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RESEARCH ARTICLE

Process Validation of Cefuroxime Axetil Film Coated Tablets

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ABSTRACT

Validation is one of the important steps in achieving and maintaining the quality of the final product. If each step of production process is validated we can assure that the final product is of the best quality. The study presented here provides the assurance that the manufacturing procedure is suitable for intended purpose and the product consistently meets predetermined specifications and quality attributes, as per specified master formula record. It also provides documented evidence for the operation sequence of manufacturing process and to determine the critical parameters and variables in the process of manufacturing of the tablets.

KEYWORDS

Process validation, Tablets, Quality, Validation Protocol, Manufacturing Process.

INTRODUCTION

The prime objective of any pharmaceutical process is to manufacture products of requisite attribute and quality consistently, at the lowest possible cost. Validation is a necessary part of a quality assurance program and is fundamental to an efficient production operation. Process validation establishes the flexibility and constraints in the manufacturing process controls in the attainment of desirable attributes in the drug product while preventing undesirable properties. Process Validation is an important and systematic approach to identifying, measuring, evaluating, documenting, and re-evaluating a series of critical steps in the manufacturing process that require control to ensure a reproducible final product.

Validation Protocol[8]

A written plan of actions stating how process validation will be conducted;

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it will specify who will conduct the various tasks and define testing parameters; sampling plans, testing methods and specifications; will specify product characteristics, and equipment to be used. It must specify the minimum number of batches to be used for validation studies, acceptance criteria and who will approve/disapprove the conclusions derived from the study. An ideal validation protocol contains the following:

a) Objective and General Information.

b) List of equipment and their qualification status.

c) Facilities qualification.

d) Manufacturing formula & manufacturing procedure narrative.

e) Process flow diagram.

f) Label claim.

g) List of critical processing parameters and critical excipients.

h) Sampling, tests and specification.

i) Acceptance criteria.

Validation Life Cycle[7]

Validation is a continuing and evolving process. The validation process extends from the very basic to a very broad theological and methodical investigation. Its scope encompasses documentation, revision control, training and maintenance of the system and process.

Validation procedure

1. Three batches of 1,20,000 tablets batch size to be manufactured as described in the batch manufacturing record.
2. Current version of standard operating procedures to be followed.
3. Record the observations at compression stage in the below specified data sheets.
4. Record the yield after compression.

