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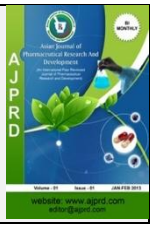

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Research Article

Process Validation of Highly Potent Antidiabetic Tablets of Voglibose 0.2 Mg

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ABSTRACT

Diabetes mellitus is chronic disorder which affecting number of persons worldwide, alpha glycoside inhibitors like Voglibose is a highly potent and tolerant alpha glycoside inhibitor as compare to other diabetic drugs, the main objective of this process validation is to provide documentary evidence that the manufacturing process of **Voglibose Tablet IP 0.2 mg** will consistently and reproducibly produce a product, which meets predetermined specifications and quality attributes. The critical process parameter was identified with the help of process capability and evaluated by challenging as per in-house specification. Three initial process validation batches (T17L004, T18L003, T19A013) of same size, method, equipment & validation criteria were taken. As per the process validation protocol critical parameter identified like sifting, dry mixing, wet granulation, drying, sifting and milling, blending &lubrication, compression at different stages and blister packing and evaluated as per process validation protocol. **Conclusion:** Based on evaluation of manufacturing process and analytical data it is concluded that the employed manufacturing process for **Voglibose Tablet IP 0.2 mg** shall be consistently& reproducibly produce a product which meeting its predetermined specification and quality attributes, hence it is considered to be validated.

Keywords: Voglibose 0.2 mg, Critical process parameter, Critical quality attributes, Process capability index.

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INTRODUCTION:

Diabetes Mellitus (DM) is a chronic metabolic disorder-affecting people worldwide, with significant morbidity and mortality caused by its micro-vascular and microsacular complication, affecting various vital organs and structure in human. Voglibose is a more potent and tolerant alpha glycoside inhibitor as compare to other diabetic drugs. Voglibose comes under the class of competitive alpha glycoside inhibitors and was first discovered in japan in 1981.

The antihyglycemic action of voglibose results from a reversible inhibition of membrane bound intenstines alpha glycosidase hydrolysed enzymes which hydrolyzed oligosaccharide and disaccharide to glucose and other monosacchride in the brush border of the small intenstine, thus the voglibose delays the the absorption as well as digestion of dietary polysaccharide by reversibly inhibiting carbohydrate diagestive enzymes like sucrose, maltose, zomaltase etc. this resultsin a reduction in PPHG.

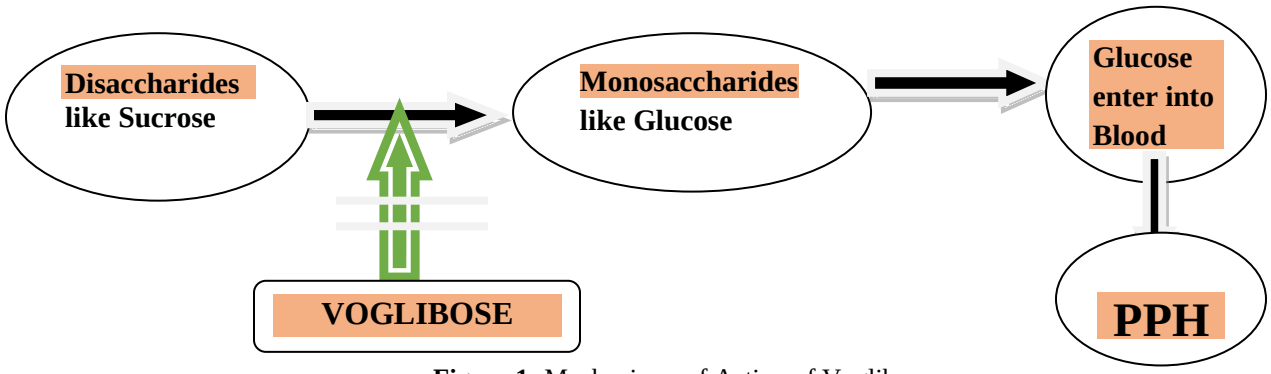


Figure 1: Mechanisms of Action of Voglibose

Voglibose may also facilitate mobilisortary alpha endogenous glycogen like GLP-1, which has an inhibitory action on glycogen, thus lowering fasting glucose levels too. Voglibose treatment has resulted in an increased released of GLP-1, which is known to enhance insulin secretion and insulin sensitivity [1].

According to Indian GMP validation study is essential part of GMP. Those required to be done as per predetermined protocols. Process validation is carried out during the development stage by means of risk analysis of the production process, which is broken down into individual steps [2]. These are then evaluated on basis of past experience to determine whether they might lead to critical situation are identified, the risk is evaluated, the potential cause are investigated and assessed for probability & extent, the teal plan are drawn up, & priorities are set [3] .The trial are then performed and evaluated & overall assessment is made. If at the end result are acceptable the process is satisfactory [4].Unsatisfactory processes must be modified & improved until a validation exercise proves them satisfactory this form of validation is essential in order to limit the risk of error occurring on the production scale [5]. This present work deals with identification of critical stage and their consequent evaluation by challenging its upper and lower specifications [6]

MATERIALS AND METHODS:

Table 1: Raw materials, specification, quantity and approved vendor

Sr. No.	Raw Materials	Specification	Qty per Tablet (In mg)	Overages	Approved Vendor
ACTIVE PHARMACEUTICAL INGREDIENTS					
1.	**Voglibose**	**IP**	**0.200**	**15.0% (Calculate on dried basis)**	Om Laboratories Ltd. Ahmadabad.
EXCIPIENTS FOR DRY MIXING					
2.	**Dicalcium Phosphate**	**IP**	**40.00**	-	India Phosphate Industrial Area Ujjain.
3.	**Maize Starch**	**IP**	**18.00**	-	Universal Starch Chem. Allied Ltd. Dhule
BINDER PREPARATION					
4.	**Maize Starch**	**IP**	**5.000**	-	Universal Starch Chem. Allied Ltd. Dhule
5.	**Methylparaben**	**IP**	**0.500**	-	Aster Industries, Nalgonda.
6.	**Propylparaben**	**IP**	**0.050**	-	Aster Industries, Nalgonda.
LUBRICANTS					
7.	**Purified Talc**	**IP**	**1.250**	-	Neelkanth Minechem, Jodhpur.
8.	**Microcrystalline**	**IP**	**55.00**	-	Vasa Pharmachem Pvt. Ltd., Ahmadabad.
9.	**Crosscarmellose**	**IP**	**3.000**	-	Prachin Chemicals Naroda, Hyderabad.
10.	**Aerosil**	**IP**	**1.000**	-	Par Drugs & Chemicals Pvt. Ltd., Bhavnagar.
11.	**Maize Starch**	**IP**	**10.00**	-	Universal Starch Chem. Allied Ltd. Dhule.
12.	**Cross Povidone**	**IP**	**2.500**	-	Boai NKY Pharmaceuticals Ltd. China.

