

Microbiology (Sterility) Laboratory Procedures

In this episode you will find procedures and practical work instructions on sterility testing concepts, principles and microbiology laboratory management guidelines for your pharmaceuticals business.

In this area you will find Standard Operating Procedures on Entry Procedure to Sterile Filling Areas, Validation of Aseptic Gowning Procedures, Microbiological Data Recording Procedure, Destruction of Biological Waste in the Microbiology Laboratory, Depyrogenation of Glassware In Micro. Lab. Oven, Media Preparation in Microbiology Laboratory, Aseptic Media Filling and Micro. Integrity Leak (Soup) Testing Procedure, Aseptic Media Filling and Soup Test Guideline, Environmental and Plant Hygiene Monitoring Procedure, Microbial Limit Testing Procedure by Using Laminar Flow Cabinets etc and many other procedures according to your need.

All procedures have reference of prepared Forms and Templates for effective record keeping and reporting purposes. Forms are attached at the end of each procedure. Templates are listed separately.

SOP List

MICLAB 005: Entry Procedure to Sterile Filling Areas

This SOP outlines the gowning procedure that must be followed by each and every person who enters a Sterile Area. The procedure is designed to reduce the risk of contaminating product with bacteria and/or particles

MICLAB 010 Validation of Aseptic Gowning Procedures

Aseptic gowning is the ability to complete the gowning procedure without compromising the sterility of the garment. This SOP outlines the sterile gowning validation procedure as required for the final sign off for the initial sterile training and the revalidation of currently trained Operators, Fitters, Electricians and Cleaners and all organization staff who are authorized to enter Sterile areas.

MICLAB 015 Microbiological Data Recording Procedure

To describe procedures for the recording of Microbiological data using the in-house hard copy and computerized recording system. All documents containing test results are legal documents and therefore it is imperative that all the information required is recorded accurately. Any changes/corrections to be made must be signed with that person's initials and dated.

MICLAB 020 Destruction of Biological Waste in the Microbiology Laboratory

To describe procedures for destroying all Laboratory Biological Waste to comply with Quarantine Regulations

MICLAB 025 Depyrogenation of Glassware In Micro. Lab. Oven

To outline the procedure for the depyrogenation of glassware using the Microbiology Laboratory Qualtex Oven.

MICLAB 030 Media Preparation in Microbiology Laboratory

To describe the procedures for the preparation of microbiological media for use in the Microbiology Laboratory.

MICLAB 035 Aseptic Media Filling and Micro. Integrity Leak (Soup) Testing Procedure

One of the requirements of cGMP is a periodic evaluation of all aseptic processes by filling media into the appropriate containers under normal production conditions. The media fill should reflect the sterility of the entire process from the Sterilizing filter to the filled primary container and should include all subsequent manufacturing steps. This SOP outlines the procedures for both Media Fills and Microbiological Leak Tests.

For Validation purposes, a Microbiological Leak Test (Soup test) or a separate Protocol to verify the entire process from the 'Bioburden Reduction Filter' to the primary container may be required.

MICLAB 040 Aseptic Media Filling and Soup Test Guideline

Media Fills are designed to verify the entire process, equipment and staff (see MICLAB 035). This process simulation should be performed as initial validation with three (3) consecutive satisfactory simulation tests per shift and repeated at defined 6 monthly intervals (twice per year per process per shift) and after any significant modification to the HVAC-system, equipment, process and number of shifts" for aseptically filled process.

Soup test has to be conducted at least once per year per shift for terminally sterilised lines and non-sterile process. Validation and re-validation media fills are to assure the sterility of the entire process. This process simulation test should imitate as closely as possible the routine aseptic manufacturing process and include all the critical subsequent manufacturing steps.

The Media Fill should challenge the "worst case" situation and should include all the possible interventions of a normal production run. The duration of the media run should be at least 4 hours or half a production shift to allow for all routine interventions.

An example of valid media fill is 10,000 units per shift for a high speed filling machines.

MICLAB 045 Environmental and Plant Hygiene Monitoring Procedure

Description for Microbiological testing of areas of the environment which may influence or affect product performance and/or quality - including, air, surfaces, personnel, clothing and disinfectants

Daily monitoring of sterile grade areas during production is to be conducted by trained production staff. The Microlab is to ensure that the necessary plates are delivered on a daily basis so monitoring can take place.

Once a test has been completed, the responsible operator is to initial the plate and make sure that the batch number of the batch running at the time of the test is written on the plate. Plates will be labeled with prompts to ensure this isn't forgotten. If no batch is running at the time of the test N/A should be put on the plate instead of a batch number.

If an area of concern is noted during routine daily testing, inform Micro immediately so that further steps can be taken.

Once a week a Microlab technician will perform environmental monitoring and a housekeeping audit of the area.

If, in monitoring any of the following areas, any of the following events occur, the Microlab staff member responsible for conducting Environmental Monitoring in that area is to launch an Environmental Monitoring Investigation by IMMEDIATELY repeating the test.

MICLAB 050 Microbial Limit Testing Procedure by Using Laminar Flow Cabinets.

To describe the procedures to be followed in conducting Microbial Limit Tests in the Laminar flow Cabinets in the Microbiology Lab.

