Supplementary Training Modules on Good Manufacturing Practice

Good Practices for Quality Control Laboratories

Part 2: Materials, equipment, instruments and other devices

World Health Organization

Quality Control

Reagents

- Reagents, chemicals, solvents and materials used in tests and assays – of appropriate quality – with COA and MSDS
- From reputable, approved suppliers
- Preparation of reagents:
  - SOPs and as recommended in pharmacopoeia
  - Clear responsibility in job descriptions
- Records for the preparation, and standardization of volumetric solutions

10.1 – 10.3

Quality Control

- Reagents clearly labelled:
  - *the contents, the manufacturer, the date received and opened, concentration, storage conditions, expiry or re-test date*
  - *When prepared in the laboratory, also the name, date of preparation, initials of person, expiry date, concentration*
- Volumetric solutions:
  - *the name, molarity or concentration, date of preparation, the date of standardization and factor, and identify the responsible technician*
- Whenever possible, transportation in original containers
- When subdivided – into clean, fully labelled containers

10.4-10.7

Quality Control

Visual inspection

- Ensure seals are intact (receiving, distribution for use)
- Suggested to record this on the label (e.g. date, name and initial)
- If tampered with, rejected, unless identity and purity can be confirmed

Water

- Considered as a reagent – use grade as in pharmacopoeia
- Precautions to avoid contamination during:
  - *supply, storage and distribution*
  - *Meet specification*

10.8 - 10.12

Quality Control

Storage of reagents

- Appropriate storage conditions
- Store also clean bottles, vials, spoons, funnels, and labels required for dispensing reagents from larger to smaller containers
- Training in safe handling of chemicals and reagents

Store keeper responsibilities:

- Appropriate store facility, inventory, expiry dates

10.13 – 10.14

Quality Control

Reference substances and reference materials

- A person nominated responsible
- Use pharmacopoeia reference substances whenever possible
- Used for testing, calibration, qualification of equipment, instruments or other devices

Registration and labelling

- Identification number assigned
  - *a new identification number to each new batch*
  - *number marked on each vial and quoted on the analytical worksheet at every use (batch number)*

11.1. – 11.6, 11.8.

Quality Control

Maintain a register for reference substances and reference materials. Record e.g.: (1)

- identification number of the material
- precise description of the material
- source
- date of receipt
- batch designation or other identification code
- intended use of the material (e.g. as an infrared reference material, as an impurity reference material for thin-layer chromatography, etc.)
- location of storage in the laboratory, and any special storage conditions

11.7

Quality Control

Maintain a register for reference substances and reference materials. Record e.g.: (2)

- Other necessary information (e.g. the results of visual inspections)
- Expiry date or retest date
- Certificate (batch validity statement) of a pharmacopoeial reference substance (i.e. certified reference material which indicates its use, the assigned content, its status (validity)
- For secondary reference substances - the certificate of analysis

11.7.

Quality Control

Reference substances prepared in the laboratory:

- Keep a file with information (properties and safety data)
- Results of all tests and verifications
- Expiry date or retest date
- Signed by the responsible analyst

11.9. – 11.11.

Quality Control

Retesting (monitoring)

- Retesting at regular intervals
  - See *WHO General guidelines for the establishment, maintenance and distribution of chemical reference substances*
- Results recorded and signed by the responsible analyst
- If OOS - retrospective check of tests performed using this reference substance
- Risk analysis and CAPA
- Stored in accordance with the storage conditions

11.12 – 11.15

Quality Control

Calibration, validation and verification of equipment, instruments and other devices

- Unique identification (number) for equipment, instruments, devices used for testing, verification and/or calibration
- Also labels indicating status of calibration and due date
- DQ, IQ, OQ, PQ as necessary
- Performance verified at appropriate intervals according to a plan
- Plan for regular calibration implemented

12.1 - 12.5

Quality Control

Examples for calibration:

- SOPs should be in place for each instrument
- pH meters to be verified with standard certified buffer solution before use
- Balances calibrated annually, verified daily, and regularly checked with test weights
- What do you think should be appropriate intervals for the calibration and verification of:
  - HPLCs, GCs, FTIRs?

12.6.