Process flow chart: Cefuroxime Axetil 500 mg

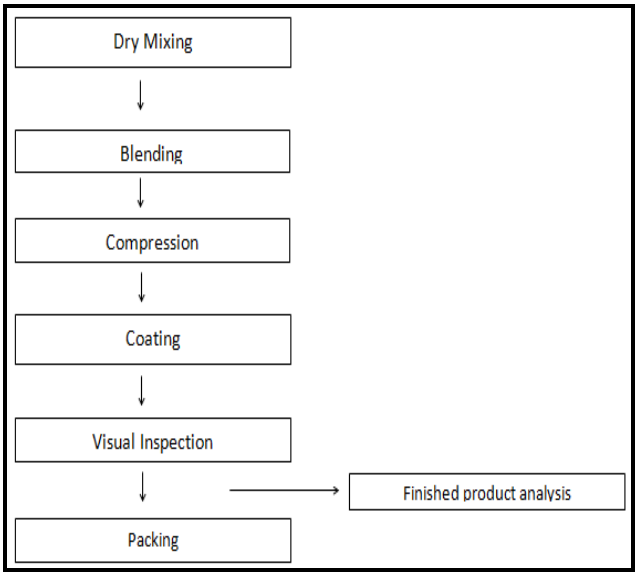

Table 1: Details of Sampling and Analysis

Sampling Device	Clean and dry Stainless Steel Sampling rod (Unit dose type)	
Sampling Container	Clean and dry 10ml vial with closures,labeled with product name , batch number, stage, Sample ID. And Sampler's name	
Sampling interval	1) After completion of 30 mins dry mixing process.	
	2) After completion of 30 mins Blending process.	
Sampling Location	1) Figure-1 for Dry mixing process. (Total 05 locations)	
	2) Figure-2 for Blending. (Total 11 locations)	
Number of Samples	05 and 11 Samples shall be taken from the Cage Blender as shown in Figure-1 & Figure-2 respectively.	
Sample Quantity	Each Sample from all locations shall be one to three times of the unit dose weight of Cefuroxime Axetil BP 500mg. Each sample shall be taken in triplicate for contingency. Entire sample quantity shall be taken for analysis and do not subdivide any sample.	
Testing	1) Content Uniformity	2) Blend Uniformity

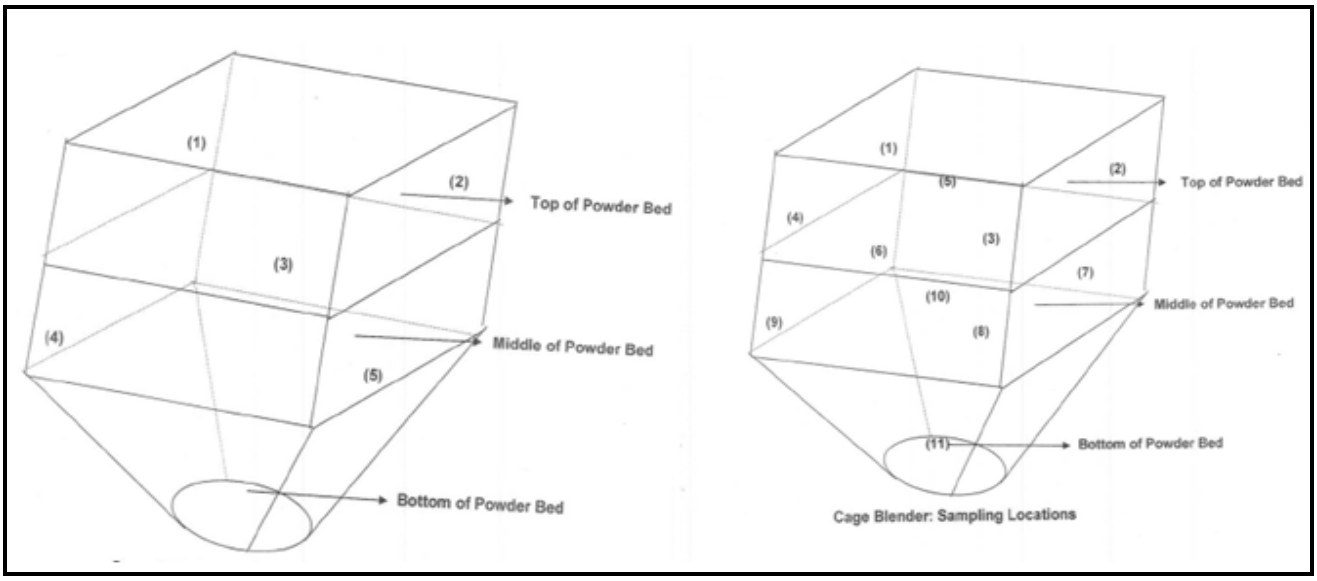

Figure 1 & 2: Sampling Locations

Table 2: Physical parameters to be observed during compression

Parameter	Standard
Description	Blue color capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.
Average mass	990 mg ± 2%
Mass variation	990 mg ± 5%
Hardness	Between 10-35kg (100-350N)
Thickness	6.30 mm ± 0.2mm
Disintegration time	NMT 5.0 mins.
Friability	NMT 1.0%

Run the compression machine at different speeds and check the samples for all above physical parameters.
Note: Approximately one third of the compression to be carried out at each speed and record the speed and timings in the BMR.

