Supplementary Training Modules on Good Manufacturing Practice

Good Practices for Quality Control Laboratories

WHO Technical Report Series, No. 957, 2010. Annex 1

World Health Organization

Quality Control

Introduction

This Module consists of four parts:

- Part 1: Management and infrastructure
- Part 2: Materials, equipment, instruments and devices
- Part 3: Working procedures, documents and safety
- Part 4: Inspecting the laboratory

Part One.

Supplementary Training Modules on Good Manufacturing Practice

Good Practices for Quality Control Laboratories

Part 1: Management and infrastructure

World Health Organization

Quality Control

Objectives

- To discuss Good Practices for Quality Control laboratories including quality systems and infrastructure
- To understand the role and importance of the Quality Control laboratory in:
  - *sampling and testing*
  - *materials, equipment and systems*
- To discuss approaches in inspecting a Quality Control laboratory

Part One.

Quality Control

General

- Many of the recommendations relevant to quality control testing at the site of the pharmaceutical manufacturer
- In line, and beyond ISO17025
- The QC laboratory provides a service and is like a manufacturing unit – its "products" include test results, advice and investigations
- It needs
  - *buildings, personnel, resources*
  - *equipment, raw materials*
  - *quality systems*

Part One.

Quality Control

General

- Activities include sampling, testing
- APIs, excipients, finished products
- Components, packaging materials
- Specifications and test methods
- Planning and organization of work

Part One.

Quality Control

In Part 1: Management and infrastructure:

- Organization and management
- Quality management systems
- Control of documentation and records
- Data processing equipment
- Personnel
- Premises, equipment, instruments and other devices
- Contracts

Part One.

Quality Control

Organization and management: (1)

- Function in accordance with national legislation
- Operate in accordance with good practice norms and standards
- See also general texts on Good Manufacturing Practices and Good Practices in Quality control
  - *WHO Technical Report Series, No. 908, 2003, Annex 4*

1.1– 1.2

Quality Control

Organization and management (2):

- Personnel
  - *Managerial and technical positions to ensure operation in accordance with quality systems*
  - *No conflict of interest*
- Organizational chart and job descriptions
- Supervision and training

1.3

Quality Control

Organization and management (3):

The laboratory should have:

- Managerial and technical personnel with authority and resources
- Arrangements to prevent commercial, political, financial and other pressures or conflicts of interest
- Policy and procedure in place to ensure confidentiality of
  - — information contained in marketing authorizations,
  - — transfer of results or reports,
  - — and to protect data in archives (paper and electronic);

1.3

Quality Control

Organization and management (4):

The laboratory should:

- Have organizational charts showing e.g. relationships between management, technical operations, support services and the quality management system
- Specify personnel responsibility, authority and interrelationships
- Nominate trained substitutes/deputies for personnel
- Provide adequate supervision of staff

1.3

Quality Control

Organization and management (5):

The laboratory should have:

- Management which has overall responsibility
- A designated quality manager (ensure compliance with the quality management system). Direct access to top management
- Adequate information flow
- Traceability of the samples (from receipt to test report completion)
- Up-to-date specifications and related documents (paper or electronic) and safety procedures

1.3

Quality Control

Organization and management (6):

- A registry should be kept and may include information on
  - receiving, distributing and supervising the consignment of the samples
  - keeping records on all incoming samples and accompanying documents.
- Ensure communication and coordination between the staff involved in the testing of the same sample in different units.

1.4. – 1.5.

Quality Control

Quality Management System (QMS)

- Establish, implement and maintain QMS covering
  - Type of activities, range and volume of testing and/or calibration, validation and verification
    - Policies, systems, programmes, procedures and instructions
- Communicated, available, understood and implemented
- Documented in a quality manual
  - *available to the laboratory personnel*
  - *maintained and updated by a responsible person*

2.1

Quality Control

The quality manual should refer to at least (1):

- Quality policy
- Organizational chart; operational and functional activities
- Operational and functional activities
- Structure of documents
- Internal QM procedures
- Procedures for tests

2.2

Quality Control

The quality manual should refer to at least (2):

- Qualifications, experience and competencies of personnel
- Initial and in-service training
- Internal and external audit
- Implementing and verifying corrective and preventive actions
- Dealing with complaints
- Management reviews
- Selecting, establishing and approving analytical procedures

2.2

Quality Control

The quality manual should contain at least (3):

- Handling of OOS results
- Reference substances and reference materials
- Participation in appropriate proficiency testing schemes and collaborative trials and the evaluation of the performance
- Selection of service providers and suppliers

2.2

Quality Control

The quality policy statement should include at least: intentions and commitment to:

