PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1.0 OBJECTIVE

1.1 To lay down the Procedure for the investigation of sterility test failure.

2.0 SCOPE

2.1 This SOP is applicable for procedure for the investigation of sterility test failure at ……

3.0 RESPONSIBILITY

3.1 Microbiologist

4.0 ACCOUNTABILITY

4.1 QC-Manager

5.0 PROCEDURE

5.1 If there is any product failure in sterility testing, immediately inform it to the department head and the concerned plant in charge.

5.2 A written note duly signed by the department head should be send to the concerned plant in-charge stating the failure and not to release the concerned batch until and unless the investigations are completed.

5.3 Divide and perform the investigation into two categories.

5.3.1 Microbiology Laboratory.

5.3.2 Production Area.

5.4 After the complete investigation if any abnormality is found in both the microbiology laboratory and the production area, it should be highlighted to the department head, Quality Assurance Manager, and concerned plant in-charge for necessary action. Perform the investigation in the following manner:

5.5 MICROBIOLOGY LAB

5.5.1 ISOLATION AND IDENTIFICATION OF THE MICROORGANISMS.

5.5.1.1 Isolate the organisms from the failed sample by streaking on Soya bean casein digest agar.

5.5.1.2 Perform the gram staining as per the GTP.

5.5.1.3 Identify the organism as per the GTP.

5.5.2 AUTOCLAVE

5.5.2.1 Check whether the autoclave is validated or not. If yes, when was the date of validation.

5.5.2.2 Check whether there had been any major maintenance of the autoclave, if yes, when was the maintenance done.

5.5.2.3 Check whether the autoclave was revalidated after the maintenance.

5.5.2.4 Check whether the autoclave was operated as per the SOP for operation of autoclave.

5.5.2.5 Check the training record of the operators for operation of autoclave.

5.5.2.6 Check the sterilization record for the temperature attained during the process for the sterilization of sterility testing materials.

5.5.2.7 Check the record for the time duration of the sterility testing materials.

5.5.2.8 Check whether the time period is as per the validation protocol.

5.5.2.9 Check the record for the use of biological / chemical indicators and if used, check whether it is working as per the specification of the indicator.

5.5.2.10 Check whether the load was sterilized as per the loading pattern.

5.5.2.11 Check the sterilization record for the quantity of the material placed in the chamber for sterilization during that particular load.

5.5.3 GARMENTS

5.5.3.1 Check whether the garments used during the testing process were sterilized.

5.5.3.2 Check with the analyst whether the garments were wet during the testing of the particular batch.

5.5.3.3 Check the sterilization record for the sterilization of the garments.

5.5.3.4 Check the record for the duration of sterilization and were they sterilized as per the loading pattern predetermined in the validation protocol.

5.5.4 DISINFECTION OF STERILITY TESTING AREA

5.5.4.1 Check the sterility testing area disinfectant record for the usage of disinfectants.

5.5.4.2 Check whether the disinfectant used was as per the schedule.

5.5.4.3 Check the date of preparation of the diluted disinfectant.

5.5.4.4 Check the expiry date of the diluted disinfectant.

5.5.5 PERSONNEL

5.5.5.1 Check whether the analyst is properly qualified and trained for testing of sterile products.

5.5.5.2 Check the training record of the analyst for the entry and exit procedure into sterility testing area.

5.5.5.3 Check whether the analyst is suffering from any contagious disease.

5.5.6 STERILITY TESTING AREA

5.5.6.1 Check whether the HVAC is validated or not.

5.5.6.2 Check whether the AHU is working properly or not.

5.5.6.3 Check whether the LAF is validated or not as per the validation protocol. Check the date when it was last validated.

5.5.6.4 Check whether there had been any major maintenance work in the sterility testing area. If yes, whether the area was requalified for testing as per the protocol or not.

5.5.6.5 Check the sterility testing room fumigation record; check the date when it was last fumigated.

5.5.6.6 Check whether the area was cleaned or not.

5.5.6.7 Check the disinfectant used for cleaning.

5.5.6.8 Check with the analyst, if there had been any power failure during the testing.

5.5.6.9 Check the temperature and RH record of the area during that particular day.

5.5.7 AREA MONITORING

5.5.7.1 Check whether area monitoring was performed on that particular day. If yes, check the counts for settle plates, swabs, air sampling and the personnel monitoring counts of the analyst.

