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RESEARCH ARTICLE

QUALIFICATION OF EQUIPMENT: BIN BLENDER AND COMPRESSION MACHINE

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Received 23 April 2012; Revised 17 April 2012; Accepted 08 May 2012, Available online 15 May 2012

ABSTRACT

Qualification is the planning, carrying out and recording of tests on equipment and systems, which will form a part of the validated process, to demonstrate that it will perform as intended. The performance qualification of the bin blender (200 L) for minimum (20%) and maximum (70%) occupancy capacities and blend uniformity at different blending time intervals and of the compression machine at different compression speeds i.e. 20 RPM to 50 RPM was done. The installation qualification (IQ) and operational qualification (OQ) protocols should be prepared, approved and performed as per the qualification master plan. Bin blenders which are used as dry mixers are used after the initial stages i.e. premixing and granulation. Compression machine is designed for high speed production capability as a modular system in tablet compressing chamber for manufacturing of tablets or press forming preparations. The prerequisites required before starting the performance qualification of equipment is that OQ should be successfully completed, all the necessary materials, procedures and testing arrangements should be made. For the bin blender samples were collected as per sampling plan at different time intervals and the collected samples analyzed for color content in each sample. For the compression machine (26 station), the tablets were checked for physical parameters such as appearance, weight variation, hardness, friability and thickness. The equipment qualification was carried out to demonstrate the efficiency of the equipment's and ended with satisfactory results.

Key words: Bin blender, compression machine, performance qualification, qualification.

INTRODUCTION

Qualification is an essential part of a pharmaceutical manufacturer's quality assurance system; it should demonstrate that facilities are suitable for their intended use and should also guarantee that the medicinal products are of an appropriate quality. Manufacturing and laboratory instruments/equipment and their supporting utilities that are used in the Good Manufacturing Practices /Good Laboratory Practices activities are to be qualified and certified for their intended purpose. Qualification of instrument/ equipment is not a single, continuous process but instead results from many discrete activities. These activities have been grouped into four phases of qualification. They are: Design qualification (DQ), Installation qualification (IQ), Operational qualification (OQ) and Performance qualification (PQ).

Schedule M states about the qualification of the equipment[1].Qualification requirements of established equipment/instruments are decided on the basis of available historical data of that equipment. (e.g., usage logs, calibration records, preventive maintenance records, change controls etc.)[2]. An item of equipment is an object that is characterized by its internal technical processes. A facility is the sum of all equipment used for a common purpose[3].The objective is to provide a method for the performance qualification of bin blender (200 L), by studying the effect of various parameters like bowl load, blending time and blender speed on mixing of available materials.

Bin blenders are used as dry mixers and the principle of blending is fall and roll over method. To verify the performance of pillar type bin blender (200 L), for minimum (20%) and maximum (70%) occupancy capacities and blend uniformity at different blending time intervals performance qualification is carried out.

The Compression machine is designed for high speed production capability as a modular system in tablet compressing chamber for manufacturing the tablets or press-forming preparations. To verify the proper working of the Compression machine (26stations) at different compression speeds i.e. 20 RPM, 30 RPM, 40 RPM and 50 RPM, the performance qualification was carried out.

Regarding the "qualification of equipment," chapter 3.34 of the GMP Guideline states: "Manufacturing equipment should be designed, located and maintained to suit its intended purpose." Annex 15 to the EU GMP Guideline specifies how this requirement must be implemented[3].

Chapter 2.5.11 of Pharmaceutical Inspection Convention /Scheme (PIC/S) [4] document PI 006 therefore expressly states that the contract giver is ultimately responsible for proper implementation of the validation work:"In such cases, the responsibility lies with the contract giver to ensure that the required standards of the quality of the work which is carried out, for program control and for documentation are met[4]."

The GMP Guidelines for documentation apply in general for the layout and compilation of qualification documents which must be authorized by the head of production and quality assurance. The documentation should be retained for at least five years once the facility or equipment has been shut down. According to Annex 15, No. 2 of the EU

GMP Guideline, a company's current qualification projects must be described in a validation master plan.

The first stage of a qualification should be the design qualification (DQ). Conformance of the design with the GMP requirements should be demonstrated and documented. Before the facility is delivered, it may be necessary to make sure that the user requirements are complied with at the manufacturer's premises (Factory Acceptance Test, FAT)[5].

The correct implementation of the aforementioned requirements when assembling/setting up the facility is documented in the installation qualification (IQ). It serves as a check of the documents that were required for the design qualification. The Operational Qualification (OQ) provides evidence that the facility is functioning on the basis of established parameters and within defined limits whereas PQ is performance testing of the facility with all production materials subsequently processed during routine operation.

