

- **Define what is Good Manufacture Practice GMP and explain its importance in Pharmaceutical productions**
 - Good Manufacturing Practice is that part of Quality Management which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the Marketing Authorisation, Clinical Trial Authorisation or product specification. Good Manufacturing Practice is concerned with both production and quality control
 - Importance: GMP is designed to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product.
- **Define QA and QC and compare between them in a tabular form**

• QC	• QA
Part of Good Manufacturing Practice	sum total of the organized arrangements
Lab based	Process/company based
Strategy of Detection/ finding the problem	Strategy of Prevention/process to avoid the problem and guarantee good quality
QC is a corrective tool	QA is managerial tool
Responsibility of specific team QC	Responsibility of everyone on the team

- **What is PQR and what are the main points which shall be included in it**
 - Annual Product Quality Review is a mandatory requirement of Good Manufacturing Practice. FDA uses the term “Annual Product Review” (APR) while “Product Quality Review” (PQR) term is used in EU-GMP guidelines. The PQR concentrates on the quality system and process to show that they continue to produce consistently good quality product.
 - A review of starting materials including packaging materials used in the product
 - A review of critical in-process controls and finished product results.
 - A review of all batches that failed to meet established specification
 - A review of all significant deviations, their related investigations, and the effectiveness of resultant corrective and preventative actions taken.
 - A review of all changes carried out to the processes or analytical methods.
 - A review of Marketing Authorization variations
 - A review of the results of the stability monitoring program and any adverse trends.
 - A review of all quality-related returns, complaints and recalls and the investigations performed at the time.
 - A review of adequacy of any other previous product process or equipment corrective actions.
 - Review of post-marketing commitments and pharmacovigilance, where applicable.
 - The qualification status of relevant equipment and utilities
 - A review of any contractual arrangements to ensure that they are up to date.
- **What is CAPA and its main use in GMP explaining the PDCA cycle**
 - Corrective and preventive action - Consists of improvements to an organization's processes taken to eliminate causes of non-conformities or other undesirable situations
 - PDCA (Plan->Do->Check->Act)
- **What is Root Cause Analysis RCA and discuss its different techniques and the main differences between them.**
 - A root cause is the identification of the source of the problem where the person(s), system, process, or external factor is identified as the cause of the non-conformity
 - The root cause analysis can be done via 5 Whys (one major cause- one root cause), Affinity-Diagram (inter-related and detailed causes, which have something in common and can be grouped to a Major Causes) and Fishbone Diagram (numerous root causes based on Cause and Effect Relationships)

- **Briefly discuss what are the main requirements mentioned by GMP guidelines concerning QC areas**
 - QC laboratories should be separated from production areas
 - Control laboratories should have suitable design with enough space to avoid mix-ups and cross-contamination
 - There should be adequate suitable storage space for samples and records
 - Separate rooms may be necessary to protect sensitive instruments from vibration, electrical interference, humidity, etc.
 - Special requirements are needed in laboratories handling particular substances, such as biological or radioactive
- **Briefly discuss what are the main requirements mentioned by GMP guidelines concerning Storage area**
 - Should be of sufficient capacity to allow orderly storage of the various categories of materials and products
 - Should be designed or adapted to ensure good storage conditions
 - Should be clean and dry and maintained within acceptable temperature limits
 - Where special storage conditions are required these should be provided, checked and monitored
 - Receiving and dispatch bays should be protected materials and products from the weather
 - Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked, and their access restricted to authorised personnel.
 - There should normally be a separate sampling area for starting materials.
 - Segregated areas should be provided for the storage of rejected, recalled or returned materials or product.
 - Highly active materials or products should be stored in safe and secure areas.
 - Printed packaging materials are considered critical to the conformity of the medicinal product and special attention should be paid to the safe and secure storage of these materials.
- **What are the qualifications of the qualified person? and if he is the responsible for releasing the batch, mention briefly his main duties**
 - A qualified person shall be in possession of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course of study, or a course recognized as equivalent by the Member State concerned, extending over a period of at least four years of theoretical and practical study in one of the following scientific disciplines : pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology. However, the minimum duration of the university course may be three and a half years where the course is followed by a period of theoretical and practical training of a minimum duration of one year and including a training period of at least six months in a pharmacy open to the public. The qualified person shall have acquired practical experience over at least two years, in one or more undertakings which are authorized to manufacture medicinal products.
 - Releasing the batch: control that GMP have been followed; The principal manufacturing and testing process have been validated; approval has been given by the head of QC;