5.5.7.2 Check whether the counts were in limits or not. If found, check whether the counts were isolated and identified.

5.5.8 PRODUCT TESTING

5.5.8.1 Check the training record of the analyst for performing the test.

5.5.8.2 Check whether the analyst is an approved in house analyst as per the analyst validation protocol.

5.5.8.3 Check the sterility record for the number of tests performed on that particular day.

5.5.8.4 Check with the analyst whether there had been any abnormality during the testing of the product.

5.5.8.5 Check the negative control for the particular media lot.

5.5.8.6 Check the negative control for the test being performed on that day.

5.5.8.7 Check the batch number of the sterility testing media used for the failed batch and the details of the sterilization from the record.

5.5.8.8 Check whether the sterilization indicators were used along with that media.

5.5.8.9 After checking all the above parameters, compile the data.

5.6 PRODUCTION AREA

5.6.1 From the batch manufacturing record, check the date of charging and unloading of the batch.

5.6.2 PERSONNEL

5.6.2.1 Check the number of operators who went inside the area from the entry log record in that particular shift in which the batch was unloaded.

5.6.2.2 From the training record, check whether all the persons entered were qualified for entering into the sterile area.

5.6.2.3 Check the training record of IPQA personnel for entry and sampling of finished goods.

5.6.2.4 Check the training record for the gowning of all the operators and IPQA personnel as per the SOP for gowning procedure.

5.6.3 AREA MONITORING OF STERILE AREA

5.6.3.1 Check the area monitoring record of the shift in which the product was unloaded.

5.6.3.2 Check for any abnormal counts in settle plate exposure, surface monitoring, air sampling and personnel monitoring. If any counts were found check whether the colonies were isolated and identified.

5.6.3.3 Check that the abnormal counts were duly informed to the plant

In-charge.

5.6.4 DISINFECTANTS

5.6.4.1 Check the disinfectant preparation record.

5.6.4.2 Check whether the disinfectant used was as per the schedule.

5.6.4.3 Check whether the disinfectant used was approved and qualified by the Quality control department.

5.6.4.4 Check the date of preparation of the diluted disinfectant.

5.6.4.5 Check the expiry date of the diluted disinfectant.

5.6.5 AREA CLEANING RECORD

5.6.5.1 Check the area cleaning record.

5.6.5.2 Check whether the cleaning was done as per the schedule.

5.6.5.3 Check whether the cleaning person who went for cleaning in that particular shift was qualified and trained to go in the sterile area.

5.6.5.4 Check whether the cleaning person was also monitored. If yes, check the counts.

5.6.5.5 Check whether the colonies were isolated and identified.

5.6.6 DIFFERENTIAL PRESSURE AND RH%

5.6.6.1 Check whether the differential pressure was correct in all the areas in hat particular shift.

5.6.6.2 Check the RH % of the area in that particular shift.

5.6.6.3 If the differential pressure and the RH % were out of the limit, check the maintenance record and whether it was informed to the maintenance department for rectification.

5.6.6.4 Check the record for the rectification done in the area.

5.6.7 HVAC AND LAF

5.6.7.1 Check the validation record of HVAC and LAF.

3.6.7.2 Check the next due date for validation.

5.6.8 MAJOR MAINTENANCE

5.6.8.1 Check the maintenance record for any major maintenance of the area or any equipment part related with the product.

5.6.8.2 Check whether the maintenance operator was qualified for entering the sterile area or not.

5.6.8.3 Check whether the operator was monitored for personnel counts, if yes check the number of colonies, if found.

5.6.8.4 Check whether the colonies were isolated and identified.

5.6.9 DHS AND AUTOCLAVE

5.6.9.1 Check the usage record for DHS and Autoclave.

5.6.9.2 Check the strip chart for any deviation during the process for container sterilization by DHS and rubber bung sterilization by autoclave.

5.6.9.3 Check the strip chart for any electrical breakdown during the process.

5.6.10 GARMENTS

5.6.10.1 Check whether the garments were sterilized.

5.6.10.2 Check the sterilization record of the garments.

5.6.10.3 After checking all the above parameters, compile the data.

5.6.11 After checking all the parameters in both the production area and microbiology laboratory, prepare an investigation report as per the Annexure-I.