Table 3: Sampling plan and testing summary

Stage	Sampling points	Sample quantity	Tests to be performed	Respons-ibility
Compression	After machine setting	50 Tablets* Both from LHS and RHS	Description, Length, Width, Thickness, Average Mass, Mass variation, Hardness, Disintegration Time, Friability	IPQA
		06 tablets****	Dissolution	QC

Speed challenge study	**Study at** **-Low speed** **-High speed**	Sample from left & right rotary	50 tablets (from LHS and RHS)	Description, Thickness, Average Mass, Mass variation, Hardness, Disintegration Time, Friability	IPQA
		Composite sample	20 tablets***	Uniformity of dosage units (on 10 tablets)	QC
Hardness challenge study	**Study at** **-Low Hardness** **-High Hardness**	Sample from left & right rotary	50 tablets (from LHS and RHS)	Description Thickness Average Mass Mass variation Hardness Disintegration Time Friability	IPQA
		Composite sample	06 tablets**** at each stage	Dissolution	QC
Compression (At optimum parameters)		[1]Sample from beginning, middle, and near end stage of compression	50 tablets from LHS and RHS at each stage	Description Thickness Average Mass Mass variation Hardness Disintegration Time Friability	IPQA
			10 tablets*** at each stage	Uniformity of dosage units (on 10 tablets at each stage)	QC
		[1]Compsite Sample from beginning, middle, and near end stage of compression	06 Tablets****	Dissolution	QC
			30 Tablets**	Assay	
Coating solution		After preparation	1 × 50 ml	Description	QC and Micro.
				Weight per ml	
			1 × 30 ml (initial)	Microbiological analysis	
			1 × 30 ml (After 24 hours)	Microbiological analysis	
		After completion of coating operation	1 × 50 ml	Description	
				Weight per ml	
			1 × 30 ml	Microbiological analysis	
Coated tablets		After completion of coating of each lot	Pooled sample of 50 tablets from IPC(s)	Description Length Width Thickness Average Mass	IPQA

			Mass variation Hardness Disintegration Time Friability	
	Pooled sample after completion of coating	12 tabs**	#Dissolution profile	QC
		150 tabs**	Finished product analysis (Chemical analysis)	
		30 tabs**	Microbiological analysis	Micro.
Packaging	[1]from initial, middle, and near end stage of packaging	01 blister at each stage of each pack style	Description of pack	IPQA
			Sealing quality	
			No of tabs in a pack	
		No. blisters in 01 sealing roller or 01 stroke at each stage of pack style	Leak test	
Finished product	Random	30 g tabs of each pack style	Microbiological analysis	Micro.

1 Entire operation shall be devided into initial, middle and end stages, based on total theoretical time required for the activity.
* Results are required to proceed further.
** Collect the sample in duplicate, one set sample to be taken for analysis and second set shall be preserved with IPQA. This preserved sample if not used shall be destroyed after analysis.
*** Collect the sample in triplicate, one set sample to be taken for analysis and second set shall be preserved with
This preserved sample if not used shall be destroyed after analysis.
**** Collect the sample in quadruplicate, one set sample to be taken for analysis and second set shall be preserved with IPQA. This preserved sample if not used shall be destroyed after analysis.
# Sampling interval shall be 05, 10, 15, 30, 45 and 60 minutes.
£ Target shall meet all the parameters of the tablets as specified.
$$ NLT 60% (Q) of the labeled amount of cefuroxime is dissolved in 15 minutes and NLT 75% (Q) of the labeled amount of cefuroxime is dissolved in 45 minutes.
TAMC: 103 cfu/ml and Pathogens: Absent

RESULTS AND DISCUSSION

Compression stage variables considered for study

Machine speed (6 - 14 RPM), Hardness.

Measured responses:

Description, Average mass, Mass variation, Hardness, Thickness, Friability, Disintegration time and Uniformity of dosage units & Dissolution.

Acceptance criteria: As per finished product specification.

