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Validation for Moxifloxacin Tablet

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Abstract

Quality Assurance includes management of the quality of raw materials, assemblies, products and component, management, production, validation and inspection processes. Validation is action of providing in accordance with principle of GMP, that any procedure, process, equipment, materials activity or system actual leads to expected results". At various stages in a validation/qualification exercise there is need for protocols, documentation, procedure, equipment, specifications and acceptance criteria for test results. The FDA has the authority and responsibility to inspect and evaluate process validation performed by manufactures. The cGMP for validated formulations (drugs) manufacturing required that drug product be produced with a high degree of assurance meeting all the attributes they are intended to process of meeting all the attributes they are intended to process. All the physical parameters of all three batches were found well within the acceptable limits.

Key-words: Quality Assurance, Validation, Good Manufacturing Practices & FDA.

Introduction

"Quality Assurance is defined as the maintenance of a desired level of quality in a service or product, especially by means of attention to every stage of the process of delivery or production. It is the systematic measurement, comparison, with a standard, monitoring of processes and associated feedback loop that confers error prevention.

QA includes principles like, "fit for purpose" and "right first time". Quality Assurance therefore incorporates GMP and other factors". QA includes management of the quality of raw materials, assemblies, products and component, management, production and inspection processes. (Potdar 2006).

Process validation (P.V.) may be defined as "a documented programmed which provide a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes." Various regulatory bodies have been various definitions to validation.

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Some consideration should be exercised when selecting the process validation strategy. Amongst these should be the use of different lots of active raw material and major excipients, batch produced on different shifts, the use of different equipment and facilities dedicated for commercial production, operating range of the critical processes, and a thorough analysis of the process data in case of re-qualification and re-validation, During the processing of the validation batches, extensive sampling and testing should be performed on the product at various stage and should be documented comprehensively.

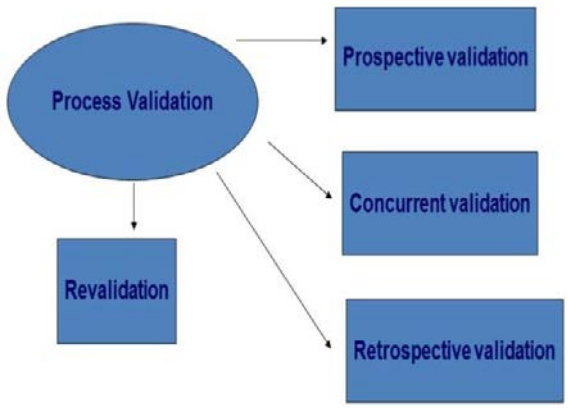

Fig. 1: General Type of Process Validation

Material and Methods

Table 1: List of Equipment used in Moxifloxacin 400 mg tablets manufacturing

S.NO.	NAME OF EQUIPMENTS	MANUFACTURER
01	Rapid Mixer Granulator	Alliance
02	Vibro Sifter	AVON Pharma
03	Fluidized Bed Processor	Alliance
04	Multi Mill	SAMS
05	Paste Kettle	SAMS
06	Octagonal Blender	SAMS
07	Tablet Compression Machine	SejongPharma
08	Metal Detector	Mr. Equipments
09	Tablet Inspection Belt	VRW Engineering
10	Disintegration Apparatus	Electrolab DT (USP)
11	Weighing Balance	Axis LC/GC
12	Moisture Analyzer	Sartorius MA45
13	Hardness Tester	ERWEKA
14	Friability Apparatus	Electrolab Friabilator (USP)

Process flow diagram (Lieberman and Lachman et al., 1987)

Fig . 2 Process flow diagram

Loss on drying (lod or moisture analyzer)

In pharmacy, the term loss on drying, commonly referred to as LOD, is an expression of moisture content on a wet-weight basis, which is calculated as follows:

