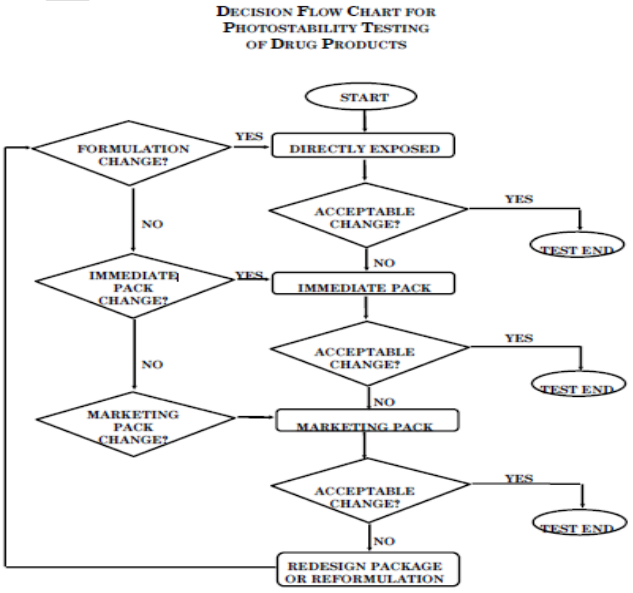
Photostability testing is carried out on a single batch of material selected as described under Selection of Batches in the Parent Guideline.

Under some circumstances these studies should be repeated if certain variations and changes are made to the product (e.g., formulation, packaging).

A systematic approach to photostability testing is recommended covering, as appropriate, studies such as:

1) Tests on the drug substance;
2) Tests on the exposed drug product outside of the immediate pack; and if necessary
3) Tests on the drug product in the immediate pack; and if necessary ;
4) Tests on the drug product in the marketing pack.

The extent of drug product testing should be established by assessing whether or not acceptable change has occurred at the end of the light exposure.



- **Light Sources**

The light sources described below may be used for photostability testing. The applicant should either maintain an appropriate control of temperature to minimize the effect of localized temperature changes or include a dark control in the same environment unless otherwise justified.

Option 1

Any light source that is designed to produce an output similar to the D65/ID65 emission standard such as an artificial daylight fluorescent lamp combining visible and ultraviolet (UV) outputs, xenon, or metal halide lamp.

D65 is the internationally recognized standard for outdoor daylight as defined in ISO 10977 . ID65 is the equivalent indoor indirect daylight standard.

Option 2

For option 2 the same sample should be exposed to both the cool white fluorescent and near ultraviolet lamp.

1. A cool white fluorescent lamp designed to produce an output similar to that specified in ISO 10977(1993) ; and

2. A near UV fluorescent lamp having a spectral distribution from 320 nm to 400 nm with a maximum energy emission between 350 nm and 370 nm.

DRUG SUBSTANCE

For drug substances, photostability testing should consist of two parts:

1) forced degradation testing and
2) confirmatory testing.

The purpose of forced degradation testing studies is to evaluate the overall photosensitivity of the material for method development purposes and/or degradation pathway elucidation.

In these forced degradation studies, a variety of exposure conditions may be used, depending on the photosensitivity of the drug substance involved and the intensity of the light sources used.

For photostable materials, studies may be terminated after an appropriate exposure level has been used.

Confirmatory studies should then be undertaken to provide the information necessary for handling, packaging, and labeling.

Normally, only one batch of drug substance is tested during the development phase, and then the photostability characteristics should be confirmed on a single batch selected as described in the Parent Guideline.

If the drug is clearly photostable or photolabile. If the results of the confirmatory study are equivocal, testing of up to two additional batches should be conducted.

- **Presentation of Samples**
  Care should be taken to ensure that the effects of the changes in physical states of sample such as sublimation, evaporation or melting are minimized.

  Possible interactions between the samples and any material used for containers or for general protection of the sample, should also be considered and eliminated.

  As a direct challenge for samples of solid drug substances, an appropriate amount of sample should be taken and placed in a suitable glass or plastic dish and protected with a suitable transparent cover if considered necessary.

  Solid drug substances should be spread across the container to give a thickness of typically not more than 3 millimeters. Drug substances that are liquids should be exposed in chemically inert and transparent containers.

- **Analysis of Samples**
  At the end of the exposure period, the samples should be examined for any changes in physical properties (e.g., appearance, clarity, or color of solution) and for assay and degradants by a method suitably validated for products.

- **Judgement of Results**
  The forced degradation studies should be designed to provide suitable information to develop and validate test methods for the confirmatory studies.

  The confirmatory studies should identify precautionary measures needed in manufacturing or in formulation of the drug product, and if light resistant packaging is needed.

  When evaluating the results of confirmatory studies to determine whether change due to exposure to light is acceptable, it is important to consider the results from other formal stability studies in order to assure that the drug will be within justified limits at time of use

DRUG PRODUCT

Normally, the studies on drug products should be carried out in a sequential manner starting with testing the fully exposed product then progressing as necessary to the product in the immediate pack and then in the marketing pack.

For some products where it has been demonstrated that the immediate pack is completely impenetrable to light, such as aluminium tubes or cans, testing should normally only be conducted on directly exposed drug product.

- **Presentation of Samples**
  Where practicable when testing samples of the drug product outside of the primary pack, these should be presented in a way similar to the conditions mentioned for the drug

substance. The samples should be positioned to provide maximum area of exposure to the light source. For example, tablets, capsules, etc., should be spread in a single layer.

If testing of the drug product in the immediate container or as marketed is needed, the samples should be placed horizontally or transversely with respect to the light source, whichever provides for the most uniform exposure of the samples.

- **Analysis of Samples**
  At the end of the exposure period, the samples should be examined for any changes in physical properties (e.g., appearance, clarity or color of solution, dissolution/disintegration for dosage forms such as capsules, etc.) and for assay.

  For solid oral dosage form products, testing should be conducted on an appropriately sized composite of, for example, 20 tablets or capsules.

- **Judgement of Results**
  When evaluating the results of photostability studies to determine whether change due to exposure to light is acceptable, it is important to consider the results obtained from other formal stability studies in order to assure that the product will be within proposed specifications during the shelf life.

QUESTION - ANSWER

Sr. No.	Questions	Answer
1	On how many batches photostability testing is carried out?	**Single batch**
2	When photo stability study is repeated?	**if certain variations and changes are made to the product**
3	How many approaches are there for stability testing?	**Four**
4	Light sources used in photostability testing is designed to produce an output similar to _____ emission standards.	**D65/ID65**
5	Which light source is internationally recognized standard for outdoor daylight defined in ISO 10977?	**D65**
6	Which light source is internationally recognized standard for indoor daylight defined in ISO 10977?	**ID65**
7	A cool white fluorescent lamp designed to produce an output similar to that specified in _____.	**ISO 10977(1993)**
8	D65/ID65 are the standard light sources which are specified in _____.	**ISO 10977**
9	What is a spectral distribution of near UV fluorescent lamp?	**320 nm to 400 nm**

10	What is a a maximum energy emission of near UV fluorescent lamp?	**350 nm and 370 nm**
11	How many types of photostability testing are there for drug substance?	**2**
12	Which are the types of photostability testing of drug substance?	**1) forced degradation testing and** **2) confirmatory testing.**