STANDARD OPERATING PROCEDURE

Title: Environmental Monitoring of Production Areas				
SOP No.:		**Department:**	Microbiology	
		Effective Date:		
Revision No.:	00	**Revision Date:**		
Supersede Revision No.:	Nil	**Page No.:**	1 of 31	

1.0 OBJECTIVE

To lay down procedure for environmental monitoring of Production areas.

2.0 SCOPE

This SOP is applicable for environmental monitoring of Production areas.

3.0 RESPONSIBILITY

Prepared by - Executive Microbiology

Checked by - Assistant Manager

Approved by – Manager QA

4.0 PROCEDURE

4.1 Viable Monitoring

4.1.1 **Passive air sampling (Settle plate exposure technique)**

4.1.1.1 Prepare and qualify Soyabean casein digest agar / Potato dextrose agar media plates of 90 mm dia as per SOP.

4.1.1.2 Alternatively ready to use agar media plates can be use for monitoring.

4.1.1.3 Perform the growth promotion test of ready to use plates as per SOP.

4.1.1.4 Transfer the media plates to sampling area in a closed container to avoid any contamination.

4.1.1.5 Label the plates with the details given below -

Monitoring type / Plate No. / Media Load No. / Sampling Date / Sign

4.1.1.6 Frequency, exposure time and recommended limits of passive air sampling (Settle plate exposure technique) are given

Table - I

Grade	Recommended Limits ** (cfu / 4 hours)	Media Used / Frequency of Exposure	Time of Exposure
A	1	SCDA / Each operating shift PDA / Weekly once in each operating shift SCDA (Anaerobic monitoring)/ Monthly	4 hours
B	3		
C	5		
D	50	SCDA / Once in a week PDA / Monthly SCDA (Anaerobic monitoring)/ Monthly	

** **In-house Limits:** To be revised after at least 100 monitoring results.

4.1.1.7 Remove the plates from the container and place the media plates on the petri plate stand, provided at each of the designated locations.

4.1.1.8 Expose the plates for a period of 4 hours.

4.1.1.9 After completion of exposure time, cover the lid of each plate and transfer to micro lab for incubation.

4.1.1.10 Incubate the Soyabean casein digest agar plates along with one unexposed plate (Negative control) of the same media load or of the same batch/lot, if using ready to use plate, at 30°C-35°C for 2 days for aerobic bacterial counts followed by 20°C-25°C for 3 days for fungal, Yeast and molds counts in the inverted position.

4.1.1.11 Incubate the potato dextrose agar plates along with one unexposed plate (Negative control) of the same media load or of the same batch/lot, if using ready to use plate 20°C-25°C for 5 days for fungal, yeast and molds counts in the inverted position.

4.1.1.12 For anaerobic environmental monitoring incubate the Soyabean casein digest agar plates along with one unexposed plate (Negative control) of the same media load or of the same batch/lot, if using ready to use plate, at 30°C-35°C for 3 days for anaerobic bacterial counts in the inverted position under anaerobic condition.

4.1.1.13 After completion of incubation period count the number of colonies per plate and record the observations as cfu/4 hrs.

4.1.1.14 Negative control (Unexposed Plate) should not show any growth.

4.1.1.15 Record the results in Annexure - I and V.

4.1.2 **Active air sampling (Volumetric Air Sampling)**

4.1.2.1 Operate the volumetric air sampler for active air sampling.

4.1.2.2 Ready to use Soyabean casein digest agar plates / cassettes are to be used for sampling.

4.1.2.3 Perform the growth promotion test of ready to use plates / cassettes as per SOP.

4.1.2.4 Transfer the media plates / cassettes to sampling area in a closed container to avoid any contamination.

4.1.2.5 Label the plates / cassettes with the details given below -

Monitoring type / Plate/cassette No. / Media Load No. / Sampling Date / Sign

4.1.2.6 Remove the plates / cassettes from the container and carry out the air sampling at the designated locations.

4.1.2.7 Operate the volumetric air sampler as per SOP and sample 1000 lit or one mt^3 air per location.

4.1.2.8 After completion of sampling cover the lid of each plates / cassettes and transfer to micro lab for incubation.

4.1.2.9 Incubate the Soyabean casein digest agar plates / cassettes along with one unexposed plate (Negative control) of the same media load or of the same batch/lot, if using ready to use plates / cassettes, at 30°C-35°C for 2 days for aerobic bacterial counts followed by 20°C-25°C for 3 days for fungal, yeast and molds counts in the inverted position.

4.1.2.10 After completion of incubation period count the number of colonies observed per plate and calculate the cfu/m^3.

4.1.2.11 Negative control (Unexposed Plate) should not show any growth.

4.1.2.12 Record the results in Annexure - II and VI.

4.1.2.13 Frequency, volume of air sampled and recommended limits of active air sampling (Volumetric air sampling) are given in table - II.

Table - II

Grade	Recommended Limits ** (cfu / m^3)	Media Used / Frequency of Air Sampling	Volume of air Sampled (In liter)
A	1	SCDA / Each operating shift	1000
B	7		
C	10		
D	100	SCDA / Weekly	

** **In-house Limits:** To be revised after at least 100 monitoring results.

4.1.3 **Personal Monitoring**

4.1.3.1 Prepare and qualify the RODAC plates by pouring sufficient Soyabean casein digest agar media as per SOP.

4.1.3.2 Pour the plates in such a way that the surface of the medium is slightly raised in comparison to the edge of the plate.

