Current Good Manufacturing Practices (cGMP)

Chapter 3

Objectives

- List common terms used in the Current Good Manufacturing Practice (cGMP) for finished pharmaceuticals
- Define cGMP and its importance
- Outline Code of Federal Regulation (CFR)

Common terms

Drug product: Finished form contains active drug and inactive ingredients.

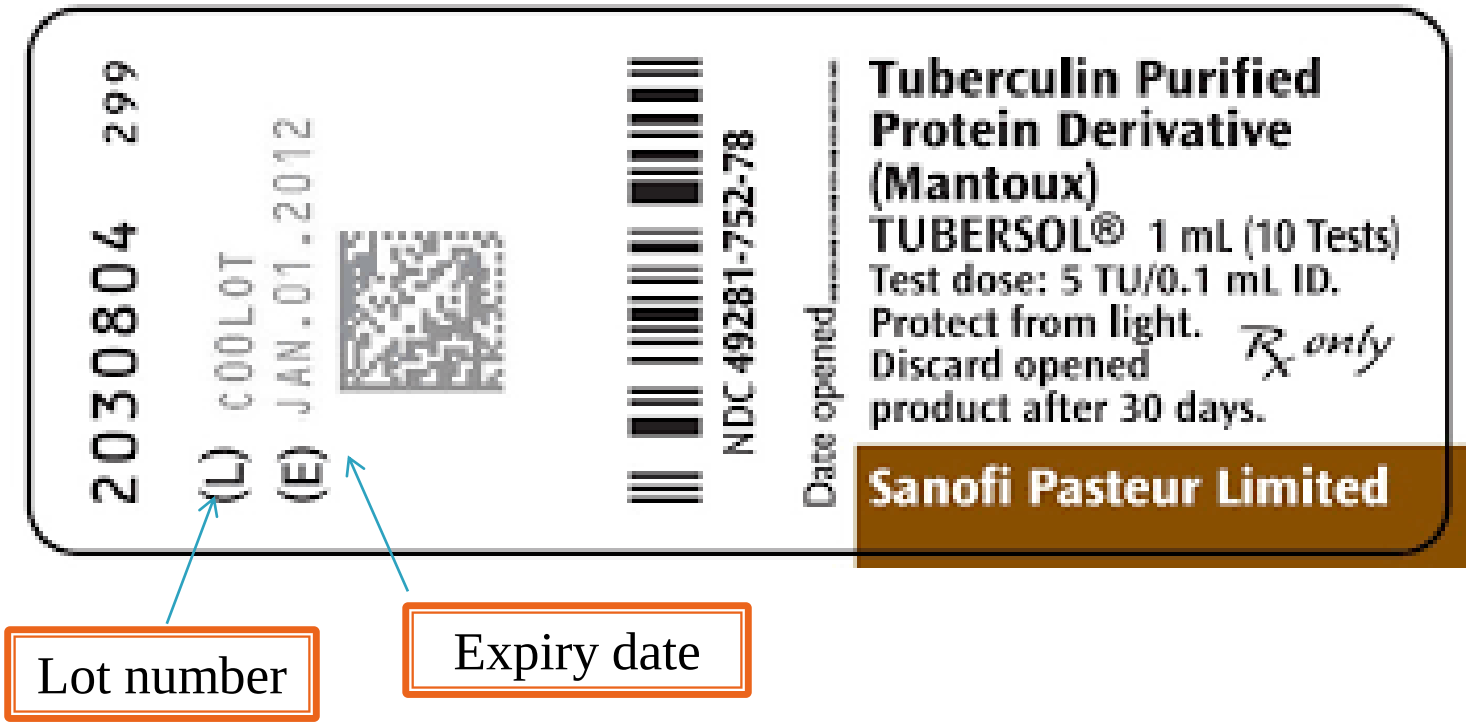
Component: Any ingredient used in manufacture of drug product.

Active pharmaceutical ingredient (API): any component have pharmacologic activity or direct effect in diagnosis, cure, mitigation, treatment or prevention of disease.

Inactive ingredient: Any component other than the active ingredients in drug product.

