

PHARMACEUTICAL MICROBIOLOGY

Pharmaceutical Microbiology Laboratory is an accredited laboratory under the Singapore Accreditation Council – Singapore Laboratory Accreditation Scheme.

Standard methods prescribed in the British Pharmacopoeia (BP), the United States Pharmacopeia (USP) and other published official methods are used in the tests. Company methods, after validation, are also used as requested by clients. Tests available are Bacterial Endotoxins (LAL) Test for Pyrogen, Microbiological Assay of Antibiotic Drugs, Disinfection Efficacy Test of Disinfectants and Antiseptics, Sterility Test of Sterilised Pharmaceutical and Biological Products, Test for Effectiveness of Antimicrobial Preservatives, Tests for Microbial Limits for Non-sterile Pharmaceutical and Biological Products, and Microbiological Identification Tests.

Pharmaceutical Microbiology Laboratory has been able to provide highly confidential analytical services to hospitals, dialysis centres and pharmaceutical firms both in Singapore and in the region. In line with the Singapore General Hospital policy, the Laboratory shall not disclose any client information and laboratory results to a third party, unless prior consent from the client is obtained.

TYPES OF TESTS

BACTERIAL ENDOTOXINS (LAL) TEST FOR PYROGEN

This is a safety test for the following:

- Parenteral pharmaceutical products and raw materials
- Medical devices
- Reverse-osmosis water and dialysate solutions for dialysis centres
- Embryo culture and flushing media for in-vitro fertilisation
- Processed and purified water for use in manufacture of pharmaceutical products

MICROBIOLOGICAL ASSAY OF ANTIBIOTIC DRUGS

This assay is to determine whether the potency of antibiotics complies with the requirement for label potency and associated limits stipulated in the USP/BP monographs for antibiotics.

DISINFECTION EFFICACY TEST OF DISINFECTANTS AND ANTISEPTICS

The disinfectants/antiseptics are tested at the use-dilutions or use-conditions prescribed on the product label to determine their efficacy.

STERILITY TEST OF STERILISED PHARMACEUTICAL AND BIOLOGICAL PRODUCTS

All pharmaceutical and biological products meant for parenteral use and any device used in conjunction with the administration of such agents, ophthalmic solutions, implants, sutures and surgical dressings are tested for sterility.

TEST FOR EFFECTIVENESS OF ANTIMICROBIAL PRESERVATIVES

Antimicrobial preservatives are substances added to dosage forms to protect them from microbial contamination. They are used primarily in multiple-dose containers to inhibit the growth of micro-organisms that may be introduced inadvertently during or subsequent to the manufacturing process or during consecutive use from the same container. The tests apply only to multi-dose parenteral, otic, nasal, topical and ophthalmic products made with aqueous bases or other vehicles in the original, unopened container.

TESTS FOR MICROBIAL LIMITS FOR NON-STERILE PHARMACEUTICAL AND BIOLOGICAL PRODUCTS

Tests for Microbial Limits are designed for the determination of the level of bioburden and the absence of specific pathogens in pharmaceutical raw materials and finished products, which are not compulsorily sterile. The bioburden limit expressed as total aerobic microbial count and absence of specific pathogens are stipulated in some of the USP/BP monographs of the non-sterile pharmaceutical products such as ointments, creams, lotions, tapes, aerosols, gels, gauze, pastes, powders, oral suspensions and syrup preparations.

MICROBIOLOGICAL IDENTIFICATIONS TESTS

The tests apply to isolated colonies from monitoring culture plates (settle plates, contact plates, air sampler strips and swabs) from microbiological monitoring of manufacture environment.