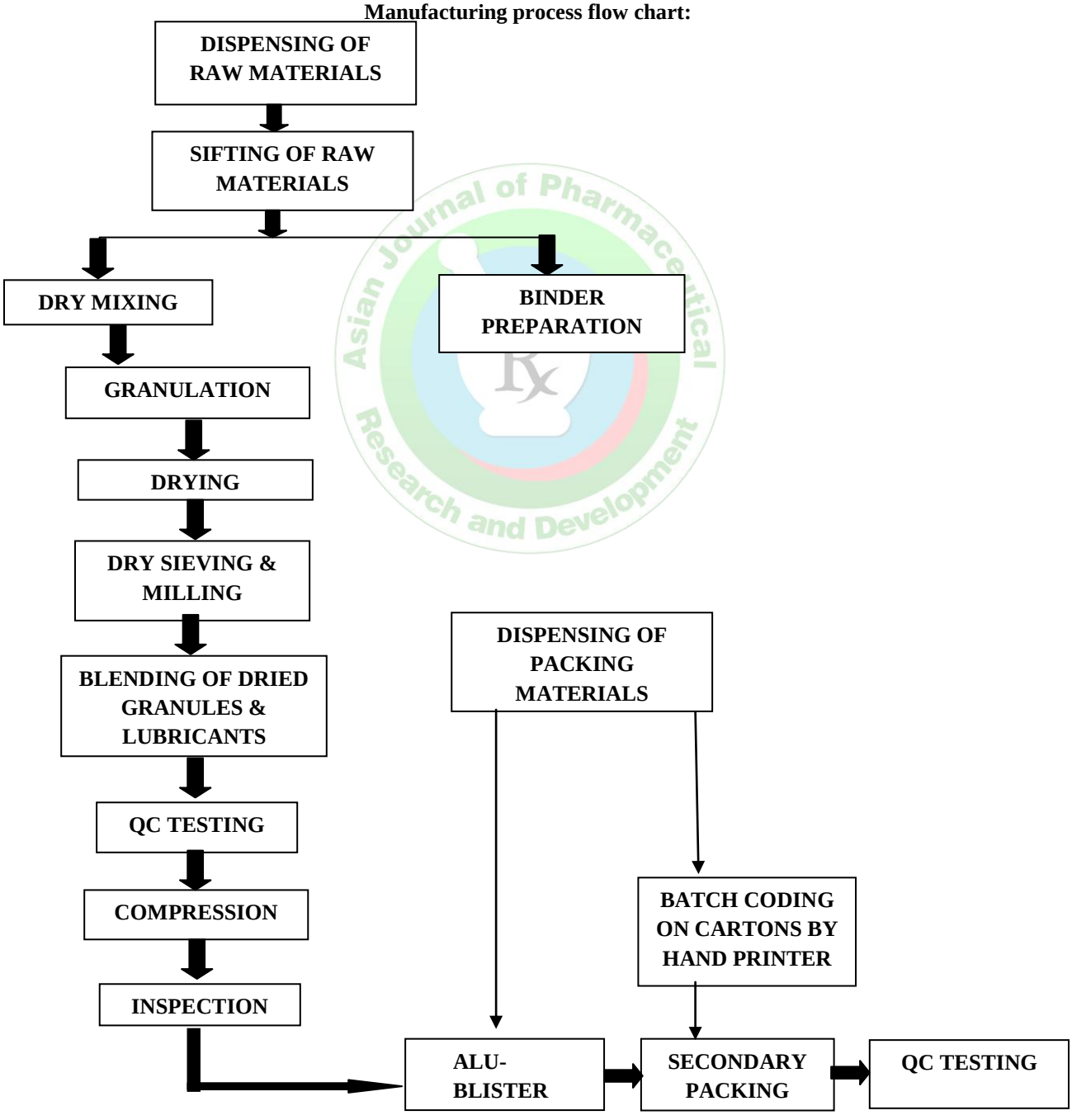
Table 2: Packing materials, specification, quantity and approved vendor

Sr. No.	Packing Materials	Qty per 1.0 Lac (In Kg)	Approved Vendor
1.	**Printed Aluminium Foil 182 mm**	**4.200**	Monalisa Packaging, MIDC, Hingna, Nagpur.
2.	**Plain Aluminium base foil 186 mm**	**14.50**	Monalisa Packaging , MIDC , Hingna, Nagpur

Table 3: Equipment's and Instruments:

Sr. No	Equipment's/Instruments	Qualification Status	Make
1.	**Vibro Sifter**	Qualified	Global Pharma Equipments, Mumbai.
2.	**Rapid Mixer Granulator**	Qualified	Elicon Pharma, Mumbai.
3.	**Paste Kettle**	Qualified	Global Pharma Equipments, Mumbai.
4.	**Fluid Bed Dryer**	Qualified	Global Pharma Equipments, Mumbai.
5.	**Multi Mill**	Qualified	Global Pharma Equipments, Mumbai.
6.	**Octagonal Blender**	Qualified	Global Pharma Equipments, Mumbai.
7.	**23 Station Rotary Tablet Press Machine**	Qualified	Shamdew Tableting Tools and Machines, Gujarat.
8.	**Tablet Deduster**	Qualified	Shamdew Tableting Tools and Machines, Gujarat.
9.	**Metal Detector**	Qualified	Shubham Multiple Services, Mumbai.
10.	**Dust Extractor**	Qualified	Shamdew Tableting Tools and Machines, Gujarat.
11.	**Tablet Inspection Tablet**	___	Rane Industries Mumbai.
12.	**Blister Packing Machine (RP MACH 1+)**	Qualified	Rapid Pack Thane, Maharashtra.
13.	**Batch Coding Machine**	Qualified	Domino Printer, Mumbai.
14.	**De-Blistering Machine**	Qualified	Shubham Multiple Services, Mumbai.
15.	**Friability Apparatus**	Qualified	Veego Instruments corporation Mumbai.
16.	**Tablet Hardness Tester**	Qualified	Veego Instruments corporation Mumbai.
17.	**Disintegration Test Apparatus**	Qualified	Veego Instruments corporation Mumbai.
18.	**High Performance Liquid Chromatography**	Qualified	Shimadzu

Manufacturing process flow chart:



Procedure

Dispensing: Dispense material as per dispensing sheet.

Sifting: Assemble Sifter as per standard operating procedure. Sift Dicalcium Phosphate and Maize Starch from 60 # sieve and collect in separate bin. Clean the sifter as per standard operating procedure.

Mixing: Transfer Dicalcium Phosphate and Maize Starch (Sifted through 60 # sieve) in Rapid Mixer Granulator and mix for 10 minutes at slow speed.

Preparation of paste: Transfer purified water into paste kettle (approx. 25 % of total weight of ingredients taking for dry mixing). Start the heater and set temperature at 100^0C. After reaching the temperature up to 100^0C add Methylparaben and Propyl paraben in paste kettle. Take equal amount of Maize starch (For paste preparation) in purified water in SS pot with gradually stirring to make slurry without any observable dry lumps of Maize Starch. Transfer the slurry into paste kettle and mix well for homogeneous paste formation with continuous shuffling by spatula.

Granulation: Slowly add Starch Paste into Rapid Mixer Granulator by switching on the impeller motor in slow speed and granulate for 10 minutes at slow speed and then at fast speed for 15-20 minutes.

(Note the impeller amperage initially and run the impeller at fast speed until the impeller amperage10±2 Amp. is obtained.)

Drying: Attached trolley contained wet lumps in to Fluid bed dryer. Load the prepared granules in FBD bowl and dry on air without heater and opening damper for 10 minutes. Shuffle the granules at regular intervals with the help of spatula, dry until the outlet temperature reaches upto 300C and inlet temperature 600C. Mill the semidried mass by using 6.0 mm multimill screen. Sieve the screened material in vibrosifter using 30# sieve. Mill sieve retained material using 2.0 mm of multimill screen. Sieve this screened material through vibrosifter using 30#, finally mill the sieve retained material using 1.0 multimill screen and sieve this screened material through 30#.

Final Drying: Dry the above sieved granules for 20 minutes until the temperature reaches upto the 35^0C. **(Temperature for moisture determination 105^0C and LOD should be less than 3%)**

Final Sieving: Sieve the dried granules through 30# sieve and collect in separate bin.

Blending and lubrication: follow the below procedure.