Batch: a specific quantity of a drug of uniform specified quality produced according to **single manufacturing order during the same cycle of manufacture.**

Lot: A batch or any portion of a batch having uniform specified quality and a distinctive identifying lot number.



Lot number, control number, or batch number: combination of letters, numbers, or symbols from which the complete history of manufacture, processing, packaging, holding, and distribution of a batch or lot of a drug product may be determined

Pop quiz

Q1)) **Regarding the pharmaceutical products production as batches, which is not true?**

A- They are useful since it is possible to make any modification to the product during the manufacturing process.

B- Batch number represents a serial number for identification complete production history of product that differs from lot number

C- The batch number is important as it may be required especially when a product is recalled

D- None of them

Common terms

Master record: **the records for** the formulation, specifications, manufacturing procedures, quality assurance requirements, and labeling of each finished product.

Master Batch record and Batch production record: contain

- Product **name**, **dosage form** and **strength**, batch size

Company logo	Batch Manufacturing Record
Product Name:	Product Code:
Batch No.:	Batch size (kg):
Manufacturing date:	Expiry date:
Prepared by:	Verified by:

MASTER BATCH FORMULA	SOP	BSCL2_2020_01
	Effective date	01/01/2016

Title: Nitrazepam Suspension 5 mg/5mL

1. Product Name

2. Batch code and number

Product License number	Batch number	Batch size	Legal category
Student id	AW3P1	100 mL	CD BENZ POM

3. Equipment

Name	Equipment Number	Calibration Status
Precision balance	QUB/EQ/01	15 Jan 2016
Analytical balance	QUB/EQ/02	15 Jan 2016
Measuring cylinder 100mL	QUB/EQ/05	20 May 2016
Graduated glass pipette 1mL	QUB/EQ/09	03 Mar 2016

Signature: *Student*	Date: *17 Apr 2016*

4. Raw materials

Name	Function	Batch number	Expiry date
Nitrazepam	*Active ingredient*	*BN00N1*	*30 Sep 2017*
Tragacanth	*Suspending agent*	*BN01T1*	*30 Sep 2017*
Conc. Cinnamon Water	*Flavouring*	*BN01C3*	*17 Apr 2016*
Amaranth	*Colouring*	*BN0104A1*	*30 Sep 2017*
D/S Chloro. Water	*Preservative*	*BN01C1*	*30 Sep 2017*
Purified Water	*Vehicle*	*QUB*	*17 Apr 2016*

Signature: *Staff*	Date: *17 Apr 2016*

-List and quantity of each component in dosage unit
-list of equipment used
-Calibration of instruments
-Specific instructions for each state in the manufacturing process.
-Statement of theoretical yield at each step in the manufacturing process
-Yield of final product
-Sampling and testing procedures (in-process control)

Parameter	Limit	Observation
Machine speed	20 rpm (15-25 rpm)	
Wt. of 20 tabs	12.00g ±2 (11.76-12.24g)	
Theoretical weight/tab	600mg	
Hardness	25Kg (20-30 Kg)	
Thickness (av. of 10 tabs)	4.10mm ±0.15mm (3.95 – 4.25mm)	
Length	10mm ± 0.1 mm (9.9 – 10.1 mm)	
Width	5 mm ± 0.1mm (4.9 – 5.1 mm)	
Disintegration time	NMT 15 mins	
Wt. variation	± 3% of Av. Wt.	
Friability (10 tabs)	NMT 1.0% w/w	

Validation Process: Establishing **documented evidence** which **provides a high degree of assurance**, that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes (process does what it purports to do). i.e **Action of proving .**

Phase I- Pre-validation qualification (Process Design), relate to drug development, pilot study and scale-up reliably.

Phase II- Process validation, verify that all established limits of the critical process parameter

Phase III- Validation Maintenance Phase, it requires frequent review of all process related documents

Validation protocol: a **prospective experimental plan** to produce documented evidence that the system has been validated.