% LOD = Wt. of water in sample -H total wt. of wet sample x100

Parameters of Evaluation **(Kania et al., 1987)**

Table 2: Parameter of Evaluation

1.	**Appearance**
2.	**Hardness**
3.	**Thickness**
4.	**Friability**
5.	**Diameter**
6	**Disintegration Time**
7.	**Group Weight**
8.	**Average Weight**
9.	**Uniformity of Weight**

Acceptance quality limit (AQL) (**Alffenaar et al., 2009)**

Acceptance Quality Limit (AQL) is to check the quality of tablets by the randomly selected of sample in to the in-process container after inspection of tablets. This program, since the judgment "accept" or "reject" is made on the basis of the sample irrespective of the conditions in the remainder of the batch. This method is although controlled manufacturing and packaging systems provides the largest measure of quality assurance, the quality level of final dosage forms has to be tested and inspected.

Table 3: Sampling plan & Inspection Level for Tablets

Sample Size Code Letter	ample Size	Acceptance Quality Limit in Non-Conforming Items					
		Critical Defect		Major Defect		Minor Defect	
		Ac	Re	Ac	Re	Ac	Re
Below 10000	**200**	**3**	**4**	**5**	**6**	**14**	**15**
10001 – 35000	**315**	**5**	**6**	**7**	**8**	**21**	**22**
35001 – 150000	**500**	**7**	**8**	**10**	**11**	**21**	**22**
150001 - 500000	**800**	**10**	**11**	**14**	**15**	**21**	**22**
500001 and above	**1250**	**14**	**15**	**21**	**22**	**21**	**22**

Ac: Acceptance; Re: Rejected

Results and Discussion

The environmental conditions during the manufacturing of Moxifloxacin granules were monitored and recorded stage wise. The stage wise temperature and relative humidity readings are tabulated below **recommended conditions,**
Temperature: 23 ± 2 C and Relative humidity: 50 ± 5 %

Table 4: Observation table for temperature

Sr. No.	Unit operation	Observation of Temperature (C)		
		Batch No. A	Batch No. B	Batch No. C
1	Dispensing	21	23	22
2	Sifting	22	22	23
3	Dry mixing	23	24	22
4	Compaction	24	23	24
5	Sifting &milling	23	21	23
6	Blending	23	22	22

Analysis reports of all the raw materials were checked and only approved raw material were dispensed.

Table 5: Usage of raw material (Active)

Active material	Batch No.	Assay	Water
Moxifloxacin	A	98.80	0.09
	B	98.81	0.06
	C	98.83	0.07
Limit :		NLT 97.0 and NMT 102.0%	NMT 0.5

Granulation process profile
Name of Equipment: Rapid Mixer granulator (600L)

Equipment make : Alliance
Speed of the Agitator : During start of activity slow speed till dough mass of and choper suitable consistency is obtained. If required run the mixer at fast speed for some time.

Table 6: LOD of Dry mixing stage (for record)

Batch No.	LOD at Temp	Weight taken (g)	Results (% W/W)
A	105^0 C	2.2456	3.20
B	105^0 C	2.2569	2.80
C	105^0 C	2.3217	2.85

Table 7: Results for blend uniformity of lubricated granules (Moxifloxacin)

Sample	Batch No. A		Batch No. B		Batch No. C	
	3 min		3 min		3 min	
	Weight taken (g)	% Assay	Weight taken (g)	% Assay	Weight taken (g)	% Assay
T1	1.625	98.0	1.280	94.4	1.276	98.9
T2	1.603	100.2	1.264	93.8	1.305	101.1
T3	1.613	98.0	1.272	97.4	1..285	100.4
T4	1.618	96.1	1.283	93.34	1.267	99.2
M1	1.623	100.1	1.279	94.7	1.267	98.7
M2	1.628	99.8	1.278	96.3	1.290	100.3
M3	1.628	101.0	1.275	95.4	1.283	99.1
B1	1.618	99.3	1.275	97.1	1.271	99.1
B2	1.618	99.6	1.278	95.5	1.279	99.9
B3	1.763	109.4	1.277	101.0	1.264	99.6
Mean		100.2		95.9		99.6
%RSD		3.5		2.34		0.79

