Quality management
GMP
Quality assurance (programs & Duties)
Documentation
How to review records
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Quality management

— An appropriate quality system encompassing the organizational structure, procedures, processes and resources.

— Systematic actions necessary to ensure adequate confidence that a product will meet given requirements for quality.

— Within an organization, quality assurance serves as a management tool, GMP and quality control are interrelated aspects.
GMP for pharmaceutical products

- GMP is that part of quality assurance which ensures that products are consistently produced and controlled to the quality standards.

GMP are aimed to diminish the risks in any pharmaceutical production. Two essential risks: cross contamination and mix-ups (confusion), false labels.
Under GMP:

- All processes are clearly defined, reviewed in the light of experience, capable of consistently of required quality that comply with their specifications.

- Qualification and validation are performed.

- All necessary resources are provided, including:
  - Qualified and trained personnel.
  - Adequate premises and space.
  - Suitable equipment and services.
- Appropriate materials, containers and labels.

- Approved procedures and instructions.

- Suitable storage and transport.

- Adequate personnel, laboratories and equipment for in-process controls.

- Procedures are written in clear and unambiguous language.

- Operators are trained to carry out procedures correctly.
- Records are made during manufacture to show all steps have been taken.

- Records covering manufacture and distribution, enable to be traced completely.

- The proper storage and distribution of the products minimizes any risk to their quality.

- A system is available to recall any batch of product.

- The causes of quality defects investigated, and prevent recurrence.
Master production protocol

The (MPP) describes the manufacturing procedure. Typically are written for upstream, downstream, formulation and fill/finish. The MPP are approved by quality assurance (QA) before manufacture.
**reconciliation**

A comparison between the theoretical quantity and the actual quantity.

**specification**

A list of detailed requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation.
Batch production record

The batch production record (BPR) describes in detail the manufacturing work carried out. The BPR template is the MPR, the difference being that the BPR comprises all data and signatures. The BPR is controlled by QA.

Certificate of analysis

The certificate of analysis (CoA) summarizes the quality control data and compares said data to the specification accept criteria.
quality assurance

- The group responsible for oversight of all activities relating to product quality

- Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product.

- The QA Unit should coordinate, monitor, and facilitate all QA activities.

- The QA Unit may include one or more individuals dedicated solely to QA functions or individuals who also perform other tasks in the establishment. In the latter situation, however, individuals should not have final oversight of their own work.
The goals of QA are decrease errors, ensure the credibility of test results, implement effective manufacturing process and system controls, and ensure continued product safety and quality.

QA includes measures to prevent, detect, investigate, assess, and correct errors. The emphasis is on preventing errors rather than detecting them.

Implementing a QA program requires a commitment of time and resources. Public health consequences require all establishments, regardless of size, invest in QA.
QA program is a system designed and implemented to ensure that manufacturing is consistently performed & product have a consistent quality.

QA is the sum of activities planned and performed to provide confidence that the quality of the product are functioning as expected and relied upon.

There are several dimensions to QA including:

(QC), CGMP, process monitoring. Other dimensions of QA standards for: personnel, facilities, procedures, equipment, testing, and recordkeeping activities.
These individuals are responsible for ensuring corrective action has been taken.

The Responsible Head or designated qualified person is also responsible for ensuring that personnel are appropriately trained to accomplish their duties.

The QA Unit reports independently from production to management.

The QA Unit should ensure that production personnel follow CGMP.

When necessary, the QA Unit should have the authority to stop production and/or release of product.
quality assurance should ensure that:

– production and control operations are clearly specified in a written form and GMP requirements are adopted;

– managerial responsibilities are clearly specified in job descriptions;

– arrangements are made for the manufacture, supply and use of the correct starting and packaging materials;

– all necessary controls on starting materials, intermediate products, and bulk products and other in-process controls, calibrations, and validations are carried out;
– products are not sold or supplied before the authorized persons certify that it has been produced and controlled and meet requirements.

– satisfactory arrangements exist to ensure, that the products are stored, distributed, and handled so that quality is maintained throughout their shelf-life.

– there is a procedure for self-inspection.

– deviations are reported, investigated and recorded.

– there is a system for approving changes that may have an impact on product quality.
– All parts of the quality assurance system should be adequately staffed, have suitable and sufficient premises, equipment, and facilities.

– Determining that SOPs exist for all manufacturing procedures, and accurately describe and define the procedures.

– Reviewing and ensuring written approval of all SOPs prior to implementation.
performance of all procedures;

– methods for periodic proficiency testing;

– methods for periodic competency evaluation of the individuals performing each procedure;

– methods for evaluating the performance of each procedure during QA audits;

– designation of each procedure as a critical or non critical control point.
– Ensuring that modifications in SOPs are documented, revised, new methods and processes are validated.

– Ensuring that SOPs for all QA unit activities exist and define the QA unit's responsibility for performing SOP review, approval, or authorization.

– Ensuring SOPs are promptly updated to reflect changes in manufacturer's directions and all SOPs and records are reviewed at least annually.
Training and Education

The QA Unit should assist in developing, reviewing, and ensuring the approval of training and educational programs for all personnel.

**Training should include:**

New employee orientation, Supervisory training, Technical training, CGMP training, Managerial training, SOP training, QA training, Computerized system training, Continuing education and training.
Competency Evaluation

QA Unit should implement a formal regular competency evaluation program.
The program should evaluate theoretical and practical knowledge of procedures.