(Stage I Sieving): Sieve collectively voglibose and Aerosil through 100# sieve, repeat the procedure again. **(Bulk 1)**

(Stage II Sieving): Sieve collectively **Microcrystalline cellulose, Maize Starch, Cross carmellose and Cross povidone through 80 #** repeat the procedure again.**(Bulk 2)**

Collectively sieving the Bulk 1 and Bulk 2 through 80# sieve. **(Bulk A)**

Collectively sieve DCP and Maize starch Granules with **Bulk A** through 30# sieve. **(Repeat the procedure 3 times)** and finally blend in octagonal blender for 30 minutes.

The pre-compression parameters of the bulk-lubricated granules were performed using Veego Tapped Density Tester USP. The pre compression parameters revealed good flow property of powder for 0.2 mg of voglibose tablets.

Compression: After performing the pre-compression parameters the lubricated granules was subjected for punching using shamdew 23 station single rotary tablet punching machine. The punching tools used were round, biconvex, 7 mm plain punch. The machine RPM was 15-25. The average punch weight of the tablets was 140 mg. The hardness, thickness, weight variation, friability and disintegration of the punched tablets were maintained in the desired range.

Hardness: Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacturing, packing and shipping. The hardness of the tablets was maintained between More than 2 Kp. Hardness was measured using digital Veego tablet hardness tester. [(2)]

Thickness: The thickness of tablets should be maintained to overcome packing problems. The thickness of punched tablets was maintained in the range of 3.10 to 3.50 mm with the average thickness of 3.30 mm. Thickness was measured using digital Vernier Caliper. [(2)]

Weight Variation: The average percentage weight variation was within ±7.5% i.e. as per the pharmacopoeia limit.

Disintegration: Disintegration time of the punched tablets was done using Veego Disintegration Test Apparatus. One tablet was placed in each of the 6 tubes of the basket and disintegration was carried out using water maintained at 37^0C. The time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded. (**Disintegration time NMT 15 minutes**) [(2)].

Friability: The friability test was performed using Tablet Friability Tester. This is important to know the mechanical strength of tablets while handling. The friability of the punched tablets. **(Friability NMT 1.0 %.)** [(2)]

Identification: Determine by thin layer chromatography, coating the plate with silica gel.

Mobile Phase- A mixture of 5 volumes of acetone, 3 volumes of ammonia water (prepared by diluting 400 ml of ammonia solution to 1000 ml with water) and 1 volume of water.

Test Solution- Disperse the quantity of powdered tablets containing about 5 mg of voglibose in 40 ml water, shake vigorously and centrifuge. Transfer the supernatant liquid to chromatographic column (prepared by pouring 1.0 ml of strongly acidic ion-exchange resin (H-type) for column chromatography (100 to 200 µm in partical diameter) into a chromatographic column 8 mm in inside diameter and 130mm in height) and allow to flow at a rate of about 5 ml

per minute. Then wash the column with 200 ml of water, and allow flowing with 10 ml dilute ammonia solution (1 in 4) at a rate of about 5 ml per minute. Filter the effluent solution two times through a membrane filter with pore size of not more than 0.22 µm. Evaporate the filtrate to dryness at 50^0 under reduced pressure, dissolve the residue with 0.5 ml of a mixture of equal volumes of water and methanol.

Reference Solution- Dissolve 20 mg of voglibose RS in 2 ml of mixture of equal volumes of water and methanol. Apply 20 µl of each solution. Allow to mobile phase to rise 12 cm. Dry the plate in air and allow to stand in iodine vapors. The principle spot obtained with the test solution corresponds to that with the reference solution, showing a yellow-brown colour and the same R_f value.

Uniformity of Content: (Determine by liquid chromatography)

Use the chromatographic system as described in the assay

Preparation of standard solution: Weight about 25 mg of voglibose RS dissolve in mobile phase and make up the volume to 50.0 ml with mobile phase. Dilute 1.0 ml of the above solution to 25.0 ml with mobile phase.

Preparation of sample: Disperse 1 intact tablet in the mobile phase with the aid of ultrasound and dilute with mobile phase in 10 ml of volumetric flask. To obtain a solution containing 0.002 per cent w/v of voglibose.

Assay: Determine by liquid chromatography

Diluents: Mobile phase.

Preparation of Mobile Phase: a mixture of 1 volume of phosphate buffer pH 6.5 prepared by dissolving 1.56 g of sodium dihydrogen phosphate dehydrate in water to make 500 ml (solution A). Dissolve 3.58 g of sodium hydrogen phosphate dodecahydrate in water to make 500 ml (solution B). To volume of solution A, add solution B until the mixture is adjusted to pH 6.5 and 2 volume of acetonitrile.

Preparation of Standard solution: Weigh about 25 mg of voglibose RS dissolve in mobile phase and make up the volume to 50.0 ml with mobile phase. Dilute 1.0 ml of the above solution to 25.0 ml with mobile phase.

Preparation of sample: Weight and crush 20 tablets in mortal pestle, weigh a equivalent quantity of 2 mg of voglibose in 50 ml mobile phase and diluted it up to 100 ml with mobile phase, Filter.

Table 4: Experimental conditions:

Column	Stainless Steel column 150 mm × 4.6 mm, packed with polyamine chemically bonded to cross linked polyvinyl alcohol polymer (5 µm)
Wavelength	(Excitation : 350 nm) (Emission : 430)
Flow rate	0.4 ml/min
Injection volume	50 µl
Column Temp.	25^0C
	Reaction coil temperature 100^0C
	Coling coil temperature 15^0C

Calculation:

$$\% \text{ Purity} = \frac{\text{Area of spl}}{\text{Area of STD}} \times \frac{\text{wt of std in mg}}{100} \times \frac{1}{25} \times \frac{100}{\text{wt of sample in mg}} \times \frac{\text{avg wt of tablet in mg}}{0.2 \text{ mg}} \times \text{Potency of std}$$

Packing: The primary packing of these tablets was done in Alu-Alu blister. 10 tablets were packed in each Alu- Alu blister

Table 5: Critical process variables

Sr. No.	Processing steps	Critical process parameters	Critical quality attributes
1.	Sifting	1.Sifter sieve size	1.Material retention 2.Integrity of sifter sieve before and after use
2.	Dry mixing	1.Speed of impeller 2.Mixing time	1. Content uniformity in dry mixture (Assay)
3.	Granulation	1.Speed of impeller 2.Granulation time 3. Amperage load	1. Uniformity of wet mass
4.	Drying	1.Drying time 2.Drying temperature	1. Loss on drying
5.	Sifting	1.Sifter sieve size	1.Material retention 2.Integrity of sifter sieve before and after use
6.	Milling	1.Mill screen size	1.Particle size distribution 2.Integrity of mill screen before and after use

7.	Blending and Lubrication	1.Blending time 2.Speed of blender	1.Description 2.Angle of Repose 3.Bulk density 4.Tapped density 5.Carr's Index 6. Hausner Ratio 7. Loss on drying 8. Content uniformity in lubricated granules
8.	Compression	1. Machine speed	1.Description 2.Average weight 3.Weight variation 4.Thickness 5.Hardness 6.Friability 7. Disintegration test 8. Assay
9.	Inspection of compressed tablet	1. Visual inspection	1. Physical defects
10.	Blister packing	1.Sealing temperature 2.Forming temperature 3.Machine speed (Strip/min) 4.Blister air pressure	1.Leak test 2.Sealing & cutting quality (Knurling) 3.Pocket formation quality 4.Overprinting details 5.Defective/empty strips

Table 6: Sampling plan with acceptance criteria:

