STANDARD OPERATING PROCEDURE

Title : Good Aseptic Practices in Aseptic Processing Area, Monitoring and Recording of Aseptic Intervention During Aseptic Processing

SOP No.:		**Department:**	Production
		Effective Date:	
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1.0 OBJECTIVE:

To lay down a Procedure for good aseptic practices in aseptic processing area, monitoring and recording of aseptic intervention during aseptic processing.

2.0 SCOPE:

This SOP is applicable for Good Aseptic Practices in Aseptic Processing Area.

3.0 RESPONSIBILITY:

Officer / Executive Production

4.0 ACCOUNTABILITY:

Head Production

5.0 ABBREVIATIONS:

Ltd.	Limited
Mfg.	Manufacturing
No.	Number
QA	Quality Assurance
SOP	Standard Operating Procedure

6.0 PROCEDURE:

6.1 Personnel qualified in gowning qualification should be allowed to enter in Aseptic area.

6.2 Before entering any aseptic environment, personnel must be trained on the topic of the cleanroom techniques and their functional responsibility.

6.3 All persons entering the aseptic processing area shall follow gowning and de-gowning procedure.

6.4 Personnel are not allowed to work in aseptic area continuously more than 4 hours. Rest for minimum 15 minute to be given to personnel working in aseptic area.

6.5 They shall follow the Personnel Hygiene guidelines in terms of health, personnel cleanliness and hygiene behavior

6.6 The personnel movement in the area shall be minimum, slow and rhythmic.

6.7 All verbal communication with the people outside the Aseptic Area shall be done through the intercom

6.8 Loud, unnecessary talk through the mask shall be not allowed. Laughing, whistling, singing and shouting shall not be allowed.

6.9 Open the doors by pushing with the help of elbow and pulling with the wrist. Ensure that two adjacent doors will not be opened simultaneously.

6.10 At a time, the in process checks shall be done by Production Chemist and IPQA Chemist. The two shall avoid being in a room together, unless required (as in manufacturing area), to reduce man movement in that particular area.

6.11 At the time of Shift changeover the person in the outgoing Shift shall leave the area, prior to the entry of the next Shift person (If required).

6.12 Eating and drinking shall not be allowed inside the aseptic processing area.

6.13 Pencil, erasers are not permitted inside the clean room. Only ball pens to be used for all purpose.

6.14 Corrugated boxes, wooden piece, bricks etc will not be allowed inside the aseptic processing area.

6.15 It has to be ensured that no skin is exposed between the gloved hands and garments part. In the same way, head gear must be tucked completely inside the uniform and hair to be covered at all times.

6.16 Any equipment, part of equipment if taken inside the clean room must be disinfected with 70% IPA before they are taken in.

6.17 No one who is physically ill or especially with respiratory or stomach disorders will enter the clean room.

6.18 Personnel items like jewelry, watch, keys, coins, combs etc. are not allowed to take inside the clean room.

6.19 Before entering the clean environment, person must understand the responsibilities of the work as well as aseptic technique / sterile behavior.

6.20 Once inside the clean room, person shall remain till the end of the work / shift and unnecessary or frequent opening of doors of either mixing or filling area or air locks shall be avoided.

6.21 Nervous relief-type manners such as head scratching or rubbing hands face or parts of the body must be consciously avoided.

6.22 Clean room garments must be discarded while leaving the aseptic area. Fresh, clean sterilized garments shall be worn when returning to work.

6.23 No flaking or corrosive material shall be allowed in the area.

6.24 Unnecessary storage of articles like files, papers and wooden articles in aseptic processing area are not allowed.

6.25 During operation, personnel movement in aseptic processing area must be minimized.

6.26 All materials, containers, equipment etc. intended for use of aseptic operation must be labeled for identification.

6.27 Used articles, Machine Parts& Other Tools etc. shall be sent out through a Dynamic Pass Box.

6.28 All equipment, SS tables, Doors, floors, walls and ceilings shall be subjected to a regular mopping/spraying and disinfection on rotational basis, using approved disinfectants schedule.

6.29 Once the actual power supply is resumed, the area should be sanitized using 70 % IPA.

6.30 Personnel must report any deviation or adverse changes in Environmental Conditions of Temperature and Humidity to shift In-charge.