- **Mention briefly the main duties of the head of QC and the head of production departments**
 - QC: to approve or reject, as he sees fit, starting materials, packaging materials, intermediate, bulk and finished products; to ensure that all necessary testing is carried out and the associated records evaluated; to approve specifications, sampling instructions, test methods and other QC procedures; to approve and monitor any contract analysts; to ensure the qualification and maintenance of his department, premises and equipment; to ensure that appropriate validations are done, to ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.
 - Production departments: 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 and to ensure their strict implementation; to ensure that the production records are evaluated and signed by an authorised person; to ensure that the qualification and maintenance of his department, premises and equipment; to ensure that the appropriate validations are done; to ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.
- **There are many levels of personnel training in pharmaceutical industries mention them and give examples**
 - Initial training
 - Specific training on the duties assigned
 - Continuing training
 - Practical effectiveness periodically assessed
 - Personnel working in areas where contamination is a hazard specific training should be given
- **Explain what Standard Operation Procedures SOP is and discuss briefly what is its content and writing style**
 - Standard operating procedure SOP: SOP is a set of written instructions that document a routine or repetitive activity followed by an organization
 - Development and use of SOPs is a part of the successful quality system
 - Terms are used same as SOPs are protocols, instructions, worksheets and operating procedures
 - Each department will have his own SOPs; production and QC etc.
 - Main purpose is to execute the processes the proper way according to same standards and procedures to minimize variation and promote quality
 - The facility should maintain a master list of all SOPs archived under supervision of QM with guarantee of easy reaching, reviewing and modifying of the documents and guarantee of keeping a reachable and updated copy of the SOPs for each significant executor
 - Content of SOP: **Name** and **address** of the company
 - SOP **Nr** and **date** for both writing and reviewing the document
 - **Aim** or objective of the SOP
 - **Scope** (area which will be covered by the SOP)
 - Process or **steps** to be carried out in **sequential order**
 - **Whose responsibility** to carry out the SOP
 - Any other useful information, sometimes **table of contents** should be done for easier and quicker reference
 - **Name** and **signature** of the person who wrote and reviewed the document
 - SOP writing style: SOP should be written in a concise, step-by-step and easy-to-read format
 - The information presented should be unambiguous and not overly complicated
 - The active voice and present verb tense should be used • The term “you” shouldn’t be used, but implied

- The document should not be wordy or overly lengthy
- In addition, follow the style guide used by the organization, e.g., font size and margins etc.
- **What is Ring test and what is its use in QC and how to calculate it according to AGES system**
 - A ring test is an inter-laboratory test that allows to evaluate the performance of testing laboratories and is based on analysis of similar homogenous samples. The aim is to enable laboratories to assess and improve their feed analysis.
 - A ring test offers to a laboratory a possibility of external quality assessment of the analytical results it produces. Any laboratory which needs independent assessment of the quality of analytical results it produces should participate in ring test and take the opportunity to compare own performance with other laboratories. Ring tests can monitor the quality of analytical results and identify assays that need improvement through for example staff training, proper use of equipment, suitable of methods among others- Ring test is essential part of quality control measure to demonstrate competency to accreditation bodies, customers and other regulatory bodies.

How do the results of the ring test allow laboratories to evaluate their performance?

In a ring test quantitative criteria (such as the z-scores) are often used for evaluation of the laboratory performance. For each assay 'z-score' is calculated:

$$z\text{-score} = \frac{|x_{lab} - \bar{x}_{RT}|}{s_{RT}}$$

x_{lab}	result of the lab
\bar{x}_{RT}	mean of the all results from the participating laboratories
s_{RT}	standard deviation of all results