4.1.3.3 Alternatively ready to use agar media plates (RODAC Plates) can be use for monitoring.

4.1.3.4 Perform the growth promotion test of ready to use plates (RODAC Plates) as per SOP.

4.1.3.5 Transfer the RODAC plates to sampling area in a closed container to avoid any contamination.

4.1.3.6 Label the RODAC plates with the details given below -

Monitoring type / Plate No. / Media Load No. / Sampling Date / Sign

4.1.3.7 Remove the RODAC plates from the container open the lid of plate and gently contact (touch) the plate over the location to be monitored.

4.1.3.8 Perform the personnel monitoring at specified area as given in Annexure - VIII.

4.1.3.9 After monitoring replace the lid of the RODAC plate and transfer to micro lab for incubation.

4.1.3.10 After monitoring decontaminate the sampled area with the help of a sterile cloth soaked in sterile 70% IPA.

4.1.3.11 Incubate the Soyabean casein digest agar RODAC plates along with one unexposed plate (Negative control) of the same media load or of the same batch/lot, if using ready to use plate, at 30°C-35°C for 2 days for aerobic bacterial counts followed by 20°C-25°C for 3 days for fungal, yeast and molds counts in the inverted position.

4.1.3.12 After completion of incubation period count the number of colonies per plate and record the observations as cfu/plate.

4.1.3.13 Negative control (Unexposed Plate) should not show any growth.

4.1.3.14 Record the results in Annexure - IV.

4.1.3.15 Frequency and recommended limits of personal monitoring are given in table - III.

Table - III

Personal Monitoring	Recommended Limits ** (cfu / contact plate)	Media Used / Frequency of Personal Monitoring
Garment	5	SCDA / After every operation
Gloves	3	SCDA / After every operation

** **In-house Limits:** To be revised after at least 100 monitoring results.

4.1.4 **Surface Monitoring (RODAC Plate Technique)**

4.1.4.1 Prepare and qualify the RODAC plates by pouring sufficient Soyabean casein digest agar media as per SOP.

4.1.4.2 Pour the plates in such a way that the surface of the medium is slightly raised in comparison to the edge of the plate.

4.1.4.3 Alternatively ready to use agar media plates (RODAC Plates) can be use for monitoring.

4.1.4.4 Perform the growth promotion test of ready to use plates (RODAC Plates) as per SOP.

4.1.4.5 Transfer the RODAC plates to sampling area in a closed container to avoid any contamination.

4.1.4.6 Label the RODAC plates with the details given below -

Monitoring type / Plate No. / Media Load No. / Sampling Date / Sign

4.1.4.7 Remove the RODAC plates from the container open the lid of plate and gently contact (touch) the plate over the location to be monitored.

4.1.4.8 Perform the surface monitoring at specified areas.

4.1.4.9 After monitoring replace the lid of the RODAC plate and transfer to micro lab for incubation.

4.1.4.10 After monitoring decontaminate the sampled area with the help of a sterile cloth soaked in sterile 70% IPA.

4.1.4.11 Incubate the Soyabean casein digest agar RODAC plates along with one unexposed plate (Negative control) of the same media load or of the same batch/lot, if using ready to use plate, at 30°C-35°C for 2 days for aerobic bacterial counts followed by 20°C-25°C for 3 days for fungal, yeast and molds counts in the inverted position.

4.1.4.12 After completion of incubation period count the number of colonies per contact plate and record the observations as cfu/plate.

4.1.4.13 Negative control (Unexposed Plate) should not show any growth.

4.1.4.14 Record the results in Annexure - III and VII.

4.1.4.15 Frequency and recommended limits of surface monitoring are given in table - IV.

Table - IV

Grade	Location	Recommended Limits ** (cfu / 24 - 30cm^2)	Media Used / Frequency of surface monitoring
A	Wall	1	SCDA / Each operating shift
	Floor	1	
B	Wall	3	
	Floor	3	
C	Wall	5	
	Floor	10	
D	Wall	50	SCDA / Weekly
	Floor	50	

** **In-house Limits:** To be revised after at least 100 monitoring results.

4.1.5 **Surface Monitoring (Swab Testing Technique)**

4.1.5.1 Carry out the surface monitoring by using swab testing in case where surface monitoring is not possible by using RODAC plate technique.

4.1.5.2 Prepare the swabs as per SOP.

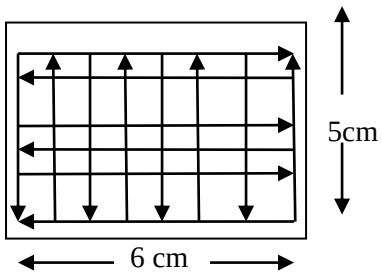
4.1.5.3 Transfer the swabs to sampling area in a closed container to avoid any contamination.