Processing step	**Justification**	**Sampling plan**	**Sample size**	**Evaluation test parameter**	**Specifications/ Acceptance criteria**
Sifting	To evaluate the sifting time during sifting process	NA	NA	Sieve size (#)	60#
				Material retention	Entire material should be pass through specified sieve
				Integrity of sifter sieve before use	Sieve should be intact without any damage
				Integrity of sifter sieve after use	
Dry mixing	To ensure proper mixing.	NA	NA	Speed of impeller	Slow speed
				Mixing time	10 minutes
Granulation	To ensure uniform binder addition. To obtain uniform granules.	NA	NA	Speed of impeller	Slow speed
					Fast speed
				Granulation time at slow speed	10 mins
				Granulation time at fast speed	15 to 20 mins
				Total granulation time	25 + 5 mins
				Amperage at end point of granulation	10 ± 2 Amps.
				Uniformity of wet mass	To be monitored

Drying	To obtain granules of desired loss on drying/moisture content.	From FBD draw unit dose samples from 6 point locations at the end of drying.	Approx 20 gm	Drying time	10 mins
				Drying temperature	
				Inlet temperature	60.0°C ± 5°C
				Outlet temperature	30.0°C ± 5°C
				Loss on drying	≤ 3.0 % w/w
Sifting	To evaluate the sifting time during sifting process	NA	NA	Sieve size (#)	*30#
				Material retention	Entire material should be pass through specified sieve
				Integrity of sifter sieve before use	Sieve should be intact without any damage
				Integrity of sifter sieve after use	
Milling	To achieve desired granules profile for blending and compression.	NA	NA	Mill screen size	2.00 mm
				Particle size distribution	Particle size should be uniform
				Integrity of sifter sieve before use	Sieve should be intact without any damage
				Integrity of sifter sieve after use	
Blending and Lubrication	To control over blending time determines even distribution of component on overall mix, which is very essential to achieve blend uniformity	From octagonal blender draw unit dose samples from 10 point locations after completion of blending and lubrication	Approx 30gm	Description	White colour free flowing granular powder.
				Blending time	30 ± 5 mins
				Speed of blender	13-15 RPM
				Bulk density	For information
				Tapped density	For information
				Loss on drying	≤ 3.0 % w/w
				Blend content uniformity (Assay)	NLT 90.00% and NMT 110.00% of labeled amount of Ofloxacin content in lubricated granule.

In process compression	To ensure die cavity fill uniformity during in process compression	Draw samples during compression at the start, middle and towards end of compression stage at target speed.	100 Tablets	Machine speed	
				Optimum speed	To be monitored
				Minimum speed	To be monitored
				Maximum speed	To be monitored
				Description	White colour, circular, slightly biconvex uncoated tablets, plain on both sides.
				Average weight	140.00mg ± 2.0% (308.70mg-321.30mg)
				Weight of 20 tablets	2.800gm ± 3.0% (2.716gm-2.884gm)
				Weight variation	± 7.5% of average weight of tablet
				Disintegration time	NMT 15 Mins.
				Thickness	3.30 mm ± 0.2mm
				Hardness	NLT 2.0Kp
				Friability	NMT 1.00%

Sampling diagram with location: Samples Should be collected in triplicate from each sampling point by using sampling thrive and samples collect approximately near to average weight of tablet)

Compression	To meet the desired product specification during compression	Pooled sample of tablets from bin	100 tablets	Description	White colour, circular, slightly biconvex uncoated tablets, plain on both sides.
				Average weight	140.00mg ± 2.0% (137.20mg-142.80mg)
				Weight variation	± 7.5.0% of average weight of tablet
				Hardness	NLT 2.0 Kp
				Friability	NMT 1.00%
				Thickness	3.30mm ± 0.2mm
				Disintegration test	NMT 15 min.
				Assay	NLT 90.00% and NMT 110.00% of 0.2 mg of Voglibose tablet IP
Visual inspection of uncoated tablet	To meet good quality level of product during visual inspection	NA	NA	Physical defects	To be monitored
Finished product analysis	To meet the desired finished product specification during finished product analysis	Pooled sample of tablets from bin	1 carton	All finished product test	As per Finished product specification given in MFR.

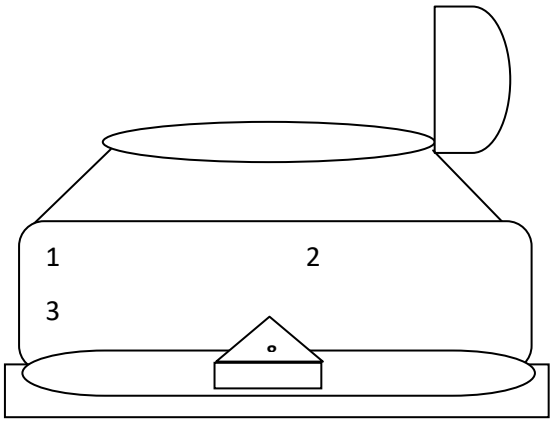


Figure 2: Schematic diagram of Rapid mixer granulator

(1) Top Left (2) Top Middle (3) Top Right (4) Middle Left (5) Middle Center (6) Middle Right (7) Bottom Left (8) Bottom Middle (9) Bottom Right

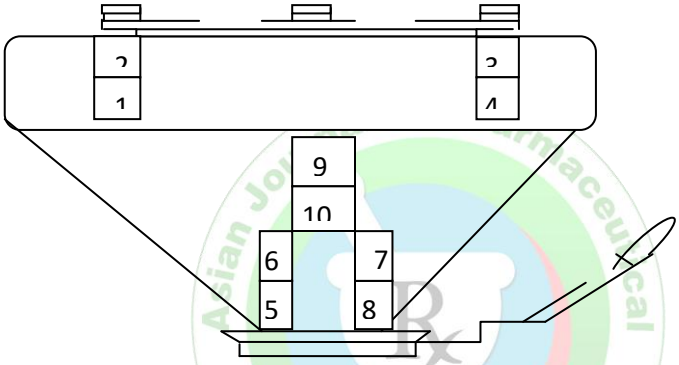


Figure 3: Schematic diagram of Octagonal blender

(1) Top Left Front (2) Top Left Back (3) Top Right Back (4) Top Right Front (5) Bottom Left Front (6) Bottom Left Back (7) Bottom Right Back (8) Bottom Right Front (9) Middle Back (10) Middle centre

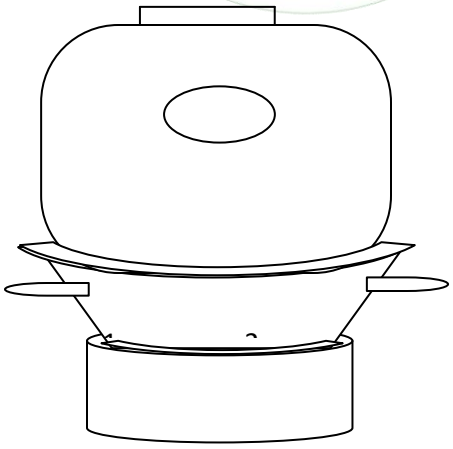


Figure 4: Schematic diagram of Fluidized bed dryer

(1) Top Left (2) Top Middle (3) Top Right (4) Middle Left (5) Middle Center (6) Middle Right (7) Bottom Left (8) Bottom Middle (9) Bottom Right

STABILITY STUDY:

Stability Studies (Accelerated & Real Time) performed with observations made during the Stability Studies of three commercial batches of Voglibose 0.2 mg. This report is applicable for stability study performed for all brands for

Voglibose 0.2 mg manufactured under mfg Lic. No. ND/56 at Snehal Pharma & Surgical Private Limited which is located in Butibori, Dist: Nagpur, Maharashtra, India which comes under Climate Zone IVb as per ICH zone classification.

