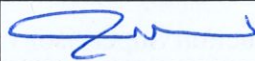
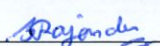

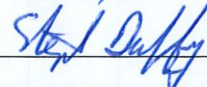


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PROCESSING INSTRUCTION: SPRAY DRIED MANNITOL BLEND (SP-504)			
Issued By/Date		Lot Number:	

	Name	Position	Signature	Date
Author:	Pouria Nooshin	Packaging Leader		26 Nov 21
Checked By:	Rajendra Sambasivam	Production Operator		26 Nov 21
Checked by (QA):	Aaron Dooley	QA Manager		26 Nov 21
Authorised by:	Stephen Duffy	Production Manager		26 Nov 21

1 PRODUCT DESCRIPTION

1.1	Product Description	Spray Dried Mannitol Blend
	Specification Number (Include version number)	SP-504-_____
	Strength	N/A
	Batch Size:	
	Blend expiry date (60 days from date of manufacture of oldest sub-batch)	
	COMPLETED BY/DATE:	

- **ENSURE SAFETY PRECAUTIONS ARE TAKEN AT ALL TIMES.**
- **FOLLOW THE STEPS IN ORDER AS SET OUT IN THE PI.**
- **REPORT ANY INCIDENTS TO THE SUPERVISOR IMMEDIATELY.**

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2 BILL OF MATERIALS

Prior to processing, the **Production Supervisor** must specify below the lot numbers, fractions & quantities of Spray Dried Mannitol to be included in the blend.

The Production Supervisor must then calculate the total assigned quantity & verify that the total is within the Blender Weight Limits specified.

Expiry date									Weight Limit: 56 kg- 60kg
Quantity (g)									
Fraction Number (s)									TOTAL (g):
Lot Number									
Quantity per unit/ Batch	56 kg- 60kg								
Specification Number	SP-503								
Material Name	Spray Dried Mannitol Individual Batch								

COMPLETED BY/DATE: _____

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Issued By/Date		Lot Number:	

3 ROOM & PRINCIPAL EQUIPMENT


3.1	Room & Principal Equipment (20RR): <ul style="list-style-type: none"> • Blending Room (B1.018) • Frewitt Coniwitt-150 Conical Mill (Tag: 00405) • Mueller CONT350-CI000-K-08357 350 Kg IBC (Tag: 00410) • Müller Blender Column Lifter (Tag 00412) • Calibrated Balances
3.2	Login to the Blending Room (B1.018) - Logbook (LB-133). COMPLETED BY/DATE: _____

4 CLEANING CHECKS

4.1	<p>Is this the first lot to be manufactured after a major clean? <input type="checkbox"/>YES <input type="checkbox"/>NO</p> <p>If Yes, Check</p> <p>If more than 5 days have elapsed since the equipment was last sanitised, then:</p> <ul style="list-style-type: none"> • Re-sanitise all product contact surfaces with 70%IPA. • Record re-sanitisation on each Equipment Cleaning Tag (FM-231) for the IBC, Mill, Column Lifter & Parts and also in the Blending Logbook (LB-133). • Ensure all surfaces are dry. • Attach each Cleaning Tag (FM-231) & Major Cleaning Records (FM-288, FM-296 & FM-286) for the IBC, Mill & Column Lifter to the processing instructions. <p>If No, this section is not applicable.</p> <p>Sign below when it is confirmed that the equipment is within the sanitisation expiry time.</p> <p>COMPLETED BY/DATE: _____</p>
-----	---

5 ROOM CONDITIONS

5.1	<p>Check EMS for alarms (as detailed in SOP-244 – from local connection in B1.034).</p> <p>If no alarms are present on the EMS regarding the pressure differential, temperature and relative humidity in Room B1.018, then it is accepted that all values are within their acceptable ranges for production to occur.</p> <p>If an alarm is present do not proceed with the batch until the conditions are restored to within acceptable limits (no alarms) or a Deviation report (FM-016) has been raised and approved.</p> <p>COMPLETED BY/DATE: _____</p>
5.2	<p>Confirm that the Nitrogen supply is turned on.</p> <p>COMPLETED BY/DATE: _____</p>

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6 ROOM CLEARANCES

6.1	<p>Ensure the room is clear of all unnecessary material – refer to SOP-142. Room clearance is performed as per FM-391 by the second trained person (not involved in completing the above steps).</p> <p>COMPLETED BY/DATE: _____</p> <p>ROOM CLEARANCE CHECKED BY/DATE: _____</p>
-----	---