4.1.5.4 Remove the swab stick from the tube and move the head of the swab slowly over the area to be sampled.

4.1.5.5 Rub the swab slowly and thoroughly back and forth over the desired surface of 30cm^2. Repeat this procedure by flipping of the swab over the same surface area in 90° from the earlier swabbing direction.

4.1.5.6 Rotate the swab throughout the procedure.

4.1.5.7 Cover an area of approximately 24 - 30 cm sq.



4.1.5.8 Using the same swab, go back over the same area using strokes perpendicular to the first.

4.1.5.9 After monitoring decontaminate the sampled area with the help of a sterile cloth soaked in sterile 70% IPA.

4.1.5.10 Aseptically transfer the swab back into tube, plug the tubes and bring to micro lab for plating.

4.1.5.11 Add 10 ml of sterile 0.1% Peptone water into each tube containing the swab.

4.1.5.12 Gently vortex the tubes and transfer the solution to a sterile filtration funnel fitted with a membrane of nominal pore size of 0.45 µm.

4.1.5.13 Twice rinse the swab with 10 ml 0.1% Peptone water, each time gently vortexing the tube and filter the rinsate through the same membrane.

4.1.5.14 After filtration, place the membrane on the pre poured plate of Soyabean casein digest agar media.

4.1.5.15 Prepare Soyabean casein digest agar media plate as per SOP.

4.1.5.16 Incubate the Soyabean casein digest agar plate at 30°C-35°C for 2 days for aerobic bacterial counts followed by 20°C-25°C for 3 days for fungal, yeast and molds counts in the inverted position.

4.1.5.17 Incubate a negative control that has been treated in a similar way as test, without sampling the surface.

4.1.5.18 After completion of incubation period count the number of colonies per plate and record the observations as cfu/24 - 30cm^2.

4.1.5.19 Negative control (without sample) should not show any growth.

4.1.5.20 Record the results in Annexure - III and VII.

4.1.5.21 Surface monitoring is to be carried out on rotational basis (weekly) by using RODAC Plate method and swab testing method alternatively.

4.2 Non Viable Monitoring (Particle Count)

4.2.1 Use air borne particle counter for monitoring of non-viable particle count in the microbiology laboratory.

4.2.2 Sample the locations under laminar airflow unit and in the room at working height.

4.2.3 In grade A & B area minimum volume of 1 m^3 to be sampled, and in grade C & D area minimum volume of 1 CFM is to be sampled.

4.2.4 Operate the air born particle counter as per SOP and after completion of sampling attach the print out generated by particle counter.

4.2.5 Record the results in Annexure - IX & X.

4.2.6 Frequency and recommended limits Non Viable Monitoring are given in table - V.

Table - V

Grade	Frequency of Non Viable Monitoring	Maximum permitted number of Particle / m3 equal to above			
		At Rest (Static)		In Operation (Dynamic)	
		0.5 µm	5.0 µm	0.5 µm	5.0 µm
A	Monthly	3500	1*	3500	1*
B	Monthly	3500	1*	350000	2000
C	Monthly	350000	2000	3500000	20000
D	Monthly	3500000	20000	Not determine	Not determine

***** The maximum permitted no. of particle at > 5.0 mm is established at 1/m3 but for reasons related to false counts associated with electronic noise ,stray light etc , a limit of 20/m3 could be considered.

4.3 Identification of colonies

4.3.1 Identify the colonies present on the plate based on colony characteristics.

4.3.2 If any new colonies other then routine micro flora observed, Isolate and identify the organism as per SOP.

4.3.3 Establish the micro flora information data as per SOP.

4.4 Trends of results

4.4.1 Monthly prepare the trends of monitoring results in the form of graph and chart.

4.4.2 Annually prepare a review report on environmental monitoring based on the available trends data.

5.0 SAFETY & PRECAUTIONS

5.1 Follow the entry, exit procedure of respective areas to enter in areas.

5.2 Use proper apparel such as shoe-covers, nose mask, and sterile garments before entering in production areas in order to avoid microbial contamination.

6.0 REVISION HISTORY

Revision No.	Reason for Revision	Superseded from & date
00	New	--------

7.0 REFERENCES

SOP .

8.0 ABBREVIATIONS

SOP	:	Standard Operating Procedure
No.	:	Number
µ	:	Micron
ml	:	Millilitre
LAF	:	Laminar Air Flow
%	:	Percentage
IPA	:	Iso Propyle alcohol
cm	:	Centimetre
°C	:	Degree Centigrade
cfu	:	Colony forming unit
mm	:	Millimeter

9.0 ANNEXURES

Annexure - I : Passive air sampling by settle plate exposure in grade A, B & C areas

Annexure - II : Active air sampling in grade A, B & C areas

Annexure - III : Surface monitoring in grade A, B & C areas

Annexure - IV : Personnel monitoring report

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Annexure - V : Passive air sampling by settle plate exposure in grade D areas

Annexure - VI : Active air sampling in grade D areas

Annexure - VII : Surface monitoring in grade D areas

Annexure - VIII: Locations of Personnel monitoring

Annexure - IX : Non-viable monitoring in grade A, B & C areas

Annexure - X : Non-viable monitoring in grade D areas

ANNEXURE - I

PASSIVE AIR SAMPLING BY SETTLE PLATE EXPOSURE IN GRADE A, B & C AREA OF PRODUCTION AREA

Date of monitoring: _____ **Report date:** _____

Media used: _____ **Sterilized medium lot no.:** _____

Shift : A **Shift : B** **Shift : C**

Time of exposure: _____ **Time of exposure:** _____ **Time of exposure:** _____

Exposed by: _____ **Exposed by:** _____ **Exposed by:** _____

Incubation temperature: 2 days at 30°C- 35°C for bacterial count followed by 3 days at 20°C- 25°C for fungal count.