Bin blenders are used as dry mixers and the principle of blending is fall and roll over method. The machine is used after the initial stages i.e. premixing & granulation. The capacity of bin blender used was 200 L.

All qualification phases must be implemented on the basis of qualification protocols that have been approved beforehand.

MATERIALS AND METHODS

MATERIALS

Bin blinder (Tapasya engineering works Pvt. Ltd.as shown in figure no. 1), Compression machine (Cadmach machinery Pvt. Ltd, CTX -26 as shown in figure no.2), Lactose(IP), MCC(IP), PVP K-30, Ponceau 4R supra (IHS), Purified water (USP), Magnesium stearate (IP).

METHODS[6,7]

Bin blinder:

Batch size: 24.0 Kg and 84.0 Kg

The batch formula for batch size of 24.0 Kg and 84.0 Kg was taken as shown in Table 1and the actual weights of the dried granules and magnesium stearate taken for the batch size of 24.0 Kg and 84.0Kg are depicted in Table2.Cleaned the equipment as per the cleaning procedure and recorded the cleaning details.

Figure 1: Pillar type bin blender.

Figure 2: Cadmach compression machine.

Table 1: Batch formula for batch size of 24.0 Kg and 84.0 Kg

S .No.	Material name	Weight (% w/w)
1	Lactose	50
2	MCC(grade)	44.5
3	PVP(grade)	5
4	Ponceau 4 R supra	0.5
	Total	100

Table 2: Weights of ingredients taken for batch size of 24.0 Kg and 84.0 Kg

S. N.		Batch size of 24.0 Kg			Batch size of 84.0 Kg		
		Dried granules		Magnesium stearate	Dried granules		Magnesium stearate
1	Tare weight (Kg)	0.250	0.250	0.020	0.250	0.250	0.020
2	Net weight (Kg)	11.30	12.46	12.71	41.740	41.420	0.240
3	Gross weight(Kg)	11.550	12.71	0.260	41.990	41.670	0.260
4	Color%	0.5	0.5	-----	0.5	0.5	------
5	Total weight	23.760		0.240	83.160		0.840

The line clearance should check before starting the process. Sifted dried granules and magnesium stearate through vibratory sifter, using SS sieve ASTM # 40 and collected in a double polythene lined HDPE / SS container and labeled accordingly.

Added dried granules (sifted through 40#) into bin blender and mixed the material for a period of 20 minutes and after

20 minutes added magnesium stearate (sifted through 40#) into bin blender and mixed the material for a period of 25 minutes.

The samples were collected as per sampling plan at different time intervals of 15, 20 and 25 minutes as depicted in Figure no.3. The samples were collected in triplicate each equivalent to three times to the weight of unit dose using appropriate unit dose sampler from different locations as per unit dose sampling procedure and transferred in to individual labeled glass vials.

