QUALITY ASSURANCE (TWO MARK QUESTIONS)

Unit-1

1. Quality control.

- The purpose of QC is to ensure the safety and efficacy of a finished drug product before released to the public.
- WHO: The sum of all procedures undertaken to ensure the identity and purity of a particular pharmaceutical.
- ISO 9000 defines quality control as "A part of quality management focused on fulfilling quality requirements".

2. Quality assurance

Quality assurance involves taking a proactive approach to ensure drug products are made in accordance with manufacturing standards and met their pre- defined product specifications.

3. ISO 14000

- ISO 14000 is a set of standards created to help companies around the world reduce their adverse impact on the environment.
- It's a framework for improved and more environmentally-conscious quality management systems by organizations large and small.
- ISO 14000 is meant to be a step-by-step guide for establishing and then achieving environmentally-friendly objectives for business practices and products.

4. Tools and elements of Qbd.

Quality by Design (QbD) is a strategic approach employed in various industries, including pharmaceuticals, manufacturing, and product development, to ensure the consistent delivery of high-quality products.
It involves a systematic and proactive process of integrating quality considerations throughout the entire product lifecycle, from conception to production.

TOOLS:

- Prior Knowledge
- Risk Assessment
- Mechanistic Model, Design of Experiments, and Data Analysis
- Process Analytical Technology

ELEMENTS:

- A quality target product profile (QTPP) that identifies the critical quality attributes (CQAs) of the drug product
- Product design and understanding including the identification of critical material Process design and understanding including the identification of critical process parameters (CPPs)
- Product design and understanding including the identification of critical material attributes (CMAs)
- Design space
- A control strategy that includes specifications for the drug substance(s), excipient(s), and drug product as well as controls for each step of the manufacturing process

5. Principles of NABL Accreditation.

- National Accreditation Board for Testing and Calibration Laboratories (NABL) is an accreditation body, with its accreditation system established in accordance with ISO/ IEC 17011.
- NABL has been established with the objective of providing Government, Industry Associations and Industry in general with a scheme of Conformity Assessment Body's accreditation which involves third-party assessment of the technical competence of testing including medical and calibration laboratories, proficiency testing providers and reference material producers.
- Accreditation process details are provided in NABL 100B- Accreditation Process & Procedure.
- Applicable fees details are provided in NABL 100A- General Information Brochure.

6. Purpose of ICH guidelines.

- 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.
- ICH aims to achieve greater harmonization worldwide for the development and approval of safe, effective, and high-quality medicines in the most resource-efficient manner.

7. GMP.

- Good Manufacturing Practice is a set of regulations, codes, and guidelines for the manufacture of drug substances, drug products, medical devices, in vivo and in vitro diagnostic products, and foods.

- A set of principles and procedures which, when followed by manufacturers for therapeutic goods, helps ensure that the products manufacture will have the required quality.

8. Q-series guidelines.

- Harmonization 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.
- Q series includes guidelines from Q1 to Q14 in ICH guidelines.

9. Quality managements.

- In the pharmaceutical industry, the quality department is playing an increasingly pivotal role in running a sustainably profitable business that is also committed to meeting the expectations of the patient and public.
- The implementation of an effective quality management system allows manufacturers to meet their ethical and regulatory obligations.
- It is a good business sense to remove defects, reduce deviation and eliminate waste.
- To achieve the highest level of safety, purity and efficacy of drug products, quality management teams are moving beyond quality control (QC) and into Quality assurance (QA).

10. Elements of TQM.

The elements of TQM are customer focus, leadership, employee involvement, process improvement, continuous learning, supplier partnerships, strategic planning, and data-driven decision-making.

11. ISO 9000

ISO 9000 is a series of international standards concerning quality management and assurance developed to help organizations establish and maintain an effective quality management system (QMS). The standards can help business entities fulfill regulatory requirements, improve continuously, and ensure customer satisfaction.

12. Total quality management.

According to ISO, TQM is defined as: "A management approach of 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 society."

13. ICH.

- "International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use".
- 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.

14. cGMP.

- cGMP refers to the Current Good Manufacturing Practice regulations enforced by the US Food and Drug Administration (FDA).
- cGMP provides for systems that assure proper design, monitoring and control of manufacturing processes and facilities.
- Adherence to the cGMP regulations assures the identity, strength, quality and purity of drug products by requiring that manufacturers of medications adequately control manufacturing operations

Unit-2

1. Purchase specifications.

- The specification is the total description of the purchase.
- The purpose of any specification is to provide purchasing personnel with clear guidelines to purchasing, and to provide vendors with firm criteria of minimum product or service acceptability. Success of the purchasing activity relies on the specification being a true and accurate statement of the buyer's requirements.
- A specification may include requirements for testing, inspection or preparing an item for delivery, or preparing or installing it for use, requirements for samples, descriptive literature, warranty, and packing.

