Supplementary Training Modules on Good Manufacturing Practice

Good Practices for Quality Control Laboratories

Part 3: Working procedures and safety

World Health Organization

Quality Control

Incoming samples

- Sampling procedure and sampling plan
- No mix-up or contamination during sampling
- Representative of the batch (statistics?)
  - See also WHO Guidelines on sampling
- Records of sampling maintained
- Ensure test request accompany sample, and appropriate tests will be used for analysis before testing starts

14.4. , 14.7.

World Health Organization

Quality Control

Test request

Test request form with a sample submitted for testing

Contains information e.g.:

- name of the person / sampler
- source of the material;
- description of the sample / material / product
- dosage form, concentration or strength, batch number
- sample size

14.5. – 14.6.

World Health Organization

Quality Control

Test request (2)

- reason for analysis
- date on which the sample was collected
- size of the consignment from which it was taken
- expiry date / retest date
- specification to be used for testing
- any other remarks or comments (e.g. discrepancies found or associated hazard) and storage conditions

14.6.

World Health Organization

Quality Control

Registration and labelling

- Registration number allocated for every sample
- Label affixed to each container of the sample
- Information recorded in a register and include e.g.:
  - registration number of the sample
  - date of receipt
  - specific unit to which the sample was forwarded for testing

14.8. - 14.10.

World Health Organization

Quality Control

Visual inspection and storage of the submitted sample

- Upon receipt - visually inspect sample. Compare against test request
- Record findings, date and sign. Record discrepancies, and queries immediately referred back to the provider of the sample
- Samples stored safely
- Appropriate storage conditions as required for that sample

14. 11. – 14.12

World Health Organization

Quality Control

Forwarding to testing / work allocation

- Sample for testing allocated to analyst or unit
- Should have competence, expertise, training
- Use specification and test procedure
- Verbal requests for testing followed up by written request

14.13 . – 14.18.

World Health Organization

Quality Control

Analytical worksheet

- Used by the analyst for recording information about the sample, the test procedure, calculations and the results of testing
- Raw data to be attached
- Provides documentary evidence either:
  - to confirm that the sample being examined is in accordance with the requirements
  - to support an OOS result and investigation
- A separate analytical worksheet for each numbered sample

15.1. – 15.4.

- Different parts (from different analysts/units) kept together

World Health Organization

Quality Control

Analytical worksheet content:

- The number of the sample
- Page numbering (e.g. 1 of 10…plus annexes)
- Dates (request, start of analysis, and completion)
- Name and signature of the analyst
- Description of the sample
- Reference to the specifications and test methods and limits
- Test equipment used

15.5.

World Health Organization

Quality Control

Analytical worksheet content:

- Reference substance used
- Results of the system suitability test
- Reagents and solvents employed
- Results obtained
- Interpretation of the results and the final conclusions
- Deviations and other remarks
- Approved and signed by the supervisor

15.5.

World Health Organization

Quality Control

- All values entered immediately on the analytical worksheet
- All graphical data attached or be traceable to an electronic record
- Completed analytical worksheet signed by the responsible analyst(s), verified and approved and signed by the supervisor
- Mistakes and amended results:
  - old and new information available
  - signed and dated by the person making the correction
  - reason for the change given on the worksheet
- SOP for amending electronic worksheets and audit trail

15.6. – 15.8.

World Health Organization

Quality Control

Selection of the specifications

- As in test request or master production instructions (as contained in the marketing authorization or product licence)
- Officially recognized pharmacopoeia - current version

Filing / archiving

- Kept safely together with any attachments, including calculations and recordings of instrumental analyses

15.9.

World Health Organization

Quality Control

Validation of analytical procedures

- All analytical procedures employed for testing should be suitable for the intended use - demonstrated by validation
- Validation done according to a validation protocol
- Includes analytical performance characteristics e.g. robustness, accuracy and precision
- Validation report
- Pharmacopoeial methods to be confirmed as suitable for use. If adapted for another use then to be validated

16.1. – 16.3.

World Health Organization

Quality Control

System suitability testing

- An integral part of many analytical procedures
- Shows that equipment, electronics, analytical operations are appropriate/suitable for the samples to be analysed
- To be performed prior to the analysis
- In case of a large number of samples analysed in sequence - then appropriate system suitability tests are to be performed throughout the sequence
- Verification not required for basic pharmacopoeial methods
  - E.g. pH, loss on drying and wet chemical methods

16.4.