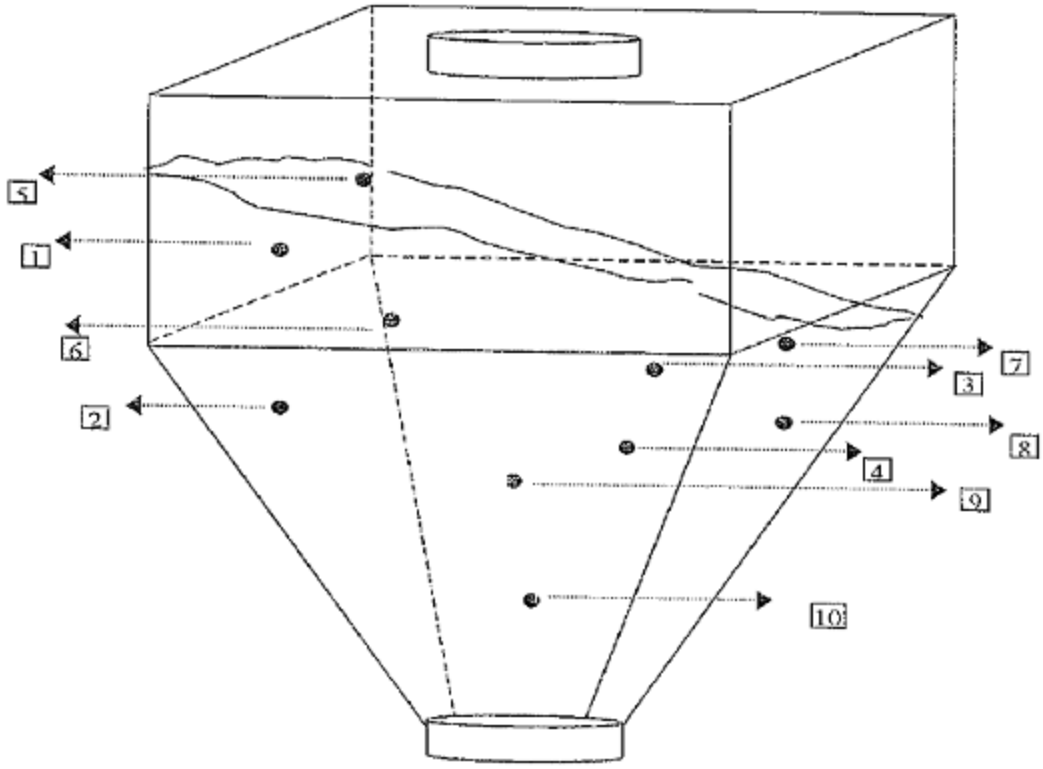

Figure 3: Sampling locations drawing for Bin blender

Sampling Location Description

Locations 1- Front Top Left; 2- Front Middle Left; 3- Front Top Right; 4- Front Middle Right; 5- Back Top Left; 6- Back Middle Left; 7 – Back Top Right; 8- Back Middle Right; 9- Centre Middle; 10 Bottom Centre

The collected samples were analyzed for color content. Content uniformity of ten samples RSD should not be more than 5%.The method used here is to quantify Ponceau 4R supra in the blend sample. Ponceau 4R supra is determined by visible spectrophotometer at 506 nm using external standard method. The above procedure with different batch sizes (24.0 kg and 84.0 kg) was followed, so as to get minimum and maximum occupancy levels in the bin blender.

Acceptance Criteria:

- Color content (assay) of all samples should be in between 90 - 110 %
- The mean of assay results at each interval should be in between 95 -105 %

Critical process control variables:

Critical process control variables of blending operation are blender occupancy, blending time and RPM. Measured parameters include blend uniformity.

Compression machine (26 station)[8]

Required quantity blend was taken as per the procedure. Cleaned the equipment as per the cleaning procedure and recorded the cleaning details. The line clearance should Checked before starting the process. Sifted blend through vibratory sifter, using SS sieve ASTM # 40 and collected in a double polythene lined HDPE / SS container and labeled accordingly. Loaded the blend in hopper and started compression with above parameters. Performed in-process checks with the frequencies specified. Compression was carried out at three different speeds and machine was being operated at both low and high compression pressures at each RPM. At each stage, 30 tablets were collected and tested for physical parameters such as appearance, weight variation, hardness, friability and thickness. The results were recorded and shown in Table 5.Acceptance criteria are shown in Table 3.

Table 3: Acceptance Criteria of various parameters

Parameter	Specification
Description	White to off-white, modified diamond shaped biconvex, beveled edge tablets.
Average weight of the tablet	600 mg ± 2%(588- 612 mg)
Weight of 20 tablets	12 ± 0.24 g (11.76 – 12.24 g)
Uniformity of weight	600 ± 5% (570 – 630 mg)
Thickness	5.80± 0.30 mm (5.50– 6.10 mm)
Hardness	10± 3.0 kp (7-13 kp)
Friability	NMT 1.0 % w/w after 100 revolutions (4 minutes)

Critical process control variables:

The control variables are compaction force (KN) and compression speed(RPM), where as measured parameters included are description, weight variation, hardness, friability and thickness. Performance of Compression machine (26 station.) was verified at different control variables such as compression pressure and compression speed (RPM).

RESULTS AND DISCUSSION

Bin blender:

a) Batch size 24.0 Kg:

Blending details: Specifications and results of process parameters are shown in Table 4.

Content uniformity of color (%) in collected samples is depicted in Table 5.

Table 4: Specifications and results of process parameters

S. No.	Process parameters	Batch size 24.0 Kg and 84.0 Kg	
		Specifications	
1.	Blending time	25 minutes	25 minutes
2.	Blender speed	Slow	Slow
3.	Blender RPM	12	12

Table 5: Content uniformity of color(%) in collected samples

S. No.	Location	Content uniformity of color(%) in collected samples					
		Batch size 24.0 Kg			Batch size 84.0 Kg		
		After 15 minutes	After 20 minutes	After 25 minutes	After 15 minutes	After 20 minutes	After 25 minutes
1.	1	99.1	97.5	101.1	100.8	100.2	101.8
2.	2	97.3	95.9	100.9	100.9	97.0	101.7
3.	3	101.8	99.2	98.9	90.2	92.7	96.8
4.	4	96.2	91.3	93.2	94.6	98.2	101.7
5.	5	101.2	98.4	99.7	91.4	97.4	102.5
6.	6	99.6	95.0	98.9	97.8	86.9	97.9
7.	7	100.3	87.4	92.7	95.5	77.5	103.7
8.	8	100.2	91.9	98.2	96.1	87.1	100.3
9.	9	100.0	98.0	99.6	95.0	93.7	102.7
10.	10	101.5	102.0	100.1	100.3	94.3	99.7
11.	Mean	99.7	95.7	98.3	96.3	92.5	100.8
12.	%RSD	1.8	4.56	3.02	3.89	7.44	2.03

