Name of Unit	Organization, Personnel, premises and equipment and Raw materials
Subject/Course name	Quality Assurance
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Learning Outcome of module-2

LO	Learning Outcome (LO)	Course Outcome Code
LO1	Students will able to understand the cGMP aspects in a pharmaceutical industry	BP606.4
LO2	To Understand the responsibilities of QA & QC departments	BP606.3

MODULE CONTENT TABLE

Topic
• Organization and Personnel: Personnel responsibilities, training, hygiene and personal records. • Premises: Design, construction and plant layout, maintenance, sanitation, environmental control, Utilities and maintenance of sterile areas control of contamination. • Equipment's and Raw Materials: Equipment selection, purchase specifications, maintenance, Purchase specifications and maintenance of stores for raw materials.

PERSONNEL

The establishment and maintenance of a satisfactory system of quality assurance and the correct manufacture and control of pharmaceutical products and active ingredients rely upon people. For this reason there must be sufficient qualified personnel to carry out all the tasks for which the manufacturer is responsible. Individual responsibilities should be clearly defined and understood by the persons concerned and recorded as written descriptions.

General

1. The manufacturer should have an adequate number of personnel with the necessary qualifications and practical experience. The responsibilities placed on any one individual should not be so extensive so as to present any risk to quality.
2. All responsible staff should have their specific duties recorded in written descriptions and adequate authority to carry out their responsibilities. Their duties may be delegated to designated deputies of a satisfactory qualification level. There should be no gaps or unexplained overlaps in the responsibilities of personnel concerned with the application of GMP. The manufacturer should have an organization chart.
3. All personnel should be aware of the principles of GMP that affect them and receive initial and continuing training, including hygiene instructions, relevant to their needs. All personnel should be motivated to support the establishment and maintenance of high-quality standards.
4. Steps should be taken to prevent unauthorized people from entering production, storage and quality control areas. Personnel who do not work in these areas should not use them as a passageway.

The head of the quality control generally has the following responsibilities:

- To approve or reject starting materials, packaging materials, and intermediate, bulk and finished products in relation to their specifications;
- To evaluate batch records;
- To ensure that all necessary testing is carried out;
- To approve sampling instructions, specifications, test methods and other quality control procedures;
- To approve and monitor analyses carried out under contract;
- To check the maintenance of the department, premises and equipment;

- To ensure that the appropriate validations, including those of analytical procedures, and calibrations of control equipment are carried out;

The head of the production generally has the following responsibilities:

- To ensure that products are produced and stored according to the appropriate documentation in order to obtain the required quality;
- To approve the instructions relating to production operations, including the in-process controls, and to ensure their strict implementation;
- To ensure that the production records are evaluated and signed by a designated person;

The head of the quality control generally has the following responsibilities:

- To approve or reject starting materials, packaging materials, and intermediate, bulk and finished products in relation to their specifications;
- To evaluate batch records;
- To ensure that all necessary testing is carried out;
- To approve sampling instructions, specifications, test methods and other quality control procedures;
- To approve and monitor analyses carried out under contract;
- To check the maintenance of the department, premises and equipment;
- To ensure that the appropriate validations, including those of analytical procedures, and calibrations of control equipment are carried out;
- To ensure that the required initial and continuing training of quality control personnel is carried out and adapted according to need.
- To check the maintenance of the department, premises, and equipment;
- To ensure that the appropriate process validations and calibrations ofcontrol equipment are performed and recorded and the reports madeavailable;
- To ensure that the required initial and continuing training of production personnel is carried out and adapted according to need.

The heads of the production and quality control generally have some shared, or jointly exercised, responsibilities relating to quality. These may include, depending on national regulations:

- Authorization of written procedures and other documents, includingamendments;
- Monitoring and control of the manufacturing environment;

- Plant hygiene;
- Process validation and calibration of analytical apparatus;
- Training including the application and principles of quality assurance;
- approval and monitoring of suppliers of materials;
- Approval and monitoring of contract manufacturers;
- Designation and monitoring of storage conditions for materials andproducts;
- Performance and evaluation of in-process controls;
- Retention of records;
- Monitoring of compliance with GMP requirements;
- Inspection, investigation and taking of samples in order to monitor factors that may affect product quality.