- Standard of service it will provide
- An effective quality management system
- Good professional practice and quality of testing, calibration, validation and verification
- Compliance with good practices guidelines
- Personnel commitments to quality and the implementation of the policies and procedures in their work

2.2a

Quality Control

Authorized, written SOPs should be established, implemented and maintained. Examples include procedures on:

- Personnel matters, including qualifications, training, clothing and hygiene
- Change control; internal audits
- Dealing with complaints
- Corrective and preventive actions

2.3

- Purchase and receipt of materials (e.g. samples, reagents)

Quality Control

SOPs (2)

- Reference substances and reference materials - procurement, preparation and control
- Internal labelling, quarantine and storage of materials
- Qualification, calibration and verification of equipment
- Preventive maintenance
- Sampling, and testing of samples, atypical and OOS results
- Validation of analytical procedures

2.3

Quality Control

SOPs (3)

- Cleaning of laboratory facilities, including bench tops, equipment, work stations, clean rooms (aseptic suites) and glassware
- Monitoring of environmental conditions, e.g. temperature and humidity
- Monitoring storage conditions
- Disposal of reagents and solvent samples; and
- Safety measures

2.3

Quality Control

- Laboratory activities systematically and periodically audited (internally and, where appropriate, by external audits or inspections) to verify compliance - CAPA
- Audits by trained and qualified personnel
- Planning and organizing internal audit
- Regular management review (e.g. annually) to cover e.g.
  - audit or inspection reports
  - investigations (complaints, atypical results) and CAPAs

2.4 - 2.5, 4.4.

Quality Control

Control of documents

- Documentation is essential part of the QMS
- Procedures to control and review all documents
- Master list maintained
  - Current versions and distribution

3.1

Quality Control

Procedures should ensure that:

- Documents have a unique number, version number and date of implementation – and are “current”
- Authorized SOPs are available near points of use
- Invalid documents are removed and replaced
- Revised documents refer to the previous document
- Documents are archived, e.g. 5 years and copies are destroyed
- Staff are trained for the new and revised SOPs

3.2 – 3.3.

Quality Control

Records

- Procedure for the identification, collection, indexing, retrieval, storage, maintenance and disposal of documents/records
- All original observations, calculations and derived data, calibration, validation and verification records, etc. and final results must be retained on record for an appropriate period of time, e.g.
  - *whole length of time the drug is on the market*
- Records to contain sufficient information to permit repetition of tests and traceability

4.1 – 4.2

Quality Control

Records must be:

- Legible, readily retrievable, stored and retained
- In a suitable environment that will prevent modification, damage or deterioration and/or loss
- Secure, confidential. Access restricted to authorized personnel.
- Electronic storage and signatures allowed - restricted access and in conformance with requirements for electronic records 4.3

Quality Control

Data processing equipment

Includes computers, automated tests or calibration equipment; used for collection, processing, recording, reporting, storage or retrieval of test and/or calibration data

- See recommendations in Appendix 5 to Annex 4 of the *Fortieth report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations*: Supplementary guidelines in good manufacturing practice: validation. Validation of computerized systems (*12*)
- Where used, requires systematic verifications of calculations and data transfers

5.1

Quality Control

- Software is documented and appropriately validated or verified
- Procedures are established and implemented for protecting the integrity of data
  - confidentiality of data entry or collection
  - storage, transmission and processing
  - access control, and audit trail
- Maintenance and an appropriate environment
- Change control
- Back up (intervals, retrievable, storage, no data loss).

5.2

Quality Control

Personnel

- Sufficient personnel with job descriptions and records proving appropriate education, training, technical knowledge and experience
- Ensure the competence of all personnel
- Staff undergoing training should be appropriately supervised and should be assessed on completion of the training.
- Permanent employees or contract workers
  - Contract workers are trained and know the QMS

6.5 – 6.4

Quality Control

Managerial and technical personnel:

- Head of laboratory (supervisor)
- Technical managers
- Analysts
- Technical staff

6.6

Quality Control

The Head of laboratory should have extensive experience in medicine analysis and laboratory management.

