PROCESS VALIDATION REPORT

FOR

PRE AND PROBIOTIC CAPSULES

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1.0 SUMMARY PLAN OF STUDY:

1.1 PRODUCT AND BATCH DETAILS:

Process Validation of Pre and Probiotic capsules was carried out on three consecutive batches. The details are as under:

BATCH DETAILS:

S.No.	BATCH NUMBER	BATCH SIZE	MFG. DATE	EXP. DATE
1.				
2.				
3.				

PRODUCT DETAILS:

Generic Name	Pre and Probiotic capsules
Product Code	
License No.	
Description	Grey/Yellow, Size "1" hard gelatin capsules cap in black colour.
Label Claim	Each Hard gelatin capsule contains: Lactobacillus acidophilus 30 mg Lactobacillus bulgaricus 15 mg Lactobacillus paracasei 45 mg Lactobacillus Plantarum 15 mg Lactobacillus casei 15 mg Lactobacillus rhamnosus 30 mg Bifidobacterium bifidum 15 mg Bifidobacterium longum 45 mg Bifidobacterium breve 15 mg Streptococcus thermophilus 30 mg Enterococcus faecium 45 mg Oligofructose q.s. } 5 Billion CFU Approved colour used in capsule shells
Shelf Life	18 months
Batch Size	1,00,000 Capsules
Pack Size	10x10's Alu-PVC Blister
Storage Condition	Store in a cool & dry place, away from direct sunlight.

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2.0 REFERENCE DOCUMENTS:

S.No.	DOCUMENTS
1.	Master Formula Record
2.	Batch Manufacturing Record
3.	Batch Packing Record
4.	Bulk Product Specification
5.	Semi-Finished Product Specification
6.	Finished Product Specification
Checked By (Sign & Date)	

NOTE: Current revision / version of document to be referred.

3.0 MANUFACTURING EQUIPMENT AND ACCESSORIES USED IN THE PROCESS:

The various equipments used for the Process Validation of Pre and Probiotic capsules are as follows:

S.No.	EQUIPMENT	EQUIPMENT NUMBER
1.0	Sifter & Sieves	
2.0	Octagonal Blender 300 Ltrs	
3.0	Capsule Filling Area	
4.0	Capsule Filling Machine	
5.0	Sorter & Elevator	
6.0	De Dusting & Polishing Machine	
7.0	Mini Capsule Sorter	
8.0	Empty Capsule Sorter	
9.0	Air Displacement Unit	
10.0	Vernier Caliper	
11.0	Disintegration Test Apparatus	
12.0	Blister Packing Machine	
13.0	Leak Test Apparatus	

All critical equipments were verified for their Installation, Operational and Performance Qualification. Further all the equipment were cleaned and operated as per relevant SOP's as indicated in the Process Validation Protocol.

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The vessels and accessories used in the Process Validation of Pre and Probiotic Capsules are as follows:

Batch Numbers			
Name of Equipment	**Equipment No.**	**Equipment No.**	**Equipment No.**
Granulation			
Octagonal Blender (300 Ltr.)			
Checked By (Sign & Date)			
Filling			
Capsule Filling Machine			
Sorter & Elevator			
De Dusting & Polishing Machine			
Mini Capsule Sorter			
Empty Capsule Sorter			
Air Displacement Unit			
Disintegration Test Apparatus			
Packing			
Blister Packing Machine			
Leak Test Apparatus			
Checked By (Sign & Date)			

The equipments and Accessories were cleaned as per the relevant SOP before use for manufacturing.

4.0 ANALYTICAL REPORT NUMBERS AND QUANTITY OF ALL RAW & PACKING MATERIALS:

RAW MATERIAL	**UOM**	**STD. QTY./Batch (Kgs.)**	**BATCH No.**					
			QTY USED	**A.R NUMBER**	**QTY USED**	**A.R NUMBER**	**QTY USED**	**A.R NUMBER**
Stomapro 127 (HG	Kg	30.00						
Oligofructose (Fructo Oligo Saccharide)	Kg	2.500						
Size 1, Cap: Grey, Body: yellow with Cap in black color	Nos.	1,00,000						

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PACKING MATERIAL	UOM	STD. QTY	BATCH No.					
			QTY USED	A.R NUMBER	QTY USED	A.R NUMBER	QTY USED	A.R NUMBER
160 mm printed Alu foil for blister packing	kg	60.00						
166 mm PVC foil for Blister packing	kg	300.00						
Printed Outer carton 10 x 10C	Nos	11300						
Shipper	Nos	11300						
Bopp Tape	Nos	110						

5.0 STAGE WISE ENVIRONMENTAL CONDITIONS:

S.No.	STAGE	BATCH NUMBER						Checked by
		Temp. (°C)	RH (%)	Temp. (°C)	RH (%)	Temp. (°C)	RH (%)	
1.	Dispensing							
2.	Blending							
3.	Filling							
4.	Primary Packing							
5.	Secondary Packing							

6.0 EXPERIMENTAL PLAN, RESULTS AND DISCUSSION:

The following critical parameters were monitored in this study:

PROCESS PARAMETERS:

- Analysis of the blend at different time intervals (05, 10 and 15 minutes) for Assay.
- Analysis of the blend (top, middle and bottom layers) from octagonal blender for Assay.
- In Process check parameters like Appearance, Average net content, Uniformity of filled weight, locking length, at different filling speed.
- Performing of leak test after every 2 hours during packing.
- Analysis of Chemical Tests of finished product.