World Health Organization

Quality Control

- In case of a major change (e.g. analytical procedure / composition of the product tested / synthesis of the API) - revalidation may be required

More guidelines and further reading:

- *WHO TRS 937, Annex 4. 2006*
- *International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)*
- *European Network of Official Medicines Control Laboratories (OMCL)*
- *General chapters of the* US Pharmacopeia *on Validation of compendial procedures and on Verification of compendial procedures*

16.5.

World Health Organization

Quality Control

Testing

- Sample tested in accordance with the work plan
- If not tested without delay - reasons given in analytical worksheet. Appropriate storage of sample needed
- When specific tests are to be done outside the laboratory – test request and samples transferred.
- Test procedures detailed and followed
- Deviations from the test procedure should be approved and documented

17.1. – 17.3.

World Health Organization

Quality Control

Evaluation of test results

- All test results recorded, reviewed and evaluated (statistically where necessary) – check that they are mutually consistent and meeting specifications – signed by analyst and supervisor
- Doubtful (atypical) and OOS results investigated (supervisor with the analyst). Checks may include (not limited to):
  - Appropriate procedures applied and followed correctly
  - Discrepancies in raw data; calculations correct
  - Qualified, calibrated equipment used; system suitability tests were done and acceptable
  - Glassware, reagents, solvents and reference substances used
- Original sample kept until the investigation is complete.

18.1. – 18.2.
18.5. – 18.6.

World Health Organization

Quality Control

Evaluation of test results

- Doubtful results can be rejected only if they are clearly due to an identified error
- When no obvious cause identified — confirmatory determination is to be performed by another analyst
- OOS SOP detailed including allowable number of retests
- **All** investigations and their conclusions recorded
- CAPA recorded

18.2. – 18.4.

World Health Organization

Quality Control

Analytical test report is:…

- …a compilation of the results and states the conclusions of the examination of a sample
- ...issued by the laboratory
- ...based on the analytical worksheet
- …free from any amendments

18.7 - 18.10

World Health Organization

Quality Control

Content of the analytical test report

- Sample registration number and laboratory test report number
- Name and address of the laboratory
- Name, description, batch number of the sample
- Reference to the specifications and procedures used, limits
- Results, date of results, and discussion of the results
- Conclusion, compliance with specification

18.11.

- Signatures (including head of the laboratory or authorized person)

World Health Organization

Quality Control

Certificate of analysis (1)

A certificate of analysis is prepared for each batch and contains e.g.:

- registration number of the sample; date of receipt;
- name and address of the laboratory;
- name, description and batch number of the sample
- reference to the specification; results of all tests performed (mean and standard deviation, if applicable) with the prescribed limits;
- conclusion (within the limits of the specification)

19.1.

World Health Organization

Quality Control

Certificate of analysis contains (2)

- Expiry date or retest date if applicable
- Date of completion of tests
- Signature of the head of laboratory or other authorized person

Note: See also The Guideline on model certificate of analysis

19.1.

World Health Organization

Quality Control

Retained samples

- As required by the legislation or by the originator of the request for analysis
- Appropriate storage conditions
- Sufficient amount to allow at least two re-analyses
- Kept in its final pack

20.

World Health Organization

Quality Control

Safety (1)

- General and specific safety instructions available based on identified risk - in line with national regulations and SOPs
- Available to each staff member and supplemented with e.g. written material, poster displays, safety data sheets, audiovisual material, occasional seminars and in line with national regulations and SOPs
- No smoking, eating and drinking in the laboratory
- Know how to use of fire-fighting equipment
- Wear laboratory coats and use eye protection

21.1. – 21.2.

World Health Organization

Quality Control

Safety (2)

- Special care - in handling highly potent, infectious or volatile substances
- Highly toxic and/or genotoxic samples only in a specially designed facility to avoid the risk of contamination
- Containers of chemicals should be fully labelled and include prominent warnings e.g. “poison”, “flammable”, “radioactive”
- Adequate insulation and spark-proofing
- Cylinders of compressed gases

21.1. – 21.2.

World Health Organization

Quality Control

Safety (3)

- Avoid working alone in the laboratory
- First-aid materials are provided and staff trained
- Protective clothing – e.g. eye protection, masks and gloves, safety showers
- Rubber suction bulbs used, safe handling of glassware, corrosive reagents and solvents
- Warnings, precautions and instructions
- Safe disposal with neutralization or deactivation

21.2. – 21.3.

World Health Organization

Quality Control

Safety (4)

- Poisonous and hazardous products
- Labeled appropriately
- Contact with reagents, solvents, vapours avoided
- Limited use of carcinogens and mutagens as reagents

21.4.

World Health Organization