7 BLENDING PROCEDURE

7.1	<p>Complete Blender set-up as per SOP-262. Ensure all safety precautions are adhered to.</p> <p>COMPLETED BY/DATE: _____</p>
7.2	<p>Install the vibrational hammer on the IBC. Confirm that the vibrator is operational – if not, alert the Production Supervisor and do not proceed with batch until fixed.</p> <p>COMPLETED BY/DATE: _____</p>
7.3	<p>Set up the Frewitt Coniwitt-150 Conical Mill (Tag 00405) according to SOP-257. Set the Mill speed to 500 rpm and use a 3 mm screen (Serial No. 432501 only). Ensure the Mill is set up correctly by testing it first. Ensure that the screen and rotor are not in contact with each other.</p> <p>COMPLETED BY/DATE: _____</p> <p>CHECKED BY/DATE: _____</p>
7.4	<p>Record the balance to be used for weighing step:</p> <p>Balance Used (Tag): _____</p> <ul style="list-style-type: none"> • Weigh each assigned fraction of Spray Dried Mannitol and record the gross weight. • Empty the contents of each bag into the IBC. • Weigh the empty bag and record the tare weight. • Calculate the net weight of each fraction added to the IBC. • Calculate the total net weight of Spray Dried Mannitol fractions added to the IBC. • Verify that the total is within the limits specified. • Complete FM-006 Inventory form for each Spray Dried Mannitol lot used. • All weights & calculations are to be checked by a 2nd Operator.

PROCESSING INSTRUCTION: SPRAY DRIED MANNITOL BLEND (SP-504)

Issued By/Date

Lot Number:

Lot Number	Fraction Number	Gross Weight (g)	Tare Weight (g)	Net Weight (g)	Completed by/Date	Checked by/Date
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
		g	g	g		
Total Powder added to IBC (56kg- 60kg)...(a):				g		

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7.5	<p>Login to the control panel. Perform the following steps as per SOP-262.</p> <p>Set the blender speed to 15 rpm. Set the blending time to 10 minutes. Enter the Lot Number of the batch to be blended in the following format MYX-XXX. The checker shall ensure the correct data as recorded below is manually entered on the Blender HMI.</p> <p>Blend Speed Entered: _____ rpm</p> <p>Blend Time Entered: _____ minutes</p> <p>Lot Number: _____</p> <p>COMPLETED BY/DATE: _____</p> <p>CHECKED BY/DATE: _____</p>
7.6	<p>Blend the batch as per SOP-262.</p> <p>If any stoppages are required record the details in the minor incident form.</p> <p>Stoppages: _____ (N/A if not required)</p> <p>Refer to Deviation: _____ (N/A if not required)</p> <p>COMPLETED BY/DATE: _____</p>
7.7	<p>Remove the blender printout. Check that Blend Speed, Blend Time and Lot Number are the same as the Blender HMI. Attach printout to PI.</p> <p>Initiate a Minor Incident Report if there is a difference observed.</p> <p>COMPLETED BY/DATE: _____</p>

8 MILLING PROCEDURE

8.1	<p>Place a tared sterile Size 2 plastic bag (with WIP label attached outlining details of batch and tare weight) underneath outlet funnel and start the Mill.</p> <p>Feed the Spray Dried Mannitol Blend gradually as detailed in SOP- 257 into the Mill hopper (to ensure no grinding of the powder occurs).</p> <p>In order to ensure each bag is closed properly, try to limit each bag maximum quantity to approximately 7,500g. Seal each bag after filling. Change the bag intermittently throughout the process and label bags as 1, 2, 3...</p> <p>COMPLETED BY/DATE: _____</p> <p>CHECKED BY/DATE: _____</p>
-----	---

PROCESSING INSTRUCTION: SPRAY DRIED MANNITOL BLEND (SP-504)

Issued By/Date

Lot Number:

8.2

Weigh minimum 50g sample from each bag for QC sampling.

Use a clean spatula to sample from different locations in each bag. Immediately reseal each bag after sampling.

Place the samples in tared, labelled sterile plastic containers & close. Care must be taken when placing the lid onto the sample container. Do not use force. Ensure lid sits evenly.

Calculate the total. All weights, calculations & sample labels must be checked by a 2nd Operator.

Balance Used (Tag): _____

Bag Number	Sample	Gross Weight	Tare Weight	Net Weight
Bag 1	QC:	g	g	g
Bag 2	QC:	g	g	g
Bag 3	QC:	g	g	g
Bag 4	QC:	g	g	g
Bag 5	QC:	g	g	g
Bag 6	QC:	g	g	g
Bag 7	QC:	g	g	g
Bag 8	QC:	g	g	g
Bag 9	QC:	g	g	g
Bag 10	QC:	g	g	g
Total Weight of Samples.....(b):				g

COMPLETED BY/DATE: _____

CHECKED BY/DATE: _____

PROCESSING INSTRUCTION: SPRAY DRIED MANNITOL BLEND (SP-504)

Issued By/Date

Lot Number:

8.3 Weigh each Spray Dried Mannitol Blend bag & calculate the total. Complete the WIP labels:

- Record the weight on the WIP label.
- Record the expiry date (from section 1 on page 1) on the WIP label

All weights, calculations & bag labels must be checked by a 2nd Operator.