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ENVIRONMENTAL CONDITIONS:

- HVAC system as well as LAF units was conforming for Installation, Operational and Performance Qualification. Differential Pressure as well as Viable counts in HVAC system and LAF units were monitored on regular basis as per relevant protocols and the same were found to be conforming to specifications.
- Purified water plant, holding tanks and distribution loops were qualified as per the protocol and the same were found to be conforming to specifications.

6.1 PROCESS PARAMETERS RESULTS:

6.1.1 Blending stage:

Mix the Prebiotic and Probiotic granules in blender for 15 minutes. The blending of Active and Excipients was checked at different time intervals (05, 10 and 15 minutes). The samples were withdrawn from different locations at different time intervals of mixing as per mentioned in the protocol and the same were sent for analysis to QC department.

6.1.1.1 Blending result of Batch Number: ……..

Sampling Time Interval	**After 5 min blending**		**After 10 min blending**		**After 15 min blending**	
	From	**To**	**From**	**To**	**From**	**To**
Sampling Location ↓	**Test Parameter**					
	Description	**Assay**	**Description**	**Assay**	**Description**	**Assay**
A (Top center)						
B (Middle Center)						
C (Bottom center)						
MEAN						
RSD NMT (2.0%)						

Remarks:_____

_____

_____

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6.1.1.2 Blending result of Batch Number: ……..

Sampling Time Interval	After 5 min blending		After 10 min blending		After 15 min blending	
	From	To	From	To	From	To

Sampling Location ↓	Test Parameter					
	Description	Assay	Description	Assay	Description	Assay
A (Top center)						
B (Middle Center)						
C (Bottom center)						
MEAN						
RSD NMT (2.0%)						

Remarks:

_____

_____

_____

_____

6.1.1.3 Blending result of Batch Number:……..

Sampling Time Interval	After 5 min blending		After 10 min blending		After 15 min blending	
	From	To	From	To	From	To

Sampling Location ↓	Test Parameter					
	Description	Assay	Description	Assay	Description	Assay
A (Top center)						
B (Middle Center)						
C (Bottom center)						
MEAN						
RSD NMT (2.0%)						

Remarks:_____

_____

_____

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6.1.2 Intermediate Process Container Samples:

Collect the material in double polythene bag intermediate-process container. After unloading the bulk withdraw 150 g composite sample from top, middle and bottom layers of the intermediate process containers. Send the sample to QC department for Assay.

PARAMETER	Acceptance Criteria	SAMPLE CODE	BATCH No.		
Description		IS_1			
Moisture content					
ASSAY (in % w/w)					

6.1.3 Filling Stage:

Setup and operate the filling machine as per respective SOP.

CONTROL PARAMETER SUMMARY FOR FILLING MACHINE:

Set the filling machine as per the below standard parameters.

PARAMETER	ACCEPTANCE CRITERIA
Appearance	
Average Fill weight	
Weight Variation	
Locking Length	

Once the machine is set as per the standard parameters above, set the machine at different speeds (lower, average and higher) and collect the capsules separately. Check the capsules produced at different speeds as per the above table. Based on the checks, arrive at optimum speed and fill the total batch at the optimum speed. The optimum speed is the highest speed at which all parameters well within the acceptance criteria.

6.1.3.1 Filling result of Batch Number: ……..

VALIDATION BATCH NUMBER				
PARAMETER	**ACCEPTANCE CRITERIA**	**LOWER SPEED 60 RPM**	**AVERAGE SPEED 85 RPM**	**HIGH SPEED 110 RPM**
Appearance				
Average Fill weight				
Weight Variation				
Locking Length				

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Set the machine at 85 rpm and fill the total batch.

RESULT OF FILLING STAGE SAMPLES:

VALIDATION BATCH NUMBER				
PARAMETER	ACCEPTANCE CRITERIA	FILLING STAGE		
		INITIAL	MIDDLE	FINAL
Appearance				
Average Fill weight				
Weight Variation				
Locking Length				
Assay				

6.1.3.2 Filling result of Batch Number: ……..

VALIDATION BATCH NUMBER				
PARAMETER	ACCEPTANCE CRITERIA	LOWER SPEED 60 RPM	AVERAGE SPEED 85 RPM	HIGH SPEED 110 RPM
Appearance				
Average Fill weight				
Weight Variation				
Locking Length				

Set the machine at 85 rpm and fill the total batch.

