STANDARD OPERATING PROCEDURE	
Department: Microbiology	**SOP No.:**
Title: Deviations & OOS in Microbiological Analysis and Monitoring	**Effective Date:**
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1.0 OBJECTIVE:

To lay down a procedure for handling of out of specification (OOS) result in Microbiological analysis and monitoring.

2.0 RESPONSIBILITY:

Quality Control Executive/ Microbiologist.

3.0 ACCOUNTABILITY:

Quality Control Manager.

4.0 PROCEDURE:

In all the reports the identified reason shall be written on a continuation sheet to the annexure provided. A copy of the above investigation report shall be maintained with the batch manufacturing records concerned to increase awareness and for any future reference

4.1 **STERILITY TEST:**

4.1.1 If evidence of microbial growth is found, the product to be examined does not comply with the test for sterility, unless it can be clearly demonstrated that the test was invalid for causes unrelated to the product to be examined .The test may be considered invalid only when one or more of the following conditions are fulfilled:

4.1.1.1 The data of the microbiological monitoring of the sterility testing facility hows a fault.

4.1.1.2 A review of the testing procedure used during the test in question reveals a fault.

4.1.1.3 Microbial growth is found in the negative controls.

4.1.1.4 After determination of the identity of the microorganisms isolated from the test, the growth of this species or these species may be ascribed unequivocally to faults with respect to the material and / or the technique used in conducting the sterility test procedure.

4.1.2 If the test is declared to be invalid it is repeated with the same number of units as in the original test.

4.1.3 If no evidence of microbial growth is found in the repeat test the product examined complies with the test for sterility. If microbial growth is found in the repeat test the product examined does not comply with the test for sterility.

4.2 ENVIRONMENTAL MONITORING:

4.2.1 If the microbial counts are found to be more than or equal to the **alert limit** then open a deviation report (annexure I) through Q.C. Head to the concerned Production head. Production personnel shall check the working discipline, supply of air, safety measures etc.

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4.2.2 If the count exceeds or reaches the **action limit** then an urgent notification to the Production head and Engineering Head through Q.C. Head shall be followed by an investigation for the same.

4.2. 2.1 Supply of air

4.2.2.2 Working discipline

4.2.2.3 Review of data from the same place and others from the incubated plates

4.2.2.4 If any of the plates does not indicate the same then no action is necessary.

4.2.2.5 If any of the plates indicates more count then perform additional cleaning , disinfection or fumigation and retraining to the operator shall be given.

4.2.2.6 All activities shall be recorded as per the annexure attached with this SOP.

4.2.2.7 More number of samplings (i.e. double the original) shall be preformed at the same location where the counts observed were beyond or equivalent to the action limit but an additional relevant parameter of monitoring shall also be performed which shall be incorporated with the same annexure.

4.2.2.8 All the batches manufactured during the said period shall be subjected to the microbial analysis for MLT / Sterility &BET in order to ensure that the batches manufactured are in accordance with the relevant finished product specifications. The investigation report shall be submitted to the Q.C. - Head

4.2.3 If the bio-burden is found out of specified limit in the core areas the identification of the organism shall be performed.

4.2.4 Stop the production immediately and check all the possible parameters, which can affect bio-burden of the area.

4.2.5 Check the pressure differential of the area, which must be within the specified limit.

4.2.6 Check the air velocity of LAF /HEPA filters, which must be within the specified limit.

4.3 If the investigation / review of manufacturing activities (e.g. sterilization process, aseptic filtration, environmental conditions, personnel practices) indicates failure of manufacturing activities, then the batch shall be considered as failed to comply sterility.

4.4 MICROBIOLOGICAL AND BET EXAMINATION OF WATER:

4.4.1 If only the alert is exceeded without finding an undesirable microorganism the release of the preparation for which this water has been used, has to be taken under hold till the result comes.

4.4.2 In case of the counts touching the action limit then all the batches manufactured shall be re analyzed by taking 25 grams and making the allowance for the larger size specimen for the analysis.