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/plate/4 hrs)	Observation (cfu/plate/4 hrs)		
						Shift		
						A	B	C
1.	Change room - 2	SP 1.1	Near return air riser	C	5			
		SP 1.2	Near return air riser					
		SP 1.3	Inside garment cubicle	A	1			
2.	Change room - 3	SP 2.1	Near return air riser	B	3			
		SP 2.2	Near return air riser					
3.	Sterile corridor	SP 3.1	Near return air riser	B	3			
		SP 3.2	Near return air riser					
		SP 3.3	Near return air riser					
		SP 3.4	Near return air riser					
		SP 3.5	Near return air riser					
		SP 3.6	Near return air riser					
		SP 3.7	Near return air riser					

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/plate/4 hrs)	Observation (cfu/plate/4 hrs)		
						Shift		
						A	B	C
3.	Sterile corridor	SP 3.8	Near return air riser	B	3			
		SP3.9	Inside dynamic pass box of bulk manufacturing - 2 airlock	A	1			
		SP3.10	Inside dynamic pass box of Bulk manufacturing - 1 airlock					
4.	Cooling zone	SP 4.1	Near return air riser	B	3			
		SP 4.2	Near return air riser					
		SP 4.3	Near return air riser					
		SP 4.4	Near return air riser					
		SP 4.5	Inside garment cubicle	A	1			
		SP 4.6	Inside dynamic pass box of CPZ					
5.	Sterile dispensing room	SP 5.1	Near return air riser	B	3			
		SP 5.2	Near return air riser					
		SP 5.3	Near return air riser					

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/plate/4 hrs)	Observation (cfu/plate/4 hrs)		
						Shift		
						A	B	C
6.	Filtration - 1	SP 6.1	Near return air riser	B	3			
		SP 6.2	Near return air riser					
7.	Filtration - 2	SP 7.1	Near return air riser	B	3			
		SP 7.2	Near return air riser					
		SP 7.3	Near return air riser					
		SP 7.4	Near return air riser					
8.	BFS - 1	SP 8.1	Near return air riser	B	3			
		SP 8.2	Near return air riser					
		SP 8.3	Near return air riser					
		SP 8.4	Near return air riser					
		SP 8.5	Near return air riser					
		SP 8.6	Near return air riser					
		SP 8.7	Near return air riser					
		SP 8.8	Near return air riser					
		SP 8.9	Near return air riser					
		SP8.10	Near return air riser					
		SP8.11	Inside Dynamic pass box	A	1			

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/plate/4 hrs)	Observation (cfu/plate/4 hrs)		
						Shift		
						A	B	C
9.	BFS - 2	SP 9.1	Near return air riser	B	3			
		SP 9.2	Near return air riser					
		SP 9.3	Near return air riser					
		SP 9.4	Near return air riser					
		SP 9.5	Near return air riser					
		SP 9.6	Near return air riser					
		SP 9.7	Near return air riser					
		SP 9.8	Near return air riser					
		SP 9.9	Near return air riser					
		SP 9.10	Near return air riser					
		SP 9.11	Inside Dynamic pass box	A	1			
10.	BFS tooling	SP 10.1	Near return air riser	B	3			
		SP 10.2	Near return air riser					
		SP 10.3	Near return air riser					
11.	Chang room - 2 Bulk manufacturing - 1	SP 11.1	Near return air riser	C	5			
		SP 11.2	Inside garment cubicle	A	1			

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/plate/4 hrs)	Observation (cfu/plate/4 hrs)		
						Shift		
						A	B	C
12.	Bulk manufacturing - 1	SP12.1	Near return air riser	C	5			
		SP12.2	Near return air riser					
13.	Chang room - 2 Bulk manufacturing - 2	SP 13.1	Near return air riser	C	5			
		SP 13.2	Inside garment cubicle	A	1			
14.	Bulk manufacturing - 2	SP 14.1	Near return air riser	C	5			
		SP 14.4	Near return air riser					
15.	Chang room - 4	SP 15.1	Near return air riser	C	5			
		SP 15.2	Near return air riser					
16.	Negative control	SP 16.1	NA	NA	Nil			

NA: Not Applicable

Remarks: The area complies / does not complies with the laid down limits.

Observation Done By:
Date:

Checked By:
Date:

ANNEXURE - II

ACTIVE AIR SAMPLING IN GRADE A, B & C AREA OF PRODUCTION AREA

Date of monitoring: _____ **Report date:** _____

Media used: _____ **Sterilized medium lot no.:** _____

Shift : A **Shift : B** **Shift : C**

Time of sampling: _____ **Time of sampling:** _____ **Time of sampling:** _____

Air Sampling done by: _____ **Air Sampling done by:** _____ **Air Sampling done by:** _____

Incubation temperature: 2 days at 30°C- 35°C for bacterial count followed by 3 days at 20°C- 25°C for fungal count.