Batch taken for study: X, Y, Z

Table 4: Product Details

Table No.	Product Details
Product Name	Cefuroxime Axetil tablets BP 500 mg
API	Cefuroxime Axetil
Area Temperature	22 ± 2ºC
Area Humidity	NMT 45%
Batch size	1,20,000

Table 5: List of equipment for manufacturing

S. No	Equipment	Qualification status
1	Double Cone Blender	Qualified
2	Compression machine	Qualified
3	Auto coater	Qualified
4	Metal detector	Qualified
5	Bottle unscramble machine	Qualified
6	Tablet/Capsule counter and filling machine	Qualified
7	Desiccant inserter machine	Qualified
8	Cotton inserter machine	Qualified
9	Inline capper machine	Qualified
10	Induction sealer machine	Qualified
11	Blister Packing machine	Qualified

Table 6.1: Speed Challenge Study (Low Speed)

Test parameter	Specification	X		Y		Z	
		LHS	RHS	LHS	RHS	LHS	RHS
Machine speed	To be established	05 rpm		05 rpm		05 rpm	
Description	Pale yellow capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.	Complies	Complies	Complies	Complies	Complies	Complies
Avg. mass	990 mg ± 2%	991 mg	993 mg	995 mg	993 mg	994 mg	992 mg
Mass variation	990 mg ± 2%	-0.6 to 1.8%	-1.0 to 1.9%	-0.5 to 1.8%	-1.1 to 1.9%	-0.6 to 1.9%	-1.0 to 1.8%
Thickness	6.30 mm ± 0.2mm	6.12 to 6.25 mm	6.14 to 6.23 mm	6.13 to 6.25 mm	6.12 to 6.22 mm	6.17 to 6.23 mm	6.14 to 6.24 mm
Hardness	Between 10-35kg (100-350N)	162 to 179 N	169 to 174 N	167 to 181 N	165 to 175 N	168 to 178 N	165 to 179 N
Disintegr-ation time	NMT 5.0 mins.	48 to 56 sec	49 to 58 sec	47 to 55 sec	48 to 57 sec	48 to 58 sec	47 to 56 sec
Friability	NMT 1.0%	0.15%	0.18%	0.13%	0.15%	0.14%	0.16%

Table 6.2: Speed Challenge Study (High Speed)

Test parameter	Specification	X		Y		Z	
		LHS	**RHS**	**LHS**	**RHS**	**LHS**	**RHS**
Machine speed	To be established	14 rpm		14 rpm		14 rpm	
Description	Pale yellow capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.	Complies	Complies	Complies	Complies	Complies	Complies
Average mass	990 mg ± 2%	992 mg	994 mg	995 mg	993 mg	994 mg	991 mg
Mass variation	990 mg ± 2%	-0.5 to 1.9%	-1.1 to 1.7%	-0.5 to 1.8%	-1.1 to 1.9%	-0.6 to 1.9%	-1.1 to 1.8%
Thickness	6.30 mm ± 0.2mm	6.11 to 6.24 mm	6.14 to 6.23 mm	6.13 to 6.25 mm	6.12 to 6.22 mm	6.17 to 6.23 mm	6.14 to 6.24 mm
Hardness	Between 10-35kg (100-350N)	161 to 180 N	169 to 174 N	167 to 181 N	165 to 175 N	168 to 178 N	165 to 181 N
Disintegration time	NMT 5.0 mins.	47 to 57 sec	49 to 58 sec	47 to 56 sec	48 to 56sec	48 to 58 sec	47 to 56 sec
Friability	NMT 1.0%	0.13%	0.18%	0.13%	0.15%	0.14%	0.17%