6.0 ABBREVIATIONS

6.1	IPQA	In process Quality Assurance
6.2	LAF	Laminar Air Flow
6.3	HVAC	Heat Ventilated Air Conditioning
6.4	AHU	Air Handling Unit
6.5	RH	Relative Humidity
6.6	DHS	Dry Heat Sterilizer

7.0 ANNEXURES

7.1 Annexure-I Sterility Test Failure Investigation Report

CHANGE HISTORY		
Supersedes SOP No.	**Change Control No.**	**Changes made**
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STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

ANNEXURE-I

INVESTIGATION REPORT FOR STERILITY TEST FAILURE

Name of the product :

Lot No./batch No. :

Date of Charging :

Date of Manufacturing :

Batch Charged By :

Shift during which the batch was charged :

Date investigation started :

PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

MICROBIOLOGY LAB INVESTIGATIONS REPORT

1.Isolation and identification of Microorganisms	
1.1 Gram nature of isolated organism	:
1.2.The organism is identified as	:
2. H.P.H.V Steam sterilizer	:
2.1.H.P.H.V.steram sterilzer is validated or not	:
2.2 If Validated when it was done	:
2.3.Is there any major breakdown	:
2.4 If yes, when it was happened	
2.5 Whether it was revalidated after breakdown	
2.6 Whether the training record for operation of HPHV steam sterilizer is present or not	
3. GARMENTS	
3.1 Whether the garments used for sterility testing is used as per hold time validation of sterilized articles.	
3.2 Whether the garments are wet at the time of conducting sterility test	
4. Disinfection	
4.1 Check the disinfectant record for the usage of disinfectants	

STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

4.2 Check the expiry date of the diluted Disinfectant

5. Personnel

5.1 Whether the analyst is trained and qualified for sterility testing

5.2 Whether the analyst is suffering from any contagious disease

6. Sterility testing area

6.1 Whether the HVAC is validated or not
6.2 If yes, when it was last validated
6.3 Whether the LAF is Validated or not
6.4 If yes, when it was last validated
6.5 Check the fumigation record, when it was last fumigated
6.6 Is there any power failure during sterility testing

7. Area monitoring

7.1 Whether area monitoring was performed on that day.
7.2 Check the counts for settle plates, Air sampling and personnel monitoring. If found whether the counts are within limits or not
7.3 Whether the counts were isolated and identified

8. Product testing

8.1 Whether the analyst is an approved in-house analyst as per the analyst validation protocol

8.2 Whether there had been any abnormality during the testing of the product

STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

8.3 Whether the negative control is OK or not	

OUT OF LAB INVESTIGATIONS

1. Review of Manufacturing Facility:	
1.1 Campaign Started on	:
1.2 Batch No.	:
	:
2. Sterilization Records:	
2.1 Steam Sterilizer	
2.1.1 Garments Cycle No.	
2.1.2 Container stoppers Cycle No.	
2.2 Dry Heat Sterilizer	
2.2.1 Cycle No.	
2.2.2 Sampling aids Cycle No.	
3. Date of last change of Compressed Air, Nitrogen Line Filters	**:**
4. Last HVAC validation Reports including DOP and air velocity results of terminal HEPA and HEPA of LAF units are OK or not	**:**
5. Environmental Monitoring Records [Period covered: 30 days prior to the manufacture of suspected batch and till date] OK or not	

STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

5.1 Plate Exposure Results	:
5.2 Active Air Sampling Results	:
5.3 Personnel Monitoring Results	:
5.4 Surface Monitoring Results	:
5.5 WFI Monitoring Records	:
5.6 Non Viable Air borne particle counts if any	:
5.7 Temperature/RH Records	:
5.8 Differential Pressure Records of area	:
5.9 Positive pressure of equipments	:
5.10 Any other abnormal Observation (Recorded and /or Reported)	:
6. Batch Production Record Review: [Review the BPR for any abnormalities in aseptic processing like duration of batch processing, no. of operating people in the room etc:	

STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

7. Identification of the organism(s) recovered during environmental / personnel monitoring in manufacturing / sterility testing facility	
7.1 Manufacturing Facility:	
7.1.1 Source (Air/Surface/Personnel)	:
7.1.2 Identity of the organism (Attach Identification Report)	:
7.2 Sterility Testing Facility	
7.2.1 Source (Air/ Surface/Personnel)	:
7.2.2 Identity of the Organism (Attach Identification Report)	:
7.3 Probable source of contamination	:
7.4 Any assignable cause of sterility positive [if found] Action Taken	: :
7.5 Action taken if other batches have Likely impact.	:
7.6 Conclusion of Investigation	:

8. Investigation Carried out by

Name	Signature	Date

STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Investigation for the Sterility test failure	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

9. Conclusion of investigation by Head of Microbiology/Quality Control Department (Reason of Failure)

10. Signatures

	Name	Signature	Date
Head- Production			
Head- QA			
Head- QC			
Head- Microbiology			