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Process validation of abiraterone acetate tablets USP 250 MG

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Abstract
To develop a process validation protocol for establishing documented evidence to ensure that process variables including the critical process parameters are under control and to demonstrate that the process consistently produces product meeting its predetermined specifications and quality attributes. To perform Concurrent process validation for Abiraterone Acetate Tablets USP 250 mg. The protocol describes the different process stages, control variables & measuring responses with justification, sampling plan, acceptance criteria the process of manufacturing of abiraterone acetate tablets up 250 mg as per manufacturing document, master card for batch no. abir01, abir02 and abir03 were validated and approved as per this validation report on the basis of statistical analysis of all critical process & mixing, compression and packing parameters, it is concluded that manufacturing process is robust and hence, stands validated.

Keywords: Process Validation, Abiraterone Acetate, Stands Validated

Introduction

Validation

Validation is a process which establishes the documentary evidence which shows that the procedures and processed which has been done in the testing and production are complaint to the particular standards at all the stages. The Process Validation is the method which proves that the processes which has been done at all the points, from product designing to its final validation, are capable to provide quality products every time when the same methods are applied. Accordingly, it is obvious that compliance with the finished product specification itself may not be sufficient to assure that the processes are valid and the manufacturer has full control over the process. As the validation is a necessary segment in Quality Assurance but also fundamental to an efficient production operation. The purpose of process validation is to make sure that the methods, which are used during the manufacturing of the dosage form, gives the consistent and high quality results. The validation of the processes ensures the product quality which may not be determines by the finished product specification. Process validation involves a series of activities taking place over the lifecycle of the product and process. This guidance describes process validation activities in three stages.

Stage

1. Process Design Stage.
2. Process Qualification Stage.
3. Continues Process Validation.

Reason for performing process validation

As the process validation is a regulatory requirement in the global health care industry for pharmaceuticals. Regulatory agencies across the world expect firms to validate their processes. Here are some points which shows the importance of process validation:

- The process validation improves the use of technology.
- It reduces the risk of failure of the product.
- It makes sure that the final customer gets the quality product every time.
- The optimization of the product is done in very well manner.
- The identification and assessment of risk can be done easily.
- It evaluates the requirement of in-process testing and evaluation.

Stages of process validation

As already mentioned in the introduction part, Process Validation has 3 stages which are mentioned below:

a) **Process Design:** The commercial manufacturing process is defined during this stage are in accordance with the development and scale-up activities
b) **Process Qualification:** In this stage, the process design is evaluated to determine, whether the process is capable of reproducible commercial manufacturing
c) **Continues Process Validation:** Further assurance is attained during regular production that the process remains in a state of control.

Process Design: Stage 1 Process Design may be defined as the evaluation and collection of data from the product designing stage during the production, which authorizes the proof that the process is qualified to provide consistent quality products. It includes R&D, design, stability parameters, in-process quality assurance and master documents.

Process Qualification: Stage 2 Process Qualification is that stage which confirms that the process design is efficient in reproducing the manufacturing process. It verifies that all pre-determined limits of the Critical Process Parameters are valid and that quality products can be produced even under "worst case" conditions.

Continues Process Validation: Stage 3 The Validation Maintenance Stage requires a frequent review of all process related documents, including validation audit reports to assure that there have been no changes, deviations, failures; changes if any in the manufacturing process, Standard operating procedures are employed, in addition to change control procedures.

Material and Method

Material

Chemicals and Reagents

Product Name Abiraterone Acetate Tablets USP 250 mg Generic Name Abiraterone Acetate Tablets USP 250 mg Product Code 4ABIR01 Dosage Form Solid oral dosage form (Uncoated tablet) Label Claim Each Uncoated tablet contains: Abiraterone Acetate USP 250 mg Excipients Q.S Standard Batch size 10,000 Tablets

Qualification of Equipment and Facility: Qualification documents of above key manufacturing equipment and utility system i.e. DM Water plant, Air Handling Unit etc., shall be reviewed for their performance and capabilities in accordance to the requirement for manufacturing of Abiraterone Acetate Tablets USP 250 mg.

Active Lactose Monohydrate BP 200, Diluent Microcrystalline Cellulose (Plain), Diluent Cross Carmellose Sodium (Vivasole), Disintegrant Paste Preparation PVPK30 (Povidone K 30).