Table 6.3: Uniformity of Dosage Units Is Performed For Speed Challenge Study

Test parameter	Specification	Observation (in %)					
		(Low speed, 5rpm)			**(High speed,14rpm)**		
Uniformity of dosage units	The acceptance value of 10 dosage units is less than or equal to 15.0	X	Y	Z	X	Y	Z
		99.7	102.1	101.7	100.2	99.1	100.7
		100.3	100.7	103.0	100.3	97.7	100.4
		98.0	102.3	102.5	99.7	98.1	101.1
		98.1	102.4	102.0	98.2	97.0	101.1
		99.8	102.9	101.5	99.7	95.9	102.9
		98.7	103.5	104.1	98.0	95.5	103.1
		100.0	102.6	100.0	99.9	96.4	103.3
		98.1	102.5	101.9	98.7	99.8	104.1
		100.7	102.8	102.0	98.7	98.7	103.2
		100.2	99.3	102.8	98.9	99.7	101.7
Mean		**99.4**	**102.1**	**102.2**	**99.2**	**97.8**	**102.2**
Minimum		**98.0**	**99.3**	**100.0**	**98.0**	**95.5**	**100.4**
Maximum		**100.7**	**103.5**	**104.1**	**100.3**	**99.8**	**104.1**
Acceptance Value		**2.5**	**3.6**	**3.3**	**2.0**	**4.4**	**3.8**

Observation: The Dissolution results at high and low speed are found within the specification limits for the batch X, Y, Z

Table 7.1: Hardness Challenge Study (Low Hardness)

Test parameter	Specification	X		Y		Z	
		LHS	RHS	LHS	RHS	LHS	RHS
Machine speed	To be established	06 rpm		05 rpm		08 rpm	
Description	Pale yellow capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.	Complies	Complies	Complies	Complies	Complies	Complies
Average mass	990 mg ± 2%	991mg	993 mg	995 mg	993 mg	994 mg	992 mg
Mass variation	990 mg ± 2%	-0.9 to 1.8%	-1.0 to 1.9%	-0.5 to 1.8%	-1.1 to 1.8%	-0.5 to 1.9%	-1.2 to 1.3%
Thickness	6.30 mm ± 0.2mm	6.38 to 6.44 mm	6.37 to 6.46 mm	6.38 to 6.45 mm	6.36 to 6.49 mm	6.38 to 6.48 mm	6.39 to 6.45 mm
Hardness	Between 10-35kg (100-350N)	105 to 128 N	107 to 129 N	110 to 130 N	112 to 139 N	109 to 128 N	128 to 145 N
Disintegration time	NMT 5.0 mins.	21 to 29 sec	22 to 34 sec	29 to 32 sec	26 to 34 sec	26 to 29 sec	22 to 24 sec
Friability	NMT 1.0%	0.22%	0.24%	0.31%	0.28%	0.36%	0.29%

Table 7.2: Hardness Challenge Study (High Hardness)

Test parameter	Specification	X		Y		Z	
		LHS	RHS	LHS	RHS	LHS	RHS
Machine speed	To be established	06 rpm		05 rpm		08 rpm	
Description	Pale yellow capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.	Complies	Complies	Complies	Complies	Complies	Complies
Average mass	990 mg ± 2%	992 mg	993 mg	995 mg	993 mg	994 mg	992 mg
Mass variation	990 mg ± 2%	-0.8 to 2.1%	-1.0 to 1.3%	-1.3 to 1.8%	-1.1 to 1.4%	-1.4 to 1.8%	-0.8 to 1.3%
Thickness	6.30 mm ± 0.2mm	6.11 to 6.16 mm	6.12 to 6.18 mm	6.12 to 6.19 mm	6.12 to 6.19 mm	6.12 to 6.18 mm	6.13 to 6.20 mm
Hardness	Between 10-35kg (100-350N)	180 to 224 N	180 to226 N	202 to 238 N	198 to 228 N	200 to 232 N	194 to 228 N
Disintegration time	NMT 5.0 mins.	48 to 59 sec	54 to 59 sec	57 to 58 sec	52 to 57 sec	56 to 59 sec	50 to 55 sec
Friability	NMT 1.0%	0.15%	0.12%	0.14%	0.16%	0.16%	0.15%

