



PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE

Department: Microbiology

SOP No.:

Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis

Effective Date:

Supersedes: Nil

Review Date:

Issue Date:

Page No.:

1.0 OBJECTIVE:

To lay down a procedure for Handling of Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis.

2.0 SCOPE:

This SOP is applicable for Out of Trend Results of Water, Personal Monitoring & Environment Monitoring in the clean areas during routine monitoring by Settle Plates, Air Sampling & Water Testing from schedule location in Quality Control area.

3.0 RESPONSIBILITY:

Officer / Executive – Microbiologist

4.0 ACCOUNTABILITY:

Head – QC

5.0 PROCEDURE:

5.1 QUALITY CONTROL DEPARTMENT

5.1.1 In case the CFU counts exceed the Alert / Action levels at any location then QC department must be intimate to QA department as per **Annexure-I**, Titled “**Quality Control Intimation Slip**”.

5.1.2 QA head shall immediately investigation as per Annexure-II, Titled “**Microbiology & Production Area Observation Report**” will contain the following details :

- A. Name of the Plant
- B. Date of monitoring
- C. Sampling method used
- D. Sampling location
- E. Microbial count exceeds Alert/Action limit
- F. CFU observed
- G. Action limits

5.2 Investigations shall be carried out in Quality control & Production department

5.3 Results shall be discussed with the Sr.Microbiologist for any unusual observations made in the area and for any difficulty faced during sampling.

5.4 Media Preparation & Sterilization Records and Negative controls of the Media shall be checked for any abnormality.

5.5 Identify the organism up to specific level from the plate showing Out of Trend result.



STANDARD OPERATING PROCEDURE

Department: Microbiology

SOP No.:

Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis

Effective Date:

Supersedes: Nil

Review Date:

Issue Date:

Page No.:

5.6 Identify the organism isolated from normal production flora/ QC flora/ Personal monitoring which are having same colony characteristics to establish the possible source of contamination.

5.7 Refer the historical review of environmental monitoring results for the site in question.

5.8 If above observations do not confirm as a cause of analytical error then check at the Production Department.

5.9 PRODUCTION DEPARTMENT

5.9.1 The Investigation shall be carried out as per the checklist given in the **Annexure-II**.

5.9.2 The QA Head shall investigate the cause of the Out of Trend results in co-ordination with Microbiology section (QC) and Production Head.

5.9.3 After investigations are over the Head Operation will send dully filled Action taken report along with the Investigation report to QC.

5.10 OUT OF TREND. INVESTIGATION FOR ALERT LEVEL :

5.10.1 The alert level can be considered as an “early warning” of potential drift from normal operating conditions and it allows the corrective actions to be taken before product quality is adversely affected.

5.10.2 Refer the previous results for the affected site.

5.10.3 Upon review of above determined results further investigation and /or additional sampling can be warranted. Instruct the in-charge (Operation in clean area) to take extra measures for disinfection of the site in question.

5.11 OUT OF TREND INVESTIGATION FOR ACTION LEVEL:

5.11.1 If there have been multiple excursions in excess of alert level (or if the action level has been exceeded) investigate the parameters shown in **Annexure-II & III**.

5.11.2 On the basis of investigation made as per **Annexure-II & III**, establish the corrective actions required and implement it.

5.11.3 After the corrective actions are taken check the effectiveness of these actions by suitable monitoring.

5.11.4 If count exceeds alert/action level for operator glove or gown check the following parameters:

A. Operator activity

B. Environmental monitoring history of operator



STANDARD OPERATING PROCEDURE

Department: Microbiology

SOP No.:

Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis

Effective Date:

Supersedes: Nil

Review Date:

Issue Date:

Page No.:

- C. Other environmental monitoring data in the working area
- D. Periodic sanitization for gloves
- E. Types of organism identified
- F. Operator's validation data during media fill
- G. Number of Operator & Helper on the day.
- H. Any maintenance activity.
- I. Entry Exit record.
- J. Personal Hygienic Record of the Operator.

5.11.5 Instruct the In-Charge, for the re qualification of the operator and give adequate training to the operator.

5.11.6 If the counts exceeds the action limits any locations in the Clean area (Class 100, 1000 & 10,000) the Production activities in the area will be stopped. The production activities shall start only after getting 3 consecutive satisfactory area monitoring results.

5.11.7 If the results of out of Trend observed in Grade 'A' areas i.e. class 100, the batch processed on the particular filling line on the day of Out of Trend should be treated after investigation performed as per **Annexure-II**, Titled "**Microbiology & Production Area Observation Report**".

5.11.7.1 If problem found at filling line and/or action level exceeded in multiple environmental monitoring tests (i.e. Settle plate count, Air sampling) at the same site the batch should be hold.

5.11.7.2 If the results of Out of Trend are found as a isolated event with definable cause or other monitoring results of the same location are found within limits and trend data is acceptable before and after Out of Trend, repeat the retesting of the batch processed on the day of Out of Trend for sterility test using double no. of units.