4.4.3 In the case of counts crossing or touching the alert limit or action limit in any type of water the same will be intimated to the production department and maintenance department. If the result cannot be attributed to the analytical error, sampling error, contamination in the container sampled then the microorganism detected must be identified / differentiated by taking sample from all other points.

4.4.4 Adequate sanitization of the system shall be ensured to eliminate the source of contamination with a rigorous check for the same.

4.4.5 All the investigations made shall be recorded in the annexure III provided with this SOP.

4.5 MICROBIOLOGICAL EXAMINATION OF RAW MATERIAL/FINISHED PRODUCT:

4.5.1 The first action is to intimate the Q.C. Head.

4.5.2 Retest the same material/product but with a sample size of 25 grams by making allowance for the larger size specimen.

4.5.3 Results for the same shall be intimated to the Q.A. Head for final decision.

5.0 REASON FOR REVISION:

Harmonization of format.

6.0 TRAINING:

Trainer	--	Head – Quality Control
Trainees	--	Quality Control Chemists & Assistants
Period	--	One day

7.0 DISTRIBUTION:

Certified Copy No. 1 : Head of Department – Quality Control
Certified Copy No. 2 : Microbiology Department
Original Copy : Head – QA

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8.0 ANNEXURES:

Annexure I : For Deviation Report to Production Department

Annexure II : Corrective Report after Sampling of Environmental Parameter in Production

Annexure III : **I**nvestigation report for failure in test for bacterial Endotoxin & MLT

9.0 REFERENCES:

In house.

PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

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ANNEXURE –I

FORMAT FORDEVIATION REPORT TO PRODUCTION DEPARTMENT
(Deviation Report About the environmental monitoring)

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Sampling point where deviation occurred: **Date:**
Name of the Product **Batch no.:**

Deviation : Parameter:
Requirement :
Results : Signature :

Corrective action in Production Department:

Cleaning, Disinfection, Change of disinfectant, Checking of LAF unit parameters , Checking of HVAC system, Education to Operators, Repair/Maintenance Work (Cross whichever is not applicable and specify actions taken).

Maintenance, Repair / Comments:

……
……
……

Name: **Signature:** **Date:**

Repeated Sampling:

Parameter: **Result:**
Comments by Q.C. Head for Approval of Production:

……
……
……

Signature:

Prepared By	Checked By	Approved By	Authorized by

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ANNEXURE - II

Format for Corrective Report after Sampling of Environmental Parameters in Production

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Date: **Deviation:**

Date of repeated Deviation:

Corrective Measures in Microbiological Lab

Checking of condition s of LAF unit during working, Checking of equipment
Growth promotion test for the media used.

Done By: Checked By:

Results of Microbiological Impurity of Finished Product:

Name: Date: Signature:

Comments of Quality of Quality of Control - Head:

Name: Date: Signature:

Comments of Quality Assurance - Head:

Name: Date: Signature:

Prepared By	Checked By	Approved By	Authorized by

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ANNEXURE –III

INVESTIGATION REPORT FOR FAILURE IN TEST FOR BACTERIAL ENDOTOXIN & MLT

REF. SOP No.:	**Revision No.:** 00 **Effective Date:**	**Page No.:** 1 of 1

Sample
Analyzed on Analyzed By Checked By

Preparation parameters for
Sampling container Procedure of sampling GP test of media
Any testing error

BET
Micro tips Test tubes Pipette
LAL reagent
Batch No. Mfg. Expiry Reconstituted on

LAL Reagent water
Batch No. Expiry Blank

Parameters of Depyrogenation/Sterilization apparatus:
Validation Status Calibration Status

Results of other samples with same conditions tested on the same day.

Details of Raw material used in finished product

Result
Test repeated
Date Result Microbiologist

ACTION TAKEN:

Production Head **Engineering Head** **Quality Control Head**

CONCLUSION:
(Results of MLT for Other Samples to be enclosed)

Microbiologist
Date:

QC Manager
Date:

Remarks from Q.C. Head
Name: Sign Date:

Prepared By	Checked By	Approved By	Authorized by