Table 7.3: Dissolution study is performed for hardness challenge study

Table 7.3.1: Dissolution (Low hardness)						
Tablet No.	**X**		**Y**		**Z**	
	15 minutes	**45 minutes**	**15 minutes**	**45 minutes**	**15 minutes**	**45 minutes**
1	85	99	87	102	91	101
2	86	99	89	100	89	99
3	83	98	86	98	88	100
4	85	98	86	100	87	102
5	86	99	90	98	88	101
6	85	100	87	99	90	100
Minimum	**83**	**98.0**	**86**	**98.0**	**87.0**	**99.0**
Maximum	**86**	**100.0**	**90**	**102.0**	**91.0**	**102.0**
Average	**84.8**	**98.8**	**87.5**	**99.5**	**88.8**	**100.5**
NLT 60% (Q) of the labeled amount of cefuroxime is dissolved in 15 minutes and NLT 75% (Q) of the labeled amount of cefuroxime is dissolved in 45 minutes						

Observation: The Dissolution results at low hardness are found within the specification limits for the batch X, Y, Z.

Table 7.3.2: Dissolution (High hardness)						
Tablet No.	**X**		**Y**		**Z**	
	15 minutes	**45 minutes**	**15 minutes**	**45 minutes**	**15 minutes**	**45 minutes**
1	89	100	83	102	83	100
2	87	101	85	99	86	99
3	88	101	85	99	82	101
4	89	99	84	98	86	99
5	89	101	84	99	87	99
6	90	101	86	99	85	100
Minimum	**87**	**99.0**	**83.0**	**98.0**	**82.0**	**99.0**
Maximum	**90**	**101.0**	**86.0**	**102.0**	**87.0**	**101.0**
Average	**88.7**	**100.5**	**84.5**	**99.3**	**84.8**	**99.7**
NLT 60% (Q) of the labeled amount of cefuroxime is dissolved in 15 minutes and NLT 75% (Q) of the labeled amount of cefuroxime is dissolved in 45 minutes						

Observation: The Dissolution results at high hardness are found within the specification limits for the batch X, Y, Z

Table 8.1: Uniformity of Dosage Units (During Compression at Optimum Parameters)

Tablet No.	Observation (in %)								
	X			Y			Z		
	Initial	Middle	End	Initial	Middle	End	Initial	Middle	End
1	99.2	98.7	100.1	101.6	101.2	102.9	100.5	102.5	101.1
2	97.7	100.0	98.4	100.4	101.7	99.8	101.8	103.1	102.1
3	99.7	100.1	99.8	102.1	100.9	101.8	100.8	100.9	100.0
4	99.5	99.6	97.9	101.3	99.8	101.7	103.1	104.0	101.4
5	99.7	99.7	99.3	101.8	101.3	100.6	101.0	102.1	101.8
6	98.8	98.4	98.7	102.9	100.2	105.1	102.1	101.5	101.2
7	99.4	97.8	98.5	100.7	101.7	100.9	100.1	102.4	99.5
8	98.1	98.1	99.7	100.7	101.5	103.0	101.0	103.0	99.7
9	100.0	99.3	99.6	103.4	102.5	102.1	102.2	102.7	100.9
10	98.8	99.8	98.2	100.0	100.0	100.4	103.1	102.6	100.7
Mean	**97.7**	**97.8**	**97.9**	**100.0**	**99.8**	**99.8**	**100.1**	**100.9**	**99.5**
Minimum	**100.0**	**100.1**	**100.1**	**103.4**	**102.5**	**105.1**	**103.1**	**104.0**	**102.1**
Maximum	**99.1**	**99.2**	**99.0**	**101.5**	**101.1**	**101.8**	**101.6**	**102.5**	**100.8**
Acceptance Value	**1.8**	**2.0**	**1.9**	**2.6**	**2.1**	**4.1**	**2.6**	**3.0**	**2.1**