Conditions	Temperature	Humidity	Frequency (Months)
Accelerated stability study	40.00 ° C ± 2º C	75.00 % RH ± 5% RH	0, 3, and 6
Real time stability study	30.00º C ± 2º C	75.00 % RH ± 5%RH	0, 3, 6, 9, 18, and 24

RESULTS:

Table 7: For Critical Process Parameters

Processing step	Critical process parameter	Acceptance criteria	Observations		
			Batch No. T17L004	Batch No. T18L003	Batch No. T19A013
Sifting	Sieve size(#)	60#	60#	60#	60#
Dry mixing	Speed of impeller	Slow speed	Complies	Complies	Complies
	Mixing time	30 ± 5 mins	30mins.	30mins	30mins
Granulation	Speed of impeller	Slow speed	Complies	Complies	Complies
	Granulation time	15± 5 mins	15mins	15 mins	15mins
	Speed of impeller	Fast speed	Complies	Complies	Complies
	Granulation time	10 ± 5 mins	10 mins	10 mins	10 mins
	Total granulation time	25 ± 5 mins	25mins	25mins	25mins
	Amperage reading	10.0 ± 2 Amps.	10.2Amps	10.5Amps	11.3Amps
Drying	Drying time	25 ± 5 mins	25mins	25mins	25mins
	Inlet temperature	60.0°C ± 5°C	57.0-62.0°C	58.0-63.0°C	58.0-62.0°C
	Outlet temperature	30.0°C ± 5°C	28.0-32.0°C	27.0-33.0°C	28.0-33.0°C
Sifting	Sieve size(#)	30#	30#	30#	30#
Milling	Screen size	2.0 mm	2.0 mm	2.0 mm	2.0 mm
Lubrication and Blending	Blending time	30 ± 5 mins	30 mins	30 mins	30 mins
	RPM of blender	13-15 RPM	14 RPM	14 RPM	14 RPM
	Sieve size(#)	30#	30#	30#	30#
Compression	Machine speed				
	Optimum speed	To be monitored	22RPM	22RPM	22RPM
	Minimum speed	To be monitored	12RPM	12RPM	12RPM
	Maximum speed	To be monitored	38RPM	38RPM	38RPM
Inspection of compressed tablet	Visual inspection	No physical defects	Complies	Complies	Complies
Blister packing (Alu-Alu)	Sealing temperature	185.0ºC ± 5ºC	183.0-188.0ºC	183.0-188.0ºC	183.0-188.0ºC
	Machine speed				
	Optimum speed	To be monitored	20-22 strips/min	20-22 strips/min	20-22 strips/min
	Minimum speed	To be monitored	14-16 strips/min	14-16 strips/min	14-16 strips/min
	Maximum speed	To be monitored	24-26 strips/min	24-26 strips/min	24-26 strips/min

Results for Critical Quality Attributes

Table 8: Observations during Sifting

Processing step	Critical quality attribute	Acceptance criteria	Observations		
			Batch No. T17L004	Batch No. T18L003	Batch No. T19A013
Sifting	Material retention	Entire material should be pass through specified sieve	Complies	Complies	Complies
	Integrity of sifter sieve before use	Sieve should be intact without any damage	Complies	Complies	Complies
	Integrity of sifter sieve after use		Complies	Complies	Complies

Table 9: Observations during Drying

Sample area	Batch No.T17L004	Batch No. T18L003	Batch No.T19A013
Top Left	2.62%	2.38%	2.72%
Top Middle	2.68%	2.44%	2.80%
Top Right	2.57%	2.46%	2.73%
Middle Left	2.71%	2.61%	2.56%
Middle Centre	2.78%	2.49%	2.88%
Middle Right	2.79%	2.53%	2.71%
Bottom Left	2.78%	2.44%	2.88%
Bottom Middle	2.65%	2.51%	2.74%
Bottom Right	2.54%	2.36%	2.82%

Table 10: Observations during Milling

Processing step	Critical quality attribute	Acceptance criteria	Observations		
			Batch No. T17L004	Batch No. T18L003	Batch No. T19A013
Milling	Particle size distribution	Particle size should be uniform	Complies	Complies	Complies
	Integrity of multimill screen before use	Sieve should be intact without any damage	Complies	Complies	Complies
	Integrity of multimill screen after use		Complies	Complies	Complies

- **Observations during Lubrication:**

Table 11: API content uniformity (Voglibose):

Sr. No.	Sample area	Batch No.T17L004	Batch No. T18L003	Batch No.T19A013
1.	Top Left Front	99.36%	98.51%	98.68%
2.	Top Left Back	99.22%	98.68%	98.59%
3.	Top Right Back	100.69%	99.80%	99.85%
4.	Top Right Front	100.60%	98.59%	99.88%
5.	Bottom Left Front	99.28%	99.88%	99.82%
6.	Bottom Left Back	100.64%	99.98%	100.68%
7.	Bottom Right Back	100.88%	100.22%	99.85%
8.	Bottom Right Front	100.55%	99.74%	100.53%
9.	Middle Back	99.45%	99.92%	99.92%
10.	Middle Centre	100.75%	99.83%	99.95%
Min.		**99.22%**	**98.51%**	**98.59%**
Max.		**100.88%**	**100.22%**	**100.68%**
Average		**100.14%**	**99.51%**	**99.78%**
SD		**0.709**	**0.648**	**0.672**
RSD (NMT 2.00%)		**0.708%**	**0.651**	**0.674%**
Process capability index (NLT-1.33)		**2.28**	**2.32**	**2.37**
Acceptance criteria		**NLT 90.00% and NMT 110.00% of labeled amount of Voglibose content in lubricated granule.**		

Table 12: Test results after Blending and Lubrication

Test	Specification	Batch No.T17L004	Batch No. T18L003	Batch No. T19A013
Description	White colour free flowing granular powder.	Complies	Complies	Complies
Angle of Repose	-	$32^0 38'$	$31^0 32'$	$32^0 22'$
Bulk density	-	0.418% w/w	0.428% w/w	0.436% w/w
Tapped density	-	0.552% w/w	0.583% w/w	0.595% w/w
Carr's Index	-	14.59	14.81	14.41
Hausner Ratio	-	1.17	1.17	1.16
LOD	≤ 3.00% w/w	**2.68%w/w**	**2.40% w/w**	**2.82% w/w**

- **In process data for compressed tablets at start, middle and end of compression stage:**

✓ **Batch No.T17L004**

Test	Specification	Start	Middle	End
Description	White colour circular, slightly biconvex uncoated tablets with plain on both sides.	Complies	Complies	Complies
Weight of 20 tablets	2.800 gm ± 3.0% (2.716 gm-2.884gm)	2.805gm	2.823gm	2.800gm
Average weight	140.00 mg ± 2.0% (137.20mg-142.80mg)	140.25mg	141.15mg	140.00mg
Weight variation	± 7.5% of average weight of tablet	137.13mg to 143.24mg	138.30mg to 144.12mg	137.17mg to 142.52mg
Hardness	NLT 2.00Kp	2.14-3.00Kp	2.15-3.85Kp	2.43-2.97Kp
Friability	NMT 1.00 %	0.214%	0.216%	0.215%
Thickness	3.30mm ± 0.2mm	3.26-3.32mm	3.28-3.34mm	3.27-3.38mm
Disintegration test	NMT 15 min.	1-3 min	2-3 min	2-3 min

