REPORT FOR
PROCESS VALIDATION STUDY
OF
VIAL DRY POWDER FILLING
Pantoprazole sodium powder for injection
USP 40 mg
PROTOCOL Ref No……
Report No:……

TABLE OF CONTENTS

1.0 POST APPROVAL SIGNATURE

This is a specific summary report for Process validation study of dry powder vials process line, which is installed in vial manufacturing area.

This Protocol is approved by the following:

Functional Area	Name	Signature	Date
Prepared by			
Quality Assurance Department			
Reviewed & Approved by			
Production Department			
Quality Control Department			
Quality Assurance Department			

2.0 OBJECTIVE

Objective of this report is to collect sufficient data to establish that the dry powder vial manufacturing line performs to meet the desired specification in consistent manner.

3.0 OVERVIEW

The manufacturing and processing of dry powder vial filling has to be performed under aseptic conditions, whereby the manufacturer has to ensure that the sterilization processes of processing equipment, manufacturing tools, and containers & closures, miscellaneous items are adequately validated to provide necessary sterility assurance.

In addition, the critical area for aseptic processing of dry powder vial filling has to be maintained as per Area classification requirements specified by different regulatory guidelines.

The sterilization processes of manufacturing aids and the aseptic manufacturing practices have to be performed in a manner, to provide high degree of sterility assurance to the product.

Considering these objectives, a process validation study is designed to demonstrate the sterility assurance levels, Vial fill weights, vial filling, sealing speeds are adequately designed.

4.0 METHODOLOGY

The process validation study was initiated as per the approach described in the Validation protocol PVP-008 and execution of Batch Manufacturing record with MPR No: ……. Process validation Study is carried out by employing three 10000 vials batch sizes.

5.0 PROCESS DESCRIPTION FOR PROCESS VALIADTION

Obtained line clearance as per– "Line and Area Clearance in Production Formulation" and record in respective BMR.

Rubber Stoppers, Machine parts & accessories, Vial Tubular Type-I, 10 ml amber color are cleaned and sterilized as per sop.

Filling machine parts were assembled aseptically and recorded in respective batch Records. Filling line was run as per standard operating procedure and activities were recorded in respective batch records & log books.

The Pantoprazole sodium sterile powder is taken in to the aseptic area and charged in to the dosing disk and adjust to the required fill weight.

After completion of vial filling bunging and sealed vials are then transferred to packing area for Visual inspection.

Aseptic filling, bunging and sealing process are done under aseptic conditions.

6.0 ACCEPTANCE CRITERIA

All the critical process steps and sampling plan should comply with the standard specifications given in the protocol.

7.0 LIST OF EQUIPMENT USED IN THE PROCESS

S.No.	Equipment Name	Equipment No.	Operation SOP No.	Cleaning SOP No.
1.0	Autoclave			
2.0	Dry Heat Sterilizer			
3.0	Vial Washing Machine			
4.0	Vial Depyrogenation Tunnel			
5.0	Dry powder vial Filling Machine			
6.0	Vial Sealing Machine			
7.0	Visual Inspection Table			
8.0	Visual Labelling Machine			
9.0	Vacuum Leak Test Apparatus			
10.0	Bung Washing Machine			
11.0	Mobile Laminar Air Flow			
† Current effective version to be referred				

8.0 SELECTION OF THE BATCH AND SIZE

Three consecutive batches (……) with batch size 10,000 10 ml Tubular USP-I amber colored Vials in each batch has been validated.

Batch Formula:

S. No	BATCH No.	NAME OF INGREDIENT	UNIT	STD Qty/Batch	DISPENSED Qty	A R No
01		Pantoprazole Sodium Sterile powder USP	KG	0.400		
		Tubular vials USP-1 10 ml Amber colored@	Nos	10200		
		Rubber stoppers(20 mm Bromobutyl) @	Nos	10200		
		20 mm Aluminiumflip off Seals (Red color) @	Nos	10200		
02		Pantoprazole Sodium Sterile powder USP	KG	0.400		
		Tubular vials USP-1 10 ml Amber colored@	Nos	10200		
		Rubber stoppers(20 mm Bromobutyl) @	Nos	10200		
		20 mm Aluminiumflip off Seals (Red color)	Nos	10200		

03		Pantoprazole Sodium Sterile powder USP	KG	0.400		
		Tubular vials USP-1 10 ml Amber colored@	Nos	10200		
		Rubber stoppers(20 mm Bromobutyl) @	Nos	10200		
		20 mm Aluminiumflip off Seals (Red color) @	Nos	10200		

@ : 5% Excess Vials shall be dispensed.

9.0 VIAL WASHING AND DEPYROGENATION

The Vial washing and Depyrogenation have been carried out as per Standard Operating Procedures. All the vial washing parameters and vial Depyrogenation temperatures are maintained as per standard parameters in all the three process validation studies. All the tunnel Depyrogenation reports are attached with the BMR.

10.0 RUBBER BUNGS AND FLIP OFF SEALS

The rubber bungs have been cleaned and sterilized as per standard operating procedures. Rubber bungs sterilization reports have been attached with BMR. The flip off seals have been sanitized as per procedure.

Sterilization Details of Components:

S.No	Batch No	Type of Components	DATE	Ster Start Time	Ster End Time	Min Temp Maintained
01		Machine Parts				
		Rubber Bungs				
		Vials				
02		Machine Parts				
		Rubber Bungs				
		Vials				
03		Machine Parts				
		Rubber Bungs				
		Vials				

Vial filling and Bunging:

Vial filling and Bunging are done as per protocol and BMR. Vial fill weight and fill speed are maintained constant in all the three process validation trials.