- **Sometimes the pharmaceutical firm needs a production contract, the main elements of it is the contract giver, the contract acceptor and the contract itself, discuss briefly**
 - **Contract Giver:** The Contract Giver is responsible for assessing the competence of the Contract Acceptor to carry out successfully the work required according to the required Guidelines of GMP
 - The Contract Giver should provide the Contract Acceptor with all the information necessary to carry out the contracted operations correctly in accordance with the marketing authorization and any other legal requirements
 - The Contract Giver should ensure that the Contract Acceptor is fully aware of any problems associated with the product or the work which might pose a hazard to his premises, equipment, personnel, other materials or other products
 - The Contract Giver should ensure that all processed products and materials delivered to him by the Contract Acceptor comply with their specifications or that the products have been released by an authorized person.
 - **Contract acceptor:** The Contract Acceptor must have adequate premises and equipment, knowledge and experience, and competent personnel to carry out satisfactorily the work ordered by the Contract Giver
 - The Contract Acceptor should ensure that all products or materials delivered to him are suitable for their intended purpose
 - The Contract Acceptor should not pass to a third party any of the work entrusted to him under the contract without the Contract Giver's prior evaluation and approval
 - The Contract Acceptor should refrain from any activity which may adversely affect the quality of the product manufactured and/or analyzed for the Contract Giver
 - **The Contract:** A contract should be drawn up between the Contract Giver and the Contract Acceptor which specifies their respective responsibilities relating to the manufacture and control of the product

- Technical aspects of the contract should be drawn up by competent persons suitably knowledgeable in pharmaceutical technology, analysis and Good Manufacturing Practice
- All arrangements for manufacture and analysis must be in accordance with the marketing authorization and agreed by both parties
- The contract must describe in detail who is responsible for releasing the batch, purchasing materials, QC analysis
- The contract should permit the Contract Giver to visit the facilities of the Contract Acceptor
- In case of contract analysis, the Contract Acceptor should understand that he is Subject to inspection by the Authority
- **What is the 3 classifications of manufacture defects in pharmaceutical industry explains them and give examples and what is the suitable action to be taken with each defect**
 - **Critical Defects** are those defects which can be life-threatening, and which require the company to take immediate action by all reasonable means, as soon as the defect becomes apparent, whether in or out of business hours. This means that all wholesalers must be alerted, and the necessary actions taken to commence recalling the product throughout the distribution chain. This illustrate how important distribution records are, including those of the wholesaler. Examples: product labelled with incorrect name; Counterfeitt or deliberately tampered with product; Microbiological contamination of a sterile product. It may mean using radio and tv news broadcasts to conduct the recall.
 - **Major Defects** are those defects which may put the patient at some risk, but which are not life-threatening. They will require the recall of the batch or product withdrawal within a few days. In some countries this is specifies as within 48 hours. Examples: Any labelling/leaflet misinformation which represents a significant hazard to the patient; Microbial contamination of non-sterile products with some risks; Non-compliance to specification. A country may decide on different time-scales for recalls, depending on the appropriate response for the product or defect concerned.
 - **Other Defects** are those defects which present only a minor risk to the patient. Any batch recall or product withdrawal would normally be initiated within a few days. In some countries this is specified as within five working days. Examples: readily visible isolated packaging/closure faults; Contamination which may cause spoilage or dirt and where there is minimal risk to the patient.
- **What is HACCP and mention its main 7 principles**
 - HACCP is a systematic method for the identification, assessment and control of safety hazards
 - 1. Conductus a **hazard** Analysis
 - 2. Determine the **critical control points** (CCPs)
 - 3. Establish target levels and **critical limit(s)**
 - 4. Establish a system to **monitor** the CCPs
 - 5. Establish the **corrective action** to be taken when monitoring indicates that a particular CCP is not under control
 - 6. Establish **procedures to verify** that the HACCP system is working effectively
 - 7. Establish **documentation** concerning all procedures and keep records appropriate to these principles and their application

- **What are the other methods of risk analysis? mention 5 and explain one in more details**
 1. Failure Mode Effects Analysis (FMEA)
 2. Failure Mode Effects and Criticality Analysis (FMECA)
 3. Fault tree analysis (FTA): This tool assumes failure of the functionality of a product or process. The results are represented pictorially in the form of a tree of fault modes. This can be used to investigate complaints or deviation in order to fully understand their root cause
 4. Hazard operability Analysis (HAZOP)
 5. Preliminary hazard Analysis (PHA)

- **In a table, compare between internal and external audit**

	Internal Audit	External Audit
Purpose of the audit	Check if the process works according to the required GMP standards	Check if the process works according to the required GMP standard
The auditors	Employed or outsourced	outside firm or “Registered Auditors”
Audit agenda	By the company internal	By the Auditor (external)
Auditor report to	Relevant managers or audit committee (if present)	Shareholders or person of responsibility
Sort of report	Tailored report about how the risks and objectives (try to improve)	Report of the truthfulness and fairness of the process (finding the faults and doesn’t have to suggest solutions)
Obligation	No, it is voluntary	Yes, when certificate or contract obligates
Period	Continuous Process	Once in a year (accordingly)