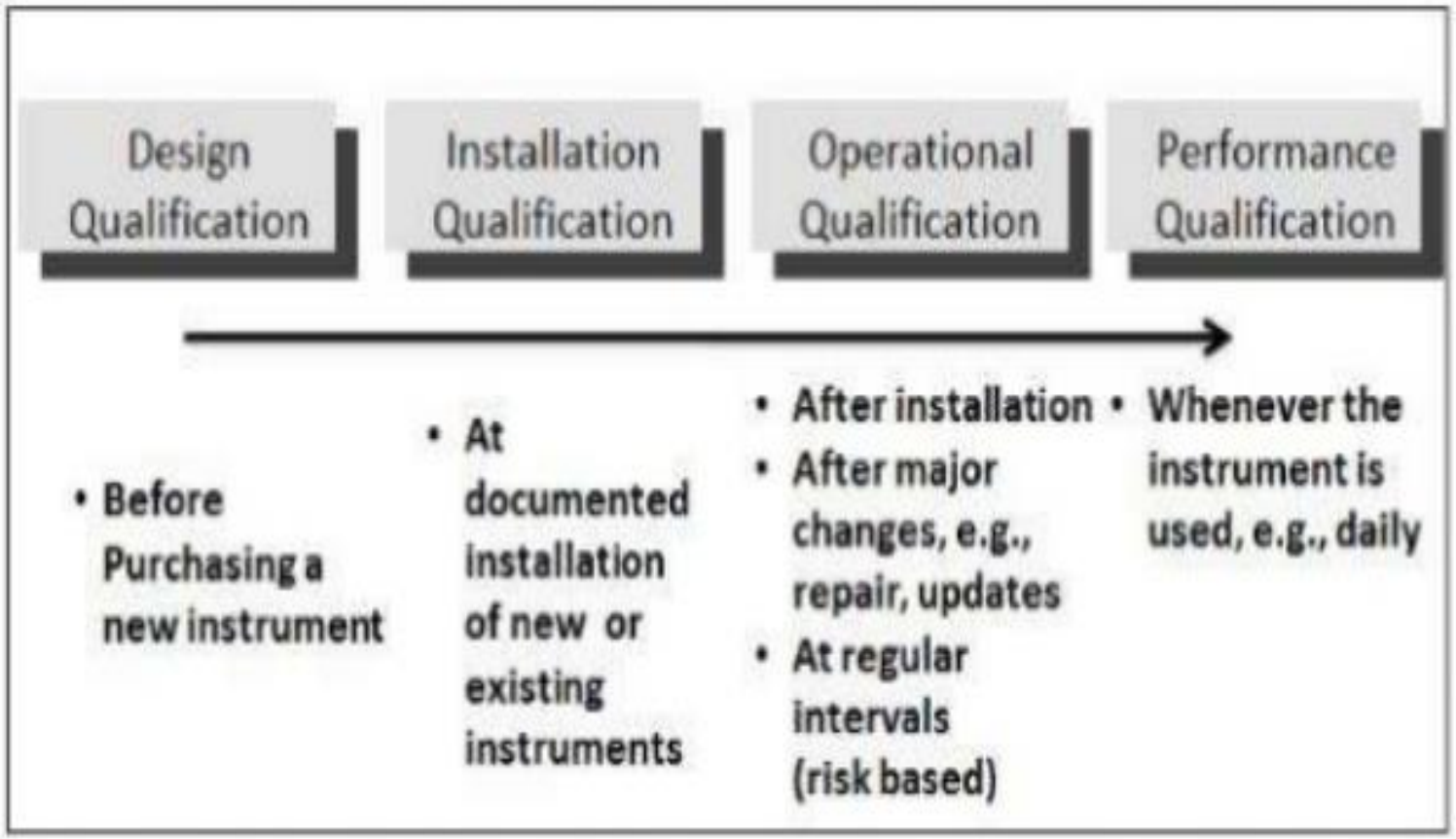
It gives idea about future performed:

- What activities are to be performed?
- Who is going to perform these activities?
- When the activities should start and when they should get over?
- What documents will be generated?
- What the policy on revalidation

Validation: Documented evidence that a system (e.g., equipment, software, controls) does what it purports to do

The major types of Validation :

- Process validation
- Cleaning validation
- Equipment validation
- Validation of analytical methods



Quality audit: A **documented activity** performed in accordance with established procedures on a planned and periodic basis to verify compliance with the procedures to ensure quality

Compliance: determine by inspection of **the extent to which the manufacturer is acting** with prescribed **regulations, standards, and practices**.

