



QUALITY CONTROL OF PHARMACEUTICAL PRODUCTS AND PRODUCTION MANAGEMENT

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ABSTRACT

Background information: For pharmaceutical goods to remain consistent, safe, and effective, quality control, or QC, is essential. Strict testing, inspections, and adherence to legal requirements are all part of the procedure to find and stop flaws or deviations in the manufacturing process. Finding live microorganisms in the air, raw materials, water, and final products is known as microbiological quality control, or QC, and it is a crucial part of the pharmaceutical industry. Scope and methods: The goal of this process is to detect and quantify microbial contamination using a variety of testing methodologies and environmental monitoring approaches. Key protocols include microbiological limit tests (MLT) for water and non-sterile products, sterility tests for products meant to be sterile, and the use of settle plates, active air sampling, and surface swabs to monitor industrial environments. By assessing the inhibition of bacterial growth, the agar diffusion method for antibiotic testing establishes the potency of antibiotic products. Standards like EU GMP Annex 1 and ISO 14644-1 must be followed in order to interpret results and guarantee regulatory compliance. Finding and conclusions: the data indicated that various products meet the requirements for pharmaceutical safety and microbiological quality. regarding the sensory study no variations were found in the overall production and storage. According to microbiological analysis , all the medicines and items are considered microbiologically safe for the use of consumers.

1.INTRODUCTION

1.1 Quality control and production management

Ensuring the quality of products is crucial for the pharmaceutical sector, as it affects not only the safety and effectiveness of treatments but also the maintenance of regulatory compliance and consumer trust. Pharmaceutical manufacturing requires both production management and quality control (QC), which work together to maintain the high standards needed in this industry. Pharmaceutical quality control consists of a number of procedures meant to guarantee that goods fulfil specified standards and are free of impurities. This entails thorough testing of the raw materials, materials used during processing, and final goods. To confirm the potency, purity, and safety of pharmaceutical goods, methods including Gas Chromatography (GC), High-Performance Liquid Chromatography (HPLC), and Mass Spectrometry (MS) are frequently used.

QC is a continuous process that involves stability testing, validation of production procedures, and adherence to Good Manufacturing Practices (GMP). It is not merely a final step. However, planning, directing, and overseeing the manufacturing processes are all part of production management in the pharmaceutical industry. An efficient, economical, and legally compliant manufacturing process is guaranteed by competent

production management. This covers everything from acquiring raw supplies to streamlining production schedules, maintaining machinery, managing the personnel, and incorporating new technology into manufacturing processes.

Production management and quality control must work together for pharmaceutical businesses to be successful. By ensuring consistency, safety, and efficacy throughout every product batch, this integration reduces the likelihood of product recalls and protects public health. Furthermore, as new technologies emerge and pharmaceutical goods become more complicated, the business is always changing, calling for constant advancements in production management and quality control procedures.

- ❖ This dissertation explores the critical aspects of quality control and production management in the pharmaceutical industry. It examines the methodologies employed in QC, the challenges faced in ensuring product quality, and the strategies for effective production management. Through an in-depth analysis, this study aims to highlight the importance of these functions in the overall pharmaceutical production process and propose recommendations for enhancing quality and efficiency in pharmaceutical manufacturing.

1.2 What is quality control in pharmaceutical industries?

a) Definition and Objective

Pharmaceutical quality control refers to the methods and actions used in operations to guarantee that the goods meet predetermined criteria for quality. Ensuring that pharmaceuticals are safe to take and function as intended without side effects is the main goal.

b) Important Elements of Quality control

Testing of Raw Materials: Before raw materials are utilized in manufacturing, quality control (QC) tests them to make sure they fulfill the required purity and quality requirements. This entails making sure the right storage conditions are met, confirming the chemical composition, and searching for impurities.

In-Process Control: In-process controls are used in manufacturing to keep an eye on the working conditions and procedures. This entails evaluating intermediates and keeping an eye on crucial variables like pressure, temperature, and humidity to make sure the production process stays within predetermined bounds.

Testing of the finished Good:

To ensure that the finished product satisfies all quality requirements, it is put through a thorough testing process. The product's safety, effectiveness, and shelf life are verified using assays for active pharmaceutical ingredients (APIs), stability testing, dissolution testing, and microbiological testing.

c) Strategies and Procedures

Analytical Chemistry: The chemical makeup and purity of pharmaceutical items are frequently examined using methods including High-Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), Mass Spectrometry (MS), and Nuclear Magnetic Resonance (NMR). Microbiological testing: Verifies that no hazardous microorganisms are present in the items. Microbial limit testing, endotoxin testing, and sterility testing are some of the techniques. Physical testing: Assesses the product's physical characteristics, including particle size distribution, dissolution rate, and tablet hardness.

d) Adherence to Regulations

Regulations imposed by national regulatory agencies, the European Medicines Agency (EMA), and the U.S. Food and Drug Administration (FDA) must be followed by pharmaceutical businesses. Strict quality control procedures are required by these standards to guarantee the effectiveness and safety of pharmaceuticals.

1.3 Microbiological Testing for Pharmaceutical Industry Quality Control

In the pharmaceutical sector, microbiological testing is an essential component of quality control (QC). It guarantees that pharmaceuticals fulfil the strict safety and efficacy requirements necessary for human use and are free of dangerous germs.

The following are the main elements and techniques of microbiological testing in the context of quality control for pharmaceuticals:

a) The goal of microbiological QC

Microbiological testing in the pharmaceutical industry is primarily used to:

Make that all products are sterile, especially those that are given parenterally (injections, infusions, etc.). Determine the extent to which non-sterile products are contaminated by microbes. Check the antimicrobial preservatives' efficacy. Make sure that the surroundings and procedures used in manufacturing are clean.

b) Types of Microbiological tests

Sterility testing:

Purpose: Verifies the absence of live microorganisms in sterile items.

Techniques: Direct inoculation and membrane filtering are the methods used.

