MANNITOL (STARTING MATERIAL)

	Name	Position	Signature	Date
Author:	Khrystyna Dunn	QA Officer		22 Jun 22
Reviewed by:	Aaron Dooley	QA Manager		23 Jun 22
Authorised by:	Edward Vaiciurgis	Head of Quality		23 Jun 22

1.0 MATERIAL IDENTIFICATION

1.1	Standard Name	Mannitol (Starting Material)
1.2	Alternate Name	Pearlitol PF
1.3	Description	A white powder. Formula, $C_6H_{14}O_6$.
1.4	Packaging	Packaging must be intact for goods to be accepted. There must be at least 2 layers of packaging. Material must be received within original packaging – polyethylene bag / paper bag.
1.5	Dimensions	Not Applicable
1.6	Weight	Not Applicable
1.7	CAS Number	69-65-8.

2.0 APPROVED SUPPLIER

2.1	Supplier	Brenntag Australia Pty Ltd.
2.2	Manufacturer	Roquette Freres. Address: 1, Rue de la Haute Loge, 62136 Lestrem France.
2.3	Product Code	Pearlitol, Material Grade PF (Pyrogen Free).

3.0 STORAGE CONDITIONS

Store in a clean place from 15°C to 30°C, protected from moisture.

4.0 HAZARD AND SAFETY

Not considered a hazardous material.

5.0 CERTIFICATES REQUIRED

5.1 Certificate must be batch specific and include a signature (an electronic signature is deemed acceptable).

5.2 Certificate of Analysis (C of A) stating that the batch meets the requirements of the current USP and Ph. Eur. for mannitol. Specific tests listed must include at least one identity test. The C of A must contain the address of the site of the manufacturer

6.0 SAMPLING REQUIREMENTS

6.1 Quantity Required

Sampling is performed in accordance with the current version of SOP-029. Inspect and sample √n+1 shippers received.

A sample of the polyethylene bag from the same √n+1 shippers received is also required.

The amount of sample to be taken for each test is as follows *(note that the total amounts to be sampled are indicated in **bold**)*;

Table 1. QC Chemistry Testing Amount Required.

Sample	Quantity (*g*)
Appearance (Per sampled pool)[1]	6
Melting Point / Range (Per sampled pool)[1]	1
Assay + Related Substances (Per sampled pool)[1]	10
Loss on Drying (Per sampled pool)[1]	4
Conductivity (Per sampled pool)[1]	40
External Chemical Testing (Per sampled pool)[1]	150
FT-IR (Per sampled container)	1
Total sample required per sampled container[2]	**120**
Retention sample required per sampled container[2]	**240**

[1]Pooling is to be performed by QC in accordance with SOP-066.

[2]Note: In cases where only 1 container is received upon delivery, please sample 150g for external testing and 120g for QC testing (Total of 270g is required). Retention required in this case would be 540g (270 x 2).

Table 2. QC Microbiological Testing Amount Required.

Sample	Quantity (*g*)
Bioburden Sample (Per sampled pool)[1]	**20**
Bioburden Retention 1 (Per sampled pool)[1]	**20**
Bioburden Retention 2 (Per sampled pool)[1]	**20**

[1]Pooling is to be performed in accordance with SOP-066.

7.0 INSPECTION, TESTING AND ACCEPTANCE LIMITS

As per result sheets 1, 2 and 3 on pages 3, 4, and 5 of this document.

Release as per FM-018.