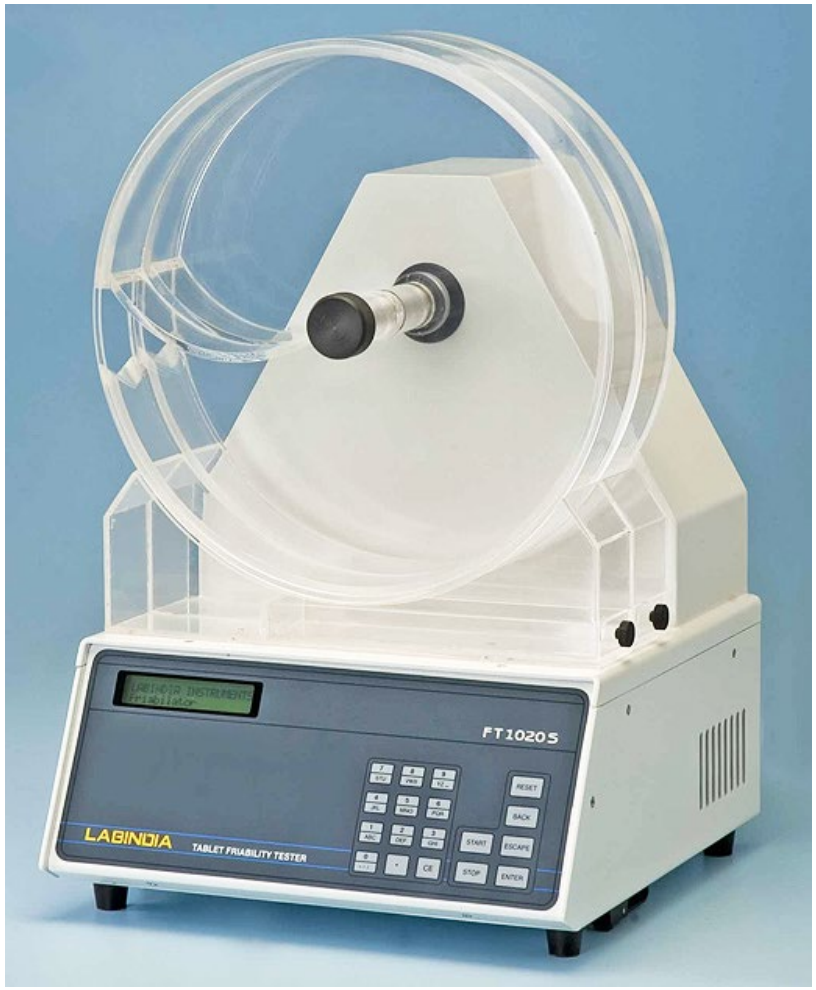
Quality Control

- In the following slides, we will look at some instruments you may find in the quality control laboratory
- Discuss which parameters may be considered during calibration and verification
- Discuss appropriate intervals for calibration and verification
- Discuss some specific aspects to be observed when using the apparatus

Quality Control

Dissolution apparatus

Quality Control



Friability tester

Quality Control

Disintegration tester

Quality Control

Quality Control

Analytical balance

Quality Control

Spectrophotometer

Quality Control

pH Meter

Inspecting the QC laboratory

- During your inspection of the QC laboratory you come across analytical equipment you are not familiar with.

- What questions could you ask?

Quality Control

- Authorized personnel to operate equipment
- SOPs readily available for use, maintenance, verification and calibration of equipment, instruments and devices
- Manuals kept
- The results of calibration and verification recorded
- SOPs for the safe handling, transport and storage of measuring equipment
- SOP for maintenance
  - e.g. regular servicing followed by verification of performance.

12.7. – 12.10.

Quality Control

Records kept of each item of equipment/ instrument/ device:

- Identity of the equipment, instrument or other device
- Manufacturer's name, model, serial number or other unique identification
- Qualification, verification and/or calibration required
- Current location
- Equipment manufacturer's instructions

12.8.

Quality Control

Records kept of each item of equipment/instrument/device:

- Dates, results and copies of reports, verifications and certificates of all calibrations, adjustments, acceptance criteria and the due date of the next qualification, verification and/or calibration
- Maintenance carried out, and the maintenance plan
- History of any damage, malfunction, modification or repair
- Use and “remarks or observations” made at the time the equipment, instruments or devices were used

12.8.

Quality Control

- Equipment, instruments and other devices - giving suspect results, shown to be defective or outside specified limits

  ….should be taken out of service

- Labelled or marked as such
- Not used until they have been repaired and requalified
- Requalify when appropriate
  - E.g. after major repair

12.11. – 12.12.

Quality Control

Traceability

- Result of analysis should be traceable (reported data, raw data, instruments, materials and reagents used)
- Includes traceability to a primary reference substance
- Also needed in case of OOS for investigations
- Calibrations or qualification of instruments should be traceable to certified reference materials and to SI units

13.1. – 13.2.