Binder Isopropyl Alcohol, Binding solvent, Lubrication Cross, Carmellose Sodium (Vivasole) Disintegrant Sodium Lauryl Sulphate BP 30.000 0.300 Surfactant Colloidal Anhydrous Silica BP 5.000 0.050 Glidden Magnesium Stearate BP 7.000 0.070 Lubricant Average Weight of Uncoated Tablets 715.00 mg ± 5%.

Process Validation Procedure

Pre –Validation Checks

Check whether relevant SOP's are available for each activity and piece of equipment used in the process and are effective. Also, check training records for concerned SOP's are available and are effective.

Standard Operating Procedures (SOP's)

Review and Training Verification Identify all process equipments and utilities. Verify the details of qualification/ calibration information for those equipments utilized during the validation testing and record the details. Identify all process equipments, test instruments and utilities. Verify the details of the qualification/ calibration for those equipments utilized during the validation testing and record the details.

Verification of analytical method validation

Ensure that the analytical test procedures involved in the protocol are validated. Review the reports for the adequacy and compliance. Record the detail.

Checks during Validation

Line Clearance

QA should give clearance before starting the activity for each batch as per the Line.

Clearance SOP. Line clearance details have to be entered in the respective BMR (s), wherever applicable.

Processing Steps

All processing steps shall be followed as per respective SOPs and BMRs. In-process checks/ critical control points shall be monitored/ verified and as per BMR and be entered in BMR. Samples will be collected as per sampling plan. Compile and review the analytical reports as per the sampling plan (Test programme and Acceptance criteria).

Recording of observations

Record the observation after execution of each stage/ procedure as per BMR and protocol.

Certificate of analysis

Certificate of analysis for Abiraterone Acetate Tablets USP 250 mg under process validation study shall be enclosed. 10.0 Stability Study: Three consecutive validated batches of Abiraterone Acetate Tablets USP 250 mg shall be subjected for Stability Study at following conditions: 1. Accelerated Stability Study at condition 40 ± 20 C, RH 75% ± 5% for period of 1, 2, 3 and 6 months. 2. Long Time stability study at condition 30 ± 20 ºC, RH 65% ± 5% for period of 3, 6, 9, 12, 18, 24 months. The stability study shall be carried out as per the established protocol. 11.0 Acceptance Criteria: The process validation study of Abiraterone Acetate Tablets USP 250 mg shall be carried out on three Consecutive commercial batches qualified equipments mentioned in Master Production and Control Record.