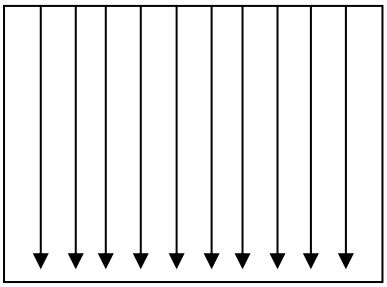
6.31 Incase more than 4 persons are required in the area then not more than 7 persons shall be allowed but for NMT 15 minutes.

6.32 If more than 7 persons for more than 15 minutes observed in the area it shall be considered as non-allowable interventions and shall be bring to the notice of QA and shall be covered during upcoming media fill..

6.33 All acrylic doors shall be closed during filling activity and only required door is opened during material charging / activity.

6.34 Wipe the Acrylic Doors of Filling Machine before closing with 70% Sterile IPA in unidirectional way from top to bottom in following manner.

Top of Door



Bottom of Door

6.35 After cleaning /wiping process is complete, sanitize the gloves with sterile 70% IPA.

6.36 Materials, Containers and Equipment introduced in Aseptic Area must be Sterilized or Disinfected prior to transfer in Aseptic Area.

6.37 Use lint free, Sterile Mops for Cleaning & Sanitization in Aseptic Areas.

6.38 Material/ article will be sterilized in autoclave with the protective bag (Decron Bag/Tyvek Bag).

6.39 Use Three Bucket system for Cleaning and sanitization of Aseptic Area as per respective SOP for Cleaning and Sanitization of Aseptic Area.

6.40 Entry to the Aseptic Processing Area is restricted to Trained and Qualified Personnel only as per List of Authorized Personnel for respective area.

6.41 Before entering in Clean Room, Personnel should understand the Responsibilities, Clean Room Techniques and behavior.

6.42 All Personnel entering the Aseptic Area shall wear primary garments first followed by secondary garments as per respective SOP.

6.43 Personnel shall remove all the personal belongings and jewelry including items such as rings, watches, etc. in primary change room lockers.

6.44 All persons shall take every precaution to avoid undue contamination of the garment during working.

6.45 Personnel should not touch wall during & after wearing primary and secondary gowning.

6.46 The sterile gloves shall be worn by personnel in aseptic area.

6.47 The sterile accessories, used for handling of sterile material shall be stored in Sterilized containers under LAF and transfer the sterilized component through mobile LAF in Aseptic Area.

6.48 Movement of Person in the Clean Areas shall be slow and careful with robotic movement.

6.49 All personnel working in aseptic area shall avoid unnecessary conversation with each other during aseptic handling

6.50 Personnel shall ensure that any activity carried out in clean area shall not compromise with the Sterility of the product.

6.51 All persons working in aseptic area shall avoid loud and unnecessary conversation with each other.

6.52 Wrong personnel practices & behavior can lead to higher viable and Non-viable counts in Aseptic Area.

6.53 Sterilized wipes and 70% sterile IPA shall be kept in Grade B nearby Grade A (Working Platform) for sanitization of hands and door panels.

6.54 All persons working in Aseptic area shall do minimum intervention under LAF during operation and if any aseptic intervention happened during operation personnel must sanitize his hands by 70 % Sterile IPA before and after attending the intervention.

6.55 Open the doors by pushing with the elbow / shoulder and pulling with the wrist.

6.56 At the time of shift changeover the personnel in the outgoing shift shall not leave the area, prior to the entry of the next shift personnel in staggered manner.

6.57 The person exiting from aseptic area shall de-gown as per respective SOP of area.

6.58 All Document recording related to aseptic area e.g. Line clearance in aseptic area, Filtration & Filling operation, In-process activity along with area monitoring and non-viable particle counts excursion shall be performed in aseptic area by personnel directly performing the activity on autoclavable paper in respective format of BMR and SOP.

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6.59 MONITORING AND RECORDING OF ASEPTIC INTERVENTIONS DURING ASEPTIC PROCESSING:

6.59.1 Aseptic Intervention carried out in routine processing in aseptic area shall be recorded as per Annexure-I, Titled "Record of Aseptic Interventions" for each batch manufacturing activity. Detail of aseptic intervention is mentioned as below.