MICLAB 055 Microbiological Monitoring of Plant Water Systems

In this SOP you will find Sampling Procedure for Bioburden and Endotoxin Samples, Bioburden Test Method and Results, Endotoxin Testing of WFI (Distilled Water), Bioburden and Bacterial Endotoxin Alert and Action Levels, Diagrammatic Representations of a typical purified Water Systems, Bioburden Waste Tank Water Sampling, Clean Steam Sampling & Testing, OOL/OOS Result Actions etc

MICLAB 060 Micro Laboratory Procedure for Sterility Testing

This sop is to describe the procedure for sterility testing of aqueous, injectable and terminally sterilized non-injectable products. To explain the correct interpretation of sterility results and to outline Stasis requirements for used sterility canisters.

MICLAB 065 Determination of Heat Resistance of Spore Forming Organisms

This SOP describes the method for calculating the Heat Resistance Factor, (D-value), of spore-forming organisms. D-Value is defined as the time required for a population of a pure culture of microorganisms to be decreased by 90% when exposed to a fixed temperature, e.g. 121°C ($\pm 1^\circ\text{C}$).

MICLAB 070 Identification of Microorganisms to Genus and Species Level

To describe the procedures for the preliminary identification of bacteria isolated from Plant Water, Environmental, Personnel, Product and Raw Material sources.

Bacteria that will require identification (ID) to **at least** genus level include organisms isolated from the manufacturing environment, personnel, in-process and finished products, plant water and other miscellaneous sources. SOP's detailing the microbiological testing procedures for each of these samples will indicate the required level of ID of recovered organisms. The following sections detail the procedures for the preliminary ID of micro-organisms. Further ID to species level is to be conducted for conformation.

MICLAB 075 Micro Evaluation on Bioburden, Non sterile and Raw Materials

This SOP describes the procedures for Microbiological Evaluation of Bioburdens, non-sterile Products & raw materials.

Bioburdens includes: Batches prior to membrane filtration, i.e. solutions; Batches prior to sterilization i.e. filled containers; Face masks; IPA.

This procedure includes Equipment preparation for Non-sterile testing, Bulk Solution Bioburden (BSB) Sampling; Filled Container Bioburdens (FCB); Raw Material Bioburdens (RMB); Surgical Face Masks; Isopropyl Alcohol (70% IPA); Speciation Procedures for Organisms found in Non-Sterile Products and Raw Materials; Out-of-Specification Procedures for Non-Sterile Products and Raw Materials; Retest and Repeat Procedures for Non-Sterile Products and Raw Materials.

MICLAB 080 Bacterial Endo Toxin Testing (LAL) - Gel Clot Method

To describe the procedure for conducting a Bacterial Endotoxin Test by the LAL Gel-Clot method. The gel-clot method for bacterial endotoxin testing described in this SOP is based on the fact that Limulus Amoebocyte Lysate (LAL) will form a firm gel in the presence of bacterial endotoxin.

MICLAB 085 Bacterial Endo Toxin Testing kCA Method

The purpose of this SOP is to outline the theory of Bacterial Endotoxin testing using Kinetic Chromogenic Analysis (KCA). And to outline the procedure for routine product testing, operator / reagent verification and product validation by KCA using the BioWhittaker KQCL (brand) reader. This Procedure also describes the routine maintenance procedures for the BioWhittaker KQCL (brand) reader.

MICLAB 090 Stock Suspension of Micro Organism

The objective of this SOP is:

- To describe the method for preparing and maintaining stock suspensions of vegetative microorganisms and spores used within the Microbiology Laboratory.
- To explain the procedure for growth promotion and media verification requirements for all media used within the Laboratory.
- To outline requirements for Stasis testing on sterility canisters after sterility testing has been completed.

MICLAB 095 Sterile Sampling Procedure for Microbiology Laboratory

To detail the procedure for taking Microbiological samples for Sterility testing, Bacterial Endotoxin testing, Bioassay testing, Microbial Limit test and Micro status testing throughout Production. This procedure includes sterilization charts, Settle plates (Fallout plates) and Personnel monitoring.

MICLAB 105 Gel Clot Validation Method

The gel clot validation method for Bacterial Endotoxin testing described in this SOP, is to determine the level of Inhibition/Enhancement of products on the LAL test for endotoxins within the allowable Maximum Valid Dilution (MVD) for each type of product. The Gel-Clot techniques detect or quantify endotoxins based on clotting of the LAL reagent in the presence of endotoxin.

To be determined for each type of product, using the highest and lowest concentration of active. If either concentration shows inhibition or enhancement, then each remaining concentration must be tested. At least three (3) Production batches of each finished product should be tested for inhibition and enhancement.

MICLAB 110 Microbiology Laboratory Investigation and Retest Procedure for Atypical and OOS Results

The purpose of this procedure is to provide guidance when investigating microbiology laboratory out of specification (OOS) results associated with raw material samples, in-process samples and finished product samples. This procedure describes the actions taken by Microbiology Laboratory staff in the event the result of a test does not conform to company specifications for microbiological release.

This procedure will also provide guidance for re-testing raw material samples, in-process samples and finished product samples when it has been decided through a laboratory investigation that retesting is justified. Retesting should be viewed as an investigational tool to aid in determination of the root cause of the discrepant laboratory result.

MICLAB 115 TOC Analyser - Operation and Calibration of Sievers 820 (brand) Analyser

To define the procedures to be followed and the responsibility for the operation, calibration and maintenance of the Sievers 820 TOC Analyser with Autosampler.

MICLAB 120 IPA Contamination Testing Procedure

To describe the test sometimes used to check the purity of the IPA used in the factory as a disinfectant.