PHARMACEUTICAL QUALITY ASSURANCE

UNIT 5 NOTES

CALIBRATION & VALIDATION

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CALIBRATION

- Calibration is the process of checking & adjusting an instrument to ensure it gives accurate & correct redings by comparing it with a standard reference.
- It simply means checking whether an instrument is giving the right value or not.

PRINCIPLE OF CALIBRATION

- The basic principle of calibration involves comparison with a standard:
  - Instrument reading is compared with a known standard value
    The difference (error) is calculated
  - If required, the instrument is adjusted to correct the error.

NEED OF CALIBRATION

- To ensure correct measurement results.
- To maintain consistency in production.
- To avoid defective products.
- To meet regulatory requirements
- To ensure proper functioning of instruments.

Scope Of Calibration

- Calibration applies to all instruments used in:
- Production area (e.g temperature, pressure devices)
- Quality Control Laboratory (e.g, pH meter, HPLC)
- Quality Assurance (QA) activities
- Warehousing (e.g, humidity, & temperature monitoring)
- Research & Development (R&D)

Calibration Procedure

- First identify the instrument to be callibrated & Check ID
- Use a certified standard with a known accurate value for comparison.
- Take readings using the instrument.
- Compare the observed readings with the standards.
- Determine the deviation b/w the observed value & the standard value.
- Adjust the instrument, if needed.
- Record all data.
- Attach a calibration label.

Importance Of Calibration

- Ensures accurate & reliable measurements.
- Maintains quality of p'ceutical products.
- Helps in compliance with GMP/GLP guidelines.
- Reduces errors in manufacturing & testing
- Ensures patient safety
- Prevents batch rejection & financial loss

Calibration Of pH Meter

- Calibration of pH meter is the process of adjusting the instrument using standard buffer solutions to ensure it gives accurate pH readings.

Principle

- The pH meter is callibrated by comparing its readings with standard buffer solutions to know pH values (usually pH 4, 7 & 9.2/10).
- The instrument is adjusted until it shows the correct pH.

Materials Required

- pH meter
- Standard buffer solutions (pH 4, 7, 9.2/10)
- Distilled Water
- Tissue paper (for drying electrode)

Procedure

① Preparation Of Instrument

- Switch on the pH meter & allow it to stabilize.
- Ensure the electrode is clean & in good condition.
- Rinse the electrode with distilled water & gently dry using tissue paper (don't rub).

② Calibration With pH 7 Buffer

- Immerse the electrode in pH 7 buffer soln.
- Allow the reading to stabilize.
- If pH ready 7, accept; if not adjust the meter to show exactly pH 7.

③ Calibration With pH 9.2/10 Buffer

- Rinse the electrode.
- Dip in alkaline buffer (pH 9.2 or 10)
- Adjust the reading accordingly.

④ Final Check

- Confirm calibration by rechecking with buffer solutions.
- After that pH meter will ready to measure pH of other substances.

VALIDATION

- Validation is the process of establishing documented evidence that a process, method or system consistently working according as required.
- In simple words validation means proving that a processes work correctly every time.

PRINCIPLE OF VALIDATION

- The basic principle of validation is 'A process should consistently produce a product that meets predeterminated specifications & quality attributes'.
- It includes:
  - Documented evidence
  - Consistency & reproductibility of results.
  - Comparison with predefined acceptance criteria.
  - Following a systematic & scientific approach.
  - Identification & Control of any variation.

PURPOSE OF VALIDATION

- To ensure consistent product quality
- To meet regulatory requirements (GMP, GLP)
- To reduce risk of errors & failures
- To ensure safety & efficacy of drugs.

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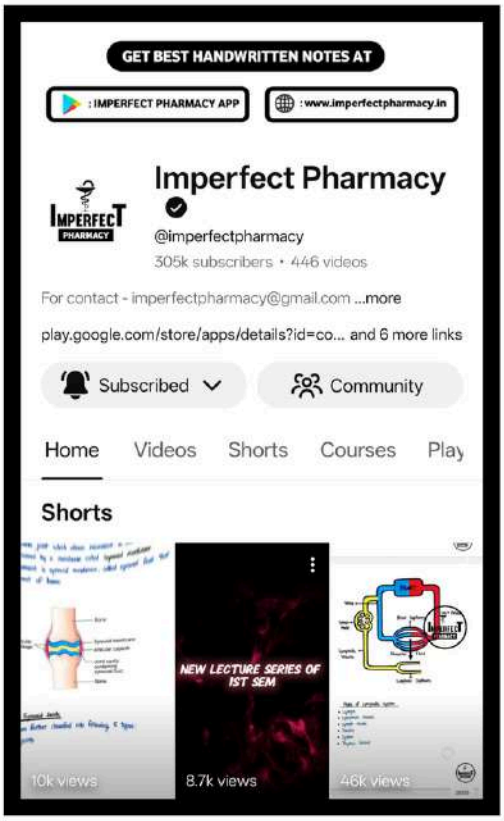