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/m^3)	Observation (cfu/m^3)		
						Shift		
						A	B	C
1.	Change room - 2	AS 1.1	Center of the room	C	10			
		AS 1.2	Inside garment cubicle	A	1			
2.	Change room - 3	AS 2.1	Center of change room	B	7			
3.	Sterile corridor	AS 3.1	Between cooling zone door & filtration - 2 door	B	7			
		AS 3.2	Between change room 3 door & BFS - 2 door					
		AS 3.3	Center of Sterile dispensing door & BFS -1 door					
		AS 3.4	Inside dynamic pass box of bulk manufacturing - 2 airlock	A	1			
		AS 3.5	Inside dynamic pass box of bulk manufacturing - 1 airlock					

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/m^3)	Observation (cfu/m^3)		
						Shift		
						A	B	C
4.	Cooling zone	AS 4.1	Center of the room	B	7			
		AS 4.2	Inside dynamic pass box of CPZ	A	1			
		AS 4.3	Inside garment cubicle					
5.	Sterile dispensing room	AS 5.1	Center of the room	B	7			
6.	Filtration - 1	AS 6.1	Center of the room	B	7			
7.	Filtration - 2	AS 7.1	Center of the room	C	10			
8.	BFS - 1	AS 8.1	Right side of BFS	B	7			
		AS 8.2	Left side of BFS					
		AS 8.3	Inside dynamic pass	A	1			
9.	BFS - 2	AS 9.1	Right side of BFS	B	7			
		AS 9.2	Left side of BFS					
		AS 9.3	Inside dynamic pass	A	1			
10.	BFS tooling	AS 10.1	Center of the room	B	7			
11.	Chang room - 2 Bulk manufacturing - 1	AS 11.1	Center of the room	C	10			
		AS 11.2	Inside garment cubicle	A	1			
12.	Bulk manufacturing - 1	AS 12.1	Center of the room	C	10			
13.	Chang room - 2 Bulk manufacturing - 2	AS 13.1	Center of the room	C	10			
		AS 13.2	Inside garment cubicle	A	1			

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/m^3)	Observation (cfu/m^3)		
						Shift		
						A	B	C
14.	Bulk manufacturing - 2	AS 14.1	Center of the room	C	10			
15.	Chang room - 4	AS 15.1	Center of the room	C	10			
16.	Negative control	AS 16.1	NA	NA	Nil			

NA: Not Applicable

Remarks: The area complies / does not complies with the laid down limits.

Observation Done By:
Date:

Checked By:
Date:

ANNEXURE - III

SURFACE MONITORING IN GRADE A, B & C AREA OF PRODUCTION AREA

Date of monitoring: _____ **Report date:** _____

Media used: _____ **Sterilized medium lot no.:** _____

Method: Contact plate / Swab

Shift : A **Shift : B** **Shift : C**

Membrane filter lot no: _____ **Membrane filter lot no:** _____ **Membrane filter lot no:** _____

Done by: _____ **Done by:** _____ **Done by:** _____

Incubation temperature: 2 days at 30°C- 35°C for bacterial count followed by 3 days at 20°C- 25°C for fungal count.

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/Contact plate / 24-30 cm2)	Observation (cfu/Contact plate / 24-30 cm2)		
						Shift		
						A	B	C
1.	Change room - 2	SM 1.1	Surface of wall / floor / door	C	05 / 10 / 05			
		SM 1.2	Inside garment cubicle	A	1			
2.	Change room - 3	SM 2.1	Surface of wall / floor / door	C	05 / 10 / 05			
3.	Sterile corridor	SM 3.1	Surface of wall / floor / door	B	3			
		SM 3.2	Surface of wall / floor / door					
		SM 3.3	Surface of wall / floor / door					
		SM 3.4	Surface of wall / floor / door					
		SM 3.5	Outer surface of dynamic pass box of bulk mfg - 1 air lock					
		SM 3.6	Outer surface of dynamic pass box of bulk mfg - 2 airlock					

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/Contact plate / 24-30 cm2)	Observation (cfu/Contact plate / 24-30 cm2)		
						Shift		
						A	B	C
4.	Cooling zone	SM 4.1	Surface of wall / floor / door	B	3			
		SM 4.2	Outer surface of DHS					
		SM 4.3	Outer surface of steam sterilizer					
		SM 4.4	Inside dynamic pass box of CPZ	A	3			
5.	Sterile dispensing room	SM 5.1	Surface of wall / floor / door	B	3			
6.	Filtration - 1	SM 6.1	Surface of wall / floor / door	B	3			
		SM 6.2	Outer Surface of holding tank					
		SM 6.3	Outer Surface of filtration tank					
7.	Filtration - 2	SM 7.1	Surface of wall / floor / door	B	3			
		SM 7.2	Outer Surface of holding tank					
		SM 7.3	Outer Surface of filtration tank					
8.	BFS - 1	SM 8.1	Surface of wall / floor / door	B	3			
		SM 8.2	Outer surface of BFS - 1					
		SM 8.3	Inside dynamic pass box	A	1			
9.	BFS - 2	SM 9.1	Surface of wall / floor / door	B	3			
		SM 9.2	Outer surface of BFS - 2					
		SM 9.3	Inside dynamic pass box	A	1			