TRAINING

1. The manufacturer should provide training in accordance with a written programme for all personnel whose duties take them into manufacturing areas or into control laboratories (including the technical, maintenance and cleaning personnel) and for other personnel as required.
2. Besides basic training on the theory and practice of GMP, newly recruited personnel should receive training appropriate to the duties assigned to them. Continuing training should also be given, and its practical effectiveness periodically assessed. Approved training programmes should be available. Training records should be kept.
3. Personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitizing materials are handled, should be given specific training.
4. The concept of quality assurance and all the measures which aid its
5. Understanding and implementation should be fully discussed during the training sessions.
6. Visitors or untrained personnel should preferably not be taken into the production and quality control areas. If this is unavoidable, they should be given relevant information in advance (particularly about personal hygiene) and the prescribed protective clothing. They should be closely supervised.
7. Consultant and contract staff should be qualified for the services they provide. Evidence of this should be included in the training records

PERSONAL HYGIENE

- All personnel, prior to and during employment, as appropriate, should undergo health examinations. Personnel conducting visual inspections should also undergo periodic eye examinations.
- All personnel should be trained in the practices of personal hygiene. A high level of personal hygiene should be observed by all those concerned with manufacturing processes. In particular, personnel should be instructed to wash their hands before entering production areas. Signs to this effect should be posted and instructions observed.
- Any person shown at any time to have an apparent illness or open lesions that may adversely affect the quality of products should not be allowed to handle starting materials, packaging materials, in-process materials or drug products until the condition is no longer judged to be a risk.
- All employees should be instructed and encouraged to report to their immediate supervisor any conditions (relating to plant, equipment or personnel) that they consider may adversely affect the products.
- Direct contact should be avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product.
- To ensure protection of the product from contamination, personnel should wear clean body coverings appropriate to the duties they perform, including appropriate hair covering. Used clothes, if reusable, should be stored in separate closed containers until properly laundered and, if necessary, disinfected or sterilized.
- Smoking, eating, drinking, chewing, and keeping plants, food, drink, smoking material and personal medicines should not be permitted in production, laboratory and storage areas, or in any other areas where they might adversely influence product quality.

PERSONNEL RECORDS

The company keeps certain records relating to each individual's employment in a personnel file. The personnel file serves as the historical record of information about the employee from the date of hire to separation and contains some pre-employment and post-employment information. The records maintained in the personnel file can serve to protect the employer in future legal proceedings, and also can help clear up misunderstandings that may occur over policy issues, pay

and benefits issues, work duties and responsibilities, disciplinary or corrective actions, and grievances.

Various federal and state laws mandate that certain personnel records must be kept. Therefore, when an employer is drafting or updating its policy or procedures regarding which records to maintain in personnel files and how long those records should be kept, it is necessary to review various applicable laws.

The following records contain information that is very confidential and/or sensitive and should be handled very carefully.

Confidentiality of Personnel Records

All files connected with an employee are considered strictly confidential and should be maintained in a secured location that is separate from other records.

Files containing confidential information are to be kept in locked cabinets or drawers with limited access.

If personnel files are stored electronically, access also must be secured and limited. Access to any personnel record should be limited only to those who have a job-related need to know the information and who have been authorized to see the file in question

Creating a Policy

Adopting a written policy will allow supervisors and the human resources department to be consistent with replies when employees request access to their files. Consider including the following items in your policy:

- Ensure that your policy complies with applicable state and federal laws.
- Define personnel file, both as the term is used within your organization and according to applicable law.
- State where, when, how often, and under what circumstances workers can review or copy their files. To maintain the integrity of records, access should be permitted under some type of supervision.
- Provide an opportunity for employees to rebut or challenge information.
- Specify who is authorized to inspect personnel files.
- Review records. Periodically, you should audit employment records and remove or correct irrelevant, outdated, misleading, or inaccurate information.

Personnel Records Maintenance and Audits

It is important to remember that all employee files are subject to audits or legal proceedings; thus, it is critical to ensure that your personnel files are kept neat and organized and contain only the required documents.

A good practice is to audit the personnel files at least once a year. During the audit, you should verify that all employee records are up-to-date and complete and that you are storing the same information for each employee. Purge the files of any duplicate information. You should also move the files of terminated employees to a separate secured storage location for the required retention period.

Maintaining neat personnel files will make it easier to review your company's employee information, either by you or an audit team. Make sure the file folders are sturdy and that documents will not easily fall out of place. Label the files with the employee's name, and keep the files in alphabetical order.