6.59.1.1 Routine Interventions (DPI Line):

S.No.	Intervention Detail
1.	Aseptic Assembling of machine parts & manipulation.
2.	Aseptic transfer of sterile material from powder container to Hopper of Filling Machine.
3.	Loading of Bungs in Hopper.
4.	Volume & Weight Adjustment(Fill Volume and Fill Weight Setting)
5.	Fill weight & volume checking & verification.
6.	Active air Sampling
7.	Passive air Sampling
8.	Shift change over
9.	Operator break & meal.
10.	Filling room door open for 2 min
11.	Tea Break for 30 min
12.	Rubber stoppering machine chute adjustment for 2 min.
13.	Product sampling.
14.	Gloves Replacement.
15.	Vials fallen & jammed

6.59.1.2 Non- Routine Interventions (DPI Line):

S.No.	Intervention Detail
1.	Stopper Misfeed & clumping
3.	Defective seals on Containers
4.	Products spillage or leakage (Breakage of vials)
5.	Conveyor or Rail adjustments
6.	AHU of Filling Area OFF for 5 min
7.	Machine break down activity for 60 min (MAJOR)
8.	No. of persons increased in filling area for 15 min during filling (not more than 07 persons).
9.	Machine Break down activities for 15 minutes (MINOR)
10.	Filling Machine Hopper Empty

11	Piston /Tips Replacement
12	Operators fatigue
13	Slowest Machine Speed
14	Highest Filling Machine Speed
15	Power Failure for 10 minutes

6.59.1.3 Routine Interventions (AMPOULE LINE):

S.No.	Intervention Detail
1.	Initial Product connection or aseptic assembly of the equipment
2.	Initial Fill Volume Adjustment
3.	Periodic Fill Volume Checking & Verification
4.	Handling of Ampoules by using forceps
5.	Operator Breaks & Meals
6.	Operator Shift Changes
7.	Maximum Filling Machine Speed
8.	Minimum filling Machine Speed
9.	Tea Break for 30 min.
10.	Product Filling Container Replacement
11.	Active air Sampling
12.	Passive air Sampling
13.	Filling room door open for 2 min
14.	Gloves Replacement
15.	Ampoules jammed

6.59.1.4 Non- Routine Interventions (AMPOULE LINE):

S. No.	Intervention Detail
1.	Sensor Adjustment or Replacement
2.	Machine break down activity for 15 min (MINOR).
3.	Machine break down activity for 60 min (MAJOR).
4.	Operator fatigue
5.	Flame setting after burner on off.
6.	Filling nozzle assembly change.
7.	No. of Persons increased (Not more than 7 persons) in Filling and Sealing area for 15 minutes during filling.
8.	Oxygen & LPG pressure low
9.	Conveyor or guide rail adjustment
10.	AHU off of filling area for 05 min
11.	Power failure for 10 minutes
12	Product spillage

6.59.1.5 Routine Interventions (THREE PIECE LINE):

S.No.	Intervention Detail
1.	Initial Product Connection or Aseptic Assembly of the Equipment
2.	Initial Fill Volume Adjustment
3.	Periodic Fill Volume Checking and Verification
4.	Vial Charging in Hopper
5.	Dropper (Fixer) Charging in Hopper
6.	Screw Cap Charging in Hopper
7.	Handling of Vial at filling location by using forceps
8.	Handling of Dropper on dropper placing machine by using forceps
9.	Handling of cap at screw capping machine by using forceps
10.	Operator Breaks and Meals.
11.	Tea Break for 15 min.
12.	Operator Shift Changes.
13.	Active air Sampling
14.	Passive air Sampling
15.	Filling room door open for 2 min.
16.	Gloves Replacement
17.	Vials jammed

6.59.1.6 Non-Routine Interventions (THREE PIECE LINE):

S.No.	Intervention Detail
1.	Sensor Adjustment or Replacement.
2.	AHU of filling area OFF for 5 min.
3.	Machine break down activity for 15 min (MINOR).
4.	Machine break down activity for 60 min (MAJOR).
5.	No. of Persons increased (Not more than 7 persons) in Filling and Sealing area for 15 minutes during filling.
6.	Highest filling machine speed
7.	Slowest filling machine speed
8.	Conveyor or guide rail adjustment
9.	Highest filling machine speed
10.	Operator fatigue
11.	Product spillage
12.	Power failure for 10 minutes

6.60 Reference Copy of Annexure-I will be issued by QA with each Batch Manufacturing record. Annexure-I shall be considered for evaluation of interventions carried out, optimize the practice as per process requirement with respect to type of intervention and how frequent occur.