SPECIAL INSTRUCTIONS FOR SAMPLE COLLECTION AND HANDLING

BACTERIAL ENDOTOXINS (LAL) TEST FOR PYROGEN

1. Deliver samples of pharmaceutical products in their unopened original containers and packages.
2. For non-sterile samples of water and solutions, collect samples in pyrogen-free, sterile polystyrene plastic containers.
3. Deliver non-sterile samples of water and solutions immediately and under chilled conditions, e.g. by using coolant packs. If coolant packs are not available, chill the samples immediately after collection in the refrigerator to 2 – 4°C and deliver the samples to reach the laboratory within six hours. If delivery within six hours is not possible, store samples under frozen condition until delivery.
4. Employ aseptic techniques throughout for the collection of samples of water and solutions. For collection of water samples from a tap:
 - (a) Remove from the tap any attachments that may cause splashing, and wipe the outlet with a piece of clean cloth to remove any dirt.
 - (b) Turn on the tap at maximum flow rate and let the water flow for 2 minutes.
 - (c) Sterilise the tap for one minute with the flame from an ignited cotton-wool swab soaked in alcohol. Alternatively, a gas burner or cigarette lighter may be used. If the tap is made of flammable material, disinfect the tap by applying a solution of sodium hypochlorite (100 mg NaOCl/L) for about 30 seconds.
 - (d) Turn on the tap and allow the water to flow for 2 minutes at medium flow rate to avoid splashing.
 - (e) While holding the cap face downwards, fill the sample container (without rinsing) and leave a small air space.
 - (f) Replace the cap.

TEST FOR MICROBIAL LIMITS

1. Deliver samples of pharmaceutical products in their unopened original containers and packages.
2. For non-sterile samples of water and solutions, collect in sterile containers.
3. Deliver non-sterile samples of water and solutions immediately and under chilled conditions, e.g. by using coolant packs. If coolant packs are not available, chill the samples immediately after collection in the refrigerator to 2 – 4°C and deliver the samples to reach the laboratory within six hours. If delivery within six hours is not possible, store samples at a temperature under 4°C but **do not freeze**. Do not let maximum elapsed time between collection and sample receipt by laboratory exceed 20 hours.
4. Observe aseptic techniques in sampling as described in Bacterial Endotoxins (LAL) Test for Pyrogen.

MICROBIOLOGICAL ASSAY OF ANTIBIOTIC DRUGS

1. Deliver samples of pharmaceutical products in their original containers and packages.
2. Samples of antibiotic raw materials for microbiological assays should be properly packed in suitable air-tight containers to prevent moisture absorption.

3. Samples of light sensitive antibiotics such as nystatin and tetracyclines should be protected from light.
4. Screw-capped plastic containers or amber-coloured glass bottles are suitable.
5. Do not expose samples to warm temperatures during transport.

STERILITY TEST OF STERILISED PHARMACEUTICAL PRODUCTS

Sample units from the batch of manufacture should be collected at random in their original containers and packages and stored in a clean environment.

SUBMISSION OF SAMPLES

1. Send in samples together with a letter providing the following information:
 - Nature of sample, date and time collected
 - Type of test required
 - Name and address of sender
 - Telephone number and facsimile number, if available
 - An undertaking that all charges will be borne by the company sending in the samples. (This is applicable only for samples where payment is not made at the time of submission of samples).
 - Whether report is to be sent by mail or collected personally.
2. Samples should be properly marked or labelled with the following particulars:
 - Name of preparation
 - Active ingredients, and preservatives, if any
 - Batch number
 - Date of manufacture
 - Expiry date
 - Manufacturer's name and address
3. Sample size: Refer to Alphabetical Test Listing – Pharmaceutical Microbiology.
4. Samples sent by post should be addressed to:
 - Officer-in-charge
 - Pharmaceutical Microbiology Laboratory
 - Department of Pathology
 - Singapore General Hospital
 - Outram Road
 - Singapore 169608
 - Tel: 6222 0446/6222 0496
 - Fax: 6227 7371
5. Test Report

When making enquiries regarding the test report, quote the laboratory reference number assigned to the sample. If this is not known, then give the date the sample was submitted and the nature of the sample.