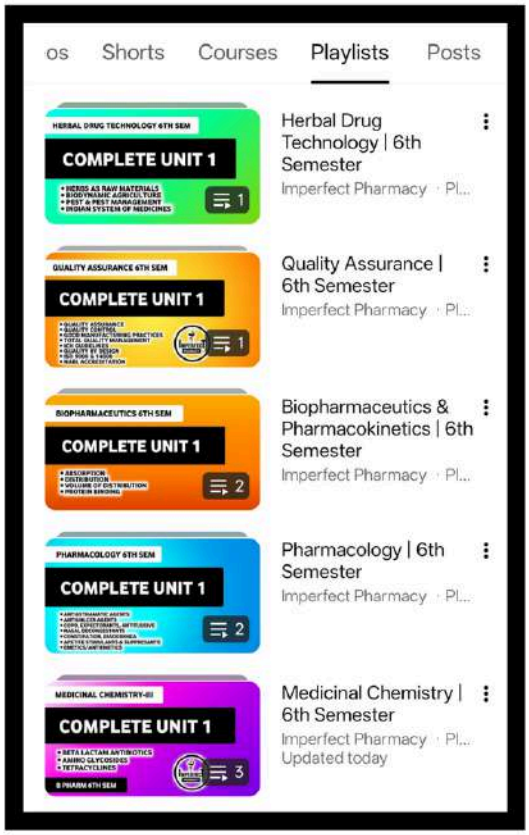

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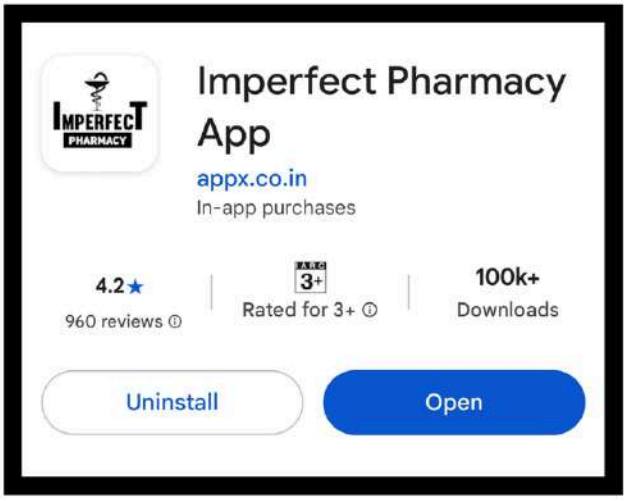

TYPES OF VALIDATION

1. Prospective Validation
2. Concurrent Validation
3. Retrospective Validation
4. Revalidation

1. PROSPECTIVE VALIDATION

- It is performed before starting routine production.
- Done during process development stage.
- Ensures processes is capable of producing desired results.
- Examples: Validating a new tablet manufacturing process before market validation.

2. CONCURRENT VALIDATION

- It is performed during actual production.
- Data is collected while manufacturing is ongoing.
- Generally used when prospective validation is not possible.
- Example: Monitoring first few batches during production.

3. RETROSPECTIVE VALIDATION

- It is based on past production data
- Uses historical records to evaluate process consistency.
- Applicable for well-established processes
- Example: Reviewing previous batch records to confirm consistency.

④ **REVALIDATION**

- It is performed when where are changes in process, equipment or materials
- It ensures that changes don't affect product quality.
- Example: Change in formulation or machine.

SCOPE OF VALIDATION

- The scope of validation includes all activities in p'ceutical industry that can affect product quality, safety & consistency.
- It involves:

① Process validation
② Equipment Validation (Qualification)
③ Analytical Method Validation
④ Cleaning Validation
⑤ Utility & Facilities Validation
⑥ Computer System Validation

IMPORTANCE OF VALIDATION

- Provides assurance of quality & consistency
- Reduces batch failures & rework
- Improves efficiency of manufacturing
- Builds confidence in processes & data.
- Required for regulatory approval

QUALIFICATION

- Qualification is the process of proving & documenting that equipment, systems or facilities are properly installed, working correctly & suitable for intended use.
- It simply means ensuring that equipment / system works properly as expected.
- Qualification is generally related with instruments.

PURPOSE OF QUALIFICATION

- To ensure equipment performs correctly
- To maintain product quality & safety
- To comply with GMP requirements
- To avoid errors in manufacturing
- To ensure consistent performance.