Responsibilities/functions include:

- All key staff have the requisite competence
- Periodic review of adequacy of existing staffing, management, and training procedures

6.6.a

- Ensuring technical management is supervised

Quality Control

Technical management to ensure that:

- Procedures are in place and implemented:
  - calibration, verification and (re-) qualification of instruments, monitoring of environmental and storage conditions
- Training programmes are current
- Materials are kept (also poisons and narcotic and psychotropic substances under the supervision of an authorized person
- Participation in proficiency testing schemes and collaborative trials where appropriate

6.6 b

Quality Control

Analysts and technical staff:

- Analysts should be qualified in e.g. pharmacy, analytical chemistry, microbiology or other relevant subjects, have knowledge, skills and ability to do the work
- Technical staff should hold diplomas in their subjects awarded by technical or vocational schools
- Quality manager to ensure compliance with the quality management system

6.6.c – e

Quality Control

Premises (1)

- Suitable size, construction and location – appropriate for the functions and operations
- Instruments and equipment, work benches, work stations and fume hoods
- Separate rest and refreshment rooms, changing areas and toilets
- Adequate safety equipment and good housekeeping
- Environmental conditions (lighting, energy, temperature, humidity, air pressure) - monitored, controlled and documented

7.1 – 7.3

Quality Control

Premises (2)

- Suitable archive facilities - protect and prevent deterioration. Access controlled
- Highly toxic substances - special precautions such as separate and dedicated unit or equipment (e.g. isolator, laminar flow work bench)
- Microbiological testing (see separate *WHO guideline)*
- In vivo biological testing – separate
- Waste removal including toxic waste

7.4 – 7.8

Quality Control

Laboratory storage facilities (1)

- Well organized for the correct storage of samples, reagents and equipment. – locked and access controlled
- Separate areas for samples, retained samples, reagents and laboratory accessories, reference substances and reference materials
- Provision for refrigeration (2–8°C) and frozen (-20°C). Controlled, monitored and recorded.

7.9 – 7.11

- Safety procedures for storage of toxic or flammable reagents

Quality Control

Laboratory storage facilities (2)

- Poisons, narcotic and psychotropic substances clearly marked
- Kept separately in locked cabinets.
- Designated responsible person to maintain a register
- Gases stored in a dedicated store, if possible isolated from the main building.
- Gas bottles avoided in the laboratory or safely secured.

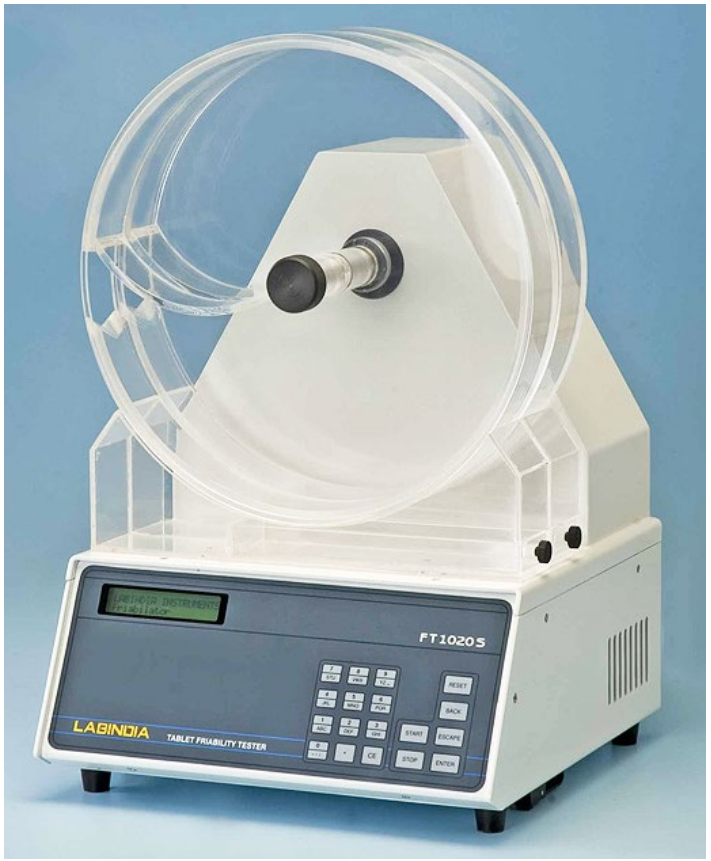
Note: Consider installation of gas generators.

7.12 – 7.13

Quality Control

Equipment, instruments and other devices

- Laboratory should have necessary equipment
- Meet requirements and specifications
- Designed, constructed, adapted, located, calibrated, qualified, verified and maintained
- Purchased from agents capable of providing full technical support and maintenance when necessary



8.1 – 8.3

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Quality Control

Contracts

Purchasing services and supplies

- Procedure for the selection and purchasing of services and supplies
- Evaluate suppliers of critical consumables, supplies and services which affect quality of testing - maintain records
- Approved suppliers list

9.1 – 9.3

Quality Control

Subcontracting of testing

- Subcontracting - in writing and, with approval
- Written contract with duties and responsibilities of each party
- Use organizations approved for the type of activity required
- Periodic assessment of the competence of contracted organization
- No delegation to a third party without prior evaluation and approval
- Register of all subcontractors

9.3 – 9.8.