✓ **Batch No.T18L003:**

Test	Specification	Start	Middle	End
Description	White colour circular, slightly biconvex uncoated tablets with plain on both sides.	Complies	Complies	Complies
Weight of 20 tablets	2.800gm ± 3.0% (2.716gm-2.884gm)	2.784gm	2.814gm	2.820gm
Average weight	140.00mg ± 2.0% (137.20mg-142.80mg)	139.20mg	140.70mg	141.01mg
Weight variation	± 7.5% of average weight of tablet	136.11mg to 142.22mg	137.40mg to 143.60mg	138.18mg to 143.20mg
Hardness	NLT 2.00Kp	2.49-2.90Kp	2.50-2.89Kp	2.69-2.81Kp
Friability	NMT 1.00 %	0.220%	0.210%	0.230%
Thickness	3.30mm ± 0.2mm	3.27-3.37mm	3.25-3.36mm	3.32-3.38mm
Disintegration test	NMT 15 min.	1-3 min	2-3 min	1-3 min

✓ **Batch No.T19A013**

Test	Specification	Start	Middle	End
Description	White colour circular, slightly biconvex uncoated tablets with plain on both sides.	Complies	Complies	Complies
Weight of 20 tablets	2.800gm ± 3.0% (2.716gm-2.884gm)	2.824gm	2.830gm	2.838gm
Average weight	140.00mg ± 2.0% (137.20mg-142.80mg)	141.20mg	141.50mg	141.90mg
Weight variation	± 7.5% of average weight of tablet	138.90mg to141.80mg	138.70mg to 142.30mg	138.10mg to 142.90mg
Hardness	NLT 2.00Kp	4.00-4.30Kp	3.10-4.20Kp	4.20-4.60Kp
Friability	NMT 1.00 %	0.303%	0.318%	0.300%
Thickness	3.30mm ± 0.2mm	3.31-3.35mm	3.27-3.34mm	3.29-3.36mm
Disintegration test	NMT 15 min.	3-4 min	2-3 min	3-4min

Compression machine speed challenge study on various test parameters:

Test parameter	Specification	Observation					
		Minimum speed			Maximum speed		
		Batch No. T17L004	Batch No. T18L003	Batch No. T19A013	Batch No. T17L004	Batch No. T18L003	Batch No. T19A013
Average weight	140.00mg ± 2.0% (137.20mg-142.80mg)	142.10mg	142.25mg	142.40mg	137.60mg	138.18mg	138.15mg
Weight variation	± 7.5% of average weight of tablet	139.25 mg to 144.14 mg	140.13mg to 145.20mg	139.10 mg to 145.30 mg	128.25mg to 145.18mg	129.11mg to 146.22mg	129.23mg to 146.30mg
Hardness	NLT 1.00Kp	4.12-5.10 Kp	4.30-5.15 Kp	4.08-5.20 Kp	1.21-1.74 Kp	1.30-1.90 Kp	1.32-2.05 Kp
Friability	NMT 1.00%	0.075%	0.088%	0.091%	0.522%	0.530%	0.601%
Disintegration test	NMT 15 min	4-5 min	3-5 min	4-5 min	1-2 min	0-1 min	0-1min
Thickness	3.30mm ± 0.2mm	3.36-3.42 Kp	3.38-4.44 Kp	3.37-3.46 mm	3.18-3.24 mm	3.20-3.24 mm	3.17-3.23 mm

Analytical Results For Compressed Tablets

Test	Specification	Batch No.T17L004	Batch No. T18L003	Batch No.T19A013
Description	White colour circular, slightly biconvex uncoated tablets with plain on both sides.	Complies	Complies	Complies
Identification test	TLC	Complies	Complies	Complies
Average weight	140.00mg ± 2.0% (137.20mg-142.80mg)	141.49mg	139.00mg	140.80mg
Weight variation	± 7.5% of average weight of tablet	139.12mg to 144.14mg	136.90mg to 140.00mg	138.50mg to 143.10mg
Hardness	NLT 2.00Kp	3.17-4.25Kp	2.39-2.90Kp	2.60-3.08Kp
Friability	NMT 1.00 %	0.350%	0.330%	0.239%
Thickness	3.30mm ± 0.2mm	3.28-3.36	3.26-3.30mm	3.30-3.38mm
Disintegration test	NMT 15 min.	1-3 min	2-3 min	2-3 min
Uniformity of content	NLT 85.00% and NMT 115.00% of Average content	Complies	Complies	Complies
Assay	NLT 90.00% and NMT 110.00% of 0.2 mg of Voglibose tablet IP	102.50%	98.50%	95.50%

Results For Blister Packing: Alu-alu blister packing in process monitoring evaluation test parameter.

Test parameter	Acceptance criteria	Batch No. T17L004		
		Initial	Middle	End
Counter sealing roller temperature	185.0ºC ± 5ºC	183.0-185.0 ºC	184.0-187.0 ºC	185.0-188.0 ºC
Leak test	None of the strips shall fail in the leak test.	Complies	Complies	Complies
Blister air pressure	5.0-7.0 Kg/cm^2	5.0-6.0 Kg/cm^2	6.0-7.0Kg/cm^2	5.0-7.0 Kg/cm^2
Sealing & cutting quality	Should be proper and uniform	Complies	Complies	Complies
Cavity formation quality	Should be free from damage	Complies	Complies	Complies
Overprinting details	Should be clear & legible	Complies	Complies	Complies
Defective/empty strip	To be nil	Complies	Complies	Complies

Test parameter	Acceptance criteria	Batch No. T19A013		
		Initial	Middle	End
Counter sealing roller temperature	185.0ºC ± 5ºC	183.0-186.0 ºC	184.0-186.0 ºC	186.0-188.0 ºC
Leak test	None of the strips shall fail in the leak test.	Complies	Complies	Complies
Blister air pressure	5.0-7.0 Kg/cm^2	5.0-6.0 Kg/cm^2	6.0-7.0Kg/cm^2	5.0-7.0 Kg/cm^2
Sealing & cutting quality	Should be proper and uniform	Complies	Complies	Complies
Cavity formation quality	Should be free from damage	Complies	Complies	Complies
Overprinting details	Should be clear & legible	Complies	Complies	Complies
Defective/empty strip	To be nil	Complies	Complies	Complies

Test parameter	Acceptance criteria	Batch No. T18L003		
		Initial	Middle	End
Counter sealing roller temperature	185.0ºC ± 5ºC	183.0-186.0 ºC	183.0-187.0 ºC	185.0-188.0 ºC
Leak test	None of the strips shall fail in the leak test.	Complies	Complies	Complies
Blister air pressure	5.0-7.0 Kg/cm^2	5.0-6.0 Kg/cm^2	6.0-7.0Kg/cm^2	5.0-7.0 Kg/cm^2
Sealing & cutting quality	Should be proper and uniform	Complies	Complies	Complies
Cavity formation quality	Should be free from damage	Complies	Complies	Complies
Overprinting details	Should be clear & legible	Complies	Complies	Complies
Defective/empty strip	To be nil	Complies	Complies	Complies

ANALYTICAL RESULTS FOR FINISHED PRODUCT:

One pooled sample from each batch of **VogliboseTablet IP 0.2mg** was collected and analyzed as per finished product specifications given in MFR No. MFRSP/TVFID2-01.The results are as follows:

Sr. No	Test	Specification	Batch No.T17L004	Batch No. T18L003	Batch No.T19A013
1.	Description	White colour circular, slightly biconvex uncoated tablets, plain on both side should be primarily packed in strip having plain aluminium foil as base foil & printed aluminium foil as lid foil. Secondarily packed in printed carton having capacity to hold 10 x 10 tablets.	Complies	Complies	Complies
2.	Printing matter	Printing matters should be as per approved specimen.	Complies	Complies	Complies
3.	Leak test	None of the strips shall fail in the leak test.	Complies	Complies	Complies
4.	Identification test	TLC	Complies	Complies	Complies
5.	Average weight	140.00mg ± 2.0% (137.20mg-142.80mg)	140.49mg	141.80mg	140.60mg
6.	Weight variation	± 7.5% of average weight of tablet	138.20mg to 143.60mg	139.50mg to 144.70mg	137.40mg to 143.23mg
7.	Hardness	NLT 1.00 Kp	3.27-3.55Kp	2.32-2.84Kp	2.63-3.03Kp
8.	Thickness	3.30mm ± 0.2mm	3.26-3.36mm	3.29-3.38mm	3.31-3.36mm
9.	Friability	NMT 1.00%	0.252%	0.180%	0.230%
10.	Disintegration test	NMT 15 min.	2-3 min	1-3 min	2-3 min
11.	Uniformity of content	NLT 85.00% and NMT 115.00% of Average content	Complies	Complies	Complies
12.	Assay	NLT 90.00% and NMT 110.00% of 0.2 mg of Voglibose tablet IP	102.50%	98.50%	95.50%

Yield details The details of yield at all stages of manufacturing were recorded in the process validation report of Voglibose Tablet IP 0.2mg.