Balance Used (Tag): _____

Spray Dried Mannitol Blend	Gross Weight	Tare Weight	Net Weight
Bag 1	g	g	g
Bag 2	g	g	g
Bag 3	g	g	g
Bag 4	g	g	g
Bag 5	g	g	g
Bag 6	g	g	g
Bag 7	g	g	g
Bag 8	g	g	g
Bag 9	g	g	g
Bag 10	g	g	g
Total Spray Dried Mannitol Blend.....(c):			g

COMPLETED BY/DATE: _____

CHECKED BY/DATE: _____

8.4 Place each bag in a second sterile plastic bag & seal the second bag.

COMPLETED BY/DATE: _____

8.5 Initiate FM-006 (Inventory Intermediate/WIP) for the Spray Dried Mannitol Blend.

COMPLETED BY/DATE: _____

8.6 Calculate the Lot expiry date below;
The expiry date for Blend (SP-504) is 60days from the date of Spray-Drying of the oldest sub-batch included in the blend.

Lot Expiry Date: _____

COMPLETED BY/DATE: _____

CHECKED BY/DATE: _____

PROCESSING INSTRUCTION: SPRAY DRIED MANNITOL BLEND (SP-504)

Issued By/Date

Lot Number:

9 YIELD

9.1 Calculate the yield. The calculation must be checked by a 2nd Operator.

Total Blend Output.....(d):	g	= (b) + (c), refer 8.2 & 8.3
Total Powder added to IBC:	g	= (a), refer 7.4
Yield:	%	= [(d) / (a)] x 100
Yield Limits:	97 – 101 %	
Yield within limits (circle):	Y / N	

COMPLETED BY/DATE: _____

CHECKED BY/DATE: _____

9.2 Photocopy the printout from the blender, sign the copy & attach to the PI.

COMPLETED BY/DATE: _____

10 LABELLING AND STORAGE

10.1 Store the labelled bags in the WIP storage area in the clean room (B1.021). Ensure all bags from the same batch are store on the same rack.
All the labels completed must be checked by the 2nd trained person for the accuracy of the details entered.

COMPLETED BY/DATE: _____

CHECKED BY/DATE: _____

11 CONSUMPTION & OUTPUT

11.1 Calculate the total consumption of all the materials used.
All consumptions must be checked by the 2nd person.

Material	Specification Number	Lot Number	Total quantity used per lot (Kg)
Spray Dried Mannitol Individual Batch	SP-503		
Spray Dried Mannitol Individual Batch	SP-503		
Spray Dried Mannitol Individual Batch	SP-503		
OUTPUT	SP-504		

COMPLETED BY/DATE: _____

CHECKED BY/DATE: _____

**PROCESSING INSTRUCTION:
SPRAY DRIED MANNITOL BLEND (SP-504)**

Issued By/Date

Lot Number:

12 MINOR INCIDENT REPORT

Record any observation made during the batch manufacture – refer to SOP-142 for minor incident definition, identification and subsequent action.

Alert the Production Supervisor immediately. **Action!**

Date/Time	Operator Initials	Incident/Observation – brief description/actions	Supervisor Evaluation - root cause, product impact, immediate action	Product Quality Impact – If N - provide brief justification If Y - reference deviation report.	Supervisor Approval – Sign/Date

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13 NAVISION & TRENDING UPDATE

13.1	Perform Navision Production Journal transactions as per SOP-165 and enter Trending as per SOP-241. COMPLETED BY/DATE: _____
------	---

14 BATCH REVIEW

14.1	Verify Navision Production Journal transactions as per SOP-165. COMPLETED BY/DATE: _____		
14.2	Ensure production journal is posted & trending is completed accurately. COMPLETED BY/DATE: _____		
14.3	Record any Associated Deviation, CR or CAR – to be completed by Production staff <table border="1" style="width: 100%;"> <tr> <td style="width: 15%;">Reports</td> <td></td> </tr> </table> COMPLETED BY/DATE: _____	Reports	
Reports			
14.4	The Process Instructions & the associated documents have been reviewed as detailed in SOP-291. COMPLETED BY/DATE: _____		

15 APPROVAL BY PRODUCTION MANAGER/PRODUCTION SUPERVISOR

These Processing Instructions & associated documents have been reviewed & the lot produced in compliance with GMP. Print Name: _____ Sign/Date: _____
--

16 ASSOCIATED DOCUMENTS AND QA REVIEW

Include details of any associated documents		
Associated Document	Document Number	Initial/Date
EMS OOL		
CAR Number(s)		
DR Number(s)		
NCPR Number(s)		
CR Number(s)		
OOS Number(s)		
BATCH DOCUMENT QA REVIEWED BY		
Print Name: _____ Sign/Date: _____		