TYPES OF QUALIFICATION

It is mainly classified into 4 types:

① Design Qualification (DQ)
② Installation Qualification (IQ)
③ Operational Qualification (OQ)
④ Performance Qualification (PQ)

① DESIGN QUALIFICATION

- It ensures that the design of equipment/ system is suitable for its intended purpose.
- It is performed before purchasing or installation.
- Example: Before buying a tablet machine, check whether its capacity, material & features meet production requirements.

② INSTALLATION QUALIFICATION

- It confirms that the equipment is installed correctly as per design & manufacturing guidelines.
- It ensures that all components, parts & connections are properly fitted.
- Example: Checking whether a machine is installed properly with correct wiring, parts & documentation.

③ OPERATIONAL QUALIFICATION

- It verifies that the equipment operators correctly under different operating conditions.
- It involves testing all functions, controls, alarms & safety features.
- Example: Running a machine at different speeds & temperatures to check proper manufacturing.

④ Performance Qualification

- It confirms that the equipment consistently performs effectively under actual working conditions.
- It involves testing during routine production.
- It ensures that the equipment produces consistent & quality output.
- Example: Producing multiple batches of tablets & checking their quality & uniformity.

Importance Of Qualification

- It confirms equipment whether is fit for use or not.
- Reduces risk of failure
- Ensures reliable production process
- Required for regulatory approval.

UV - VISIBLE SPETROPHOTOMETER

UV - Visible Spectrophotometer is an analytical instrument used to measure the absorption of ultravoilet (200- 400 nm) & visible (400- 800 nm) light by a substance.

PRINCIPLE

- UV- visible spectroscopy measures how much light a sample absorbs or transmitts at specific wavelengths.
- The amount of light absorbs is related to the concentration of the absorbing species.

INSTRUMENTATION

The essential part in instrumentation of UV- Visible Spectroscopy, includes:

- Light Sources
- Monochromator
- Sample Holder
- Detector
- Recorder

Qualification Of UV - Visible Spectrophotometer

Qualification of UV - Visible Spectrophotometer is the process of ensuring that the instrument is properly installed, operates correctly, & gives accurate and reliable results.

Stages Of Qualification

Qualification should be performed in 4 stages :

1. DQ of UV - Visible Spectrophotometer
2. IQ of UV - Visible Spectrophotometer
3. OQ of UV - Visible Spectrophotometer
4. PQ of UV - Visible Spectrophotometer

① Design Qualification

- It confirms that the design & specification of UV - Visible spectrophotometer meet the intended analytical requirements.
- It involves checking parameters like wavelength range (200-800nm), accuracy, resolution & software features.

② Installation Qualification

- It verifies that the UV - Visible Spectrophotometer is installed correctly as per manufacturer guidelines.
- It checks :
  - Proper installation of components
  - Availability of utilities (power supply)
  - Manuals & documents.

③ Operational Qualification

- It ensures that the UV - Visible Spectrophotometer operates properly within specified limits.
- It includes tests such as:
  - Wavelenght accuracy
  - Photometric accuracy
  - Stray (Unwanted) light test
  - Resolution Test

④ Performance Qualification

- It confirms that the instrument performs consistently during routine use.
- It involves:
  - Analysis of standards samples
  - Checking reproductibility & accuracy

Analytical Method Validation

- Analytical method validation is the process of proving that an analytical / testing method is suitable, reliable & accurate for its intended purpose.
- It ensures that the test method gives correct & consistent results.

Purpose

- To ensure accuracy & reliability of test results.
- To confirm this method is fit for intended use.
- To meet regulatory requirements (ICH, GMP)
- To maintain quality control of drugs.

Parameters Of AMV

- Accuracy
- Precision
- Specificity
- Linearity
- Range
- Limit of Detection
- Limit of Quantitation
- Robustness

① Accuracy

- Accuracy means how close your result it to the true value.
- If the actual value is 100 & your results is 99 or 101 → it is accurate.
- It is checked by using standard / reference samples.

② Precision

- Precision means same result again & again when test is repeated.
- It shows consistency of the method.

③ Specificity

- It is the ability to measure only the required drug (analyte) without interference.
- Other substances like impurities, excipients should not affect result.

④ Linearity

- It shows that result is directly proportional to concentration.
- If concentration doubles → absorbance should also increase proportionally.

⑤ Range

- Range is the minimum to maximum concentration where method works properly.
- Within this range, method gives accurate & precise results.

⑥ Limit Of Detection

- It represents lowest amount of drug that can be detected but not accurately measured.
- Example: Drug present at 0.01 mg can be detected but not quantified properly.