2. Personal records.

It maintains

- The minimum health requirement of personnel working in the factory must be given in writing.
- A pre- employment medical examination inclusive of eye- testing must be insisted.
- Periodic health check-ups should be carried to all personnel's.
- Special attention to be paid to persons with any communicable disease.
- Employees went for medical leave should submit a medical certificate from medical officer /nurse before join to work.
- Staffs should report about any infectious diseases of their (or) of the family enabling their temporary transfer to other work areas.

3. Control of contamination.

- Air is main source of contamination and so the prevention of dust particle in air can also cause the control of number of microorganisms
- This can be achieved by series of treatments or by air cleaning It must be done as follows:
- Air first must be passed through primary filter mad of glass or wool. This primary filter must remove the larger particles. Next pass through a passage narrowing electrostatic precipitator
- Finally, the air is passed through HEPA filter and thus it may filter up to the particle size of 0.3 microns and may remove with better efficiency.
- Direction of air flow is horizontal or vertical. The laminar flow may be carried out and it may sweep the enterer confined area with uniform velocity with maximum eddies.

4. Roles of head of production department

- To ensure that products are produced and stored according to the appropriate documentation in order to obtain the required quality.
- To approve the instructions relating to production operations and to ensure their strict implementation.
- To ensure that the production records are evaluated and signed by an authorized person before they are sent to the Quality Control Department

- To check the maintenance of his department, premises and equipment.
- To ensure that the appropriate validations are done.
- To ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.

5. Raw materials

- "It is defined as the starting material used in manufacturing of finished product".
- Raw materials including ingredients, processing aids, and packaging, are the foundation of finished food products.
- As such, they must meet not only your specifications, but also regulatory requirements.

6. Training

The manufacturer should provide training for all the personnel whose duties take them into production areas or into control laboratories (including the technical, maintenance and cleaning personnel), and for other personnel whose activities could affect the quality of the product.
Training of employees:

- Training may also be defined as the acquisition of technology which permits employees to perform their present jobs to standards.
- It involves human performance on the job, the employee is presently doing or is being hired to do.
- “A person is called trained person when he has appropriate knowledge, skill & attitude”

7. Personnel hygiene

- Good personal hygiene is required in pharmaceutical industries to safeguard the product and avoid any type of contamination that affects quality of medicinal product.
- Detailed hygiene programs should be established and adapted to the different needs within the factory.
- They should include procedures relating to the health, hygiene practices and clothing of personnel.

- These procedures should be understood and followed in a very strict way by every person whose duties take him into the production and control areas.

8. Sanitation

As per GMP guidelines, Sanitation says; "Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a clean and sanitary condition"

Sanitation is the reduction of microbiological contamination. It is usually achieved by the use of chemicals.

Sanitation is the process of

- Removal of dust and dirt and other waste materials
- Minimizing the risk of cross contamination between different products in the same area
- Reducing the number of microorganisms in work areas
- Controlling pests so that these do not affect the quality of materials to be used in the manufacturing of drugs.

9. Environmental control

Thermal pollution control:

Various off stream cooling system are required to handle thermal discharge from process. There different ways for controlling thermal pollution.

- Wet cooling towers
- Dry cooling towers

Water pollution:

There is a great problem to handling a liquid waste effluent is more complex than gas effluent. The treatment could be done by

- Physical treatment
- Chemical treatment

- Biological treatment

Air control:

There are two major categories:

- Those suitable for removing particulate matter
- Those associated with removing gaseous pollutant
- Removed by chemical And Physical way

10. Maintenance of sterile area

Sterile products are manufactured in the area specially designed and maintained. Since most of the sterile products are injected directly into human body, it must be very careful in designing and maintaining sterile area.

Sterile area provided for manufacturing of sterile products are given below:

- Equipment and component washing area
- Water for injection preparation and compounding area
- Filling and sealing area
- Multiple air lock entrance
- Sterilization area containers visual examination area
- Quarantine area

Filling and sealing area must be separated from other areas in such a way that aseptic condition is maintained by sealing the partitions.