8.0 SHELF LIFE

8.1 Minimum Remaining Shelf Life — Product will only be accepted if it has at least 12 months shelf life remaining.

8.2 Expiry Date — Expiry date shall be 3 years from the date of manufacture as specified by the manufacturer.

8.3 Retest date — No retest for shelf life extension is permitted beyond the manufacturer's retest date

9.0 RESULT SHEET

Result Sheet 1 of 4

Lot number_____

TEST NAME	TEST METHOD	SPECIFICATION	RESULT	RESULT RECORD LOCATION	INITIAL / DATE
Appearance	TM-014	White or almost white, crystalline powder or free-flowing granules.			
Identification (by Infrared Absorption)	TM-036	Complies with pharmacopeial mannitol reference spectrum.			
Appearance of solution	TM-014	Clear and colourless.			
Melting Range	TM-037	Between 165°C and 170°C			
Melting Point	TM-037	Between 165°C and 170°C			
Assay	TM-006	98.0% to 101.5% of D-mannitol (dried substance)			
Related Substances	TM-006	Sorbitol ≤2.0%			
		Isomalt (Total of both peaks) ≤0.2%			
		Maltitol ≤0.2%			
		Individual Unidentified Substances ≤0.10%			
		Total Impurities ≤2.0%			
Reducing Sugars	As per the current edition of the Ph. Eur. and USP	Maximum 0.1% (calculated as glucose equivalent)			

Results of tests and inspections are within specification. **Sign**_____**Date** _____

Result Sheet 2 of 4

Lot number_____

TEST NAME	TEST METHOD	SPECIFICATION	RESULT	RESULT RECORD LOCATION	INITIAL / DATE
Loss on Drying	TM-015	Not more than 0.5% of its weight over 4 hours at 105°C			
Conductivity	TM-019	Not more than 20µs/cm			
Nickel	ICP-ES, as per Intertek Method AM00722 Or As per the current edition of the Ph. Eur.	Not more than 1.0ppm			
Certificate of Analysis states that the batch meets the requirements of the current Ph. Eur / USP for mannitol. Specific tests listed include at least one identity test.					

Results of tests and inspections are within specification. **Sign**_____**Date** _____

MANNITOL (STARTING MATERIAL)

Result Sheet 3 of 4

Lot Number _____

TEST NAME	TEST METHOD	SPECIFICATION	RESULT	RESULT RECORD LOCATION	INITIAL / DATE
Total Viable Aerobic Count and Prescribed Organisms	Total Viable Aerobic Count **As per current USP/Ph. Eur (harmonised) and FM-210**	$<10^2$ colony forming units per gram			
	Total Combined Yeast/Mould Count **As per current USP/Ph. Eur (harmonised) and FM-210**	$<10^1$ colony forming units per gram			
	Test for *E. Coli* **As per current USP/Ph. Eur (harmonised) and FM-210**	Absence of *Escherichia coli* in 1 gram			
	Test for *Salmonella* **As per current USP/Ph. Eur (harmonised) and FM-210**	Absence of *Salmonella* in 10 grams			
	Tests for *S. aureus* and *P. aeruginosa*. **As per current USP/Ph. Eur (harmonised) and FM-210**	Absence of *S. aureus* and *P. aeruginosa* in 1 gram			
	Bile Tolerant Gram Negative Bacteria **As per current USP/Ph. Eur (harmonised) and FM-210**	Absence of Bile-Tolerant Gram Negative Bacteria in 1 gram			

Results of tests and inspections are within specification. **Sign**_____**Date** _____

Result Sheet 4 of 4

Lot number_____

Polyethylene bag testing

TEST NAME	TEST METHOD	SPECIFICATION	RESULT	RESULT RECORD LOCATION	INITIAL / DATE
Identification (by Infrared Absorption)	TM-060	Complies with reference spectrum.			

Results of tests and inspections are within specification. **Sign**_____**Date** _____