⑦ Limit Of Quantification

- Lowest amount that can be measured accurately & precisely.
- Example: Drug at 0.05 mg can be measured with accuracy & precision.

⑧ Robustness

- Ability of method to remain unaffected by small changes.
- Example: Slight change in temperature, pH or wavelength.

VALIDATION MASTER PLAN

- Validation Master Plan (VMP) is a document that provides an overall plan & strategy for all validation activities in a pharmaceutical facility.
- It provides roadmap for all validation activities in a company.

PURPOSE OF VMP

- To define how validation will be carried out
- To ensure systematic & organized validation activities
- To meet regulatory requirements (GMP)
- To maintain consistency in validation approach
- To assign roles & responsibilities
- To ensure proper documentation & control

GUIDELINES OF VMP

- VMP should be well-structured & clearly written
- It should be approved by Quality Assurance (QA)
- It must follow GMP & regulatory guidelines
- All validations activities should be planned & documented
- It should define roles & responsibilities clearly
- It should be periodically reviewed & updated.

Content Of VMP

- Introduction: Title page with Document No. & Version info
- Scope: Areas covered: Process, Equipment, Cleaning etc.
- Responsibilities: Roles of QA, QC, Production Department etc.
- Validation Policy: Company's approach & strategy.
- List of Equipments / System: Items requiring validation
- Documentation: Validation Protocols, Validation Reports etc.
- Change Control: Handling changes in system/process.

Importance Of VMP

- It acts as a guideline for all validation activities
- Ensures proper planning & execution
- It helps in regulatory inspections
- Improves quality assurance system

WAREHOUSING

Warehousing is the process of storing raw materials, packaging materials & finished products under suitable conditions to maintain their quality, safety & identity until use or distribution.

TYPES OF WAREHOUSES

- Raw Material Store: For storing APIs & excipients
- Packeging Material Store: For packeging Materials
- Finished Goods Store: For final products
- Quarantine Area: For materials under testing
- Rejected Area: For rejected or damaged materials
- Returned Goods Area: For returned products
- Cold Storage Area: For temperature - sensitive products

Good Warehousing Practices

Good Warehousing Practices (GWP) are a set of guidelines that ensure proper storage, handling & distribution of pharmaceutical products so that their quality, safety & efficacy are maintained.

Objectives Of GWP

- To maintain product quality during storage
- To prevent contamination, mix-ups & damage
- To ensure proper stock control & traceability
- To comply with regulatory requirements

Elements Of GWP

① Warehouse Design & Layout

- Warehouse should be clean, well-ventilated & properly constructed.
- It must have adequate space for storage & movement.
- It should have separate areas for:
  - Raw Materials
  - Finished Products
  - Rejected / returned goods
  - Quarantine materials
  - Proper lighting

② Environmental Control

- Maintain required temperature & humidity.
- Use of air conditioning, refrigeration if needed.
- Environment should be continuously monitored using calibrated instruments.

③ Storage Conditions

- Products stored as per label instructions.
- There should be proper racks.
- There should be special storage for sensitive products.

④ Stock Management

- Follow FIFO (First in First out) & FEFO (First Expiry First out)
- There should be proper labelling of all materials.
- Avoid overstocking & stock-outs

⑤ Material Handling

- Carefully load / unload materials to avoid damage.
- Use of proper equipment for transportation (such as trolleys).
- Avoid mix-ups & cross-contamination.
- Materials should be handled by trained professionals.

⑥ Documentation & Records

- Maintain records such as :
  - Good reciepts records
  - Stock registers
  - Distribution records

⑦ Security & Safety

- Access should be restricted to authorized personnel only
- There should be protection against theft & unauthorized entry (alarm).

⑧ Handling Of Returned/Expired Goods

- There should be separate storage area for returned/ expired products & it must be clearly labelled.
- Return goods should be properly investigated.
- Expired products should be disposed as per guidelines.

Importance Of GWP

- Maintains drug quality & stability
- Reduces risk of errors & contamination
- Ensures regulatory compliance
- Improves efficiency in storage & distribution.

MATERIAL MANAGEMENT

Material management is a process of planning, purchasing, storing, controlling & distributing materials required for production in an efficient & economical way.

STEPS OF MATERIAL MANAGEMENT

- Selection of suppliers
- Procurement of raw materials, packaging materials etc.
- Checking quantity & condition of materials
- Documentation & entry in records
- Proper storage condition (temperature, humidity)
- Use of FIFO/ FEFO methods.
- Maintain stock levels
- Avoiding wastage & expiry.
- Supplying materials to production temperature.

ADVANTAGES

- Helps in smooth production process.
- Reduces losses & wastage.
- Ensures quality & GMP compliance.
- Improves overall efficiency.

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