The following items should be kept in a basic personnel file:

Records related:

1. Employment
   - Employment application and resume.
   - Any communications with applicant surrounding employment application.
   - College transcripts.
   - Employment interview report.
   - Job descriptions and employee's acknowledgment of receipt.
   - Hiring, promotion, demotion, transfer, layoff, rates of pay, other forms of compensation, and education records.
   - Correspondence regarding the terms and conditions of employment—an offer or acknowledgment letter which may be given prior to the beginning of employment.
   - Current employment contract or addendums.
   - Other employment practices.
   - Letters of recognition.
   - Applicable certificates and licenses.
   - Checklist from new employee orientation showing subjects covered.

- Copy of pre-employment and orientation notices given to the employee. Acknowledgment of receipt of employee handbook.
- Acknowledgment of receipt of sexual harassment policy, etc.
- Disciplinary notices or documents.
- Test documents used by an employer to make an employment decision. Termination records.

II. Performance Appraisals and Disciplinary Actions

- Progress reports or notes by supervisors and managers.
- Performance appraisal forms.
- Performance improvement program records.
- Disciplinary (formal and informal) actions and supporting documentation.
- Report of coaching/counseling session.
- Follow-up

III. Training and Development

- Training history records.
- Training program applications/requests.
- Safety training/meeting attendance/summary forms.
- Commendations.

IV. Employee Separations

- Exit interview form.
- Exit interviewer's comment form.
- Record of documents given with final paycheck.
- Severance agreement, if applicable.

The following items should be maintained in separate files:

Medical Records: The Americans with Disabilities Act requires employers to keep all medical records separate. Many states have privacy laws to protect employees. All medical records, including physical examinations, medical leaves, worker' compensation claims, and drug and alcohol testing should be kept separate.

Equal Employment Opportunity: To minimize claims of discrimination, it is important to keep source documents that identify an individual's race and sex in a separate file. Additionally, if

internal/external charges are investigated, it is recommended that these files also be maintained separately.

Immigration (I-9) Forms: It is recommended that these forms be maintained chronologically by year. Keeping this information in a separate file reduces the opportunity for an auditor to pursue and investigate unrelated information.

Invitation to Self-Identify Disability or Veterans Status: This information is required to be maintained by federal contractors. Laws prohibit employment decisions on the basis of certain protected classes; however, managers have the right to access an employee's file for a number of operational issues. Unless there is a need to know for accommodation purposes, these files should be maintained separately to reduce a potential source of bias.

Safety Training Records: OSHA may audit company's training records. Keeping this information separate will protect the employer from an auditor pursuing and investigating other information in the personnel file.

Investigation records

Garnishment forms/child support orders

Background check information

PREMISES

***Principle*.** Premises must be located, designed, constructed, adapted, andmaintained to suit the operations to be carried out.

General

- The layout and design of premises must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt, and, in general, any adverse effect on the quality of products.
- Where dust is generated (e.g. during sampling, weighing, mixing and processing operations, packaging of powder), measures should be taken to avoid cross-contamination and facilitate cleaning.
- Premises should be situated in an environment that, when considered together with measures to protect the manufacturing process, presents minimum risk of causing any contamination of materials or products.
- Premises used for the manufacture of finished products should be suitably designed and constructed to facilitate good sanitation.

- Premises should be carefully maintained, and it should be ensured that repair and maintenance operations do not present any hazard to the quality of products.
- Premises should be cleaned and, where applicable, disinfected according to detailed written procedures. Records should be maintained.
- Electrical supply, lighting, temperature, humidity and ventilation should be appropriate and such that they do not adversely affect, directly or indirectly, either the pharmaceutical products during their manufacture and storage, or the accurate functioning of equipment.
- Premises should be designed and equipped so as to afford maximum protection against the entry of insects, birds or animals. There should be a procedure for rodent and pest control.
- Premises should be designed to ensure the logical flow of materials and personnel.

Ancillary areas

- Rest and refreshment rooms should be separate from manufacturing and control areas.
- Facilities for changing and storing clothes and for washing and toilet purposes should be easily accessible and appropriate for the number of users. Toilets should not communicate directly with production or storage areas.
- Maintenance workshops should if possible be separated from production areas. Whenever parts and tools are stored in the production area, they should be kept in rooms or lockers reserved for that use.
- Animal houses should be well isolated from other areas, with separate entrance (animal access) and air-handling facilities.