S.No	Batch No	Date	Vial Filling		Fill Weight	
			Start	End	Maximum	Minimum
01						
02						
03						

VIAL SEALING

All the vials are filled and sealed as per BMR and sealed vials are checked for leak tests and found pass. The sealing machine speed is maintained constant in all the three validation batches.

S.No	Batch No	Vial Sealing			Leak Test
		Date	Start time	End time	
01					PASS
02					PASS
03					PASS

Yield and Reconcillation:

Three process validation batches yield percentages are calculated as per BMR and are within in limits.

S.No	Batch No	Date	Batch yield %	Reconcillation %
01				
02				
03				

Result and Evaluation

All the in process and finished product samples are analyzed and are within limits.

S. No	BATCH No	Type of Samples	Stage	Analysis For	Result	A R No
01		Empty Vials	From Filling Line	BET	PASS	
				Sterility	PASS	
		Rubber	From Filling Line	BET	PASS	

S. No	BATCH No	Type of Samples	Stage	Analysis For	Result	A R No
		Bungs		STERILITY	PASS	
02		Empty Vials	From Filling Line	BET	PASS	
				Sterility	PASS	
		Rubber Bungs	From Filling Line	BET	PASS	
				STERILITY	PASS	
03		Empty Vials	From Filling Line	BET	PASS	
				Sterility	PASS	
		Rubber Bungs	From Filling Line	BET	PASS	
				STERILITY	PASS	

14.0 FINISHED PRODUCT SPECIFICATIONS

S. No	TEST		SPECIFICATION			
1.0	Description		A labelled USP type I glass vial containing white to off white free flowing powder after reconstitution gives clear and transparent solution.			
2.0	**Identification:**					
	By HPLC Method		The retention time of the major peak in the chromatogram of the sample solution corresponds to that in the chromatogram of working standard in assay test.			
	By Chemical Method:		It gives a reaction of sodium.			
3.0	**Reconstitution for injection**					
	A	for injection	To reconstitute add 10 ml sodium chloride injection IP 0.9%w/v shake well			
	B	for infusion	To reconstitute add 100 ml sodium chloride injection IP 0.9% w/v shake well			
4.0	**Constituted solution**					
	A	Completeness of solution	The reconstitute solution should become clear			
	B	Clarity of	Constituted solution should as clear			

S. No	TEST	SPECIFICATION			
	solution	as diluent			
5.0	pH of reconstituted solution	9.0 to 12.0			
6.0	**Related Substances (By HPLC)**				
	Impurity A	NMT= 0.2%			
	Impurity B	NMT =0.1%			
	Impurity C	NMT=0.1%			
	Impurity E	NMT=0.1%			
	Impurity D+F	NMT=0.2%			
	Any unspecified impurities	NMT=0.1%			
	Total Impurities	NMT=0.5%			
7.0	Water content (by KF)	NMT= 3.0% w/w			
8.0	Bacterial Endotoxins	Not more than 1.25 EU/mg			
9.0	Sterility test	The contents of the sealed containers should comply with the test of sterility.			
10.0	**Particulate matter:**				
	Visible Particulate Matter	Free from any visible particulate matter			
11.0	**Sub-visible Particulate Matter**				
	10 micron or larger	6000 per vial			
	25 micron or larger	600 per vial			
12.0	Uniformity of Weight	Not more than two of the individual weights deviate from the average weight by more than 10% and none deviates by more than 20 %.)			
13.0	Uniformity of dosage units	Between 85% to 115% of label claim and RSD NMT 6.0%			
14.0	**Assay** Each Vial Contains Pantoprazole sodium USP eq .to Pantoprazole 40 mg	90% to 110%			

15.0 SUMMARY

15.1 A summary has been prepared based on the data generated on three consecutive Process Validation Batches

15.1.1 Qualifications of the facility and utilities like qualification of HVAC, area for viable and non-viable counts, Compressed air, Nitrogen, pure steam system, and Water system etc. are completed.

15.1.2 The qualification of equipment like Autoclave, Dry heat sterilizer, Vial washing machine, Tunnel, Filling, capping machines, sealing machine are completed .

15.1.3 All concerned persons which includes Production, Microbiology, and Maintenance departments are given training on Process validation Study. All necessary aspects related to the process validation are explained in the training program.

15.1.4 All the concerned persons are given training on Entry, Exit and gowning Procedure for Aseptic Processing Area (APA).

15.1.5 All the SOP's related to Aseptic manufacturing process, cleaning and sanitization, fumigation and Environmental monitoring etc. are completed before starting Process validation.

15.1.6 Environmental monitoring for viable and non-viable particle counts, temperature, Relative humidity, Differential pressure record and water Analysis Reports are reviewed before starting the process validation and are in compliance.

15.1.7 All the equipment's used in process validation have been qualified before process validation study.

16.0 CONCLUSION

The process validation have been conducted with as per protocol and as per the results of validation studies and evaluation of results, it can be concluded that the aseptic manufacturing process, sterilization process of equipment's and components, environmental control and monitoring program and aseptic practices of personnel were adequate to manufacture the sterile drug product in the facility and the process used for the manufacturing of Pantoprazole sodium powder for injection 40 mg/vial of batch size 10000 vials is capable of producing the consistent results as per protocol .