6.61 Apart from mentioned routine and non-routine intervention, interventions shall be recorded in same format and shall be covered in upcoming media fill (If not covered).

6.62 If any other intervention occurs during routine filling and sealing process then record and specify the same in the **Annexure-I.**

6.63 Trend shall be preapred on the basis of intervention occurred and recorded during ruotine filling process.

6.64 On the basis of this trend simulation of each intervention shall be performed upto maximum frequency on next media fill (Once in Six Month).

6.65 On the basis of this trend simulation of each intervention shall be performed upto maximum frequency on next media fill (Once in Six Month).

6.66 PROCEDURE TO PERFORM THE INTERVENTION:

6.66.1 When any intervention is to be performed under grade A, ensure that the filled vials should be removed from filling track to avoid any contamination.

6.66.2 During transfer of Vial/Dropper/Cap from bench type LAF to respective hopper, sanitize the pack with IPA 70 % solution then place on the surface of machine. Sanitize the scissor, cut the poly bag and pour into respective hopper slowly slowly.

6.66.3 During assembling of sterilized machine parts in grade A sanitize the hands before to perform each Intervention.

6.66.4 During removal of stucked/jammed vials in the chute ensure the filled vials available in the filling track should be removed before to perform this intervention.

6.66.5 During removal of stucked/jammed dropper in the chute ensure the filled vials available in the filling track should be removed before to perform this intervention.

6.66.6 During tea break, lunch break and shift change over remove all the filled and sealed vials from the filling and capping track.

6.66.7 During filling if any minor or major breakdown occurs then after performance such intervention replace the hand glove and sanitize with IPA 70 % before start the filling operation.

7.0 ANNEXURE:

ANNEXURE NO.	TITLE OF ANNEXURE	FORMAT NO.
Annexure-I	Record of Aseptic Interventions / Activity	

ENCLOSURES: SOP Training Record.

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8.0 DISTRIBUTION:

- Controlled Copy No.01 Quality Assurance
- Controlled Copy No.02 Production
- Master Copy Quality Assurance

9.0 REFERENCES:

Not Applicable.

10.0 REVISION HISTORY:

CHANGE HISTORY LOG

Revision No.	Change Control No.	Details of Changes	Reason for Change	Effective Date	Updated By

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ANNEXURE-I
RECORD OF ASEPTIC INTERVENTIONS

Date : **Production Line :**

Product Name : **Batch No. :**

B. Size (In L) : **B. Size (In Nos.) :**

I-Aseptic Manipulation (Routine Intervention)

Intervention	Number of frequency count					Total No.	Checked By
Aseptic assembling of sterilized machine parts.	1	2	3	4	5		
Initial Product Connection	1	2	3	4	5		
Addition of Sterile Powder from container to Hopper of filling machine.	1	2	3	4	5		
Initial Fill Volume Adjustment	1	2	3	4	5		
	6	7	8	9	10		
Periodic Fill Volume/ Weight Checking & Verification	1	2	3	4	5		
	6	7	8	9	10		
	11	12	13	14	15		
	16	17	18	19	20		
	21	22	23	24	25		
Dropper/ Rubber Stopper charging in Hopper	1	2	3	4	5		
	6	7	8	9	10		
	11	12	13	14	15		
	16	17	18	19	20		
	21	22	23	24	25		
	26	27	28	29	30		
	31	32	33	34	35		
	36	37	38	39	40		
	41	42	43	44	45		
	46	47	48	49	50		