Storage areas

- Storage areas should be of sufficient capacity to allow orderly storage of the various categories of materials and products with proper separation and segregation: starting and packaging materials, intermediates, bulk and finished products, products in quarantine, and released, rejected, returned or recalled products.
- Storage areas should be designed or adapted to ensure good storage conditions. In particular, they should be clean, dry, sufficiently lit and maintained within acceptable temperature limits. Where special storage conditions are required (e.g. temperature, humidity) these should be provided, controlled, monitored and recorded where appropriate.

- Receiving and dispatch bays should be separated and protect materials and products from the weather. Receiving areas should be designed and equipped to allow containers of incoming materials to be cleaned if necessary before storage.
- Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and their access restricted to authorized personnel. Any system replacing the physical quarantine should give equivalent security.
- Segregation should be provided for the storage of rejected, recalled, or returned materials or products.
- Highly active and radioactive materials, narcotics, other dangerous drugs, and substances presenting special risks of abuse, fire or explosion should be stored in safe and secure areas.
- Printed packaging materials are considered critical to the conformity of the pharmaceutical product to its labelling and special attention should be paid to sampling and the safe and secure storage of these materials.
- There should normally be a separate sampling area for starting materials. (If sampling is performed in the storage area, it should be conducted in such a way as to prevent contamination or cross-contamination.)

Weighing areas

- The weighing of starting materials and the estimation of yield by weighing should be carried out in separate weighing areas designed for that use, for example with provisions for dust control. Such areas may be part of either storage or production areas.

Production areas

- In order to minimize the risk of a serious medical hazard due to crosscontamination, dedicated and self-contained facilities must be available for the production of particular pharmaceutical products, such as highly sensitizing materials (e.g. penicillins) or biological preparations (e.g. live microorganisms).
- The production of certain other highly active products, such as some antibiotics, hormones, cytotoxic substances and certain non-pharmaceutical products, should not be conducted in the same facilities. In exceptional cases, the principle of campaign working in the same facilities can be accepted provided that specific precautions are taken and the necessary validations (including cleaning validation) are made. The manufacture of technical poisons,

such as pesticides and herbicides, should not be allowed in premises used for the manufacture of pharmaceutical products.

- Premises should preferably be laid out in such a way as to allow the production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels.
- The adequacy of the working and in-process storage space should permit the orderly and logical positioning of equipment and materials so as to minimize the risk of confusion between different pharmaceutical products or their components, to avoid cross-contamination, and to minimize the risk of omission or wrong application of any of the manufacturing or control steps.
- Where starting and primary packaging materials and intermediate or bulk products are exposed to the environment, interior surfaces (walls, floors and ceilings) should be smooth and free from cracks and open joints, should not shed particulate matter, and should permit easy and effective cleaning and, if necessary, disinfection.
- Pipework, light fittings, ventilation points and other services should be designed and sited to avoid the creation of recesses that are difficult to clean. As far as possible, for maintenance purposes, they should be accessible from outside the manufacturing areas.
- Drains should be of adequate size and designed and equipped to prevent back-flow. Open channels should be avoided where possible, but if they are necessary they should be shallow to facilitate cleaning and disinfection.
- Production areas should be effectively ventilated, with air-control facilities (including filtration of air to a sufficient level to prevent contamination and cross-contamination, as well as control of temperature and, where necessary, humidity) appropriate to the products handled, to the operations undertaken and to the external environment. These areas should be regularly monitored during both production and non-production periods to ensure compliance with their design specifications.
- Premises for the packaging of pharmaceutical products should be specifically designed and laid out so as to avoid mix-ups or cross-contamination.
- Production areas should be well lit, particularly where visual on-line controls are carried out.

Quality control areas

- Quality control laboratories should be separated from production areas. Areas where biological, microbiological or radioisotope test methods are employed should be separated from each other.
- Quality control laboratories should be designed to suit the operations to be carried out in them. Sufficient space should be given to avoid mix-ups and cross-contamination. There should be adequate suitable storage space for samples, reference standards (if necessary, with cooling), solvents, reagents and records.
- The design of the laboratories should take into account the suitability of construction materials, prevention of fumes and ventilation. There should be separate air supply to laboratories and production areas. Separate air-handling units and other provisions are needed for biological, microbiological and radioisotope laboratories.
- A separate room may be needed for instruments to protect them against electrical interference, vibration, contact with excessive moisture and other external factors, or where it is necessary to isolate the instruments.

