Supplementary Training Modules on Good Manufacturing Practice

Good Practices for Quality Control Laboratories

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
Supplementary Training Modules on Good Manufacturing Practice

Good Practices for Quality Control Laboratories

Part 1: Management and infrastructure
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
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
Quality Control

General

- Activities include sampling, testing
- APIs, excipients, finished products
- Components, packaging materials
- Specifications and test methods
- Planning and organization of work
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
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
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
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);
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
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
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.
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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
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
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
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
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
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
- 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
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
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
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*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
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.
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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
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).
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**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
Managerial and technical personnel:

- Head of laboratory (supervisor)
- Technical managers
- Analysts
- Technical staff
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
- Ensuring technical management is supervised
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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
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.
**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

**Quality Control**
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
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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.
- Safety procedures for storage of toxic or flammable reagents
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.
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
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
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.