Sr. No	Batch No.	Stage	Theoretical yield	Practical yield	% of yield	Limits	Observations
1.	T17L004	Sifting and Milling	13.510 Kg	13.447 Kg	99.53%	**NLT 95.00%**	Complies
		Blending and Lubrication	27.997 Kg	27.964 Kg	99.88%	**NLT 99.00%**	Complies
		Compression	27.997 Kg	27.642 Kg	98.73%	**NLT 98.00%**	Complies
		Packing	2,00,000 Tablets	1,95,740 Kg	97.87%	**NLT 95.00%**	Complies
2.	T18L003	Sifting and Milling	13.510 Kg	13.445 Kg	99.52%	**NLT 95.00%**	Complies
		Blending and Lubrication	27.995 Kg	27.892 Kg	99.63%	**NLT 99.00%**	Complies
		Compression	27.995 Kg	27.847 Kg	99.47%	**NLT 98.00%**	Complies
		Packing	2,00,000 Tablets	1,94,600 Tablets	97.30%	**NLT 95.00%**	Complies
3.	T19A013	Sifting and Milling	13.510 Kg	13.410 Kg	99.26%	**NLT 95.00%**	Complies
		Blending and Lubrication	27.960 Kg	27.916 Kg	99.84%	**NLT 99.00%**	Complies
		Compression	27.960 Kg	27.466 Kg	98.23%	**NLT 98.00%**	Complies
		Packing	2,00,000 Tablets	1,95,680 Tablets	97.84%	**NLT 95.00%**	Complies

Stability report

✓ **T17L004**

Tests	Conditions	Results						
		Testing Frequency (In Months)						
		0	3	6	9	12	18	24
Appearance	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Physical Properties:								
Change of Colour	Accelerated	No Change	No Change	No Change	NA	NA	NA	NA
	Real Time	No Change	No Change	No Change	No Change	No Change	No Change	No Change
Capping	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Cracking	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Interaction with packaging material	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Odour	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not	Not Observed	Not Observed	Not	Not	Not	Not

		Observed			Observed	Observed	Observed	Observed
Water content	Accelerated	2.49	2.55	2.38	NA	NA	NA	NA
	Real Time	2.63	2.24	2.50	2.44	2.26	2.65	2.45
Hardness (Kp)	Accelerated	3.27-3.55	3.29-3.68	3.26-4.25	NA	NA	NA	NA
	Real Time	3.17-3.50	2.29-3.18	2.56-3.23	2.85-3.11	3.79-4.88	2.69 -3.76	2.98-3.61
Disintegration Test (Minutes)	Accelerated	2-3	2-3	2-3	NA	NA	NA	NA
	Real Time	2-3	2-3	1-2	2-3	2-4	2-3	2-3
Assay (%)	Accelerated	102.50	101.90	100.89	NA	NA	NA	NA
	Real Time	102.50	100.42	100.63	100.45	99.98	100.14	99.89
Container & Closure System								
Plain Aluminium Foil	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Printed Aluminium Foil	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Secondary Pack	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies

Tests	**Conditions**	**Results**						
		Testing Frequency (Months) (Bacteria NMT 10^3 cfu/gm)						
		0	**3**	**6**	**9**	**12**	**18**	**24**
Microbial Contamination								
Total Bacterial Count	Accelerated	35	30	40	NA	NA	NA	NA
	Real Time	35	40	41	38	45	34	31
Total Fungal Count	Accelerated	Nil	Nil	Nil	NA	NA	NA	NA
	Real Time	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Escherichia coli	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Salmonella Species	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Shigella Species	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Pseudomonas aeruginosa	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Staphylococcus aureus	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent

✓ **Batch No. T18L003**

Tests	Conditions	Results						
		Testing Frequency (In Months)						
		0	3	6	9	12	18	24
Appearance	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Physical Properties:								
Change of Colour	Accelerated	No Change	No Change	No Change	NA	NA	NA	NA
	Real Time	No Change	No Change	No Change	No Change	No Change	No Change	No Change
Capping	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Cracking	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Interaction with packaging material	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Odour	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Water content	Accelerated	2.40	2.56	2.42	NA	NA	NA	NA
	Real Time	2.42	2.50	2.48	2.62	2.45	2.66	2.61
Hardness (Kp)	Accelerated	2.39-2.90	2.42-2.68	3.02-3.60	NA	NA	NA	NA
	Real Time	2.11-2.48	2.56-2.71	2.32-2.42	2.19-2.98	3.01-3.66	2.10-2.92	3.11-3.65
Disintegration Test (Minutes)	Accelerated	2-3	2-3	2-3	NA	NA	NA	NA
	Real Time	2-3	1-3	2-3	2-4	2-3	2-3	2-3
Assay (%)	Accelerated	98.50	99.52	98.61	NA	NA	NA	NA
	Real Time	98.50	99.27	99.18	99.97	98.26	98.05	97.92
Container & Closure System								
Plain Aluminium Foil	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Printed Aluminium Foil	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Secondary Pack	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies

Tests	Conditions	Results						
		Testing Frequency (Months) (Bacteria NMT 10^3 cfu/gm)						
		0	3	6	9	12	18	24
Microbial Contamination								
Total Bacterial Count	Accelerated	24	29	31	NA	NA	NA	NA
	Real Time	32	29	41	42	38	28	19
Total Fungal Count	Accelerated	Nil	Nil	Nil	NA	NA	NA	NA

	Real Time	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Escherichia coli	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Salmonella Species	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Shigella Species	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Pseudomonas aeruginosa	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Staphylococcus aureus	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent

✓ **B. No. T19A013**

Tests	**Conditions**	**Results**						
		Testing Frequency (In Months)						
		0	**3**	**6**	**9**	**12**	**18**	**24**
Appearance	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Physical Properties:								
Change of Colour	Accelerated	No Change	No Change	No Change	NA	NA	NA	NA
	Real Time	No Change	No Change	No Change	No Change	No Change	No Change	No Change
Capping	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Cracking	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Interaction with packaging material	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Odour	Accelerated	Not Observed	Not Observed	Not Observed	NA	NA	NA	NA
	Real Time	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed	Not Observed
Water content	Accelerated	2.82	2.76	2.78	NA	NA	NA	NA
	Real Time	2.82	2.79	2.48	2.49	2.56	2.39	2.39
Hardness (Kp)	Accelerated	2.60-3.08	2.66-2.98	2.87-3.25	NA	NA	NA	NA
	Real Time	2.67-3.11	2.60-3.56	2.45-2.89	2.64-3.50	2.80-3.17	2.89-3.45	2.46-3.09
Disintegration Test (Minutes)	Accelerated	2-3	2-4	2-4	NA	NA	NA	NA
	Real Time	2-3	2-4	2-3	2-3	2-3	2-4	2-3
Assay (%)	Accelerated	95.50	96.21	95.78	NA	NA	NA	NA
	Real Time	95.50	95.52	95.78	95.45	95.49	95.55	95.49
Container & Closure System								
Plain Aluminium Foil	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies

Printed Aluminium Foil	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Secondary Pack	Accelerated	Complies	Complies	Complies	NA	NA	NA	NA
	Real Time	Complies	Complies	Complies	Complies	Complies	Complies	Complies

Tests	**Conditions**	**Results**						
		Testing Frequency (Months) (Bacteria NMT 10^3 cfu/gm)						
		0	**3**	**6**	**9**	**12**	**18**	**24**
Microbial Contamination								
Total Bacterial Count	Accelerated	24	29	31	NA	NA	NA	NA
	Real Time	32	29	41	42	38	28	19
Total Fungal Count	Accelerated	Nil	Nil	Nil	NA	NA	NA	NA
	Real Time	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Escherichia coli	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Salmonella Species	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Shigella Species	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Pseudomonas aeruginosa	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Staphylococcus aureus	Accelerated	Absent	Absent	Absent	NA	NA	NA	NA
	Real Time	Absent	Absent	Absent	Absent	Absent	Absent	Absent

CONCLUSION:

After evaluation of above validation data of three batches it is concluded that,

Sifting: The sifting of Dicalcium phosphate, Maize starch, Maize starch (Paste) and Voglibose, Purified talc, Microcrystalline cellulose, Maize starch, Croscarmellose sodium, Crospovidone, Aerosil was carried out using Vibro sifter fitted with sieve **30# and 60#** respectively.

Conclusion: The sifting of Dicalcium phosphate, Maize starch, Maize starch (Paste) and Voglibose, Purified talc, Microcrystalline cellulose, Maize starch, Croscarmellose sodium, Crospovidone, Aerosil with sieve **30# and 60#** is considered to be satisfactory.

Dry mixing: The dry Mixing of Dicalcium phosphate, Maize starch and Maize starch (Paste) were performed in RMG for **10 minutes** keeping impeller slow speed in all three consecutive validation batches.

Conclusion: Based on the obtained data, it can be concluded that dry mixing of Dicalcium phosphate, Maize starch and Maize starch (Paste) for **10minutes** keeping impeller slow speed is considered to be satisfactory.

Wet granulation: The wet granulation of the product was performed in RMG. The binder solution was added to the dry mix and mixing was performed for **10 minutes** keeping impeller slow speed & then again for **15-20 minutes** keeping impeller fast speed for all three consecutive process validation batches. The total kneading time was kept for **25 minutes.** The amperage reading for impeller at the end point of granulations was **10.2-11.3 Amps.**

Conclusion: Based on the obtained data it can be recommended that, Add binder solution to the dry mix powder and mixing is to be performed for **10 minutes** keeping impeller slow speed & then again for **15-20 minutes** keeping impeller fast speed considered being satisfactory for all three consecutive process validation batches. The total granulation time is kept for **25 minutes.** The amperage reading for impeller at the end point of

granulations is considered to be satisfactory at **10.2-11.3 Amps**.

Drying: The drying activity of all three consecutive batches was carried out in Fluid bed dryer. After the drying stage the pooled samples were withdrawn for loss on drying which were also found within the in-process specification. The inlet temperature was observe between **57.0-63.0ºC** and outlet temperature between **27.0-33.0ºC** in all three consecutive process validation batches. The final drying time was kept for **20 minutes.**

Conclusion: Based on data of the drying and LOD obtained from the samples after drying process provides evidence that the final drying time of **20 minutes** with inlet temperature of **57.0-63.0ºC** and outlet temperature **27.0-33.0ºC** was sufficient to ensure required drying of granules till LOD of the dried granules is **≤ 3.0 % w/w**

Sifting and Milling: The sifting of dried granules was carried out using Vibro sifter fitted with **30#**. Milling of dried granules done through multi mill fitted with **2.0mm** screen with knives in forward direction**.**

Conclusion: The sifting of dried granules with sieve **30#** is considered to be satisfactory. The granules obtained from multi mill fitted with **2.0mm** screen with knives in forward direction at slow speed which can be evident from good flow properties of granules. The percentage yield of dried materials at sifting and milling stage was found to be **99.26% to 99.53%.**

Blending and Lubrication: The blending and lubrication of granules carried out in octagonal blender. Firstly, dried granules were blended without lubricants for **10 minutes** and with specified quantity of lubricants with Voglibose for **30 minutes.** The speed of blender was kept at **14 RPM** in all three consecutive validation batches. Total blending time was **40 minutes**. The samples were withdrawn for description, Angle of repose, bulk density, tapped density, carr's index, hausner's ration, Loss on drying and API content uniformity, which are found meeting to the acceptance criteria.

Conclusion: Based on the obtained analytical data it can be concluded that, the total blending time for **40minutes** in specified octagonal blender is capable to ensure proper mixing of the specified quantity of lubricants with Voglibose and granules having good flow properties to the blend. The percentage yield of lubricated granules at blending and lubrication stage was found to be **99.63% to 99.88%.**

Compression: The samples collected during the compression operation were found to be complying as per the acceptance criteria with respect to the parameters evaluated. The minimum speed of compression for all three batches was kept at **12RPM** and maximum speed of compression for all three consecutive process validation batches was kept at **38RPM**. The optimum speed was kept at **22RPM** in all three consecutive validation batches.

Conclusion: Based on the obtained analytical data it can be concluded that, at compression stage all the physical test parameters of all three consecutive process validation batches were found well within the acceptable limits. The percentage yield of compressed tablet at compression stage was found to be **98.23% to 99.47%.**

Blister packing (Alu-Alu): The samples collected during the blister packing (Alu-Alu) operation were found to be complying as per the acceptance criteria with respect to the physical test parameters evaluated. The machine optimum speed for all three batches at initial, middle and end of blister packing (Alu-Alu) stage was kept at from **20-22 strips/min.** The sealing temperature was observed between **183.0-188.0ºC** respectively in all three consecutive process validation batches. The blister air pressure was observed between **5.0-7.0 Kg/cm^2.**

Conclusion: Based on the obtained evaluation data it can be concluded that, at blister packing (Alu-Alu) stage all the physical test parameters of all three consecutive process validation batches were found well within the acceptable limits. The percentage yield of packed tablet at final packing stage was found to be **97.30% to 97.87%.**

Process capability index (Cpk): The minimum process capability index values for API content uniformity during lubrication stage were found within acceptance criteria and shows that process was capable to produce product meeting its predetermined specification.

Stability Study: A preliminary assigned shelf life of 24 months had been derived from the primary and supportive data obtained from the accelerated stability and real time study. Accelerated stability study and real time stability study confirms the stability of Voglibose 0.2 mg tablet during testing.

- At present 24 months stability study of batch no. T17L004, T18L003 and T19A013 are completed. There are no deviations observed in the accelerated and Real Time stability studies.
- All the analytical data derived during process validation of Voglibose Tablet IP 0.2mg with reference to MFR (Master Formula Record) and BMR (Batch Manufacturing Record).
- The results from the analytical data of process validation of Voglibose Tablet IP 0.2mg were excellent and very near to true values.
- Based on evaluation of above manufacturing process and analytical data it is concluded that the employed manufacturing process for Voglibose Tablet IP 0.2mg shall be consistently & reproducibly produce a product which meeting its predetermined specification hence it is considered to be validated.

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