Guidelines: Followed by pharmacopeial standards (e.g., USP <71>, EP, JP).

Microbial Limits Testing:

Purpose: Determines whether a given pathogen is present in non-sterile items as well as the overall number of aerobic viable microorganisms.

Techniques: presence/absence testing, Most Probable Number (MPN), and plate count techniques.

Guidelines: Adhering to pharmacopeial standards (e.g., USP <61>, <62>) for conduct.

Environmental Monitoring:

Goal: Maintains the manufacturing environment's microbiological balance and cleanliness.

Techniques: Personnel monitoring with contact plates, swabs, and settle plates; air sampling; surface sampling.

Regulations: Followed GMP guidelines for execution.

Antibiotic Assay:

Purpose: evaluates the effectiveness of antimicrobial preservatives in goods as its purpose.

Techniques: Include inoculating the product with a known amount of particular microorganisms and tracking the decrease in those numbers over time.

Rules: Followed by pharmacopeial guidelines (e.g., USP <51>, EP 5.1.3).

1.4 Importance of Microbiological Quality control

To guarantee the efficacy, safety, and quality of pharmaceutical products, the pharmaceutical business relies heavily on microbiological quality control, or QC. The following major areas where microbiological QC is important can be highlighted:

a) Security of Patients

Preventing contamination involves making sure that goods are free of dangerous bacteria, which can lead to illnesses or unfavorable reactions. This is especially important for patients with impaired immune systems or those getting sterile items, such as injectables. Endotoxin control involves identifying and limiting pyrogens, or endotoxins, which can result in serious side effects include fever and septic shock.

b) Adherence to Regulations

Meeting Standards: Complies with stringent regulations established by national regulatory organizations, the FDA, and the EMA, among others. Recalls of products, legal repercussions, and loss of market authorization are all possible outcomes of noncompliance. GMPs, or good manufacturing practices: guarantees compliance with GMP, which includes regulations for preventing microbiological contamination during the production process.

c) Product Stability and Effectiveness

Effectiveness of Preservatives: confirms the antimicrobial preservatives' efficacy in products, guaranteeing that they stay safe and effective for the duration of their shelf life. Stability testing evaluates a product's capacity to withstand different environments while maintaining its intended level of potency and safety.

d) Assurance of Quality

Consistent Quality: Prevents contamination that can jeopardize the integrity and general quality of pharmaceutical products.
Environmental Monitoring: Guarantees that the industrial environment is kept under control and observed in order to avoid contamination.

e) Economic Impact:

Reduces the need for expensive product recalls and production halts brought on by contamination problems. By detecting contamination early in the production process, it also lowers waste.
Market Reputation: Preserves pharmaceutical businesses' standing in the marketplace by guaranteeing the release of safe, high-quality goods that inspire customer confidence and brand loyalty.

f) Research and development

New Product Development: Supports the creation of novel pharmaceutical medicines by guaranteeing their microbiologic safety and efficacy from the outset of research to the point of commercialization.
Process validation: Assists in the effective scale-up from pilot to full production by guaranteeing that new manufacturing processes are reliable and free of microbiological contamination.

g) Public Health Disease Control:

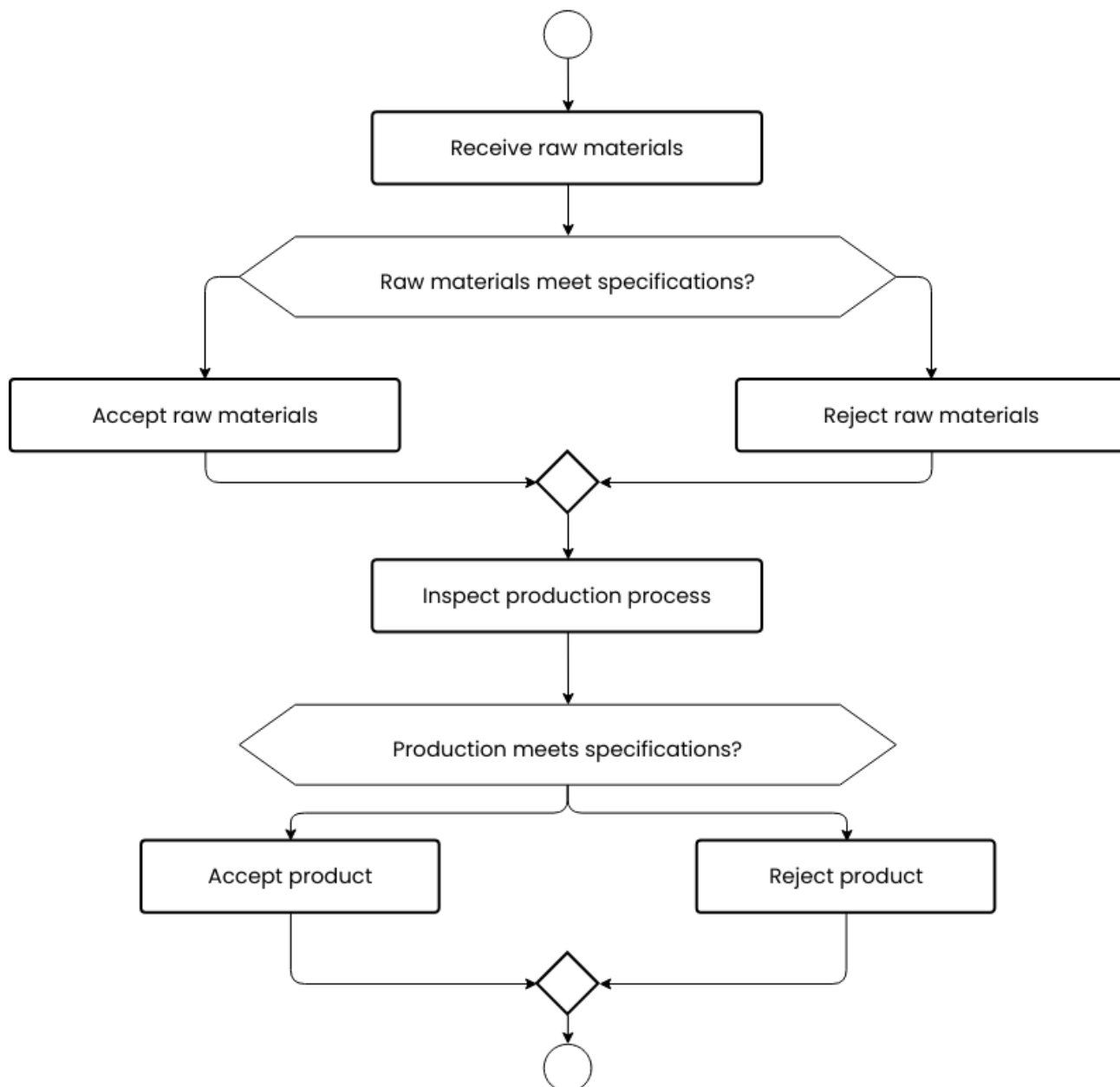
By making sure that pharmaceutical goods do not contribute to microbial resistance or new infections, public health plays a critical role in preventing the development of infectious diseases.