Result and Discussion

Processing Stage	Critical Parameters	Specifications	Batch No.		
			ABIR01	ABIR02	ABIR03
Lubrication	Lubrication Time	To be established	40 min	40 min	40 min
	% LOD	NMT 2.0%	1.47%	1.50%	1.63%
	% Assay of Abiraterone Acetate	95% -105%	100.40	99.41	99.70
Compression (Beginning sample)	Flow property of Granules	Uniform Flow without any Stoppage.	Uniform Flow without any Stoppage.	Uniform Flow without any Stoppage.	Uniform Flow without any Stoppage.
	Description	White coloured oval shaped uncoated tablet, having both side plain	White coloured oval shaped uncoated tablet, having both side plain	White coloured oval shaped uncoated tablet, having both side plain	White coloured oval shaped uncoated tablet, having both side plain
	Weight of 20 Tablets	14300.0 gm ± 3%	14306.0	14306.4	14307.6
	Average Weight	715.0 mg ± 5%	715.3	715.3	715.3
	Breadth	9.50 ± 0.3 mm	9.52	9.52	9.52
	Length	16.0 ± 0.2 mm	16.2	16.1	16.0
	Thickness	6.00 ± 0.3 mm	6.2	6.1	6.2
	Hardness	NLT 3.0 kg/cm2	5.0 kg/cm2	4.2 kg/cm2	4.1 kg/cm2
	Friability	NMT 1.0%	0.18%	0.15%	0.23%
	Disintegration Time	NMT 15 min	2.38 min	2.50 min	2.35 min
	Dissolution Test	NLT 85% (Q)	99.84%	99.75%	100.23%
Processing Stage	**Critical Parameters**	**Specifications**	**Batch No.**		
			ABIR01	**ABIR02**	**ABIR03**
	Assay Abiraterone Acetate	NLT 90% and NMT 110% of the labeled amount	99.16%	99.50%	99.78%
Compression (Middle Sample)	Flow property of Granules	Uniform Flow without any Stoppage.	Uniform Flow without any Stoppage.	Uniform Flow without any Stoppage.	Uniform Flow without any Stoppage.
	Description	White coloured oval shaped Uncoated tablet, having both side plain	White coloured oval shaped uncoated tablet, having both side plain	White coloured oval Shaped uncoated tablet, having both side plain	White Coloured oval shaped uncoated tablet, having both side plain
	Weight of 20 Tablets	14300.0 gm ± 3%	14307.5	14306.3	14310.2
	Average Weight	715.0 mg ± 5%	715.3	715.3	715.5
	Breadth	9.50 ± 0.3 mm	9.55	9.50	9.53
	Length	16.0 ± 0.2 mm	16.2	16.1	16.2
	Thickness	6.00 ± 0.3 mm	6.3	6.0	6.2
	Hardness	NLT 3.0 kg/cm2	4.7 kg/cm2	4.3 kg/cm2	4.2 kg/cm2
	Friability	NMT 1.0%	0.14%	0.25%	0.15%
	Disintegration Time	NMT 15 min	2.45 min	2.45 min	2.54 min
	Dissolution Test	NLT 85% (Q)	99.78%	100.17%	99.84%
	Assay	90%-105 of			
	Abiraterone	the labeled	99.39%	99.37%	99.14%
	Acetate	amount			
Processing Stage	**Critical Parameters**	**Specifications**	**Batch No.**		
			ABIR01	**ABIR02**	**ABIR03**
	Flow property of Granules	Uniform Flow without any Stoppage	Uniform Flow without any Stoppage	Uniform Flow without any Stoppage	Uniform Flow without any Stoppage
	Description	White coloured oval shaped Uncoated tablet, having both side plain	White Coloured oval shaped uncoated tablet, having both side plain	White coloured oval shaped uncoated tablet, having both side plain	White coloured oval shaped uncoated tablet, having both side plain
Compression (End Sample)	Weight of 20 Tablets	14300.0 gm ±3%	14308.7	14306.6	14307.2
	Average Weight	715.0 mg ±5%	715.4	715.3	715.3
	Breadth	9.50 ± 0.3 mm	9.50	9.54	9.50
	Length	16.0 ± 0.2 mm	16.1	16.2	16.1
	Thickness	6.00 ± 0.3 mm	6.1	6.1	6.1
	Hardness	NLT 3.0 kg/cm2	4.2 kg/cm2	4.2 kg/cm2	4.2 kg/cm2
	Friability	NMT 1.0%	0.22%	0.19%	0.26%
	Disintegration Time	NMT 15 min	2.52 min	2.31 min	2.44 min
	Dissolution Test	NLT 75% (Q)	99.46%	99.89%	99.92%
	Assay	90%-105%			
	Abiraterone	the abled	99.52%	99.66%	99.25%
	Acetate	amount			

Documentation: Result recording data of various stages following documents are reviewed and prepared during process validation study.

Bulk Stage %: Assay of lubricated bulk

Sr. No.	Sampling Location in RMG	Sample No.	% Assay of Batch No.		
			ABIR01	ABIR02	ABIR03
1	Top	Right	99.49%	100.45%	101.47%
2		Centre	99.84%	98.45%	98.90%
3		Left	100.45%	100.82%	101.71%
4	Middle	Right	101.41%	100.56%	98.93%
5		Centre	99.57%	99.79%	100.46%
6		Left	100.72%	98.90%	101.70%
7	Bottom	Right	99.26%	98.89%	98.56%
8		Centre	101.25%	99.37%	100.24%
9		Left	99.45%	100.64%	99.89%
Average % Assay =			100.40	100.41	100.16%
% RSD (Not more than 2.0%) =			0.81%	1.17%	1.20%

Compression Stage: Individual weight of 20 tablets

Batch No: abir01 (Beginning sample)

Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt.(mg)
1	715.8	5	715	9	715.4	13	715.2	17	714.8
2	715.9	6	715.1	10	715.3	14	715.4	18	714.9
3	715.4	7	715.8	11	715.2	15	714.7	19	715.1
4	715.6	8	715.6	12	715.2	16	715.6	20	715
Weight of 20 Tablets (14.30 gm ± 5%)					14306 mg				
Average Weight (715 mg ± 5%)					715.3 mg				
Minimum Weight					714.7 mg				
Maximum Weight					715.9 mg				
Sr. No.	**Avg. Wt. (mg)**	**Sr. No.**	**Avg. Wt. (mg)**	**Sr. No.**	**Avg. Wt. (mg)**	**Sr. No.**	**Avg. Wt. (mg)**	**Sr. No.**	**Avg. Wt.(mg)**
1	715.2	5	715.2	9	714.8	13	715.6	17	715.4
2	715.3	6	715.2	10	715.8	14	715.1	18	715.3
3	715	7	715.2	11	715.9	15	715.8	19	715.2
4	715.3	8	715.4	12	715.4	16	715.6	20	715.8
Weight of 20 Tablets (14.30 gm ± 5%)					14307.5 mg				
Average Weight (715 mg ± 5%)					715.375 mg				
Minimum Weight					714.8 mg				
Maximum Weight					715.9 mg				

Batch No: ABIR01 (Middle Sample)

Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt.(mg)	Sr. No.	Avg. Wt. (mg)
1	715.2	5	715.2	9	714.8	13	715.6	17	715.4
2	715.3	6	715.2	10	715.8	14	715.1	18	715.3
3	715	7	715.2	11	715.9	15	715.8	19	715.2
4	715.3	8	715.4	12	715.4	16	715.6	20	715.8
Weight of 20 Tablets (14.30 gm ± 5%)					14307.5 mg				
Average Weight (715 mg ± 5%)					715.375 mg				
Minimum Weight					714.8 mg				
Maximum Weight					715.9 mg				

Batch No: ABIR01 (End Sample)

Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt.(mg)	Sr. No.	Avg. Wt.(mg)
1	715.4	5	715.2	9	715.4	13	715.9	17	715.8
2	715.2	6	715.4	10	715.8	14	715.4	18	715.6
3	715.2	7	715.8	11	715	15	715.6	19	715.4
4	715.2	8	715.2	12	715.8	16	715.1	20	715.3
Weight of 20 Tablets (14.30 gm ± 5%)					14308.7 mg				
Average Weight (715 mg ± 5%)					715.4 mg				
Minimum Weight					715 mg				
Maximum Weight					715.9 mg				

Compression stage: Individual weight of 20 tablets

Batch No.: ABIR02 (Beginning Sample)

Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt.(mg)	Sr. No.	Avg. Wt.(mg)
1	715.2	5	715.4	9	715	13	715.2	17	715.4
2	715.4	6	715.8	10	715.3	14	715.2	18	715.8
3	715.8	7	715.4	11	715	15	715.4	19	715
4	715.3	8	715.2	12	715.2	16	715.2	20	715.2
Weight of 20 Tablets (14.30 gm ± 5%)					14306.4 mg				
Average Weight (715 mg ± 5%)					715.32 mg				
Minimum Weight					715 mg				
Maximum Weight					715.8 mg				

Batch No: ABIR02 (Middle Sample)

Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt.(mg)	Sr. No.	Avg. Wt.(mg)
1	715.2	5	715.2	9	715.4	13	714.9	17	715.8
2	715.6	6	715.2	10	715.2	14	715.2	18	715.6
3	715.4	7	715.1	11	715	15	715.8	19	715.4
4	715.2	8	715.9	12	714.8	16	715.1	20	715.3
Weight of 20 Tablets (14.30 gm ± 5%)					14306.3 mg				
Average Weight (715 mg ± 5%)					715.315 mg				
Minimum Weight					714.8 mg				
Maximum Weight					715.9 mg				

Batch No: ABIR02 (End Sample)

Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg Wt. (mg)
1	715.2	5	714.9	9	714.8	13	715.8	17	715.3
2	715.3	6	714.8	10	715.9	14	715.9	18	715.2
3	715.4	7	714.7	11	715.2	15	715.4	19	715.3
4	715.8	8	715.6	12	715.1	16	715.6	20	715.4
Weight of 20 Tablets (14.30 gm ± 5%)					14306.6 mg				
Average Weight (715 mg ± 5%)					715.33 mg				
Minimum Weight					714.7 mg				
Maximum Weight					715.9 mg				

Compression stage: Individual Weight of 20 Tablets

Batch No: ABIR03 (Beginning Sample)

Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt. (mg)	Sr. No.	Avg. Wt.(mg)	Sr. No.	Avg. Wt.(mg)
1	715.8	5	714.8	9	715.2	13	715.9	17	715.4
2	715.2	6	714.9	10	715.4	14	715.4	18	715.8
3	715.2	7	715.2	11	715.8	15	715.6	19	715.8
4	715.1	8	715.4	12	715	16	715.3	20	715.4
Weight of 20 Tablets (14.30 gm ± 5%)					14307.6 mg				
Average Weight (715 mg ± 5%)					715.38 mg				
Minimum Weight					714.8 mg				
Maximum Weight					715.9 mg				

Compression stage: In-process checks during compression

Batch No. ABIR01 (Beginning Sample)

Sr.	Thickness	Length	Breadth	Hardness	Friability	DT	Assay for Abiraterone Acetate	Dissolution
No.	6.0 ± 0.3 mm	16.0 ± 0.2 mm	9.50 ± 0.2 mm	NLT 3.0 kg/cm2	NMT 1.0%	NMT 15.0 min	90% - 105%	NLT 85% (Q)
1	6.1	16.1	9.51	4.5 kg/cm2	---	---	---	---
2	6.1	16.1	9.51	5.0 kg/cm2	---	---	---	---
3	6.2	16.2	9.52	5.5 kg/cm2	---	---	---	---
4	6.2	16.2	9.52	5.0 kg/cm2	---	---	---	---
5	6.2	16.1	9.52	4.5 kg/cm2	---	---	---	---
Avg.	6.2 mm	16.2mm	9.52 mm	5.0 kg/cm2	0.18%	2.38 min	99.84%	99.16%

Batch No. ABIR01 (Middle Sample)

Sr. No.	Thickness 6.0±0.3 mm	Length 16.0±0.2 mm	Breadth 9.50 ± 0.2 mm	Hardness NLT 3.0 kg/cm^2	Friability NMT 1.0%	DT NMT 15.0 min	Assay for Abiraterone Acetate 90% - 105%	Dissolution NLT 85% (Q)
1	6.3	16.2	9.55	5.0 kg/cm2	---	---	---	---
2	6.3	16.2	9.55	5.0 kg/cm2	---	---	---	---
3	6.2	16.2	9.55	4.5 kg/cm2	---	---	---	---
4	6.2	16.2	9.51	4.5 kg/cm2	---	---	---	---
5	6.3	16.1	9.51	4.5 kg/cm2	---	---	---	---
Avg.	6.3 mm	16.2mm	9.55 mm	4.7 kg/cm2	0.14%	2.45 min	99.78%	99.39%

Discussion on the results

The process as detailed in the Master card for Abiraterone Acetate Tablets USP 250 mg Batch No. ABIR01, ABIR02 and ABIR03 have been followed for manufacturing of the product.

The equipment utilized for the manufacturing and processing of these batches of 10,000 Tablets are as per list of qualified equipment's mentioned in Master Production and Control Record.

The raw material used for manufacturing process is produced from approved vendors only and shall be approved by Quality Control.

Sampling and analysis was done in accordance with the protocol. The in process tests at dry mixing, compression & packaging stages meet the specified requirements.

Based on the analytical data of batch, dry mixing time of 20 min and the analytical results of which were found satisfactory.

Compression was done at speed of 30000 tablets/hour and the in-process results were found satisfactory.

Packing was done at speed of 30-50 strokes/min, 150 °C (forming), 160 °C (sealing) temperature, the results of appearance and leak test were found satisfactory.

Each batch complied with the finish product specification.

References

1. Guidance for Industry: Process Validation: General Principles and Practices. Website: www.fda.gov
2. European Medical Agency: Guideline on process validation for finished products - information and data to be provided in regulatory submissions.
3. Commission Regulation (EC) No 712/2012 of 3 August 2012 amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products.
4. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.
5. Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products.
6. Eudralex volume 4 (GMP guidelines), Annex 15 (Qualification and validation).
7. Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, II a, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorizations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures.
8. ICH Q8 (R2) (Pharmaceutical development).
9. ICH Q9 (Quality risk management).
10. ICH Q10 (Pharmaceutical quality system).
11. ICH Q11 (Development and manufacture of drug substances (chemical entities and biotechnological / biological entities.
12. www.wikipedia.com
13. T. Higuchi, E Brochmann, H Hanssen Pharmaceutical analysis 1st edition.
14. Studies regarding the process validation of pharmaceutical formulations released through association of oncology product.