- **In a table, compare between the 3 kinds of internal audit**

	Tier One	Tier Two	Tier Three
Carried out	Staff of a section or department of company	Local Quality assurance Group	Cooperate Compliance Group and external Consultant
Purpose	Require Short time and Focusing on house keeping and documentation	Require Longer period and more focus on system than housekeeping	More focusing of assess the readiness of regulatory audit
Frequency	More	Less	Even less
Qualification	Receive Some Basic Training	More exklusive Trainings	Highly trained and experienced or specialist with the expert knowledge of GMP

- **What is the main information which shall be included in the patch packaging record?**

- The name and batch number of the product
- The date(s) and ties of the packaging operations
- Identification of the operator(s) who performed each significant step of the process and the name of any person who checked these operations
- Records of checks for identity and conformity with the packaging instructions, including the results of in-process control
- Details of the packaging operations carried out

- Whenever possible samples of printed packaging materials used, including specimens of the batch coding, expire dating and any additional overprinting
- Notes on any special problems or unusual
- Reconciliation of packaging materials including issues, use returns and destruction
- Approval by the person responsible for the packaging operations.
- **What is the main information which shall be included in the receipt paper?**
 - The name of the material on the delivery note and the containers
 - The in-house name and or code of materials
 - Date of receipt
 - Suppliers name and manufacturers name
 - Manufactures batch or reference number
 - Total quantity and number of containers received
 - The batch number assigned after receipt
 - Any relevant comment
- **What are the different kinds of water which are used in Pharmaceutical production? and mention examples for its different uses (you can include it in schematic form) (scheme for Pharmaceutical water system)**
 - Drinking water / potable water - Pre-Filtration; removal of specific ions
 - Bulk Purified water (BPW) – protect from recontamination, protect from microbial proliferation
 - Bulk Highly Purified Water (BHPW) - protect from recontamination, protect from microbial proliferation
 - Bulk Water for Injection (BWFI) - distillation as the final purification step.
- **What HVAC refers to? And what can HVAC do (function) and what can't HVAC do for a pharmaceutical production facility?**
 - **Heating Ventilation and Air-Conditioning**
 - Control **airborne particulate**, dust and micro-organisms through air filtration using HEPA filters
 - Maintains **room pressures** (in areas that must remain cleaner than surrounding areas (+ve))
 - Reduces **contamination** by air flow from cleaner areas toward adjoining space through doors, ceiling openings (reduces chances of contamination)
 - Maintains space **moisture** (by cooling to dew point temperature and using desiccant dehumidifiers)
 - Maintains space **temperature** (can affect product directly or indirectly) All to minimize and prevent contamination and cross contamination
 - Cannot clean up contaminated surfaces, room or equipment
 - Do not compensate for workers who do not follow procedures
- **What are the main components of the AHU (Air Handling Unit)?**
 - HVAC system comprises of **Air Handling Unit (AHU)** connected to a **ductwork ventilation system** that distributes the conditioned air through the building and returns it to the air handler (AHU).
 - • **Air Handling Unit (AHU)** is a device used to condition and circulate air as a part of HVAC. It is usually a large metal box containing a **blower, heating or cooling elements, filter racks or chambers, sound attenuators and dampers**
- **Discuss the main chapters of GDP 2013 explaining the main differences than GMP**
 - The obvious difference between GDP and GMP is that GDP covers the wholesale distribution of medicines, whereas GMP covers their manufacture
 - • There is overlap between the two – to maintain product quality after a batch has been released from the manufacturing site, as well as to monitor and control complaints, problems and to permit a recall
 - • The European Union's guidelines on Good Distribution Practice (GDP) were updated at the end of 2013

- **Explain the main difference between ISO 9001 version 2008 and 2015 explaining the connection with the 2015 and the PDCA cycle**
 - The first three clauses in ISO 9001:2015 are largely the same as those in ISO 9001:2008, but there are considerable differences between ISO 9001:2008 and ISO 9001:2015 from the fourth clause onwards. The last seven clauses are now arranged according to the PDCA cycle (Plan, Do, Check, Act)
- **What is AMBO 2009? and Mention the main points covered by AMBO 2009 in Austria**
 - Regulation on Operating Instruction for Medicinal Products
 - Pharmaceutical Quality Assurance
 - Facility organization and personnel
 - Facility Equipment
 - Production Area
 - Quality Control
 - Documentation
 - Storage area
 - GDP