10.0 DOCUMENT CHANGE HISTORY

Version	Date Effective	Section	Description and Rationale
16	01Jul22	2.0	Updated product code. Updated supplier as per CR934.
15	30Nov20	6.1	Added note to also sample the polyethylene plastic bags as per CR850
		Result Sheet 4	Added results table for Polyethylene bag testing as per CR850.
14	06-Nov-20	1.4	Added statement regarding material being received in original packaging as per CR850.
		2.1	Supplier name changed from Axieo to DKSH Performance Materials as per CR919.
		3.0	Added storage condition of 15°C to 30°C as per CR850.
		All	Formatting updated to current template TE-017-07.
13	13-May-19	3.0	Remove statement "should not exceed 30°C as this has been incorrectly stated since version 1 of this document. Product is stored in warehouse at 15°C to 25°C. refer to CR No.824
		6.1	Remove reference to sampling for water content, as water content is now longer a required test as per CR No.564.
		Result Sheet 1	Remove Assay: D-mannitol anhydrous test as per CR564
		Result Sheet 1	Remove reducing sugars tested as per Ph. Eur 7th Edition and include that remaining Reducing Sugars test is to be compliant with the current edition of USP as well as the Ph. Eur. in accordance with CR No.564.
		Result Sheet 2	Remove the Water Content and Lead test and as per CR564. Remove the Heavy Metals test as per CR789.
12	16-Mar-18	All	Formatting updated to current template TE-017-06. This included adding a new section 4 for hazards and safety.
		Result Sheet 2	Reference to Probe changed to Intertek as per CR762.
		Result Sheet 3	Added detail to test method column for micro tests noting that the methods used are all as per current USP/Ph.Eur (harmonised) for clarity.
11	17-Oct-16	5.1	Reinstatement of water content test as this test will be required for compliance with marketing authorisation for Bronchitol-Pharmaxis Russia, as detailed in CR564.
		Results Sheet 1 and 2	Anhydrous assay specification reinstated as well as water content, Lead limit test and reducing sugars as per Ph. Eur. 7th edition. This is to ensure compliance with marketing authorisation for Bronchitol-Pharmaxis Russia, detailed in CR564.
10	25-Aug-16	2.1	Nuplex Specialties changed to Axieo as per CR606.
		All	Formatting altered due to updated template TE-017-05.

		5.1	Removal of water content and bacterial endotoxins tests, no longer required as per CR564. Added note below Table 2 to refer to SOP-066 for pooling requirements.
		Results Sheet 1, 2 and 3	Assay specification now based on dried substance instead of anhydrous, removed water content, removed reducing sugars test as per Ph. Eur. 7th edition, removed Lead limit test, removed absence of all Psuedomonads test, removed bacterial endotoxins test and loss on drying specification changed from NMT 0.3% to NMT 0.5% all in accordance with CR564. Added option for Nickel limit test to be performed as per Ph. Eur. current edition as per CR660. E. Coli specification "in 1 gram" and Salmonella specification "in 10 grams" added to be consistent with how other specifications are stated.
9	01-Jul-15	All	Formatting altered due to updated template TE-017-04.
		5.1	Clarified √n+1 sampling plan as per CAR561. Adjusted Tables 1 and 2 to reflect updates to testing requirements as per CR564.
		Result Sheet 1, 2 and 3	Testing requirements and specifications changed in accordance with CR564 requirements.
8	19-Apr-13	All	Update document to current version of the template TE-017-03 as per SOP-021.
		2.1	Supplier name change from "APS Food & Nutrition" to "Nuplex Specialties" as per CR452.
		7.1	Change the minimum remaining shelf life of mannitol starting material to "12 months" as per CR438.
		Result Sheet 2 of 3	Correct the test method "As per the current edition of the Ph Eur" to "As per the current edition of USP" as per DR1773 for Reducing Sugars, Acidity, Chloride, Sulphate and Arsenic.
7	06-May-11	1.1	Update Standard Name as per title of document.
		1.2	"Pearlitol PF" as Alternate Name.
		2.1	Update name of approved supplier to "APS Food & Nutrition" from "Med-Chem Ingredients Pty Ltd". CR345.
		5.1	Update of quantity required for each testing per sampled pool/per sampled container under reduced sampling plan, as per completion of CR295. Refer to SOP-029 for sampling.
		Result sheet 1 of 3, Page 3 of 6	Update unidentified related substances specification from "≤0.1%" to "≤0.10%" in compliance with the current Ph. Eur as per CR299.
6	14-Apr-10	All	Document format updated in accordance with SOP-021.
		5.0	Referenced SOP-066 for sample pooling requirements.
		5.1	Sampling requirements summarised in table format. Specified amounts per individual container and per pooled sample.

		Result Sheet	In Results Sheet 1 of 3 Test Method for Specific Rotation changed from “As per the current edition of the USP” to “as per TM-038” as stated in CR#230.
		Result Sheet	Identification by Infrared Absorption method changed to TM-036 from “as per current USP and Ph. Eur” as stated in CR#252.
		Result Sheet	Microbial tests changed to harmonised method as per CM-09-024-03 and CR#231.

END OF DOCUMENT