Equipment

- Equipment must be located, designed, constructed, adapted, and maintained to suit the operations to be carried out. The layout and design of equipment must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt, and, in general, any adverse effect on the quality of products.
- Equipment should be installed in such a way as to minimize any risk of error or of contamination.
- Fixed pipework should be clearly labelled to indicate the contents and, where applicable, the direction of flow.
- All service pipings and devices should be adequately marked and special attention paid to the provision of non-interchangeable connections or adaptors for dangerous gases and liquids.
- Balances and other measuring equipment of an appropriate range and precision should be available for production and control operations and should be calibrated on a scheduled basis.
- Production equipment should be thoroughly cleaned on a scheduled basis.

- Laboratory equipment and instruments should be suited to the testing procedures undertaken.
- Washing, cleaning and drying equipment should be chosen and used so as not to be a source of contamination.
- Production equipment should not present any hazard to the products. The parts of the production equipment that come into contact with the product must not be reactive, additive, or absorptive to an extent that would affect the quality of the product.
- Defective equipment should be removed from production and quality control areas. If this is not possible, it should be clearly labelled as defective to prevent use.
- Closed equipment should be used whenever appropriate. Where open equipment is used or equipment is opened, precautions should be taken to minimize contamination.
- Non-dedicated equipment should be cleaned according to validated cleaning procedures between productions of different pharmaceutical products to prevent cross-contamination.
- Current drawings of critical equipment and support systems should be maintained.

Sanitation

The sanitation of clean areas is particularly important. They should be cleaned frequently and thoroughly in accordance with an approved written programme. Where disinfectants are used, more than one type should be employed. Monitoring should be regularly undertaken to detect contamination or the presence of an organism against which the cleaning procedure is ineffective. Interactions between different cleaning materials should be validated. Appropriate cleaning validation should be carried out to ensure disinfectant residuals can be detected and are removed by the cleaning process.

Disinfectants and detergents should be monitored for microbial contamination; dilutions should be kept in previously cleaned containers and should only be stored for defined periods unless sterilized. Disinfectants and detergents used in Grade A and B areas should be sterile before use.

A disinfectant programme should also include a sporicidal agent since many common disinfectants are ineffective against spores. The effectiveness of cleaning and disinfectant procedures should be demonstrated.

Fumigation of clean areas may be useful for reducing microbial contamination in inaccessible places.

Maintenance of Pharmaceutical Clean Area: FDA Recommendation

FDA recommendations on the pharmaceutical clean area and supporting area maintenance in sterile manufacturing unit. Maintenance of pharmaceutical clean area has its importance in sterile manufacturing. Sterility of the sterile products is the most important factor for the product quality and it can be achieved only by the proper maintenance of the manufacturing area. Areas surrounding the core manufacturing area are known as supporting areas. These supporting areas have different functions as storage of in process materials, cleaned equipment, material transfer etc. These areas should be designed to minimize the particulate and microbial contamination in the core manufacturing area where the product is exposed to the air. Different activities in surrounding areas should be conducted according to the cleanliness class of the area. Less critical activities such as equipment washing should be done in the 1,00,000 class area. The adjacent area to the aseptic area (class 100) should be maintained at least at class 10,000. The manufacturer can maintain it as class 1000 or 100 depending upon the activities done in the pharmaceutical clean area.

Buffer Area and Its Maintenance in Sterile Manufacturing Facility Separation of areas used in manufacturing operation is necessary to prevent the contamination. The areas of higher air cleanliness class should have proper airflow and higher pressure differential than the less cleanliness class areas. Rooms maintained at higher cleanliness class should have positive pressure differential than the adjacent rooms. According to FDA, the pressure differential should be at least 0.05 inch of water.

At the opening of door, the air should flow from the higher cleanliness room to lower to prevent the entrance of the contamination. Pressure differential should be maintained throughout the manufacturing process runs and it should be monitored and recorded in every shift as directed by FDA for the pharmaceutical clean area. Any deviation found from the limits must be investigated. To maintain the clean room area and its air quality it is required to maintain the desired air flow. For the supporting areas of class 1,00,000 airflow should be maintained to get at least 20 air changes per hour. It would be difficult to maintain this area below these air changes.

As per FDA guidance, an automated monitoring system should be established for that detects the critical changes those can alter the area cleanliness. As for differential pressure, low pressure in any of the classified areas should be detected and an alarm should be raised for the same to prevent the entrance of unclassified air into the area.

