PROCESS VALIDATION REPORT FOR ACYCLOVIR STERILE

PROTOCOL Ref No.:
REPORT NUMBER:

TABLE OF CONTENTS

1.0 POST APPROVAL SIGNATURE

Signature of this summary report approval page indicates agreement with the process validation of Acyclovir sterile approach, evaluation of results, conclusion and recommendations described in this document.

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			
Microbiology Department			
Quality Assurance Department			

2.0 OBJECTIVE

The objective of the process validation report to summarize to conclude the results of process validation of all stages in the Acyclovir sterile, which is being manufactured.

3.0 PURPOSE & SCOPE

Process validation report provided the documented evidence that the manufacturing process of Acyclovir Sterile is capable of delivering the product meeting the pre-defined Specifications.

4.0 VALIDATION PLAN & METHODOLOGY

4.1 Prerequisites for Process Validation:

⇒ Training has been given to concern purpose which involve the Process validation Procedure, Documentation Practices for filling of report, Overall strategy of Validation process, General precautions / guidelines followed during validation.

⇒ The batches are manufactured as per the Batch manufacturing record issued from quality assurance.

⇒ Three consecutive batches of standard weight of 110 kg were taken for process validation study.

⇒ The raw material used for manufacturing were from approved vendors and approved by quality control.

⇒ The qualification of all the equipment's used in manufacturing process are ensured.

⇒ The calibration and preventive maintenance of equipment's used in process validation are ensured.

⇒ The cleaning and sterilization of equipment's used in the process validation are completed before process validation.

⇒ The analytical methodologies followed during testing of finished products are validated.

4.2 Product description

Product Name : Acyclovir Sterile

Batch size : 110.00 kg

MPR Ref No : ……..

4.3 Batch Formula of Acyclovir Sterile

List of Raw Material required in the manufacture of the product is given below. Prior to the start of validation study all the input raw material were tested as per standard testing procedure and the quality is found to be in compliance with the predefined specifications.

S.No.	Name of Ingredient	Quantity/Batch		Specification No	STP No
		Unit	Quantity		
1.	Acyclovir USP	KG	110.00*	RS009	RP009
2.	ENO Carbon	KG	0.500$	RS016	RP016
3.	Sodium Hydroxide	KG	q.s	RS015	RP015
4.	Water For Injection USP	KG	424.00@	RS001	RP001
5.	Aluminum Canisters with lid, 20lts capacity.	Nos	13.00	PS002	PP002

* This quantity is based on 100%w/w assay.
@ Water for Injection shall be dispensed by production personnel, it will not appear in the final product except in traces.
$ It will not appear in the final product.
NA Not Applicable.
q.s Quantity Sufficient

The input of the raw materials in all the 3 Consecutive Batches are taken as per standard quantities with reference to batch formula.

S.No.	Name of Ingredient	Std quantity		Actual Batch Quantity		
		Unit	Qty			
1.	Acyclovir USP	KG	110.00*			
2.	ENO Carbon	KG	0.500$			
3.	Sodium Hydroxide	KG	q.s			
4.	Water For Injection USP	KG	424.00@			
5.	Aluminum Canisters with lid, 20lts capacity.	Nos	13.00			

4.4 Raw Material Quality Data

The quality data of Raw Material were compiled as per approved specification and all raw materials are within specification.

S.No.	Name of Ingredient	Std quantity		AR No		
		Unit	Qty			
1.	Acyclovir USP	KG	110.00*			
2.	ENO Carbon	KG	0.500$			
3.	Sodium Hydroxide	KG	0.200			
4.	Water For Injection USP	KG	424.00@			
5.	Aluminum Canisters with lid, 20lts capacity.	Nos	13.00			

4.5 List of Major Equipment's used during process validation of Acyclovir Sterile

S.No.	Equipment Name	Equipment No.	Operation SOP No.	Cleaning SOP No.
1.	Lyophilizer			
2.	Autoclave			
3.	Dry Heat Sterilizer			
4.	Solution preparation tank			
5.	Solution holding vessel			
6.	Process line Cartridge Filter (1.2µm)			
7.	Process line Cartridge Filter (0.2µm)			
8.	Process line Cartridge Filter (0.2µm)			
9.	Sparkler Filter			
10.	Peristaltic Pump			
11.	Powder Processing System			
† Current effective version to be referred				

4.6 Obtained Yield Details

The output of the three consecutively charged batches gives consistency in the product yield.