Validation

The QA unit should ensure that adequate validation procedures have been performed. Complaints, errors and problems at critical control points should be reviewed to determine the need for revalidation or revision of validation procedures.
Equipment

The QA Unit should ensure that procedures are in place for equipment qualification, process validation, and revalidation after repairs to ensure the proper function.

There should be written procedures for equipment qualification, calibration, validation, maintenance, and monitoring.
Documentation

- Good documentation is an essential part of the quality assurance. Its aims are to define the specifications and procedures for all materials, methods, control; to ensure that all personnel know what and when to do it; to ensure that authorized persons have all the information necessary to release, to ensure the existence of documented evidence, traceability, and to provide records. It ensures the availability of the data needed for validation, review and statistical analysis.
- Documents should be approved, signed and dated by the appropriate responsible persons.

- Documents should have unambiguous contents: the title, and purpose should be clearly stated. They should be in an orderly fashion and be easily checked.

- Documents should be regularly reviewed and kept up to date and superseded documents should be retained for a specific period of time.

- Where documents require the entry of data, these entries should be clear, legible and sufficient space should be provided for entries.
Specifications and testing procedures

- Testing procedures described in documents should be validated in the context of available equipment before they are adopted for routine testing.

- There should be authorized and dated specifications, for identity, content, purity and quality, for starting, packaging materials, finished products, for water, solvents and reagents.

- Each specification should be approved, signed and dated, and maintained by quality control, quality assurance unit.

- Periodic revisions of the specifications may be necessary to comply with new editions of pharmacopoeia.

- Pharmacopoeias, reference standards, other reference materials should be available in the quality control laboratory.
Specifications for starting and packaging materials

Including:

- The designated name and internal code reference.
- the reference, if any, to a pharmacopoeia monograph.
- qualitative and quantitative requirements with acceptance limits, other data may be added.
- the supplier and the original producer of the materials.
- directions for sampling and testing, or a reference to procedures.
- storage conditions and precautions.
- the maximum period of storage before re-examination.
- The material should be examined for compliance with the specification.
**Master formulae**

A set of documents specifying the starting materials with their quantities, packaging materials, description of procedures to produce a specified quantity of a finished product as well as in-process controls.

**Master formula should exist for each product and batch size.**

**Including:**

- the name of the product, with a product reference code.
- A description of the dosage form, batch size.
- A list of all starting materials, amounts, described using the designated name and a reference that is unique to that material.
- A statement of the expected final yield with the acceptable limits.

- A statement of the processing location and the principal equipment to be used.

- The methods, or reference to the methods, to be used for preparing and operating the critical equipment, assembling, calibrating, Sterilizing.

- Detailed step-wise processing instructions.

- The instructions for any in-process controls with their limits.

- The requirements for storage, container, labeling, special storage conditions.

- Any special precautions to be observed
**Batch processing records**

A batch processing record should be kept for each batch processed. The method of preparation of such records should be designed to avoid errors.

Before any processing begins, a check should be made, the equipment, work station, documents, or materials not required for the planned process, This check should be recorded.

During processing, information should be recorded at the time each action is taken, and after completion the record should be dated and signed by the person responsible for the processing operations.
- The name, number of the batch.
- Dates and times of completion.
- The name of the person responsible for each stage of production.
- The initials and different significant steps operator(s), checker's).
- The batch number, control number, quantity of each starting material, amount of any recovered or reprocessed material.
- Any relevant processing operation or event and the major equipment used.
- The in-process controls performed, results obtained.
- The amount of explanations yield, deviations of expected yield.

Even if it is as simple as the lights going out
**Master production record**

To assure uniformity from batch to batch, master production shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person.

**Master production shall include:**

- The name of the product and a description of the dosage form.
- The measure of each active ingredient per dosage.
- List of all components with specific codes to indicate any special quality characteristic.
- An accurate statement of the weight, using the correct weight system for each component. Reasonable variations may be permitted.
- A statement concerning any calculated excess of component.

- A statement of theoretical weight or measure at appropriate phases.

- A statement of theoretical yield, including the maximum and minimum percentages.

- A description of the drug product containers, closures, and packaging materials.

- Complete manufacturing and control instructions, sampling and testing procedures, specifications and precautions to be followed.
How to Review Manufacturing Records for Compliance

- **Learn cGMPs.**
  The main purpose of the batch record is to have written proof of what was added.

  GMP, referred to cGMP are laws that dictate certain criteria to be followed. Following these parameters reassures that the product is as safe as it can be.

- **Look at What was Done.**
  Compare the steps performed with regulations states should be done. For example, If the regulation require a second signature for the ingredient's added, look at the record and make sure a second signature is present. Determining GMP compliance is always the reviewer's goal.
- **Performing the Actual Review**

The QA person should verify that each requirement in the regulation was met while the drug was being made. They should also verify that the process and requirements listed in the batch record were completed.

- **Confirm Lab Results in Batch Record**

The QA person compares the batch record laboratory results to the actual laboratory printed report and ensure the results were accurately transferred from the report to the batch record. After being verified everything, they must sign the document as approve and released the production.
- Compliance reviews are very important.

By reviewing the batch record, Quality Assurance have an opportunity to catch errors before the product is released for public consumption or before an error cost the company thousands of dollars.
"First impressions are lasting impressions"

Therefore,

Have Required Training!

ammonia OR pneumonia