Contamination control strategy

Sterile pharmaceutical drug products and substances/ constituents manufactured to GMP standards need assurance of quality, sterility or bio burden control (depending on the manufacturing stage) to ensure patient safety. Such assurance that CQAs and patient safety are not compromised by contamination can only be provided with thorough product, process and risk knowledge together with risk-based control aligned with ICHQ9 principles. Control should be implemented through Quality by Design (QbD principles) and risk control measures defined by risk assessments. It is universally accepted that it is not possible to inspect or justify GMP/ cGMP compliance with monitoring data or media fill results alone, as such an approach offers little assurance of robust processes and assured quality in GMP.

A 'contamination control strategy' should include a strategy for environmental control of product manufacturing environments for assurance that product sterility is not compromised and patient safety is not put at risk by loss of microbial control or deviations/ excursions within the controlled environments.

Strategies in contamination control will vary depending on whether the product is aseptically processed/ manufactured, terminally sterilized, is subjected to sub-optimal heat treatment, or if a non-sterile ingredient or constituent that may require bio-burden control is used.

Relating to the important risks to patients from direct contamination and cross contamination in sterile product manufacturing, it is considered a prerequisite that a control strategy must set out the approach to control and manage such contamination risks so the approach is clear to manufacturers, auditors and GMP inspectors alike. The control strategy should take a holistic view across all elements that potentially impact contamination control including design (process and facility), process validation and manufacturing practice, in accordance with current approaches for Process Validation

There is a risk of cross contamination from chemical adulteration or residues between processes, product-to-product cross contamination, biological entities cross contamination and that which occurs between patients via cells or genes where manufacturing of therapeutic products is concerned.

EQUIPMENTS & RAW MATERIALS

Definition of Equipment

1. Equipment may be defined as any piece of plant, machinery, instrument etc, which is used for carrying out a specific activity or operation e.g. mixer, dryer, HPLC etc,
2. Equipment can be a single piece or it may consists of a set of integrated pieces to perform a common activity e.g. water purification plant.

EQUIPMENT SELECTION

While selecting the equipment, following points should be considered:

i. Design

The design of the equipment should meet user requirements, for which the equipment is selected. For this purpose User Requirement Specification (URS) should be prepared. URS will vary from equipment to equipment but this should at least answer the following questions'.

- Which kind of operation we are going to perform using this equipment?
- What capacity it should have in terms of holding and in terms of output?
- Which materials we are going to use in this equipment and do they have any interaction with the material of construction?
- How this equipment will be cleaned?
- Whether we are going to face any problem in validating the cleaning operation?
- Do we have trained operators to operate this equipment?
- 'What will be the starting and stopping time for the equipment?
- Whether maintenance of this equipment causes any contamination to the product being handled?
- What is the level of technology used?

Based on such information the user requirement specification is made and sent to the supplier who prepares the design qualification of design specification.

ii. Size

Size of the equipment is decided based on the volumes of materials, which we are going to handle. Batch sizes are also directly related to the size of the processing equipment. In case of size of equipment following things should be considered:

- Physical dimensions of the machinery (length x height x width).

- Size of the room in which the machine is going to be installed and the path in the plant through, which it will be transported.
- Holding and output capacity of the equipment
- Minimum-and maximum volume of materials we are going to handle and whether the equipment is able to process those minimum and maximum volumes.

iii. Location

Decision of locating the equipment in the plant depends upon the logical process movement Following are the factors which influence the location of the equipment:

- Utility services required.
- Potential danger of contamination and mix-ups.
- Material handling and movement.
- Movement for processing and cleaning
- Men movement for repair and maintenance.

iv. Construction

Following four main factors should be considered:

- Ease of cleaning the equipment and surrounding area.
- Ease of operation of the equipment.
- Ease of maintenance of the equipment.
- The material of construction (MOC)

DOCUMENTS REQUIRED WITH EQUIPMENT

1. Machine/Equipment manuals/SOP.
2. Machine/Equipment layout drawing, showing the position of the equipment in the rooms.
3. Equipment validation reports.

PURCHASE SPECIFICATIONS FOR EQUIPMENTS

While purchasing equipment following parameters/ specifications should be considered:

- Operating criteria are adequate for the process- size, speed and effectiveness. Availability of spares and servicing (Spare parts should be easily available).
- Ease of maintenance and cleaning.
- Environmental issues (Equipments disseminating dust may cause contamination to other products being manufactured and Equipment producing noise)

- Construction material (material used for construction of equipment should be non reactive with A.P.I, Raw materials and products being manufactured).
- Availability of process controls (e.g. Automatic weight adjustment on tablet press and temperature records on oven).
- Cost of equipment.
- Availability of SOP, design and maintenance manuals from supplier with equipments those are important for operating, handling, validation and qualification.