RESULT OF FILLING STAGE SAMPLES:

VALIDATION BATCH NUMBER				
PARAMETER	ACCEPTANCE CRITERIA	FILLING STAGE		
		INITIAL	MIDDLE	FINAL
Appearance				
Average Fill weight				
Weight Variation				
Locking Length				
Assay				

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6.1.3.3 Filling result of Batch Number: ……..

VALIDATION BATCH NUMBER				
PARAMETER	**ACCEPTANCE CRITERIA**	**LOWER SPEED 60 RPM**	**AVERAGE SPEED 85 RPM**	**HIGH SPEED 110 RPM**
Appearance				
Average Fill weight				
Weight Variation				
Locking Length				

Set the machine at 85 rpm and fill the total batch.

RESULT OF FILLING STAGE SAMPLES:

VALIDATION BATCH NUMBER				
PARAMETER	**ACCEPTANCE CRITERIA**	**FILLING STAGE**		
		INITIAL	**MIDDLE**	**FINAL**
Appearance				
Average Fill weight				
Weight Variation				
Locking Length				
Assay				

6.1.4 RESULT OF FILLING COMPOSITE SAMPLE:

PARAMETER	**ACCEPTANCE CRITERIA**	**BATCH NUMBER**		
Appearance				
Average Fill weight				
Weight Variation				
Locking Length				
Assay				

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7.0 PACKING OPERATION:

Perform packing operation as per recommended instructions. Over-coding of batch details on, labels and Corrugated Boxes shall be verified.

During packing, withdraw strips every 2 hour intervals for leak testing (Monitor and record the Sealing temperature of sealing machine.

IN PROCESS CHECKS (PRIMARY AND SECONDARY PACKING):

Note: * Put C for Complies and NC for Not Complies

VALIDATION BATCH NUMBER									
Date	**Time**	**Temp. (°c)**	**RH (%)**	**Qty. / blister 1x10'**	**Leaktest C/NC**	**Over coding detail on blister pack C/NC**	**Quality of Leaflet and blister pack C/NC**	**Over coding details on Printed carton C/NC**	**Over coding details on Shipper C/NC**

Note: * Put C for Complies and NC for Not Complies

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

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VALIDATION BATCH NUMBER									
Date	**Time**	**Temp. (°c)**	**RH (%)**	**Qty. / blister 1x10'**	**Leaktest C/NC**	**Over coding detail on blister pack C/NC**	**Quality of Leaflet and blister pack C/NC**	**Over coding details on Printed carton C/NC**	**Over coding details on Shipper C/NC**

Note: * Put C for Complies and NC for Not Complies

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

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VALIDATION BATCH NUMBER									
Date	**Time**	**Temp. (°c)**	**RH (%)**	**Qty. / blister 1x10'**	**Leak test C/NC**	**Over coding detail on blister pack C/NC**	**Quality of Leaflet and blister pack C/NC**	**Over coding details on Printed carton C/NC**	**Over coding details on Shipper C/NC**

The formalized, final 3-batch validation sequence provides the necessary process validation document required to show product reproducibility and a manufacturing process in a state of control.

The test data and results show process reproducibility and consistency among validated batches of Prebiotic and Probiotic Capsules. Description, moisture content, average fill weight, weight variation, locking length, assay, package integrity, have been addressed both during in-process and final product testing. All the parameters fall well within in-house acceptance criteria for Prebiotic and Probiotic Capsules.

Testing has been sufficient to establish process reproducibility and demonstrate, with a high degree of certainty that the product, Prebiotic and Probiotic Capsules and process are under control.

8.0 STAGE WISE YIELD VARIFICATION:

S.No.	STAGE	ACCEPTANCE CRITERIA OF YIELD (IN %)	OBSERVED YIELD (IN %) BATCH No.		
1.	Blending	NLT 99.00 %			
2.	Capsule Filling	NLT 98.00 %			
3.	Packing	NLT 97.00 %			

Conclusion: Based on the évaluation of analytical data of three batches, It is evident that result of % RSD at 25 minutes of blending are well within the acceptance criteria, hence Lubrication time of 25 minutes shall be followed in future batches.

9.0 CONCLUSION:

Based on the analytical data and comparative results of critical process steps of 03 validation batches. It is obvious that all critical process steps involved in the manufacturing i.e. Description, moisture content, average fill weight, weight variation, locking length, assay are well within the acceptance criteria hence are well controlled. Manufacturing procedure and critical process parameters followed for validation batches are consistent and reproducible and demonstrate with a high degree of certainty of the product. Hence same manufacturing and packing procedure shall be followed in future for all commercial production batches of Prebiotic and Probiotic Capsules.

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10.0 REPORT APPROVAL:

PREPARED BY

S.No.	NAME	DESIGNATION	SIGNATURE	DATE

REVIEWED BY

S.No.	NAME	DESIGNATION	SIGNATURE	DATE

APPROVED BY

S.No.	NAME	DESIGNATION	SIGNATURE	DATE