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/Contact plate / 24-30 cm2)	Observation (cfu/Contact plate / 24-30 cm2)		
						Shift		
						A	B	C
10.	BFS tooling	SM 10.1	Surface of wall / floor / door	B	3			
11.	Chang room - 2 Bulk manufacturing - 1	SM 11.1	Surface of wall / floor / door	C	05 / 10 / 05			
		SM 11.2	Inside garment cubicle	A	1			
12.	Bulk manufacturing - 1	SM 12.1	Surface of wall / floor / door	C	05 / 10 / 05			
		SM 12.2	Outer surface of mfg.tank		5			
13.	Chang room - 2 Bulk manufacturing - 2	SM 13.1	Surface of wall / floor / door	C	05 / 10 / 05			
		SM 13.1	Inside garment cubicle	A	1			
14.	Bulk manufacturing - 2	SM 14.1	Surface of wall / floor / door	C	05 / 10 / 05			
		SM 14.2	Outer surface of mfg.tank		5			
15.	Chang room - 4	SM 15.1	Surface of wall / floor / door	C	05 / 10 / 05			
16.	Negative control	SM 16.1	NA	NA	Nil			

NA: Not Applicable

Remarks: The area complies / does not complies with the laid down limits.

Observation Done By:
Date:

Checked By:
Date:

ANNEXURE - IV

PERSONNEL MONITORING REPORT OF PRODUCTION AREA

Date of monitoring: _____ **Report date:** _____

Media used: _____ **Sterilized medium lot no.:** _____

Shift : A **Shift : B** **Shift : C**

Done by: _____ **Done by:** _____ **Done by:** _____

Incubation temperature: 2 days at30°C- 35°C for bacterial count followed by 3 days at 20°C- 25°C for fungal count.

S.No	Name of the Person	Location	Observation cfu / Contact plate							
			PM1.1	PM1.2	PM1.3	PM1.4	PM1.5	PM1.6	PM1.7	PM1.8
		Limit → / Shift ↓	5	5	3	3	5	5	5	5
1.										
2.										
3.										
4.										
5.										
6.										
7.										
8.										
9.										
10.	Negative control	NA								

PM 1.1: Forehead; **PM 1.2:** Chest; **PM 1.3:** Right hand Gloves; **PM 1.4:** Left hand gloves;
PM 1.5: Right Arm pit; **PM 1.6:** Left Arm pit; **PM 1.7:** Left inner fore hand; **PM 1.8:** Right inner fore hand
NA: Not Applicable

Remarks: Complies / Does not complies.

Observation Done By: **Checked By:**

Date: **Date:**

ANNEXURE - V

PASSIVE AIR SAMPLING BY SETTLE PLATE EXPOSURE IN GRADE D AREA OF PRODUCTION AREA

Date of monitoring: _____ **Report date:** _____

Media used: _____ **Sterilized medium lot no.:** _____

Time of exposure: _____ **Exposed by:** _____

Incubation temperature: 2 days at 30°C- 35°C for bacterial count followed by 3 days at 20°C- 25°C for fungal count.

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/plate/4 hrs)	Observation (cfu/plate/4 hrs)
1.	Change room - 1	SP 16.1	Near return air riser	D	50	
2.	Air lock Material	SP 17.1	Near return air riser	D	50	
		SP 17.2	Inside static pass box to mfg - 1			
3.	Air lock CPZ	SP 18.1	Near return air riser	D	50	
4.	CPZ	SP 19.1	Near return air riser	D	50	
		SP 19.2	Near return air riser			
		SP 19.3	Near return air riser			
		SP 19.4	Near return air riser			
		SP 19.5	Inside static pass box			
5.	(Change room -1) Bulk manufacturing - 1	SP 20.1	Near return air riser	D	50	
6.	(Change room -1) Bulk manufacturing - 2	SP 21.1	Near return air riser	D	50	
7.	Air lock Material	SP 22.1	Near return air riser	D	50	
		SP 22.2	Inside static pass box to mfg - 2			

Sr. No.	Name of the Room	Plate No.	Name of the Location	Grade	Limit (cfu/plate/4 hrs)	Observation (cfu/plate/4 hrs)
8.	(Air lock) Polymer granule transfer	SP 23.1	Near return air riser	D	50	
9.	Polymer granule transfer	SP 24.1	Near return air riser	D	50	
10.	Material Air lock for Sterile dispensing	SP 25.1	Near return air riser	D	50	
11.	Negative control	SP 26.1	NA	NA	Nil	

NA: Not Applicable

Remarks: The area complies / does not complies with the laid down limits.

Observation Done By:
Date:

Checked By:
Date:

ANNEXURE - VI

ACTIVE AIR SAMPLING IN GRADE D AREA OF PRODUCTION AREA

Date of monitoring: _____ **Report date:** _____

Media used: _____ **Sterilized medium lot no.:** _____

Time of sampling: _____ **Air sampling done by:** _____

Incubation temperature: 2 days at 30°C- 35°C for bacterial count followed by 3 days at 20°C- 25°C for fungal count.