Floors of the areas must be hard, smooth, impervious It should not affect by detergents and disinfectants.

Walls and ceiling materials should be smooth and low particle shedding and easy to clean.

Air locks should provide air seals to provides pressurization of aseptic room.

11. Mix-up

Mix ups can be defined as presence of undesired material into desirable material, which can generally be visibly seen.
Ex: Paracetamol mixes with diclofenac
Tablet of one product into another, which having different size, shape.

12. Cross contamination

Contamination of starting material or intermediates or finished product by another material or product during the production is called as cross-contamination.

Ex:- Fine dust of one product into another product

13. Responsibilities of the Head of Quality Control Department

- To approve or reject, as he sees fit, starting materials, packaging materials, and intermediate, bulk and finished products.
- To evaluate batch records.
- To ensure that all necessary testing is carried out
- To approve specifications, sampling instructions, test methods and other Quality Control procedures
- To approve and monitor any contract analysts
- To check the maintenance of his department, premises and equipment
- To ensure that the appropriate validations are done
- To ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.

14. Responsibilities of the Head of the quality assurance Department

- Establish Quality Assurance Procedures.
- Direct Quality Control Personnel.
- Report Quality Issues to Production Management Personnel.
- Maintain Quality Assurance Records.
- Analyse Production and Quality Control Reports.
- Responsible for Defining QA strategy, approach and execution in development projects.
- Responsible for Leading and directing the QA leadership team.
- Monitoring of all the QA activities, test results, leaked defects, root cause analysis and identifying areas of improvement. Implement steps required to improve the processes.
- Manage training and continuous learning of QA staff by means of short courses, conferences, meetups, certifications, etc.
- Provide technical expertise in Test Automation, Testing Methodologies, Testing Processes, Tools and Techniques across the teams.

Unit-3

1. Non clinical laboratory

- Nonclinical laboratory study means in vivo or in vitro experiments in which test articles are studied prospectively in test systems under laboratory conditions to determine their safety.
- The term does not include studies utilizing human subjects or clinical studies or field trials in animals.
- The term does not include basic exploratory studies carried out to determine whether a test article has any potential utility or to determine physical or chemical characteristics of a test article.

2. General provision of GLP.

- It prescribes GLP for conducting non-clinical laboratory studies that support research and marketing permits of products regulated by FDA.
- Applicability to studies performed under grants and contracts.
- Inspection of the testing facility.

3. Secondary packing materials

- Secondary packaging is outside the primary packaging - used to group primary packages together.
- Secondary packaging designates the packaging used to group various pre-packaged products together. As secondary packaging is not in direct contact with the actual product, its use and application usually differ distinctly from those of primary packaging, although the purpose of both types may at times converge.
- Ex: paper, paperboard, cardboard and cartons.

4. Test and Control articles

- Test article means any food additive, colour additive, drug, biological product, electronic product, medical device for human use, or any other article subject to regulation under the act or under sections 351 and 354–360F of the Public Health Service Act.
- Control article means any food additive, colour additive, drug, biological product, electronic product, medical device for human use, or any article other than a test article, feed, or water that is administered to the test system in the course of a nonclinical laboratory study for the purpose of establishing a basis for comparison with the test article.

5. Hydrolytic resistance test for glass containers

- This test is used only with containers that have been exposed to Sulphur dioxide fumes under controlled humidity conditions. Such a treatment neutralizes the

surface alkali. Now the glass becomes chemically more resistant.

- The principle involved in the water attack test is to determine whether the alkali leached form the surface of a container is within the specified limits or not.
- Since the inner surface is under test entire container (ampoule) has to be used.
- The amount of acid that is necessary to neutralize the released alkali from the surface is estimated, the leaching of alkali is accelerated using elevated temperature for a specified time.
- Methyl red indicator is used to determine the end point. The basic is acid-base titration.

6. Test system

- The OECD GLP Principles define a test system as an "apparatus used for the generation of physical/chemical data". It is the equipment or apparatus to which the test item or reference item is applied during the conduct of a study.
- Physical, chemical and biological test systems are there.
- Test system means any animal, plant, microorganism, or subparts thereof to which the test or control article is administered or added for study.

7. GLP

In 1981 an organization named OECD (Organization for Economic Co-operation and Development) produced GLP principles that are international standard of the OECD Council
Good Laboratory Practice (GLP) is a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.
Principles of Good Laboratory Practice apply to all non-clinical health and environmental safety studies as required by regulations for the purpose of registering or licensing of:

- pharmaceuticals,
- pesticides,
- food additives
- feed additives,
- cosmetic products,
- veterinary drug products and similar products,
- biocides,
- Industrial chemicals.