Table 8.2: Tablet parameters during compression at optimum parameters

Test parameter	Specification	X		Y		Z	
		LHS	RHS	LHS	RHS	LHS	RHS
Machine speed	For information	10 rpm		10 rpm		10 rpm	
Description	Pale yellow capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.	Complies	Complies	Complies	Complies	Complies	Complies
Average mass	990 mg ± 2%	991-993 mg	991-993 mg	990-991 mg	989-991 mg	992-994 mg	992-994 mg
Mass variation	990 mg ± 2%	-0.8 to 1.8%	-1.2 to 1.9%	-1.5 to 1.8%	-1.2 to 1.7%	-1.1 to 1.9%	-1.2 to 1.7%
Thickness	6.30 mm ± 0.2mm	6.12 to 6.19 mm	6.12 to 6.19 mm	6.12 to 6.19 mm	6.16 to 6.20 mm	6.12 to 6.20 mm	6.13 to 6.21 mm
Hardness	Between 10-35kg (100-350N)	174 to 208 N	169 to 209 N	198 to 222 N	196 to 226 N	194 to 226 N	198 to 224 N
Disintegration time	NMT 5.0 mins.	47 to 59 sec	52 to 59 sec	57 to 58 sec	52 to 57 sec	56 to 59 sec	51 to 55 sec
Friability	NMT 1.0%	0.16 to 0.26%	0.12 to 0.19%	0.13 to 0.16%	0.17 to 0.22%	0.18 to 0.19%	0.082 to 0.19%

Assay	NLT 95.0% and NMT 110.0% of the labeled amount of cefuroxime($C_{20}H_{22}N_4O_{10}S$)	98.7%			98.5%			99.2%		
Dissolution%	NLT 60% (Q) of the labeled amount of cefuroxime is dissolved in 15 minutes	89	87	87	90	92	92	84	85	88
		88	88	88	90	91	92	87	82	84
	NLT 75% (Q) of the labeled amount of cefuroxime is dissolved in 45 minutes	100	100	98	102	103	101	99	99	101
		103	102	98	101	102	102	99	102	100

Table 9: Coating details

Parameter	Specification	Batch X	Batch Y	Batch Z
Inlet temperature	50 – 60 ºC	51.5 – 52.3 ºC	51.2 – 52.1 ºC	51.7 – 52.3 ºC
Outlet temperature	40 – 50 ºC	41.5 – 42.5 ºC	41.3 – 42.2 ºC	41.1 – 42.2 ºC
Spray rate	60 – 80 g/min	60 – 80 g/min	60 – 80 g/min	60 – 80 g/min
Diameter of nozzle	1.00 mm	1.00 mm	1.00 mm	1.00 mm
Atomizing air pressure	1 – 3 kg/sq.cm	3 kg/sq.cm	3 kg/sq.cm	3 kg/sq.cm
Pan rpm	2 – 5 rpm	2.8 – 4.1 rpm	2.5 – 4.3 rpm	2.2 – 4.6 rpm
Peristaltic pump rpm	10 – 20 rpm	14 – 15 rpm	14 – 15 rpm	14 – 15 rpm
% Weight gain	1.5 – 2.5% w/w	2.03%	2.09%	2.19%

Table 10: Coated Tablet Details

Parameter	Specification	Observation		
		Batch X	Batch Y	Batch Z
Description	**	Complies	Complies	Complies
Length	19.1 ± 0.1 mm	19.12 to 19.15 mm	19.11 to 19.14 mm	19.13 to 19.15 mm
Width	9.1 ± 0.1 mm	9.12 to 9.15 mm	9.12 to 9.15 mm	9.13 to 9.16 mm
Thickness	6.40 ± 0.2mm	6.26 to 6.33 mm	6.25 to 6.34 mm	6.24 to 6.31 mm
Average mass	1010 mg ± 2%	1012 mg	1014 mg	1016 mg
Mass variation	1010 mg ± 5%	-0.9 to 0.8%	-1.2 to 1.8%	-1.0 to 1.3%
Hardness	Between 10-35kg (100-350N)	206 to 216 N	198 to 219 N	202 to 218 N

Disintegration time	NMT 5.0 mins.	53 to 58 sec	52 to 57 sec	56 to 59 sec
** Blue color capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.				

Packing Process

After the inspection, the tablets were packed in different pack styles as per the Batch Packaging Record.