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Intervention	Number of frequency count					Total No.	Checked By
	51	52	53	54	55		
	56	57	58	59	60		
	61	62	63	64	65		
	66	67	68	69	70		
	71	72	73	74	75		
	76	77	78	79	80		
Vials charging in Hopper	1	2	3	4	5		
	6	7	8	9	10		
	11	12	13	14	15		
	16	17	18	19	20		
	21	22	23	24	25		
	26	27	28	29	30		
	31	32	33	34	35		
	36	37	38	39	40		
	41	42	43	44	45		
	46	47	48	49	50		
	51	52	53	54	55		
	56	57	58	59	60		
	61	62	63	64	65		
	66	67	68	69	70		
	71	72	73	74	75		
	76	77	78	79	80		
	81	82	83	84	85		
	86	87	88	89	90		
	91	92	93	94	95		

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Intervention	Number of frequency count					Total No.	Checked By
	96	97	98	99	100		
	101	102	103	104	105		
	106	107	108	109	110		
	111	112	113	114	115		
	116	117	118	119	120		
	121	122	123	124	125		
	126	127	128	129	130		
	131	132	133	134	135		
	136	137	138	139	140		
	141	142	143	144	145		
	146	147	148	149	150		
	151	152	153	154	155		
	156	157	158	159	160		
Screw Cap / Aluminum seal charging in Hopper	1	2	3	4	5		
	6	7	8	9	10		
	11	12	13	14	15		
	16	17	18	19	20		
	21	22	23	24	25		
	26	27	28	29	30		
	31	32	33	34	35		
	36	37	38	39	40		
	41	42	43	44	45		
	46	47	48	49	50		
	51	52	53	54	55		
Handling of Vials/ Dropper/ Screw	1	2	3	4	5		

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Intervention	Number of frequency count					Total No.	Checked By
Cap/ Ampoules/ Rubber stopper/ Aluminum seal by using forceps	6	7	8	9	10		
	11	12	13	14	15		
	16	17	18	19	20		
Operator Breaks & Meals	1	2	3	4	5		
Tea Break for 30 min	1	2	3	4	5		
Operator Shift Changes	1	2	3	4	5		
Environmental Monitoring (Settle plate/Active air sampling)	1	2	3	4	5		
	6	7	8	9	10		
Filling room door open for 2 min	1	2	3	4	5		
	6	7	8	9	10		
Rubber stopper/Dropper chute adjustment for 2 min	1	2	3	4	5		
In process product sampling	1	2	3	4	5		
Gloves Replacement	1	2	3	4	5		
	6	7	8	9	10		
Vials/Ampoules/ Rubber Stopper/ Aluminum Seal jammed	1	2	3	4	5		

II-Aseptic Manipulation (Non-Routine Intervention):

Intervention	Number of frequency count					Total No.	Checked by
Sensor Adjustment or Replacement	1	2	3	4	5		
Rubber stopper/Dropper miss feed and clumping in chute.	1	2	3	4	5		
	6	7	8	9	10		
Piston/Tips/Syringe/filling nozzle replacement	1	2	3	4	5		
AHU of Filling Area OFF for 05 Minute	1	2	3	4	5		
LAF of filling machine off for 5 minute	1	2	3	4	5		
Machine Break down activities for 15 Minutes (MINOR)	1	2	3	4	5		

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Intervention	**Number of frequency count**					**Total No.**	**Checked by**
Machine Break down activities for 60 Minutes (MAJOR)	1	2	3	4	5		
Power Failure for 10 Minutes	1	2	3	4	5		
Increase in No. of Persons for 15 Minutes (Not more than 7 persons)	1	2	3	4	5		
Highest filling machine speed	1	2	3	4	5		
Slowest filling machine speed	1	2	3	4	5		
Defective seal in container	1	2	3	4	5		
Conveyor or guide rail adjustment	1	2	3	4	5		
Operator fatigue	1	2	3	4	5		
Product spillage or leakage(Breakage of Vials)	1	2	3	4	5		
Flame setting after burner on off	1	2	3	4	5		
Oxygen and LPG pressure Low	1	2	3	4	5		
Any other intervention which is not mentioned in above list.							
	1	2	3	4	5		
	1	2	3	4	5		
	1	2	3	4	5		

Checked By:
Production
Sign & Date

Reviewed By:
Quality Assurance
Sign & Date