8. CPCSEA guidelines.

Committee for Control and Supervision of Experiments on Animals (CCSEA) is constituted under the Prevention of Cruelty to Animals (PCA) Act, 1960. CCSEA is duty bound to take all such measures as may be necessary to ensure that animals are not

subjected to unnecessary pain or suffering before, during or after performance of experiments on them.
The main functions of CCSEA are:

- Registration of establishments conducting animal experimentation or breeding of animals for this purpose.
- Approval of Animal House Facilities on the basis of reports of inspections conducted by CCSEA.s
- Permission for conducting experiments involving use of animals.
- Conduct / Support of Conference / workshop on Animal Ethics.

9. Quality assurance unit

Quality assurance unit means any person or organizational element, except the study director, designated by testing facility management to perform the duties relating to quality assurance of nonclinical laboratory studies.

Unit-4

1. Master formula records.

- "A document or set of documents specifying the starting materials with their quantities and the packaging materials, together with a description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process controls."
- There shall be Master Formula records relating to all manufacturing procedures for each product and batch size to be manufactured. These shall be prepared and endorsed by the competent technical staff i.e. head of production and quality control.

2. Quality audit.

- The audit in simple terms could be defined as the inspection of a process or a system to ensure that it meets the requirements of its intended use.
- International organization for standardization (ISO) defines the audits as "Systematic, independent and documented process for obtaining audit evidence and evaluating them objectively to determine the degree to which the verification criteria are met"
- In the pharmaceutical industry, audits are virtual means for assessing compliance with the established objectives defined in the quality system and thus paving the way for the continuous improvement program by providing feedback to management.

3. Handling of return good.

Bulk/ finished product when sent back to Manufacturer, distributor, importer is known as returned goods

- Approved written procedures for holding, testing, reprocessing of returned products to be followed
- Records of such products be maintained, name, label potency, lot/batch no., reason of return, quantity returned, date of disposition, ultimate disposition
- Proper identification & placed under quarantine
- Should be destroyed if quality is unsatisfactory- packaging, labelling, container, carton etc creates doubt about safety, identity, strength, quality, or purity
- After critical assessment the QC of goods like testing for purity, strength, identity, safety, etc may be taken for resale or relabelling. Actions should be recorded in writing.
- If it looks that the returned products involve some related batches also then such reference sample from such batches shall be investigated

4. SOP.

Standard Operating Procedure (SOP) is a set of written instructions that document a routine or repetitive activity.
The process if SOP includes

1. SOP preparation
2. SOP review and approval
3. Frequency of revisions and reviews
4. Implementing SOP
5. Management of SOP

Benefits of SOP

- To ensure that processes continue uninterrupted and are completed on a prescribed schedule.
- To ensure that no failures occur in manufacturing and other processes
- To ensure that approved procedures are followed in compliance with company and government regulations.
- To serve as a training document for teaching users about the process.
- To serve as a checklist for co-workers and auditors.
- To serve as an historical record for the changeover.
- To serve as an explanation in review of accident investigations.

5. Waste disposal

- Return to Manufacturer: The unused drugs with disposal problems like Anti-cancer or which have nearby expiry are returned
- Landfill: For solid waste, old method to place waste directly to land.
- Waste immobilization (encapsulation): Immobilization of waste in plastic or steel drums is done before disposing. Cleaning of drums later must be done adequately to prevent traces of materials

- Waste inertization: Remove Packaging materials → Remove dosage forms ex. Blister pack→ Add water+cement+lime →Grind → homogenous paste → transport to landfill
- Sewer: For large qty's of Liquid dosage forms: Syrups, IV fluids, dilute with water → Flush in small qty's over a period of time For Small qty's after dilution can be flushed by fast flowing water
- Medium temperature incineration: High Temp. incinerators are used for more than 1% halogenated compounds. Medium temperature furnaces operating at min. 850°C used to treat expired solid dosage forms.

6. Quality review.

- A Quality Review is a record of the performance against Quality Goal at regular intervals.
- A Quality Review is an inspection with a specific structure, defined roles, and procedure designed to ensure a product's completeness and adherence to quality standards.

7. Evaluation of complaints.

- Evaluation steps: Receiving, Investigating, Root Analysis of cause, Handling, Recording.
- Complaint thru email/ toll free number etc.
- Open the investigation form that includes customer personal details like name, address etc.
- Information about the complaint related to product ex. Batch no., lot no., product name, Mfg. & expiry date etc.
- Maintain complete documentation
- Decide the proper remedy Interdisciplinary teams required
- Record the complaint: product detail, type of defect, testing retention samples, review of batch production, distribution records etc

8. Distribution records.

Distribution records are written data related to distribution of drug products from the manufacturer to the distributors.
The complete data regarding all batches of drug products should be maintained.
Objectives:

- To immediately recall, investigate or to take remedial measure against the defective product.
- Maintenance of records of finished product is essential to facilitate complete recall of batch if necessary.
- investigate or to take remedial measure against the defective product.

9. Batch manufacturing record

- Batch manufacturing record is a written document from the batch that is prepared during the pharmaceutical manufacturing process.
- It contains actual data of the batch manufacturing and whole manufacturing process step by step.
- All stages are included in the batch manufacturing record from the issuance of the raw material to the final packaging.
- Every batch has a separate BMR having the batch history of batch production.
- Documents and the proofs are attached to the BMR during the manufacturing process.

10. Product recall

- Recalling means withdrawing or removing the product from distribution network as of quality issues/ adverse drug reactions.
- Recall can be done by Manufacturer or distributor.

Types of recall:
Class I: Probability that product may cause serious adverse health issues/ death
Class II: Product may cause temporary Adverse health issues or serious adverse health issues are remote
Class III: Product may not cause any adverse health consequences

11. Complaints

- A statement that says something is unsatisfactory or unacceptable about the product/ packaging in terms of any defect in pharmaceutical product
- May be received from Pharmacists, Physicians, wholesalers, Retailers, Patients. Therefore, as per GMP, Industry has their own procedures to maintain records, investigation and review steps of complaints & accordingly a system to recall the product from the market.

12. Types of quality audit

Quality audits are performed to verify the effectiveness of a quality management system. The quality audit system mainly classified in three different categories:

- Internal Audits
- External Audits
- Regulatory Audits

Internal audit:
This type of audit is also known as First-Party Audit or self-audit. Those auditing and those being audited all belong to the same organization. Internal audit is a professional

activity that consists of advising organizations on how to achieve their goals in a better way.

External audit:
This type of audit is also known as Second-Party Audit. It refers to a customer conducting an audit on a supplier or contractor.

Regulatory Audits:
This type of audit is also known as Third-Party Audit. Neither customer nor supplier conducts this type of audit. A regulatory agency or independent body conducts a third-party audit for compliance or certification or registration purposes.

Unit-5

1. Validation master plan.

- Validation in general requires a meticulous preparation and careful planning of the various steps in the process.
- It should provide an overview of the entire validation operation its organizational structure, its content and planning.
- It should be a summary document and should therefore be brief, concise and clear.
- It is a document that summaries the firm's overall philosophy intentions and approach to be used for establishing performance adequacy.

2. Good warehousing practice.

- Good warehousing practices (GWP) means storing supplies so that products are always available, accessible, and in good condition.
- A suitable space is provided to raw material, handling of raw & packaging materials required for manufacturing, including packaging of pharmaceuticals.
- Maintaining proper storage condition for pharmaceutical products and paramedical is vital to ensure their quality, safety and efficacy.

3. Materials management.

- According to The International Federation of Purchasing and Materials Management defines material management as "A total concept having its definite organization to plan and control all types of materials, its supply, and its flow from raw stage to finished stage so as to deliver the product to customer as per his requirements in time.
- This involves materials planning, purchasing, receiving, storing, inventory control, scheduling, production, physical distribution and marketing.

4. Calibration

- Calibration is a process that demonstrates a particular instrument or device produces results within specified limits, as compared to those produced by a definite standard over an appropriate range of measurements.
- Calibration is the process of adjusting an instrument or equipment to meet the manufacturer's specification.
- Calibration is performed using primary reference standard.

5. Types of validation.

- Process Validation
- Method Validation
- Equipment validation
- Cleaning Validation
- Computerized system validation

- Process validation: The collection of data from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products.

- Method validation: Method validation is the process to confirm that the analytical procedure employed for a specific test is suitable for its intended use. The method needs to be validated or revalidated.

- Equipment validation: Action of proving of providing that any equipment works correctly and leads to the expected results is equipment qualification. It is not single step activity but instead result from many activities.

- Cleaning validation: A process of attaining and document in sufficient evidence to give reasonable assurance, given the current state of science and technology, that the cleaning process under consideration does, and/or will do, what it purpose to do."

- Computer system validation: In the context of drug manufacturing, CSV involves validating the computer systems (software and hardware) used in critical processes to ensure data integrity, security, and reliability.

6. User requirement specification.

- User Requirement Specification (URS) is a list of all requirements of buyer regarding the equipment to be purchased.
- URS is prepared by the equipment user department.
- It is sent to equipment manufacturer to make it as desired criteria.

7. Factory acceptance test.

- A Factory Acceptance Test (FAT) follows the qualification stage of the design qualification (DQ) and it includes a series of testing done on equipment, carried out at the system manufacturer's site in order to verify that the vendor has accomplished responsibilities and regulatory and client user requirements.
- The primary reasons for implementing a FAT include: convincing customers that they are purchasing high quality equipment/system; ensuring that every component and control work accordingly to its functionality; saving effort, time and money; and evaluating if the equipment operates in accordance with design specifications.

8. Process validation.

As per FDA Nov 2008, 'The collection of data from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products.

Types of Process validation:
- Prospective validation
- Retrospective validation
- Concurrent validation
- Revalidation

9. Precision

The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple sampling of a homogenous sample.
Precision is the measure of the degree of repeatability of an analytical method under normal operation and is normally expressed as the percent relative standard deviation (%RSD) or the coefficient of variation (% CV) for a statistically significant number of samples.

According to the ICH, precision should be performed at three different levels:

- repeatability,
- intermediate precision, and
- reproducibility.

10. LOD

The limit of detection (LOD) is defined as the lowest concentration of an analyte in a sample that can be detected, not quantitated.

$$LOD = 3.3\sigma / S$$

Here σ is the standard deviation of the response and S is the slope of the calibration curve.

11. LOQ

The limit of quantitation (LOQ) is defined as the lowest concentration of an analyte in a sample that can be determined with acceptable precision and accuracy under the stated operating conditions of the method.

$$LOQ = 10\sigma / S$$

Here σ is the standard deviation of the response and S is the slope of the calibration curve.

12. Validation

- Food and drug administration (FDA): Establishing documented evidence that establishes a high degree of certainty that a particular process will consistently produce a product meeting its pre-determined specifications and quality attributes.

- World health organization (WHO): Action of providing that any procedure, process, equipment, material, activity, or system actually leads to the expected results.

- ISO: Validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled.

- European committee (EC): Action of providing in accordance with the principles of good manufacturing practice that any procedure, processes, equipment material, activity or system actually leads to the expected results. In brief validation is a process for effective Quality Assurance.

13. Qualification

It is the action of proving and documenting that equipment or ancillary systems are

properly installed, work correctly and actually lead to the expected results.
Activities have been grouped into four phases:

- Design Qualification (DQ)
- Installation Qualification (IQ)
- Operational Qualification (OQ)
- Performance Qualification (PQ)

14. Accuracy

- It is defined as the closeness of agreement between the actual (true) value and means an analytical value obtained by applying a test method number of times.
- Spike and recovery studies are performed to measure accuracy; a known sample is added to the excipients and the actual drug value is compared to the value found by the assay.
- Accuracy is expressed as the bias or the % error between the observed value and the true value (assay value/actual value x 100 %.)
- The accuracy is acceptable if the difference between the true value and mean measured value does not exceed the RSD values obtained for the repeatability of the method.

15. Cleaning validation

A process of attaining and document in sufficient evidence to give reasonable assurance, given the current state of science and technology, that the cleaning process under consideration does, and/or will do, what it purposes to do." Objective:
• To minimize cross contamination.
• To determine efficiency of cleaning process
• To do troubleshooting in case problem identified in the cleaning process and give suggestions to improve the process

16. Revalidation

- Revalidation provides the evidence that changes in a process and / or the process environment, introduced either intentionally or unintentionally, do not adversely affect process characteristics and product quality.
- This approach is essential to maintain the validated status of the plant, equipment, manufacturing processes and computer systems.
- Categories:
  Re-validation in cases of known change (including transfer of processes from one company to another or from one site to another)
  Periodic Re-validation is carried out at scheduled intervals.

17. Site Acceptance Test (SAT)

- A Site Acceptance Test (SAT) is the qualification stage followed by the FAT and it includes a series of testing done on equipment, carried out at the owner representative site.
- The SAT provides documented evidence that the equipment/system has been delivered in good condition and has not been affected by the transportation.