Table 11: The yield of product at different stages is found

Sr. No	BATCH YIELD DETAILS			
	Stage	% YIELD		
		X	Y	Z
1	After compression	93.42%	94.80%	94.93%
2	After Coating	90.60%	92.88%	93.06%
3	After Inspection	83.53%	90.22%	90.23%
4	After packing	97.37%	98.12%	97.80%

Table 12: Finished Product Analysis

A pooled sample of 150 tablets for chemical analysis & 30 g tablets for microbial analysis were sampled and analysed as per the finish product specification.					
Parameter		**Specification**	**Batch X**	**Batch Y**	**Batch Z**
Description		Blue color capsule shaped biconvex film coated tablets with 123 debossed on one side and plain on another side.	Complies	Complies	Complies
Identification	**i) By IR**	Should be similar as reference standard	Complies	Complies	Complies
	ii) By HPLC	The retention time for the major peaks for Cefuroxime axetil Diastereomer A and B in the chromatogram of the assay preparation correspond to those in the chromatogram of the Standard preparation, both relative to the internal standard as obtained in the assay.	Complies	Complies	Complies
	iii) For colorant	UV Spectrum Absorbance maxima at 630±3%	Complies	Complies	Complies
	iv) For Titanium Dioxide	A yellow orange color develops.	Complies	Complies	Complies
Average mass		1010 mg ± 2%	1012 mg	1014 mg	1016 mg

Uniformity Of Dosage Units	The acceptance value of 10 dosage units is less than or equal to 15.0	2.0			2.1			2.4			
Dissolution %	NLT 60% (Q) of the labeled amount of cefuroxime is dissolved in 15 minutes	89	87	87	90	92	92	84	85	88	
		88	88	88	90	91	92	87	82	84	
	NLT 75% (Q) of the labeled amount of cefuroxime is dissolved in 45 minutes	100	100	98	102	103	101	99	99	101	
		103	102	98	101	102	102	99	102	100	
Assay	NLT 95.0% and NMT 110.0% of the labeled amount of cefuroxime($C_{20}H_{22}N_4O_{10}S$)	98.7%			98.5%			99.2%			
Water (By KF, w/w)	NMT 4%	2.80%			3.51%			2.76%			
Total Related Substances	NMT 1.5%	0.97%			0.86%			0.77%			
Disintegration time	NMT 5.0 mins.	53 to 58 sec			52 to 57 sec			56 to 59 sec			
Microbiological Tests											
Total aerobic microbial count	Less than 10^3 cfu/g	06 cfu/g			05 cfu/g			04 cfu/g			
Total combined yeast and mold count	Less than 10^2 cfu/g	Nil			Nil			Nil			
Pathogens	Absent	Absent			Absent			Absent			

The validation of Cefuroxime Axetil tablets was conducted for a batch size of 1,20,000 tablets for compression stage due to change in the compression machine from 16 station single rotary to 49 station double rotary machine as per change control. Hence the compression stage was validated for the batches no. X, Y, Z.

1. The batches were manufactured as per batch manufacturing record.
2. The equipment utilized for manufacturing and processing of these batches were as per list of equipment.
3. The raw material used for manufacturing was from approved vendors and was released for manufacturing by QC.
4. The critical process parameters were evaluated with respect to quality attributes of the products.
5. Sampling for in-process control samples was carried out as per sampling procedure and plan.
6. Critical in-process controls were conformed to the specification.
7. Product of these batches was conformed to specifications.

CONCLUSION

The compression was done considering the aspects of compression process. The physical parameters checked include individual weight variation, thickness, hardness, friability and disintegration time in both LHS & RHS. The analytical data on content uniformity & Dissolution of compressed tablets are found to be well within the limits of acceptance criteria as described in the specification. From the above, it is concluded that compression process for Cefuroxime Axetil tablets is validated. The finished product report of the batch no. X, Y, Z shows that the product meets the acceptance criteria. On the basis of data generated from the above 03 batches of Cefuroxime Axetil 500 mg film coated tablets, it is concluded that the manufacturing process of cefuroxime Axetil tablets BP 500 mg is capable of producing a product meeting its quality attributes and predetermined specifications.

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