Sr. No.	Name of the Room	Plate No.	Name of the Location	Limit (cfu/m^3)	Observation (cfu/m^3)
1.	Change room - 1	AS 16.1	Center of room	100	
2.	Air lock Material	AS 17.1	Center of room	100	
		AS 17.2	Inside static pass box to mfg - 1	100	
3.	Air lock CPZ	AS 18.1	Center of the room	100	
4.	CPZ	AS 19.1	Center of the room	100	
		AS 19.2	Inside static pass box	100	
5.	(Change room -1) Bulk manufacturing - 1	AS 20.1	Center of the room	100	
6.	(Change room -1) Bulk manufacturing - 2	AS 21.1	Center of the room	100	
7.	Air lock Material	AS 22.1	Center of the room	100	
		AS 22.2	Inside static pass box to mfg - 2	100	
8.	(Air lock) Polymer granule transfer	AS 23.1	Center of the room	100	
9.	Polymer granule transfer	AS 24.1	Center of the room	100	
10.	Material Air Sterile dispensing	AS 25.1	Center of the room	100	
11.	Negative control	AS 26.1	NA	Nil	

NA: Not Applicable

Remarks: The area complies / does not complies with the laid down limits.

Observation Done By: **Checked By:**

Date: **Date:**

ANNEXURE - VII

SURFACE MONITORING IN GRADE D AREA OF PRODUCTION AREA

Date of monitoring: _____ **Report date:** _____

Media used: _____ **Sterilized medium lot no.:** _____

Method: Contact plate / Swab

Membrane filter lot no: _____ **Done by:** _____

Incubation temperature: 2 days at 30°C- 35°C for bacterial count followed by 3 days at 20°C- 25°C for fungal count.

Sr. No.	Name of the Room	Plate No.	Name of the Location	Limit (cfu/Contact plate / 24-30 cm2)	Observation (cfu/Contact plate / 24-30 cm2)
1.	Change room - 1	SM 16.1	Surface of wall / floor / door	50	
2.	Air lock Material	SM 17.1	Surface of wall / floor / door	50	
		SM 17.2	Inside static pass box to mfg - 1		
3.	Air lock CPZ	SM 18.1	Surface of wall / floor / door	50	
4.	CPZ	SM 19.1	Surface of wall / floor / door	50	
		SM 19.2	Outer surface of DHS		
		SM 19.3	Outer surface of Steam sterilizer		
		SM 19.4	Inside static pass box		
5.	(Change room -1) Bulk manufacturing - 1	SM 20.1	Surface of wall / floor / door	50	
6.	(Change room -1) Bulk manufacturing - 2	SM 21.1	Surface of wall / floor / door	50	
7.	Air lock Material	SM 22.1	Surface of wall / floor / door	50	
		SM 22.2	Inside static pass box to mfg - 2		
8.	Air lock-Polymer granule transfer	SM 23.1	Surface of wall / floor / door	50	
9.	Polymer granule transfer	SM 24.1	Surface of wall / floor / door	50	
10.	Material Air Lock for Sterile dispensing	SM 25.1	Surface of wall / floor / door	50	
11.	Negative control	SM 26.1	NA	Nil	

NA: Not Applicable

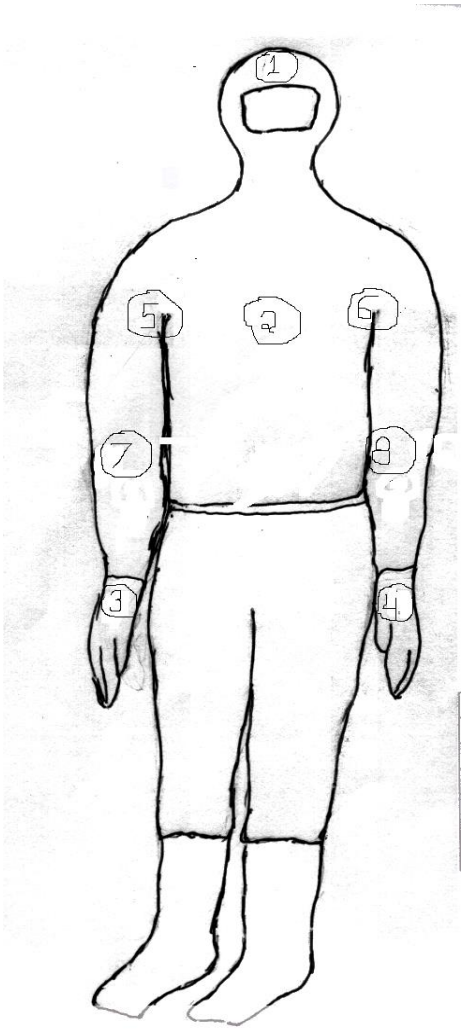
Remarks: The area complies / does not comply with the laid down limits.