S.No.	Batch No	Start Date	End Date	Obtained Qty (Kgs)
1.				
2.				
3.				

5.0 RESULT AND EVALUATION

5.1 In process Analysis Data

The in process samples have been analyzed as per the standard testing method (IP003) of Acyclovir sterile and the results are within specifications.

S.No.	Sample Stage	Analysis For		Results		
			Limits	AACV13001	AACV13002	AACV13003
1.	WFI Sample from (PDE-029) before batch charging	BET	Should Pass	PASS	PASS	PASS
2.	After product solution preparation from (PDE-029)	pH	11-12			
3.	After product solution receiving in aseptic area from (PDE-031)	pH	11-12			
		Sterility	Should pass			
		BET	Should pass			
4.	During Solution filling in to Lyo trays(Start)	pH	11-12			
		Sterility	Should pass			
		BET	Should pass			
5.	During Solution filling in to Lyo trays(Middle)	pH	11-12			
		Sterility	Should pass			
		BET	Should pass			
6.	During Solution filling in to Lyo trays(End)	pH	11-12			
		Sterility	Should pass			
		BET	Should pass			
		Moisture content	NMT 5.5%			
		Assay	98-101%			

5.2 Finished Product Analysis Data

S. No.	TEST	SPECIFICATION			
1	**Characters:**				
	Appearance	A white or almost white, crystalline powder			
	Solubility	Freely soluble in water			
2	**Identification:**				
	By HPLC	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	Clarity of solution 1g in 10ml water	The solution is clear and absorbance<0.1 AU at 430 nm			
4	**Related Substances (By HPLC):**				
	Guanin (Imp-B)	Not more than 1.0%			
	Impurity at RRT 0.7	Not more than 0.15%			
	Any other specified impurity	Not more than 0.5% (each)			
	Any Unspecified Impurity	Not more than 0.1%			
	Sum of all Impurities	Not more than 1.0%(other than guanine)			
5	Water content (by KF)	Not more than 5.5%w/w			

S. No.	TEST	SPECIFICATION			
	determined on 0.5g sample				
6	pH(50 mg/ml)	11 to 12			
7	Assay (By HPLC)	NLT 98.0% and NMT 101.0% on the anhydrous basis.			
8	**Residual Solvents:**				
	Ethyl acetate	5000ppm			
	Methanol	3000ppm			
9	Bulk Density (un-tapped)	Informative			
10	Tapped Density 100 Taps	Informative			
11	Bacterial Endotoxins	NMT 0.174 EU/mg			
12	Sterility test	Should pass the test			
13	Visible Particulate Matter	Free from any visible particulate matter			
14	Sub-Visible Particulate Matter				
	10 micron or larger	6000			
	25 micron or larger.	600			

6.0 SUMMARY

Three batches of Acyclovir Sodium sterile (Batch No.: …. were manufactured consecutively to validate all the major operations of the manufacturing process for critical steps. The batches were manufactured as defined in the approved master manufacturing record and batch production record. No unauthorized or unrecorded modifications had taken place.

All the equipment's used in the manufacture of the Acyclovir Sterile were cleaned followed by 'sterilization in place' as defined in the standard operating procedures. All the process operations are monitored critically and observations are recorded. As defined in the protocol, wherever required, in-process testing is carried out during manufacturing.

Process or analytical deviations are not reported during validation. Samples drawn as per the plan and from pre-defined locations all the results are well within the specification. All the three batches are tested as per predefined specification and testing procedure of finished product. The analytical results are tabulated indicates that there in consistency in the results and all the batches are passing as per predefined specification for the product.

Prior to the start of validation study all the input raw material were tested as per standard testing procedure and the quality is found to be in compliance with the predefined specifications. The analytical methodologies followed during testing of finished products are validated .All the equipment's used during manufacturing were qualified for DQ / IQ / OQ / PQ. The vendor (Manufacturer) of the critical (Key) raw material is qualified. The data generated during validation is reviewed and complied.

7.0 CONCLUSION

The process parameters, in process and finished product analysis indicate that the Manufacturing process of Acyclovir Sterile is capable to produce a finished Product that meets its predefined specifications and quality attributes consistently.