MAINTENANCE OF EQUIPMENTS

a) Equipment's shall be maintained at appropriate intervals to prevent the malfunction that can affect the process used for manufacturing.

b) Written procedures shall be established and followed for the maintenance of equipments used for manufacturing and the procedures shall include:

i. Maintenance schedule (Frequency of maintenance, calibration, validation).

ii. Assignment of responsibility for maintenance of equipment.

iii. A description of method/procedures used for maintenance.

iv. Protection of equipment.

v. Inspection of equipment before use.

c) All the records related to equipment maintenance shall be kept for further use.

Definition of raw material

"It is defined as the starting material used in manufacturing of finished product".

Purchase specifications for raw materials

Regarding purchasing of raw materials following points should be considered:

- Cost of raw material.
- Identity, purity and quality of raw material.
- Vendor selection: Materials should be purchased and sourced only from approved suppliers and manufacturers. Choice of vendor should be primarily based on quality consideration and Supplier/Manufacturer of the material should have his name listed in companies approved vendors list.
- All raw materials should be checked for following things:

i. Name of the manufacturer/ supplier.

ii. Name of the product/material. iii.

iii. Batch numbers.

iv. Date of manufacture and date of expiry.

v. Quantity received and number of containers or packages.

vi. Condition of containers and materials.

- Storage conditions: (Appropriate special storage conditions e.g. store at low temperature, low humidity away from direct light etc. or sterile material etc.) should be clearly mentioned.
- Labels on raw materials should bear the following information :

a) The name and code number of the product.

b) The batch number given by the supplier/ manufacturer.

c) Storage conditions.

d) Melting/ boiling point.

e) Molecular weight.

f) Expiry date of the product

g) Handling hazards associated with raw material.

h) Precautions/Safety measures.

i) Instructions for sampling.

j) Frequency of re-examination of stored raw material.

MAINTENANCE OF STORE FOR RAW MATERIALS STORAGE AREA

1.There should be a sufficient area/ Capacity for the storage of raw materials.

2.The area used for storage of raw materials should be clean, dry and maintained within acceptable limits of environmental conditions.

3.There should be a well equipped and appropriately designed reception area for receipt of raw materials.

4.There should be a Separate area for sampling.

5.There should be separate areas for storage of rejected, recalled or returned material.

6.There should be a separate Safe and secure area for storage of narcotics, psychotropic, hormones, steroids, highly active, dangerous and risky material to avoid hazards and contamination of other products. G. There should be a separate area for in-process materials, bulk products and finished products.

7.There should be separate areas for retained samples.

STORAGE CONDITIONS

The raw materials in the store should be stored according to its storage conditions required: For example:

- For general product: Room temperature should be 30◦C and Relative humidity should be 60%.
- Products requiring storage in air conditioning (Temperature should be 25± 2◦C &Relative humidity should be 45 to 55%)
- Products requiring Low temperature storage (Temperatureshould be 2 to 8◦c)
- Separate area for sterile product storage in AC under sterile conditions.
- Light sensitive material in amber color container.

Labeling of material in storage area

- Designated name of product and code
- Batch no. given by supplier
- Storage conditions
- Handling procedure
- Hazards and risks associated with it.
- Precaution to be taken.
- Safety Measures
- Expiry date or date beyond which retesting is necessary.

VERY SHORT QUESTIONS (2marks)

1. What is cross contamination?
2. What is Quarantine?
3. What is calibration?
4. What is bioburden.
5. What is HVAC?
6. Write down the factors affecting selection of equipment.
7. What is ULPA?
8. What is electrostatic discharge?
9. How static charge can be eliminated
10. How many types of contaminations are there in pharma industries?
11. What should be the frequency of HEPA filter integrity testing?

SHORT QUESTIONS (5 marks)

1. What role does the head of production department and quality control department play in fulfilling the objectives of GMP?
2. Write a note on raw material maintenance
3. Discuss about the equipment cleaning, calibration and maintenance.

LONG QUESTIONS (10 marks)

1. Discuss in detail the contamination sources in pharma industry.
2. Discuss the primary objectives of environmental monitoring along with the preparation of environmental monitoring programs.