Table 8: % Yield of lubricated granules

Limit	% Yield*		
	Batch No. A	Batch No. B	Batch No. C
NLT 98.0%	98.07	99.07	98.35

Table 9: Equipment Qualification Details

SR. NO.	NAME OF EQUIPMENTS	QUALIFIED STATUS
01	Vibro Sifter	Qualified
02	Rapid Mixer Granulator	Qualified
03	Fluidized Bed processor	Qualified
04	Multi Mill	Qualified
05	Paste Kettle	Qualified
06	Octagonal Blender	Qualified
07	Tablet Compression Machine	Qualified
08	Metal Detector	Qualified
09	Tablet Inspection Belt	Qualified
10	Disintegration Apparatus	Qualified
11	Weighing Balance	Qualified
12	Moisture Analyzer	Qualified
13	Hardness Tester	Qualified
14	Friability Apparatus	Qualified

Table 10: Environmental Condition for Tablets

Time	Temperature (°C)			Humidity (%)			Comply Or Non Comply
	B.No.1	B.No.2	B.No.3	B.No.1	B.No.2	B.No.3	
Initial	23	24	22	52%	53%	52%	Comply
Middle	22	23	23	53%	52%	53%	Comply
End	23	22	23	51%	50%	54%	Comply

All environmental conditions of three batches are recorded during the granulation, compression and inspection process. (Temperature was recorded in every starting of process, every one hours and end of process of activity) On the basis of analytical testing procedure the results were recorded and analysis report was prepared under the acceptance criteria.

Table 11: Analysis Report

Testing Parameter	Specification	Results		
		Batch No.1	Batch No.2	Batch No.3
Appearance	Yellow coloured capsule shaped biconvex uncoated tablets plain on both sides	Comply	Comply	Comply
Wt. of 30 tablet	18.00g ± 2.5% (17.55g to 18.45g)	Comply	Comply	Comply
Average weight of 30 tablet	600.00mg ± 2.5% (585.00mg to 615.00mg)	Comply	Comply	Comply
Uniformity of weight	600.00mg ± 5% (570.00mg to 630.00mg)	Comply	Comply	Comply
Thickness	5.25mm ± 0.20mm (5.05mm to 5.45mm)	Comply	Comply	Comply
Hardness	140N to 200N	Comply	Comply	Comply
DT	NMT 15 minute	Comply	Comply	Comply
Friability	NMT 1.0% W/W	Comply	Comply	Comply

On the basis of analytical testing procedure all results recorded and comply under the acceptance criteria.

Conclusion

The dry mixing of Moxifloxacin 400mg Tablets was performed in RMG for 10 min. keeping impeller "slow" and chopper "off" in all three consecutive process validation lots. The wet granulation of the Moxifloxacin 400mg Tablets was performed in RMG, binder solution added in 1-3 min into the dry mix keeping impeller and chopper slow speed for all three consecutive lots of first batch. The wet mixing was done in 2 min keeping impeller and chopper fast speed for all three consecutive lots of first batch. The total granulation time was kept 4 min. The ampere load attained for impeller is 20.0-25.0 for in all three consecutive process validation lots.

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 15 RPM and the maximum speed of compression for all three batches was kept at 25 RPM. The Optimum speed was kept 20 RPM in all three validation batches. The samples collected for minimum speed, maximum speed in first batch & at initial, middle & end, composite stage of compression from remaining two batches from three validation batches were found to be complying as per the acceptance criteria. All the physical parameters of all three batches were found well within the acceptable limits.

A careful design and validation of system and process controls can establish a high degree of confidence that all, batches produced were meets their intended specification. Now the manufacturing process of Moxifloxacin 400mg Tablets was validated and it conform that by following this validated manufacturing process, produced a quality product consistently at lowest possible cost. Future work will be progressed to establish stability study of these systems by chemical analysis for long term and short-term evaluation.

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