The color content (%) of some samples (20 minutes) was found to be out of limits (90-110%).The mean of assay results for 15 minutes, 20 minutes and 25 minutes of mixing were found to be within the limits (95-105%) and the RSD values for content uniformity of six samples were found to be within the limits (NMT 5%).

The reason for these results was found to be excess of blending time i.e. 20 minutes (without lubrication). Hence to verify the performance of bin blender the minimum occupancy capacity was fixed as 20% of blender capacity and blending time was recommended for 15 minutes (without lubrication) and 5 minutes for lubrication.

b) Batch size 84.0 Kg:

Blending details: Specifications and results of process parameters are shown in Table 4.

The sample results are depicted in Table 5.The color content (%assay) of all samples (90-110%), the mean of assay results (95-105%) and the %RSD values for content uniformity of ten samples were found to be within limits(NMT 5%) at 15 minutes and 25 minutes.

 ISSN: 2250-1177 CODEN: JDDTAO

The reason for these results was found to be excess of blending time i.e. 20 minutes (without lubrication).Thus to verify the performance of bin blender the maximum occupancy capacity was fixed as 70% of blender capacity and blending time was recommended for 15 minutes(without lubrication) and 5 minutes for lubrication.

Compression machine:

The results are mentioned in Table6 for various parameters such as uniformity of weight, thickness, hardness and friability at different RPM i.e. 20 to 50 RPM. It was found to be within the limits. Thus the compression machine's performance qualification was completed and it was ready for use.

Table 6: Results of the performance qualification of compression machine

Speed of the compression machine	Weight variation (mg)			Thickness (mm)		Hardness (KP)		Friability (%)
	Max.	Min.	Average	Max	Min	Max	Min.	
20 RPM	608	590.2	599.0633	5.74	5.64	12.1	8.0	0.11
30 RPM	611.3	592.2	604.2267	5.75	5.65	11.0	7.0	0.16
40 RPM	611.8	592.3	604.0967	5.75	5.64	11.4	7.0	0.15
50 RPM	618.233	591.6	605.2333	5.77	5.66	12.4	7.2	0.15

CONCLUSION

Qualification is an essential part of a pharmaceutical manufacturer's quality assurance system. The performance qualification of bin blender (200 L) was done for minimum (20%) and maximum (70%) occupancy capacities and content uniformity at different time intervals. Based on above results it was concluded that the blender can be used for the intended purpose. The performance qualification of the compression machine (26 stations) was done at different compression speeds i.e. 20 to 50 RPM. The physical parameters such as weight variation, thickness, hardness and friability results were found to be within limits and thus bin blender (200 L) and compression machine (26 station) were successfully qualified.

ACKNOWLEDGEMENTS:

The authors are grateful to the management of the Aizant Drug Research Solutions Private Limited, Hyderabad for providing the facilities.

CONFLICT OF INTEREST: Nil

REFERENCES

1. Schedule M; Part 1- Good manufacturing practices for premises and materials;7.0 Equipment.http://cdsco.nic.in/html/GMP/Schedule M (GMP).
2. Nash, Robert A, et al. Pharmaceutical Process Validation 3rded. Informa Healthcare. 2003; P. 860.
3. Bharadia, Praful D, Jignyasha AB. A review of current implementation strategies for validation of cleaning processes in the pharmaceutical industry. http://cat.inist.fr/?aModele=afficheN&cpsidt=17762178. 2008 Mar 20.
4. PIC/S, PI-006-3 Recommendations on Validation Master Plan Installation and Operational Qualification Non-Sterile Process Validation Cleaning Validation. 2007. http://www.picscheme.org.
5. Validation Online. "INSTALLATION QUALIFICATION". 2008 Mar 17.http://www.validation-online.net/installation-qualification.html.
6. United States Pharmacopeia. <1058>Analytical Instrument Qualification.
7. Bansal S, et al. Qualification of Analytical Instruments for Use in the Pharmaceutical Industry: A Scientific Approach. AAPSPharmSciTech2004, 5(1) Article 22.
8. Heyden Y. Vander et al. "Guidance for robustness/ruggedness tests in method validation". J.Pharmaceut.Biomed.Anal.2001, 24 (5 - 6):P. 723–753.