Production of vaccinations: Maintains the sterility and safety of vaccinations, which are essential for stopping and managing infectious diseases around the world.

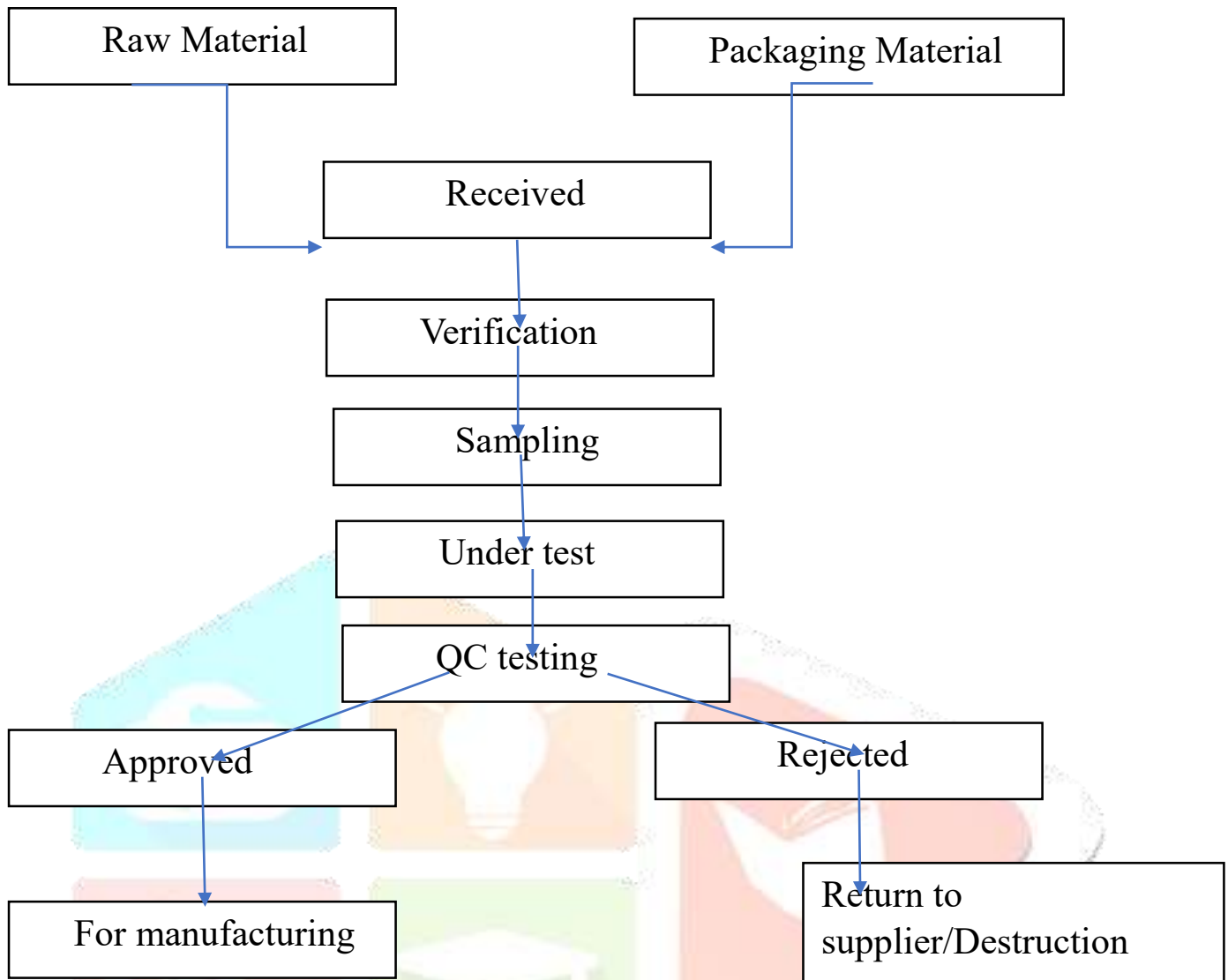
2. REVIEW OF LITERATURE

Any research study must include a review of the literature since it offers a thorough summary of the body of information already in existence and points out any gaps that the current study seeks to address. The literature study covers a range of topics related to production management and pharmaceutical product quality control (QC), including regulatory frameworks, technical breakthroughs, techniques, and industry issues.