Common terms

Certification: **Documented testimony** by **qualified authorities** that a system qualification, calibration, validation, or revalidation has been performed appropriately and that the results are acceptable.

Quarantine: An area that is marked, designated, or set aside for the holding of incoming components **prior to acceptance testing and qualification** for use

Quality Relationship

Quality assurance: all evidence needed that activities relating to quality are being performed adequately.

Quality control: process through which industry measures actual quality performance, compares it with standards.

Quality control unit:
the organizational element designated by a firm to be responsible for work related to quality control

In 1937, a public health disaster tragically (**liquid Sulfanilamide formulation** contained a poison, it killed 107 people) drove home the need for a stronger federal law

In 1941, nearly 300 people were killed or injured by one company's sulfathiazole tablets, a **sulfa drug tainted with the sedative** phenobarbital.
That incident caused FDA to drastically **revise manufacturing** and **quality control requirements**, leading to what would later be called GMPs

What are cGMPs?

GMP: regulations are established by the Food and Drug Administration (FDA) to ensure that minimum standards are met for drug product quality

In another words, Rules set up by the FDA that drug manufacturers need to follow in order to ensure that a safe , effective and high quality product is manufactured

cGMP, employ technologies and up-to-date (“current”) in order to comply with the regulation

Why GMP is important?

It is designed to saves costs, minimize risks involved in any pharmaceutical production that cannot be eliminated through testing the final product, improve the standard of drugs worldwide.

<u>Some of the main risks</u>** are

- <u>Unexpected contamination of products</u>,
- <u>Incorrect labels on containers</u>,
- <u>Insufficient or too much active ingredient</u>,

Principle of GMP

- Written step by step operating procedure and work instruction
- Carefully following written procedures
- Promptly and accurately documenting work for compliance and traceability
- Validating work ensures that system is doing what they are designed to do
- Develop a good design for the facility and the equipment from the beginning

- Properly maintaining facilities and equipment
- Clearly defining, developing and demonstrating job competence
- Protecting products against contamination by making cleanliness a continual habit Practice good Hygiene
- Design the quality in product manufacturing “effective control of quality”

- cGMP Code of Federal Regulations (CFR) **Finished Pharmaceuticals, Biologic products, Medicated articles, Medical devices**

Outline of Current Good Manufacturing Practice Regulations

- Subpart A--General Provisions
- Subpart B--**Organization and Personnel**
  - Personnel qualifications
  - Personnel responsibilities
  - Consultants
- Subpart C--**Buildings and Facilities**
  - Design and construction features
  - Lighting
  - Ventilation, air filtration
  - Plumbing Sewage and refuse warehousing
  - Washing and toilet facilities
  - Sanitation, Maintenance

- Subpart D—**Equipment**
  Equipment design, construction
  Equipment cleaning and maintenance
- Subpart E**--Control of Components and Drug Product Containers and Closures**
- Subpart F**--Production and Process Controls**
  Written procedures,
  Charge-in of components
  Calculation of yield
  In-process testing of materials and products
- Subpart G**--Packaging and Labeling Control**
- Subpart H**--Holding and Distribution**
- Subpart I**--Laboratory Controls**
- Subpart J**--Records and Reports**
- Subpart K**-- Returned and Salvaged Drug Products**

Organization and Personnel

- ✓ deals with responsibilities of **quality control unit**, **employees**, and **consultants**.
- ✓ quality control unit have responsibility for all functions that affect product quality. This includes **accepting** or **rejecting** product components, product specifications, finished products, packaging, and labeling. Adequate laboratory facilities shall be provided, written procedures followed, and all records maintained.
- ✓ All personnel required to have **education, training, and experience.** Appropriate programs of education and training, and performance evaluations are essential for maintaining quality assurance.