

**ANNEXURE -III**  
**MICROBIOLOGICAL ENVIRONMENTAL FAILURE INVESTIGATION FORM**

**A) Corrective and Preventive Action Request (CPAR) Form Number:**

**B) Failure Results**

<b>Failure Result</b>	
Sample Type	
Location (Department/Room Name/ Location)	
Date and Shift of sampling	
Observed Value	
Alert Limit	
Action Limit	

**C) Investigation Plan:**

**a) To find out the source of contamination from the common sterility determinant factor as follows**

- 1.0 Articles transferred to aseptic area
- 2.0 Personnel entering and working in the aseptic area
- 3.0 Aseptic area cleaning and disinfection
- 4.0 Air supply system (LAF and HVAC system)

**b) To review the trends of environmental monitoring results**

**D) Investigation Report:**

**1.0 Articles**

- 1 Check that articles are transferred and stored in Critical Aseptic Zone (CAZ) using standard procedures
  - i. List the articles, which are present in the CAZ before and since the date of failure and refer the SOP no and their recent validation report reference for efficiency of sterilization or disinfection
  - ii. Check that articles present in the area are within it validated period of holding in CAZ
  - iii. Check that articles are monitored by swab testing while transferring into CAZ after disinfection and results are within acceptance limit
  - iv. Check that critical components are stored under unidirectional air flow zones
  - v. Interview the personnel for transfer of any article deviating the standard procedure
  - vi. Carry out the swab testing on each articles present in the area after getting the out of limit result and report the result

Sr. No	Name of the article	SOP No for sterilization or disinfection	Validation Ref No	Storage location	Standard Location	Actual storage time	maximum storage period (Standard)	Whether swab tested Yes/ No/ NA	Current swab test result

Investigation Remarks:

**(Investigation Carried out By)**

**Checked By:**

2.0 **Personnel:**

- 1.0 Check that personnel has followed the standard practices during Aseptic operation:
- i. List the personnel who were present in Aseptic area for the past three days and on the date of failure
  - ii. Check that personnel are qualified to enter in the aseptic zone
  - iii. Check that all personnel were monitored for bioburden on or before the date of failure and check the trend
  - iv. Recheck the bioburden of the personnel after aseptic gowning for investigation
  - v. Recheck the gowning procedure for each personnel involved to ensure that no deviation happened
  - vi. Evaluate the personnel for his aseptic and behavioral practices.
  - vii. Check that personnel are not suffering from any contagious diseases.

Sr. No	Personnel Name	Past trend of the personnel monitoring	Current personnel monitoring result	Gowning practice	Aseptic practices and behaviour	Medical history

Sr. No	Personnel Name	Past trend of the personnel monitoring	Current personnel monitoring result	Gowning practice	Aseptic practices and behaviour	Medical history

2.0 Check the data of personnel residence period in aseptic area and report the maximum period. Check that maximum residence period should not be more than that established in process simulation study.

Maximum Residence period observed:

Established residence period:

3.0 Check that total number of personnel present at a time in the aseptic area and ensure that it should not be more than that established in process simulation study

Total number of personnel present at a time (observed) :

Established number:

**(Investigation Carried out By)**

**Checked By:**

**3.0 Area Cleaning and Disinfection**

- 1.0 Check whether the disinfectants were prepared as per the procedure for disinfectant preparation.
  - i. Check whether the disinfectants were used within its 'Used Before' period.
  - ii. Check whether disinfectant used are scheduled.
  - iii. Check whether the Disinfectant sample tested for bioburden meet the requirement.
  - iv. Check whether the pre and post filtration integrity of the disinfectant filter meets the requirement

Sr No	Name of the disinfectant used	Whether it is scheduled	Standard conc	Actual conc used	Bioburden result of disinfectant	Used within scheduled period	Filter Integrity meet the standard

- 2.0 Check the trend of bioburden counts and type in WFI used for the preparation of disinfection and check the type of the organism has any co relation with the organism identified from the Environmental Monitoring failure results.

Observation :

3.0 Check the Sterilization of cleaning aids (e.g. Buckets, mops etc) used in three days before and on the date of failure;

Sr No	Date of Sterilization	Load as per the Validated diagram	Sterilization as per the validated diagram

4.0 Check that time period between two cleaning and disinfection operation is within the established time limits.

Maximum Time Period Observed:

Established Time Period:



5.0 Perform the swab testing from the area, which are difficult to clean and disinfect.

Sr. No	Date of Monitoring	Difficult to Clean Locations	Results

**(Investigation Carried out By)**

**Checked By:**

4.0 **LAF and HVAC system:**

1.0 Check the class 100, unidirectional air flow zones for its proper functioning as below-

- i. Check velocity of air at the working zone (for Grade A or class 100) and at the filter downstream for Grade B or Class 10,000 area
- ii. Check the viable and nonviable airborne particulate count in increased number of location as done during qualification study
- iii. Carryout the swab testing in the Filter grill
- iv. Check HEPA filter integrity test in case of frequent failure (more than 3 times)
- v. Check air change rate which should be within the design limit or within  $\pm 20\%$  of the installed value.
- vi. Check temperature, RH and Differential pressure of the area and ensure within established standard limit

Acceptance criteria:

Air velocity:	
Air change rate:	
Minimum pressure differential	
Temperature:	
RH:	
HEPA filter integrity test result:	
Nonviable particulate count:	
Viable particulate count:	
Swab test:	

Location	Maximum Air velocity at the working zone	Air change rate	Minimum Pressure Differential observed	Maximum Temperature observed	Maximum RH observed	DOP test result	Maximum air borne nonviable particulate count	Maximum viable count	Swab test result

**(Investigation Carried out By)**

**Checked By:**

**5.0 Other Microbiological monitoring record:**

- i. Check the trend of environmental isolate from the same area.
- ii. Check the frequency of appearing
- iii. Correlate the isolated organism in the failure sample to find out probable source.

**Observation and Comments:**

**(Investigation Carried out By)**

**Checked By:**

**E) Conclusion of Investigation:**

**F) Root Cause Analysis:**

Investigation Team	Name	Signature	Date
Production			
Microbiology			
Quality Assurance			