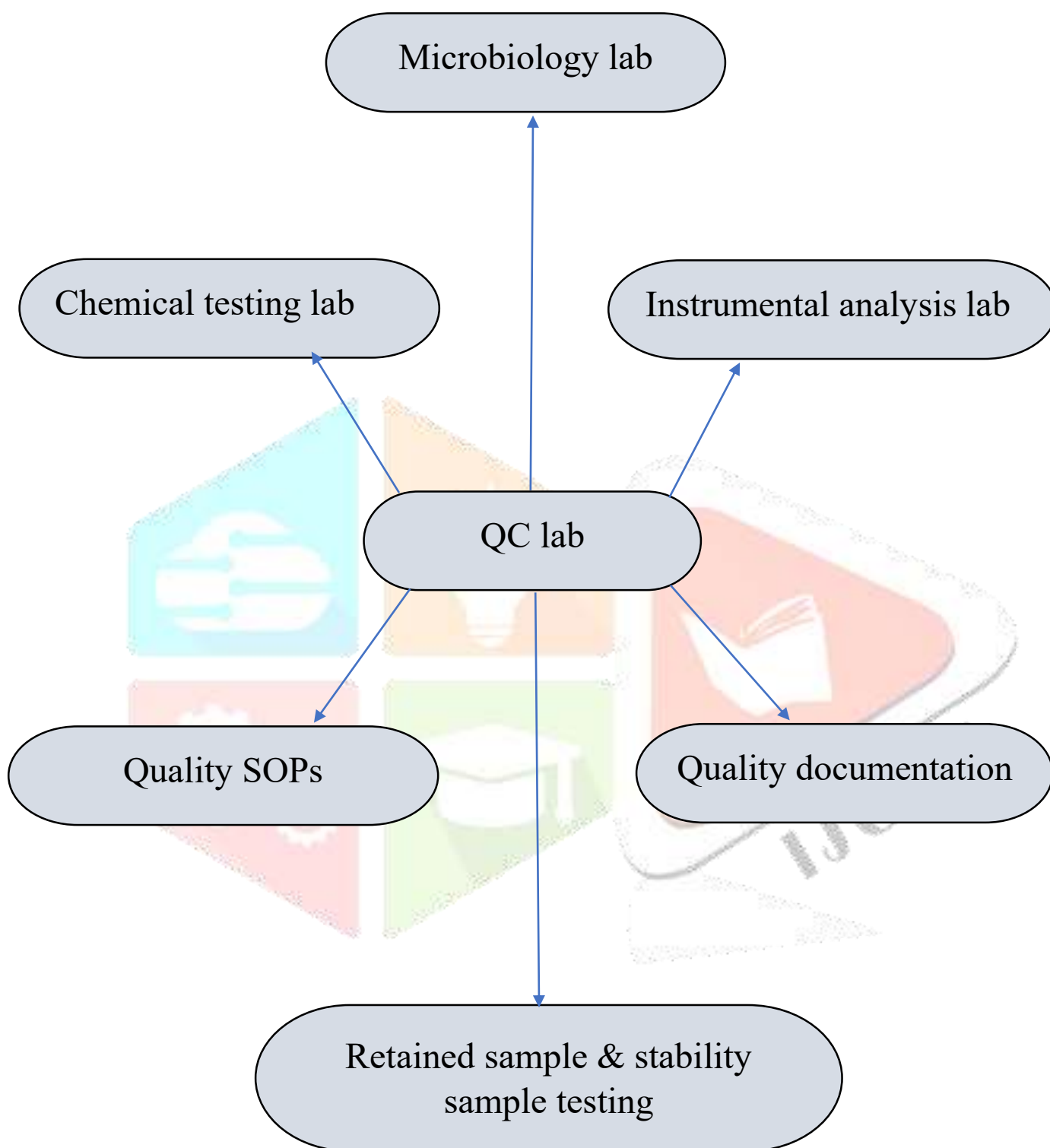
➤ 2.1 Process flow chart for Quality control



➤ 2.2 RM QC testing flow chart



➤ 2.3 Specifications of QC lab



3.MATERIALS AND METHODS

3.1 Media preparation

In pharmaceutical microbiology labs, media preparation is a basic procedure that is necessary for growing and identifying microorganisms in a variety of (QC) assays. The reliability of microbiological test results is strongly impacted by the quality and consistency of the prepared media, which makes this procedure essential for guaranteeing product safety and regulatory compliance.

material required :

prepared media powders
distilled water
weighing balance
pH meter
autoclave
conical glass bottle
sterile petri dishes
sterile test tubes
lab coat , gloves , masks

procedure :

- wash the glasswares with 2%teepol (detergent)and autoclave all the glasswares
- weigh the required amount of culture media powder using the balance
- add the weighed powder to an appropriate volume of disttled water.
- if required gently heat to let it dissolve properly
- measure or check the pH with pH meter and adjust if required
- autoclave the media at 15 psi (121 degree Celsius) for 15-20 min for sterilization
- let the media to cool down and pour it into the required plates or tubes under LAF
- To verify sterility, incubate a representative sample of the prepared media for 24 to 48 hours at 35 to 37°C. If the media is sterile, there shouldn't be any signs of microbial development.

some of the common media used during the study:

➤ SCDA: Soyabean Casein Digest Agar

The general-purpose culture medium also called Tryptic Soy Agar (TSA), is widely used in the pharmaceutical sector. It is appropriate for the detection and counting of bacteria and fungus since it facilitates the development of a broad range of microorganisms.

composition:

papaic digest of soyabean meal 5g
pancreatic digest of casein 15g
chloride 5g
sodium
agar 15g

➤ SCDM: Soyabean Casein Digest Medium

also called tryptic soya broth. It is also a general purpose broth medium used for variety of microorganisms

composition:

17.0g of pancreatic digest of Casein
3.0 g of papaic digest of soybean meal
5.0 g of sodium chloride

2.5 g Dipotassium phosphate
2.5 g dextrose

➤ **FTM: Fluid Thioglycollate Medium**

it is a general purpose medium used for the growth of aerobic and anaerobic microorganisms. particularly used in sterility testing in pharma industries. it is non selective medium

composition:

15g pancreatic digest of casein
5g yeast extract
5.5g dextrose
2.5g sodium chloride
0.5g L-cystine
0.5g Sodium Thioglycollate
0.75g agar
1mg resazurin

3.2 Environmental monitoring

A crucial component of (GMP) in the pharmaceutical sector, environmental monitoring (EM) makes sure that the manufacturing environment does not jeopardize the efficacy and safety of pharmaceutical products. EM is a technique for detecting and controlling microbiological and particle contamination that involves the systematic sampling and analysis of air, surfaces, people, and utilities.

3.2.1 Air monitoring

Air sampling techniques

Active air sampling:

In order to identify airborne microorganisms, active air sampling entails pulling a predetermined volume of air through a microbiological capture apparatus, such as liquid impingers or agar plates.

Passive air sampling:

Using exposed agar plates, passive air sampling (also known as settling plates) collects microorganisms and settling particles over a predetermined time.

SETTLE PLATE METHOD OR PLATE EXPOSURE METHOD (passive air sampling)

Material required:

Preincubated SCDA plates
Incubator
Monitoring stations or stands
Sterile forceps
Timers
Sterile swabs (optional)
Colony counters
SOPs

Procedure:

- Each agar plate should be labelled with the following pertinent information:
Location (such as a crucial area or cleanroom)
The exposure date, the beginning of the exposure
- At the designated monitoring stations, arrange the labelled sterile agar plates.
- Make sure the plates are positioned correctly in terms of height and orientation. To capture settling particles, the agar surface should be facing upwards and the lid should be on the bottom of the plate.
- Plates should be exposed for a predetermined amount of time, usually between 1-4 hrs depending on risk assessment and regulatory requirements. To precisely track the exposure length, use a timer.
- Using sterile forceps, carefully cover each plate with its lid after the exposure period to avoid contamination.
- Make sure the plates are safely covered and returned to the lab without causing any damage to the samples that were gathered.
- The exposed plates should be incubated in the following conditions:
For 48–72 hours, at 30–35°C ideal for bacterial development.
(20–25°C) for 5-7 days (or as directed by regulatory requirements) to promote fungal development.
- Count the colony-forming units (CFUs) on each plate following incubation by plate count method. manually count the colonies or use a colony counter.

3.2.2 Surface monitoring and Personnel monitoring

Visual examination, surface sampling (with swabs, contact plates, or other instruments), and analytical procedures like chemical, microbiological, or particle counting are examples of surface monitoring approaches. When necessary, the data gathered from surface monitoring is utilized to identify possible sources of contamination, evaluate how well cleaning and sanitation practices are working, and take appropriate corrective and preventive action.

Sterile environments are maintained with the use of personnel monitoring. People who work in cleanrooms are mostly responsible for the majority of contamination found in a facility. Normal human nail, hand, and hair flora, for instance, can be helpful in an investigation to determine the source of contamination.

Here are a few instances of staff monitoring:
Hands under observation: Observed at the start and finish of each manufacturing run. Forearms and uniforms were observed: once every seven days.

Surface and Personnel sampling can be done by two techniques:

Contact plate

Swab analysis

BY SWAB SAMPLING ANALYSIS

Material required:

Sterile cotton swabs

Buffer solutions like saline solution

Sterile containers or tubes

Sterile forceps

SCDA media

Sterile petri plates

Incubator

Gloves, face masks, PPE (if required)

Procedure:

- Put the sample identifying information on the labels of the sterile tubes or containers.
- Making sure not to contaminate it, remove the sterile swab from its packing.
- Moisten the swab in tube containing 10 ml of 0.9% saline solution.
- Take the swab sample by Applying sufficient pressure and rotate the swab while firmly swabbing the targeted surface area or the hands or armpits of the workers to ensure that any pollutants are collected.
- Use different swabs for each portion of the surface when dealing with larger areas.
- After sampling carefully place the swab in the tube containing saline solution and agitate the swab in the solution to make sure the collected microorganisms are released.
- Under LAF, Pipette out 1ml of enrichment solution and pour into the sterile petri plate. (90 mm dia)
- Pour 15-20 ml prepared SCDA into plate.
- Repeat the same for other plates also
- Incubate for 2 days at 32.5°C for TABC
- Then Incubate for 3 more days at 22.5°C for TYMC
- Examine the plates for microbial growth and compare the outcomes in the light of predetermined limits according to acceptable standards.

3.3 Microbial limit testing for water and non-sterile products

The pharmaceutical industry uses the microbial limit test as a crucial quality control tool to guarantee the microbiological safety and quality of non-sterile pharmaceutical goods. The principal purpose of this test is to identify and measure any microorganisms—like bacteria and fungi—that may be present in the finished product or any of its constituent parts.

The standard procedure for doing the microbiological limit test is to follow the guidelines given by pharmacopoeias, such as the European Pharmacopoeia, the United States Pharmacopeia (USP), or other pertinent regulatory authorities.

3.3.1 TOTAL AEROBIC MICROBIAL COUNT

Material Required:

Media for microbiological growth:

For the total aerobic microbial count, use either Soybean-Casein Digest Agar (SCDA) or Tryptic Soy Agar (TSA).

FTM for counting mold and yeast

If necessary, further differential or selective media

Diluents:

Peptone water or buffered saline solution for sample dilution

Sterile tubes or containers:

For the inoculation and dilution of samples

Pipette tips or sterile pipettes:

for putting samples on medium and inoculating them

Sterile spreaders or loops :

For uniformly distributing the sample across the agar plates

Incubator:

To incubate the inoculation medium at designated temperatures (usually between 20 and 25°C for yeasts and molds and between 30 and 35°C for bacteria),

Autoclave

Colony counter or magnifying lens

Laminar flow hood

Procedure:

MLT of water

- Sample collection
Aseptically gather water samples in sterile containers. Utilize suitable sampling methods to prevent contamination.
Indicate on the samples all pertinent details, including the date, time, and sampling location.
- Sample Setup and Diluting
A. Direct Examination:

The water sample can be analyzed straight, without dilution, if a low microbial load is anticipated.

B. Serial dilution :

Use successive dilutions to achieve countable colony-forming units (CFUs) on the agar plates if a larger microbial load is anticipated.

Assemble sterile dilution blanks using the proper diluents , saline solution (10^{-1} , 10^{-2} , and 10^{-3} dilutions, for example).

- Spread Plate or Pour Plate Plating Method:
Pour Plate Method: Combine 1ml of the diluted or water sample with 15-20 ml of melted agar that has been chilled to between 45 and 50°C, then transfer the mixture into sterile Petri dishes.

Spread Plate Method: Using a sterile spreader, evenly distribute a specified volume (usually 0.1 mL) of the water sample or diluted sample pipetted out onto the surface of agar plates that have already been prepared.
- Incubation
For the Bacterial Count, incubate the plates for 48–72 hours at 30–35°C. Incubate the plates for 5–7 days at 20–25°C (or according to specific criteria) in order to count the fungi.
- Counting the Colonies:

Determine how many colony-forming units (CFUs) each plate has after the incubation period. If required, count the colonies manually or with the aid of a colony counter.
- Calculate the CFU/ml

MLT for non-sterile products

Making sure non-sterile items, like tablets, capsules, syrups, ointments, and other dosage forms, are safe and of high quality requires this test.

Material required:

Same as MLT of water

Procedure:

- Preparing the Sample:

Weigh and prepare the product sample aseptically in accordance with the instructions. The standard sample amount is 10 grams or 10 ml, however this could change depending on the particular test specifications.

- Setting Up the Sample and Diluting It
A. The First Suspension:

To attain a particular concentration (e.g., a 1:10 dilution), dissolve or suspend the sample in a sterile diluent (0.9% saline solution). It might be necessary to combine homogenization, shaking, and mechanical agitation for this.

B. Dilution in Sequence:

To get a countable quantity of microorganisms, perform serial dilutions. This usually entails making a number of dilutions tenfold (e.g., 10^{-1} , 10^{-2} , and 10^{-3}).

- Techniques for Plating

A. Plate Pour Method:

Place a determined amount of the prepared sample, or diluted sample, into a sterile Petri dish (typically 1 mL). After cooling to between 45 and 50°C, pour the melted agar into the dish and swirl to gently incorporate. Before incubating, let the agar harden.

B. Spread Plate Technique:

Place a specified amount (often 0.1 mL) of the sample or a diluted sample on the surface of agar plates that have been poured and solidified beforehand. To equally disperse the sample across the agar surface, use a sterile spreader.

- Incubation:

For TAMC, SCDA plates should be incubated for 48–72 hours at 30–35°C. For a fungal count, incubate plates for five to seven days at 20 to 25°C.

- Colony counting :
After the completion of incubation period count the CFUs on each plate.

3.3.2 TEST FOR PATHOGENS

Materials and equipments:

Water or product sample
Diluents eg NaCl saline solution
Enrichment media SCDM
Selective media (MacConkey broth, MacConkey Agar, Certimide Agar, Mannitol Salt agar, XLDA, RVSB)
Sterile petri plates
Sterile pipette tips and pipette
Incubators
LAF
Gloves, lab coat and other personal protective equipments

Procedure:

- Enrichment – Add 10ml of sample into 100ml SCDM and incubate at 32.5 degree Celsius for 18-24 hrs.

a) Test for *E.coli*:

Transfer 1ml of SCDM enrichment to 100ml of MacConkey Broth & incubate at 43 degree Celsius for 2 days.
Streak from MCB to surface of MacConkey agar plate and incubate at 32.5 degree Celsius for 3 days

b) Test for *S. aureus*:

Directly streak the incubated SCDM enrichment on plate of Mannitol salt agar and incubate at 30-35 degree Celsius for 3 days.

c) Test for *P. aeruginosa*:

Directly streak SCDM enrichment on plate of Citremide Agar and incubate at 32.5 degree Celsius for 3 days.

d) Test for Salmonella:

Transfer 10 ml of sample to 100 ml of SCDM and incubate for 1 day at 32.5 degree Celsius. Take 0.1 ml of incubated solution to 10 ml of RVSB and incubate for 2 days

Streak this on XLDA plate and incubate at 32.5 degree Celsius for 2 more days.

3.4 Sterility testing

A crucial step in quality control is sterility testing, which verifies that pharmaceuticals and medical equipment meant to be sterile are free of potentially harmful germs. For items such as injectables, ophthalmic solutions, and specific surgical equipment that are labeled as sterile, this testing is necessary. Pharmacopeial standards such the European Pharmacopoeia (EP), United States Pharmacopeia (USP), and others usually provide recommendations that the sterility test must adhere to.

Materials and equipments:

Sterile LAR

Sterile culture media – FTM, SCDM

Sterile container or vials for sample collection

Foreceps

Scissors

Incubator

Autoclave

Glass tubes

Gloves, masks , gown

Procedure :

Direct inoculation method

Inoculation

A predetermined amount of the product sample should be directly injected into FTM and SCDM culture medium

The product type and guidelines should determine the inoculation volume, which is typically 1–10 mL for liquid solutions or dissolved solid materials.

Incubation

For 14 days, incubate FTM tubes at 30-35°C.

For 14 days, incubate SCDM tubes at 20–25°C.

Analysis

Every Day Observation: Check the media every day for any indications of microbial development, such as sedimentation, pellicle production, or turbidity.

Interpreting the Findings:

The product passes the sterility test if, after the 14-day, no growth is seen in either medium.

Controls

Use verified microorganisms as positive controls to ensure the test protocol is validated. Make sure these bacteria can grow in the culture media. To investigate whether the test environment is contaminated, use negative controls, such as sterile media.

3.5 Antibiotic assay

Antibiotic assays are used to measure an antibiotic's concentration or potency in a particular sample. These tests are crucial for confirming that antibiotics fulfil the necessary requirements for safety and efficacy. Chemical assays (like High-Performance Liquid Chromatography, HPLC) and microbiological assays (like the agar diffusion method and broth dilution method) are two frequently used techniques for antibiotic testing. The steps for performing an antibiotic analysis using the microbiological approach are outlined in this comprehensive guide:

Agar Diffusion Method

The disk diffusion method, also referred to as the agar diffusion method, is a popular microbiological test for figuring out how strong antibiotics are in prescription drugs. Through the use of a paper disk placed on an agar surface, the antibiotic's ability to inhibit bacterial growth is measured using this technique. This is a step-by-step instruction that explains how to use the agar diffusion method for pharmaceutical product antimicrobial assays:

Material required:

Petri plates
Pipette and tips
Forceps
Standard antibiotic solution
Test antibiotic sample
Filter paper disks
Culture media: Mueller Hinton agar
Microbial organism: *E.coli*
Incubators
Autoclave
Cappilers or rulers
Lab coat , masks, gloves
Swab or loop

Getting Standards and Samples Ready:

Weigh the antibiotic precisely and dissolve it in a suitable solvent (such as buffer or distilled water) to create a stock solution. A range of standard concentrations can be obtained by diluting the stock solution.

Utilizing the same solvent as the standards, prepare the test samples.

Preparing the Inoculum:

Make a sterile saline or broth suspension of the microbiological test organism. To achieve the turbidity of a 0.5 McFarland standard (about $1-2 \times 10^8$ CFU/mL), adjust the suspension.

How to Prepare an Agar Plate:

Fill sterilized Petri plates with Mueller-Hinton Agar and let it set. To establish a homogenous lawn of bacteria, swab the microbial suspension onto the agar plate surfaces. To guarantee uniform covering, turn the plate sixty degrees and scrub once more using a sterile cotton swab.

Setting Up the Disk:

Sterile filter paper disks should be soaked in both the standard and test antibiotic solutions. Permit surplus solution to escape. For conventional antibiotics, an alternative is to utilize professionally manufactured antibiotic disks.

Position of the Disk:

Using sterile forceps, carefully position the soaked disks so they are uniformly spaced and not too close to the plate's border on the inoculated agar surface. Add test sample and standard antibiotic disk in different concentrations.

The period of incubation

The plates should be incubated for 16–18 hours at 35–37°C.

A standard curve can be made by graphing the inhibition zone diameters of the standard antibiotic concentrations. The concentration is shown on the x-axis, while the inhibition zone diameter is shown on the y-axis.

Analysis

Examine the test samples' inhibition zone widths in relation to the reference curve

Based on the matching zone diameters on the standard curve, calculate the test antibiotic's concentration.

Controls:

When confirming the correctness of the test technique, use positive controls that contain known amounts of the standard antibiotic. To verify the test organism's viability and look for contamination, use negative controls, which are sterile media devoid of the antibiotic.

4. OBSERVATION AND RESULTS

4.1 Environment monitoring Report by plate count method

4.1.1 Microbiological lab- Sterility room

Media: SCDA

Incubation temp.& period: 22.5 for 72 hrs

32.5 for 48 hrs

Position of Plates	Fungal Colonies	Bacterial Colonies	Alert limit CFU	Action limit CFU
Air lock 1	Nil	09	25	50
Air lock 2	Nil	02	10	25
Air lock 3	Nil	Nil	1	3
Pass box	Nil	Nil	1	3
LAF Room	Nil	Nil	1	3
Laminar flow	Nil	Nil	Nil	1
Negative control	-ve	-ve	-ve	-ve
Positive control	+ve	+ve	+ve	+ve

Remarks: ok

4.1.2 Microbiological lab – Antibiotic assay room

Media: SCDA

Incubation temp.& period: 22.5 C for 72 hrs

32.5 C for 48 hrs

Position of Plates	Fungal Colonies	Bacterial Colonies	Alert limit CFU	Action limit CFU
Air lock 1	Nil	07	25	50
Air lock 2	Nil	03	10	25
Air lock 3	Nil	Nil	1	3
Pass box	Nil	Nil	1	3
LAF Room	Nil	Nil	1	3
Laminar flow	Nil	Nil	Nil	1
Negative control	-ve	-ve	-ve	-ve
Positive control	+ve	+ve	+ve	+ve

Remarks : ok

4.1.3 Production area: Ophthalmic section

Media: SCDA

Incubation temp.& period: 22.5 C for 72 hrs

32.5 C for 48 hrs

Position of Plates	Bacterial colonies	Fungal Colonies	Bacterial Colonies	Fungal colonies	Alert limit CFU	Action limit CFU
Pass box	06	Nil	04	NA	10	25
Air lock 1	14	Nil	NA	NA	25	50

Air lock 2	03	Nil	03	Nil	10	25
Air lock 3	Nil	Nil	Nil	Nil	1	3
Passage	06	Nil	Nil	Nil	10	25
Manufactrng Room	02	Nil	Nil	Nil	10	25
Filtration Room	Nil	Nil	Nil	Nil	1	3
Vial filling room	Nil	Nil	Nil	Nil	1	3
Vial sealing M/C	Nil	Nil	Nil	Nil	1	3
Negative control	-ve	-ve	-ve	-ve	-ve	-ve
Positive control	+ve	+ve	+ve	+ve	+ve	+ve

Remarks : ok

4.2 Personnel monitoring report by Swab and Finger dab method

4.2.1 Area: Microbiology lab

Media: SCDA

Incubation temp.& period: 22.5 C for 72 hrs

32.5 C for 48 hrs

Name of person	Observation Cfu / five fingers				Observation Cfu /swab			
Right hand		Left hand			Forehead		Arm pits	
	Fungal	Bact.	Fungal	Bact.	Fungal	Bact.	Fungal	Bact.
Vijay	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Parwinder	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Komal	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil

Negative control: -ve

LIMITS: For swab: < 5cfu/plate

For finger dab: < 1cfu/plate

Remarks: the count observed for each person are within the prescribed limit

4.2.2 Area: Ophthalmic section

Media: SCDA

Incubation temp.& period: 22.5 C for 72 hrs

32.5 C for 48 hrs

Name of person	Observation Cfu / five fingers				Observation Cfu /swab			
Right hand		Left hand		Forehead		Arm pits		
	Fungal	Bact.	Fungal	Bact.	Fungal	Bact.	Fungal	Bact.
Jairam	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Prince	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Sunil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Rahul	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Anoop	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Ravi	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil

Negative control: -ve

LIMITS: For swab: < 5cfu/plate

For finger dab: < 1cfu/plate

Remarks: the count observed for each person are within the prescribed limit

4.3 Sterility testing report

4.3.1 product name: Labmid injection

batch no.: 24FA01

sample quantity: 20 ampoules

media used: FTM, SCDM

incubation temp. and period : FTM for 14 days at 30-35C

SCDM for 14 days at 20 to 25 C

Day	SCDM blank	FTM blank	SCDM+ Product	FTM+ product	Remarks
1	-ve	-ve	-ve	-ve	ok
2	-ve	-ve	-ve	-ve	ok
3	-ve	-ve	-ve	-ve	ok
4	-ve	-ve	-ve	-ve	ok
5	-ve	-ve	-ve	-ve	ok
6	-ve	-ve	-ve	-ve	ok
7	-ve	-ve	-ve	-ve	ok
8	-ve	-ve	-ve	-ve	ok
9	-ve	-ve	-ve	-ve	ok
10	-ve	-ve	-ve	-ve	ok
11	-ve	-ve	-ve	-ve	ok
12	-ve	-ve	-ve	-ve	ok
13	-ve	-ve	-ve	-ve	ok
14	-ve	-ve	-ve	-ve	ok

+ve control: +ve

note: -ve =no growth , +ve= growth

remarks: sample complies with test of sterility

4.3.2product name: Amilab 500 injection

batch no.: 24 EA02

sample quantity: 20 ampoules

media used: FTM, SCDM

incubation temp. and period : FTM for 14 days at 30-35C

SCDM for 14 days at 20 to 25 C

Day	SCDM blank	FTM blank	SCDM+ Product	FTM+ product	Remarks
1	-ve	-ve	-ve	-ve	ok
2	-ve	-ve	-ve	-ve	ok
3	-ve	-ve	-ve	-ve	ok
4	-ve	-ve	-ve	-ve	ok
5	-ve	-ve	-ve	-ve	ok
6	-ve	-ve	-ve	-ve	ok
7	-ve	-ve	-ve	-ve	ok
8	-ve	-ve	-ve	-ve	ok
9	-ve	-ve	-ve	-ve	ok
10	-ve	-ve	-ve	-ve	ok
11	-ve	-ve	-ve	-ve	ok
12	-ve	-ve	-ve	-ve	ok
13	-ve	-ve	-ve	-ve	ok
14	-ve	-ve	-ve	-ve	ok

+ve control: +ve

note: -ve =no growth , +ve= growth

remarks: sample complies with test of sterility

4.4 Microbial Limit Test

4.4.1 MLT of Water for injection

Total aerobic viable count observation

Bacterial count Observed cfu	Fungal count observed cfu	Total aerobic viable Count observed cfu
Nil	Nil	Nil

-ve control : -ve

4.4.2 Pathogen observation

Pathogens	Primary test	Secondary test	Present/ absent
<i>E.coli</i>	-ve	NA	absent
<i>Salmonella</i>	-ve	NA	absent
<i>S.aureus</i>	-ve	NA	absent
<i>Paeruginosa</i>	-ve	NA	absent

limit: specified pathogens should be absent

remarks : water sample complies as per the specifications

4.4.1 MLT of potable water

Total aerobic viable count observation

Bacterial count Observed cfu	Fungal count observed cfu	Total aerobic viable Count observed cfu
04	Nil	04

-ve control : -ve

4.4.2 Pathogen observation

Pathogens	Primary test	Secondary test	Present/ absent
<i>E.coli</i>	-ve	NA	absent
<i>Salmonella</i>	-ve	NA	absent
<i>S.aureus</i>	-ve	NA	absent

<i>Paeruginosa</i>	-ve	NA	absent
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limit: specified pathogens should be absent

remarks : water sample complies as per the specifications

4.5 Antibiotic Assay

4.5.1

sample: Antibiotic tablet (Amoxicillin)

method: agar diffusion

Sample	Diameter of inhibition zone (mm)	Concentration (mg/tablet)
Standard 1(10mg/ml)	15mm	10mg
Standard 2 (20mg/ml)	25mm	20mg
Standard 3 (30mg/ml)	35mm	30mg
Tablet sample	20mm	15mg

Result: The pill sample had a 15 mg concentration of antibiotics per tablet.

4.5.1

sample: Antibiotic tablet (ciprofloxacin)

method: agar diffusion

Sample	Diameter of inhibition zone (mm)	Concentration (mg/tablet)
Standard 1(5mg/ml)	10mm	5mg
Standard 2 (15mg/ml)	20mm	15mg
Standard 3 (25mg/ml)	30mm	25mg
Tablet sample	15mm	10mg

Result: The pill sample had a 15 mg concentration of antibiotics per tablet.

5.SUMMARY

During my 4 month program at Laborate pharmaceuticals India Ltd, I gained invaluable experience and hands on experience in various aspects of pharma industries. The study's main areas of focus were measure of colony forming units Cfu present in the environment aspects as well as in the product material itself , that may contaminate the final finished product. the study shows that all the environmental conditions were under the acceptable limits set by pharmacopeial standards. microbial analysis of All the injections liquid vials were overall found to be ok under standards. the marked or labelled concentrations of the antimicrobials on particular products were checked and verified up to the mark .

The study was concluded on the note that Quality assurance and quality control department works regularly on improving the quality of the finished products , therefore these microbiological tests were included to analyse the hazards or to be risks from the root level and specific measures were taken for the same to maintain the product quality and safety.

6.REFERENCES

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