5.11.7.3 If the results of out of Trend observed in Grade 'B' or 'C' areas i.e. class 1000, 10000 the batch processed on the day of Out of Trend results, will be tested additionally for sterility test using double the quantity required for the test.

5.11.7.4 The batch filled on the day of Out of Trend should be released only after getting.

- Sterility test results of repeat testing.
- After establishment of relationship between Out of Trend result and possible cause.

6.0 REFERENCES

Not Applicable



PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE

Department: Microbiology

SOP No.:

Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis

Effective Date:

Supersedes: Nil

Review Date:

Issue Date:

Page No.:

7.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure-I	Quality Control Intimation Slip	
Annexure-II	Microbiology & Production Area Observation Report	
Annexure-III	Water System Observation Report	

ENCLOSURES: SOP Training Record

8.0 DISTRIBUTION:

- Controlled Copy No. 01 Quality Assurance Department
- Controlled Copy No. 02 Quality Control Department
- Master Copy Quality Assurance Department

9.0 ABBREVIATIONS:

Ltd. Limited
No. Number
QA Quality Assurance
QC Quality Control
SOP Standard Operating Procedure

10.0 REVISION HISTORY:

CHANGE HISTORY LOG

Revision No.	Details of Changes	Reason for Change	Effective Date	Updated By
00	New SOP	Nil	Nil	Nil



PHARMA DEVILS
MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE

Department: Microbiology	SOP No.:
Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis	Effective Date:
Supersedes: Nil	Review Date:
Issue Date:	Page No.:

ANNEXURE-I
QUALITY CONTROL INTIMATION SLIP

To, Quality Control Department	From, Quality Assurance Department
---	---

To,
Head QA

Dated:

Sub:

Dear Sir,

This is to inform you that following microbial count is exceeding the alert Limit

.....
.....

Microbiologist:
Date:

Checked by:
Date:

Approved by:
Date:



PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE

Department: Microbiology	SOP No.:
Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis	Effective Date:
Supersedes: Nil	Review Date:
Issue Date:	Page No.:

ANNEXURE-II MICROBIOLOGY & PRODUCTION AREA OBSERVATION REPORT

Name of the area		Action Limit	
Class or Grade		Microbial count Exed	
Date of monitoring		Number of cfu observed	
Sampling Method		Monitored by	

MICROBIOLOGY OBSERVATION

S.No.	Particulates	Observation
1	Date of Expose media preparation	
2	Sterilization Cycle No.	
3	In Growth Promotion Test , Inoculums Preparation Report No.	
4	Growth Promotion Test Status of media lots	
5	Preincubation Details	Negative Control
		Positive control
6	Incubators cleaning status	
7	Incubators Performance Qualification	
8	Temperature & Pressure Monitoring Record of incubator	
9	Identification of organism up to species level	
10	Grams characters	
11	Colony shape	
12	Area cleaning / Fogging Record	
13	AHU record	
14	Disinfectant efficiency	
15	Disinfectant used	
16	Personal hygienic record	

PRODUCTION OBSERVATION

S.No.	Particulates	Observation
1	Temperature And Rh Monitoring	
2	Differential Pressure Monitoring	
3	Cleaning status	
4	Fogging status	
5	Personnel qualification	
6	AHU Validation	
7	LAF Validation	



PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE

Department: Microbiology

SOP No.:

Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis

Effective Date:

Supersedes: Nil

Review Date:

Issue Date:

Page No.:

8	Personnel Hygienic Record	
9	Entry Exit record	
10	Garment condition	
11	Maintenance work	
12	Stop production and through cleaning (wall, ceiling, floor, door and machine etc.).	
13	Leakage	
14	Number of Staff, Operator & Helper on the day.	
15	Periodic Sanitization of Gloves & Garments	
16	Staff, Operator & Helper data during media fill	
17	Disinfectant Efficiency Record	
18	Disinfectant Used	
19	Cleaning Record	

Microbiologist:

Date:

Checked by:

Date:

Approved by:

Date:



PHARMA DEVILS

MICROBIOLOGY DEPARTMENT

STANDARD OPERATING PROCEDURE

Department: Microbiology

SOP No.:

Title: Handling of OOT and OOS Results During Microbial Limit Test, Environment Monitoring and Water Analysis

Effective Date:

Supersedes: Nil

Review Date:

Issue Date:

Page No.:

ANNEXURE-III WATER SYSTEM OBSERVATION REPORT

S.No.	Particulates	Observation
1.	Date of media preparation	
2.	Sterilization Cycle No.	
3.	In Growth Promotion Test , Inoculums Preparation Report No.	
4.	Growth Promotion Test Status of media lots	
5.	Pre -Incubation Details	Negative Control
		Positive control
6.	Incubators cleaning status	
7.	Incubators Performance Qualification	
8.	Temperature Monitoring Record	
9.	Identification of organism up to species level	
10.	Grams characters	
11.	Colony shape	
12.	Water system sanitization Record	
13.	Water sampling record	
14.	Sampling Qualification	
15.	Method of Sampling	