ALPHABETICAL TEST LISTING – PHARMACEUTICAL MICROBIOLOGY

BACTERIAL ENDOTOXINS (LAL) TEST FOR PYROGEN

Specimen required	: Parenteral drugs : three bottles/batch Administration devices : 10 pieces/batch Reverse-osmosis water and dialysate solutions for dialysis centres, culture and flushing media for in-vitro fertilisation, processed and purified water for manufacture and raw materials: at least 10 – 20 mL or 10 – 20 gm in pyrogen-free, sterile polystyrene plastic containers
Method	: Bacterial Endotoxins Test, United States Pharmacopeia (USP) /British Pharmacopoeia (BP)
Test results	: Parenteral drugs/medical devices: Pass or fail endotoxin limit stipulated in the USP/BP monograph of the drug or US FDA Guidelines RO water/dialysats: Pass or fail the US Advancement of Medical Instrumentation (AAMI) Guideline or ISO Standard
Turnaround time	: 1 – 2 working days
Day(s) test set up	: Monday – Saturday

MICROBIOLOGICAL ASSAY OF ANTIBIOTIC DRUG

Specimen required	: Antibiotic preparations: Capsules/tablets – 30 nos. Raw material – 2 gm Ampoules (injections) – 6 nos. Ointment tubes – 3 nos. Vials (injections) – 6 nos. Bottles (syrup) – 2 nos. Collect samples of raw materials and light-sensitive antibiotic drugs in screw-capped plastic containers or amber-coloured glass bottles. Do not expose sample to warm temperatures during transport.
Method	: United States Pharmacopeia (USP)/British Pharmacopoeia (BP)
Test results	: Pass or fail potency assay limits stipulated in the USP/BP monograph of the antibiotic drug
Turnaround time	: 2 – 4 working days
Day(s) test set up	: Monday – Friday

DISINFECTION EFFICACY TEST OF DISINFECTANTS/ANTISEPTICS

Specimen required	: 100 mL
Method	: Kelsey-Sykes Capacity Test, ISO or other standard tests
Test results	: Pass or fail the standard tests
Turnaround time	: 4 – 30 working days
Day(s) test set up	: 5 – 14 days from date of request

STERILITY TEST OF STERILISED PHARMACEUTICAL PRODUCTS

Specimen required	: Parenteral drugs and administration devices, ophthalmic preparations, surgical dressing, sutures and other sterilised pharmaceutical products, packed in unopened original containers. Generally 10 – 20 sample units (containers) per batch of manufacture. Refer to sample size stipulated in BP for various batch sizes of production.
Method	: United States Pharmacopeia (USP) /British Pharmacopoeia (BP)
Test results	: Pass or fail the Tests for Sterility USP /BP
Turnaround time	: 15 working days
Day(s) test set up	: Monday – Saturday

TEST FOR EFFECTIVENESS OF ANTIMICROBIAL PRESERVATIVES

Specimen required	: 100 mL in original, unopened container
Method	: United States Pharmacopeia (USP) /British Pharmacopoeia (BP)
Test results	: Pass or fail the USP/BP Tests for Effectiveness of Antimicrobial Preservatives
Turnaround time	: 5 weeks
Day(s) test set up	: 1 week from day of request

TESTS FOR MICROBIAL LIMITS FOR NON-STERILE PHARMACEUTICAL PRODUCTS

Specimen required	: 20 mL or 20 gm
Method	: United States Pharmacopeia (USP) /British Pharmacopoeia (BP)
Test results	: Pharmaceutical drugs: Total Aerobic Microbial Count – Pass or fail CFU limit stipulated in the USP/BP monograph of the preparation Pathogens – Detected or Not detected/gm or mL RO water/dialysats: Pass or fail the US Advancement of Medical Instrumentation (AAMI) Guideline, or ISO Standard
Turnaround time	: Total Aerobic Microbial Count: 2 – 7 working days Pathogens: 5 – 7 working days
Day(s) test set up	: Monday – Saturday