Observation Done By: **Checked By:**

Date: **Date:**

ANNEXURE - VIII

LOCATION OF PERSONNEL MONITORING OF PRODUCTION AREA



Sampling Location	No.
Fore head	1
Chest	2
Right hand gloves	3
Left hand gloves	4
Right arm pit	5
Left arm pit	6
Right inner fore hand	7
Left inner fore hand	8

ANNEXURE - IX

NON - VIABLE MONITORING IN GRADE A, B & C AREA OF PRODUCTION AREA

Date of monitoring: _____Particle Counter ID No.: _____

Monitoring done by: _____Monitoring condition: Static / Dynamic

Grade	Maximum permitted number of Particle / m3 equal to above			
	At Rest (Static)		In Operation (Dynamic)	
	0.5 µm	5.0 µm	0.5 µm	5.0 µm
A	3500	1*	3500	1*
B	3500	1*	350000	2000
C	350000	2000	3500000	20000

*** The maximum permitted no. of particle at > 5.0 mm is established at 1/m3 but for reasons related to false counts associated with electronic noise ,stray light etc , a limit of 20/m3 could be considered.**

Sr. No.	Name of the Room	Location No.	Grade	Observation	
				0.5 µm	5.0 µm
1.	Change room - 2	PC 1.1	C		
		PC 1.2			
		PC 1.3	A		
2.	Change room - 3	PC 2.1	B		
		PC 2.2			
		PC 2.3			
3.	Sterile corridor	PC 3.1	B		
		PC 3.2			
		PC 3.3			
		PC 3.4			
		PC 3.5	A		
		PC 3.6			

Sr. No.	Name of the Room	Location No.	Grade	Observation	
				0.5 µm	5.0 µm
4.	Cooling zone	PC 4.1	B		
		PC 4.2			
		PC 4.3	A		
		PC 4.4			
5.	Sterile dispensing room	PC 5.1	B		
		PC 5.2			
		PC 5.3			
6.	Filtration - 1	PC 6.1	B		
		PC 6.2			
		PC 6.3			
7.	Filtration - 2	PC 7.1	B		
		PC 7.2			
		PC 7.3			
8.	BFS - 1	PC 8.1	B		
		PC 8.2			
		PC 8.3			
		PC 8.4			
		PC 8.5			
		PC 8.6			

Sr. No.	Name of the Room	Location No.	Grade	Observation	
				0.5 µm	5.0 µm
9.	BFS - 2	PC 9.1	B		
		PC 9.2			
		PC 9.3			
		PC 9.4			
		PC 9.5			
		PC 9.6			
10.	BFS tooling	PC 10.1	B		
		PC 10.2			
		PC 10.3			
11.	Chang room - 2 Bulk manufacturing - 1	PC 11.1	C		
		PC 11.2			
		PC 11.3			
12.	Bulk manufacturing - 1	PC 12.1	C		
		PC 12.2			
		PC 12.3			
13.	Chang room - 2 Bulk manufacturing - 2	PC 13.1	C		
		PC 13.2			
		PC 13.3			
14.	Bulk manufacturing - 2	PC 14.1	C		
		PC 14.2			
		PC 14.3			
15.	Change room - 4	PC 15.1	C		
		PC 15.2			
		PC 15.3			

Remarks: The non-viable particle count of sampled area complies / does not complies with the laid down specifications.

Done By: **Checked By:**

Date: **Date:**

ANNEXURE - X

NON - VIABLE MONITORING IN GRADE D AREA OF PRODUCTION AREA

Date of monitoring: _____Particle Counter ID No.: _____

Monitoring done by: _____Monitoring condition: Static / Dynamic

Grade	Maximum permitted number of Particle / m3 equal to above			
	At Rest (Static)		In Operation (Dynamic)	
	0.5 µm	5.0 µm	0.5 µm	5.0 µm
D	3500000	20000	Not defined	Not defined

*** The maximum permitted no. of particle at > 5.0 mm is established at 1/m3 but for reasons related to false counts associated with electronic noise ,stray light etc , a limit of 20/m3 could be considered.**

Sr. No.	Name of the Room	Location No.	Observation	
			0.5 µm	5.0 µm
1.	Change room - 1	PC 16.1		
		PC 16.2		
		PC 16.3		
2.	Air lock Material	PC 17.1		
		PC 17.2		
3.	Air lock CPZ	PC 18.1		
		PC 18.2		
4.	CPZ	PC 19.1		
		PC 19.2		
		PC 19.3		

Sr. No.	Name of the Room	Location No.	Observation	
			0.5 µm	5.0 µm
4.	CPZ	PC 19.4		
		PC 19.5		
5.	(Change room -1) Bulk manufacturing - 1	PC 20.1		
		PC 20.2		
6.	(Change room -1) Bulk manufacturing - 2	PC 21.1		
		PC 21.2		
7.	Air lock Material	PC 22.1		
		PC 22.2		
8.	(Air lock) Polymer granule transfer	PC 23.1		
		PC 23.2		
9.	Polymer granule transfer	PC 24.1		
		PC 24.2		
		PC 24.3		
		PC 24.4		
10.	Material Air Lock for Sterile dispensing	PC 25.1		
		PC 25.2		

Remarks: The non-viable particle count of sampled area complies / does not complies with the laid down specifications.

Done By:
Date:

Checked By:
Date: