Prospective Process Validation Study of Glibenclamide 2.5 mg Tablets

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ABSTRACT

The present study provides a high degree of assurance that a specific process for manufacturing of Glibenclamide Tablets will consistently produce a product meeting its predetermined quality attributes and specifications. It mainly comprises the stages to be followed to evaluate and qualify the acceptability of manufacturing process of Glibenclamide 2.5 mg tablets. The process is limited to the three batches manufactured of specific batch size with specified equipments and control parameters for tablets. It involves All parameters related to the each step were evaluated by respective standard test involved in the manufacturing. Sampling, testing plan and acceptance criteria for each step were monitored. The analytical results of all stages were found to be within the acceptable limit. Other tests related to compression such as hardness, thickness, disintegration and dissolution for all three batches were found within the acceptable limit.

Key words: Glibenclamide, Blend Uniformity, Assay of Glibenclamide, Process validation of Glibenclamide, Glibenclamide tablets.

1. INTRODUCTION

Validation is defined as process of founding through a documented database programme, which provides a high degree of assurance that a specific process will constantly produce a product meeting its pre-determined specifications and critical quality attributes. The word validation simply means, ‘assessment of validity’ or ‘action of proving effectiveness’ a validated manufacturing process is one, which has been proved to do what it purports to or is represented to do. Validation essentially contains process qualification (the qualification of materials, equipment, system, buildings and personnel i.e. Design Qualification, Installation Qualification, Operation Qualification, Performance Qualification).

Process Validation is defined as the collection and evolution of data from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products. It assures Quality, Safety, and efficacy. (According to 2011 United State of Food and Drug Administration (USFDA) guideline). The process validation is the analysis of data collected throughout the design and manufacturing of a product in order to endorse that the process gives consistent production of products with given standard. The main aim of process validation of Glibenclamide is to ensure various inputs lead to consistent and great quality productions and it continuing process that must be regularly improved as manufacturing feedback is gathered. Glibenclamide, also known as glyburide, is an anti-diabetic drug in the class of medications known as sulfonlurea and thoroughly related with sulfonamide antibiotics.
Glibenclamide is a sulfonylurea derivative and is recommended for the treatment of type II diabetes mellitus. In its oral administration, Glibenclamide go through the hepatic first pass effect; such that only 45% of the drug is absorbed and considering its short half-life, the persistent has to take the drug in several divided doses to maintain the desired therapeutic effect. Gastrointestinal adverse effects of Glibenclamide have been reported for the drug, which decreases the patients’ compliance. The Glibenclamide fall in class II of the biopharmaceutical classification system, which means the drug is poorly water soluble and soluble in ethanol (5 mg/mL), Dimethyl sulfoxide - DMSO (25 mg/mL), chloroform (1:36), methanol (1:250), while showing a good permeability in the gastrointestinal mucosa\(^1\)\(^8\).

1.1 Stages of Process Validation
- Process Design Stage
- Process Qualification Stage
- Continued Process Verification Stage

1.2 Process Validation should be considered in following situation
- When implementing new processes for manufacturing
- When new equipment’s installed in manufacturing plant
- Process and equipment which are having altered suit changing the priority
- Processes were ended product test is poor

2. MATERIALS AND METHODS

Prospective process validation was performed on the three batches of Glibenclamide 2.5 mg Tablets. The three consecutive batches were labeled as (Batch X, Batch Y, and Batch Z) \(^3\)\(^9\).

List of Equipment and Stages indicate list of equipment’s which are used in manufacturing process of glibenclamide 2.5 mg tablets and give the involvement of equipment in which manufacturing stage with their make which are mentioned in table 1.

Details of Input Material indicates material or ingredients which are used in the manufacturing of glibenclamide 2.5 mg tablets with their category which shows in table 2.

Sampling and Testing Plan indicates the planning for sampling and testing with their manufacturing stage, procedure, quantity to be sampled and acceptance criteria for sampling for the manufacturing of glibenclamide 2.5 mg tablets which describe in table 3.

Manufacturing Process flow chart indicates the manufacturing stages of manufacturing process of glibenclamide 2.5 mg tablets depicted in Figure 1.

3. RESULT AND DISCUSSION

This results and discussion is limited to evaluation of three consecutive batches of glibenclamide 2.5 mg tablets for prospective process validation. Three manufacturing batches are validated in prospective process validation the batches are labeled as Batch X, Batch Y and Batch Z at blend stage, compression stage and packing stage.

Product Details
Product Name: Glibenclamide Tablets 2.5 mg
Label Claim: Each tablet contains Glibenclamide BP 2.5 mg.

3.1 Dry Mixing

Dry mixing was carried out in Rapid Mixer Granulator for 10 minutes and samples were collected from eleven different six locations for Blend Uniformity. The blend uniformity test was performed and acceptance criteria for it is individual values should be between 90.0 % to 110.0 % of the labeled amount of Glibenclamide with RSD not more than 5 % the results are described in table 4.

% RSD of Glibenclamide Tablets for all three validation batches were found within the specification. Based on % RSD data of Glibenclamide Tablets for three validation batches, it was evident that the dry mixing throughout the sampling locations and all results are found within acceptable limit.

3.2 Drying Analysis

The drying analysis carried for the % LOD of dried granules of Glibenclamide analysis. The samples were collected from the fluidized bed dryer bowl from top, middle bottom side the results are shown in table 5.

% loss of drying of dried granules of Glibenclamide was within the range 7.30 to 7.89 w/w at 120 OC for 20 minutes respectively for all three validation batches, which were within the acceptable limit.

3.3 Analytical Data for Lubricated Blend

Blending was carried out by Octagonal Blender for 13 minutes and samples were collected from 12 different locations (12-points) for test Blend Uniformity such as upper site, middle site, lower site and bottom. The results are as follows in table 6.
% RSD of Glibenclamide for all three validation batches were within the range 1.07 to 1.15, which were found within the acceptance criteria. % RSD of Glibenclamide for all three validation batches, it was evident that there was no segregation occurs in the blender and mixing is homogeneous throughout the sampling locations.

3.4 Analysis of Lubricated Blend

Lubricated blend analysis is done by description of blend, assay, loss on drying, bulk density, tapped density and sieve test parameters their results are described in table 7.

Description, Assay, loss on drying, bulked density, tapped density sieve test of lubricated blend of Glibenclamide for three validation batches was within the acceptable specification and criteria.

3.5 Physical Characteristics of Lubricated Blend

Physical characteristics of lubricated blend were done by description of lubricated blend, bulk density, tapped density, loss on drying, angle of repose and particle size distribution parameters and their results are shown in table 8.

The physical parameter of lubricated blend such as description, bulk density, tapped density, loss on drying, angle of repose and particle size distribution for three validation batches was satisfactory and found consistent within acceptable limit. No significant observation related to the flow of the blend was observed throughout the compression activity.

3.6 Compression stage physical parameters

During compression, samples from compression machine at minimum speed and maximum speed were collected of three consecutive batches for performing physical parameters. The physical parameters checks as description, average weight, uniformity of weights, thickness, hardness, friability, disintegration, assay, dissolution test performed. The results are as follows of table 9.

Physical parameter of Glibenclamide tablet at Minimum Speed (2200 Tabs/min) and Maximum Speed (2750 Tabs/ Min) of compression for three validation batches X, Y, Z were found in the range within the acceptance criteria and specification.

3.7 Compression stage analytical results

Compression stage analysis in their content uniformity, assay by HPLC and dissolution were checked at minimum speed and maximum speed as same as to physical parameters and results describe in table 10.

% dissolution of Glibenclamide at Optimum speed of compression for three validation batches X, Y, Z were found in the range which were within the acceptance criteria.

3.8 Analysis of Compressed Tablet

The analysis of compressed tablets is done by assay, content uniformity and dissolution rate of Glibenclamide compressed tablets results are shown in table 11.

Assay, content uniformity and dissolution rate of Glibenclamide at initial, middle, end and composite stage of compression at optimum were found within the acceptable limit that is Glibenclamide2.38 to 2.63 mg/tablets.

4. CONCLUSION

The prospective process validation of Glibenclamide 2.5 mg tablet has been performed for three batches and all the parameters and results were found within the acceptance limit at all stages such as dry mixing, wet granulation, drying, milling, lubrication, and compression. Based on the results of the validation data for three batches, it was concluded that the manufacturing process used for formulation of Glibenclamide 2.5 mg tablet will consistently producing the stable product meeting its predetermined specifications and quality attributes. Hence, it can be concluded that the method employed in the manufacture of the given product is considered to be validated and can be routinely followed.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.
### Table 1. List of Equipments

| Sr. No. | Equipment                                | Make                        | Stages Involved In                      |
|---------|------------------------------------------|------------------------------|-----------------------------------------|
| 1       | Weighing balance                         | Mettler Toledo               | All stages                              |
| 2       | Vibratory sifter (30inch)                | PHARMA FAB                   | Sifting of raw materials                |
| 3       | Rapid Mixer Granulator                   | BOWMEN & ARCHER             | Dry mixing and granulation              |
| 4       | Fluid bed drier (250 kg)                 | BOWMEN & ARCHER             | Drying                                  |
| 5       | Multi-mill(50 T0 250 Kg/Hrs)             | PHARMA FAB                   | Sizing                                  |
| 6       | Octagonal Blender (1200 Lit)             | BECTOCHEM                    | Blending                                |
| 7       | Compression machine.                     | CALMACH                      | Compression                             |
| 8       | Friability test apparatus                | ELECTROLAB                   | To check friability                     |
| 9       | Hardness tester                          | ELECTROLAB                   | To check hardness                       |
| 10      | Dissolution Apparatus                    | Electrolab (USP)            | Dissolution Testing                     |
| 11      | Disintegration apparatus                  | Electrolab (USP)            | To check disintegration time            |
| 12      | Blister Packing Machine                   | Elmach Pack                  | For Packing of Tablets                  |
| 13      | Metal Detector                           | Sivo System PVT LTD         | To Detect metal traces in tablets       |
| 14      | UV Spectrophotometer                      | Shimadzu                     | For Analysis                            |
| 15      | HPLC                                     | Shimadzu                     | For Analysis                            |

### Table 2. Detail input of material

| Sr. No | Ingredients                     | Specification | Category       |
|--------|---------------------------------|---------------|----------------|
| 1      | Glibenclamide                   | BP            | Active Ingredient |
| 2      | Lactose Monohydrate             | Ph. Eur       | Diluents        |
| 3      | Maize Starch                    | Ph. Eur       | Binder          |
| 4      | Povidone K30                    | BP            | Diluents        |
| 5      | Magnesium Stearate (Vegetable Grade) | EP          | Lubricant       |
| 6      | Purified Water                  | BP            | Solvent         |
Table 3. Sampling and testing plan

| Stage                          | Sample Location                                                                                       | Sample Size              | Test                      |
|-------------------------------|-------------------------------------------------------------------------------------------------------|--------------------------|---------------------------|
| Dry mixing                    | After completion of drying, draw composite sample from 11 different location of RMG after 5,10,15 min. of mixing of API and excipients | Approx. 300 mg /each location | Blend uniformity          |
| Drying                        | Samples of dried granules shall be withdrawn from 5 sampling points comprising left, right, center, front, back layer of FBD bowl. | Approx. 5.0 g /each location | Loss on Drying            |
| Lubrication Stage             | Unit dose samples shall be withdrawn from 11 different location of the blender comprising of upper, middle, lower layer and bottom layer after 3 minutes mixing with Lubricant in Octagonal blender. | Approx. 1100 mg.          | Blend uniformity          |
| Lubricated Blend              | Approximately 300 g of lubricated bulk blend to be sampled for physical characteristic evaluation. | Approx. 300 g            | Physical characteristics  |
| Compression Stage             | During compression, samples to be collected & mixed from both sides of press(RHS and LHS) at initial, middle and at the end of compression operation | 150 Tablets at each stage | Description              |
| a. Minimum speed              |                                                                                                       |                          | 2. Bulk density Tapped density |
| b. Optimum speed              |                                                                                                       |                          | 3. Angle of repose         |
| c. Maximum speed              |                                                                                                       |                          | 4. Particle size analysis  |
| Finished Product              | After final compression of tablets before packing this analysis is carried.                            | 150 Tablets              | 5. Assay                  |
|                               |                                                                                                       |                          | 6. Friability              |
|                               |                                                                                                       |                          | 7. Hardness                |
|                               |                                                                                                       |                          | 8. Thickness               |
|                               |                                                                                                       |                          | 9. Dissolution             |
|                               |                                                                                                       |                          | 10. Content uniformity     |
### Table 4. Dry mixing stage blend uniformity results

| Sr. No. | Location | Acceptance Criteria                                                                 | Batch X | Batch Y | Batch Z |
|---------|----------|-------------------------------------------------------------------------------------|---------|---------|---------|
| 1       | T1       | Individual values should be between 90.0 % to 110.0 % of labeled amount of Glibenclamide with RSD NMT 5 %. | 101.5   | 101.5   | 101.5   |
| 2       | T2       | 101.1                                                                               | 101.1   | 101.1   | 101.1   |
| 3       | T3       | 100.8                                                                               | 100.8   | 100.8   |         |
| 4       | B1       | 100.4                                                                               | 100.4   | 100.4   |         |
| 5       | B2       | 100.9                                                                               | 100.9   | 100.9   |         |
| 6       | B3       | 101.1                                                                               | 101.1   | 101.1   |         |

Minimum: 100.4, Maximum: 101.5, Mean: 100.9, % RSD: 0.3

T: Top, B: Bottom

### Table 5. Results of Drying Homogeneity Analysis

| Sr. No | Limit 7.3 to 8.0 w/w at 120 °C for 20 minutes | Batch X | Batch Y | Batch Z |
|--------|-----------------------------------------------|---------|---------|---------|
| 1      | Top                                           | 7.31    | 7.30    | 7.33    |
| 2      | Middle                                        | 7.80    | 7.82    | 7.81    |
| 3      | Bottom                                        | 7.87    | 7.86    | 7.89    |

### Table 6. Result of Blend Uniformity of Lubricated Blend

| Sr. No | Location | Acceptance Criteria                                                                 | Batch X | Batch Y | Batch Z |
|--------|----------|-------------------------------------------------------------------------------------|---------|---------|---------|
| 1      | U1       | Individual values should be between 90.0 % and 110.0 % of labeled amount of Glibenclamide with RSD not more than 5.0 % | 96.9    | 96.8    | 96.7    |
| 2      | U2       | 98.8                                                                               | 98.9    | 98.7    |         |
| 3      | U3       | 98.2                                                                               | 98.3    | 98.5    |         |
| 4      | M1       | 100.1                                                                              | 100.3   | 100.2   |         |
| 5      | M2       | 98.3                                                                               | 98.2    | 98.4    |         |
| 6      | M3       | 98.3                                                                               | 98.5    | 98.3    |         |
| 7      | L1       | 98.6                                                                               | 98.5    | 98.4    |         |
| 8      | L2       | 100.4                                                                              | 100.6   | 100.5   |         |
| 9      | L3       | 100                                                                                 | 99.9    | 100.1   |         |
| 11     | BO       | 99                                                                                 | 99.2    | 99.3    |         |

Minimum: 96.9, Maximum: 100.4, Mean: 98.86, % RSD: 1.07

|         | Minimum | Maximum | Mean   | % RSD  |
|---------|---------|---------|--------|--------|
|         | 96.9    | 100.4   | 98.86  | 1.07   |

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Table 7. Results of Assay of Lubricated Blend

| Test                  | Acceptance Criteria                                                                 | Observation              |
|-----------------------|-------------------------------------------------------------------------------------|--------------------------|
| Description           | White granules free from extraneous matter (Blend)                                  | Complies                 |
| Assay                 | 2.375 mg to 2.625 mg of Glibenclamide per average weight of Blend NMT 95.0 % and NMT 105.0 % of label claim of Glibenclamide | 97.2 97.8 98.1          |
| Loss on Drying        | For information only                                                                 | 8.65 8.78 8.33          |
| Bulk Density          | For information only                                                                 | 0.6946 mg/ml 0.7130 mg/ml 0.6888 mg/ml |
| Tapped Density        | For information only                                                                 | 0.81 g/ml 0.86 g/ml 0.79 g/ml |
| Sieve Test            | For information only                                                                 | Sieve No. % of Sample passes |
|                       | 20 #                                                                                | 93.1 % 94.3 % 93.4 %     |
|                       | 40 #                                                                                | 68.0 % 68.8 % 69.2 %     |
|                       | 60 #                                                                                | 60.1 % 59.8 % 61.2 %     |
|                       | 80 #                                                                                | 56.9 % 57.2 % 56.7 %     |
|                       | 100 #                                                                               | 46.8 % 47.2 % 46.3 %     |

Table 8. Physical Characteristic of Lubricated Blend

| Sr. No. | Parameter                        | Batch X  | Batch Y  | Batch Z  |
|---------|----------------------------------|----------|----------|----------|
| 1       | Description                      | White Colored Powder Blend | White Colored Powder Blend | White Colored Powder Blend |
| 2       | Bulk density gm/ml               | 0.65     | 0.62     | 0.65     |
| 3       | Tapped density gm/ml (500 taps)  | 0.68     | 0.68     | 0.69     |
| 4       | Loss On Drying                   | 1.98%    | 1.51%    | 1.55%    |
| 5       | Angle of Repose                  | 24.09    | 23.38    | 24.09    |
| 6       | Particle Size Distribution       | Cumulative Retention (%)  | Cumulative Retention (%)  | Cumulative Retention (%)  |
|         | Above 20#                        | 1.72 %   | 98.3 %   | 98.3 %   |
|         | Above 60#                        | 24.59 %  | 49.4 %   | 75.4 %   |
|         | Above 80#                        | 40.61 %  | 28.2 %   | 59.4 %   |
|         | Above 100#                       | 45.56 %  | 24.1 %   | 54.6 %   |
Table 9. Compression stage Physical parameters Batch X, Batch Y and Batch Z

| Test          | Acceptance Criteria                                                                 | Minimum Speed (2200 Tabs/min) | Maximum Speed (2750 Tabs/Min) |
|---------------|-------------------------------------------------------------------------------------|-------------------------------|-------------------------------|
|               |                                                                                     | LHS  | RHS  | LHS  | RHS  |
| **Batch X**   |                                                                                     |      |      |      |      |
| Description   | White circular tablets debossed with GL/2.5 on one side                              | Complies | Complies | Complies | Complies |
| Average Weight| 80.0 mg ± 5 % (76.0 to 84.0 mg)                                                     | 83.7 mg | 82.3 mg | 80.9 mg | 80.7 mg |
| Uniformity Weight| NMT 2 tablets deviate by more than ±10 % from the average weight and none deviate by ±20 % from the average weight. | -2.03 to +1.55 % | -1.58 % to +2.07 % | -2.35 % to +2.60 % | -3.35 % to +5.33 % |
| Hardness      | 19.6 N to 49.0 N                                                                   | Min – 32 | Max - 44 | Min – 31 | Max - 35 | Min – 29 | Max – 28 |
| Thickness     | 2.50 to 3.00 mm                                                                     | Min – 2.79 | Max – 2.85 | Min – 2.74 | Max – 2.79 | Min – 2.73 | Max – 2.72 |
| Friability    | Not more than 1 % w/w                                                                | 0.28 % | 0.24 % | 0.26 % | 0.24 % |
| Disintegration| Not more than 8 minutes                                                              | 01 min 44 sec | 01 min 02 sec | 01 min 12 sec | 01 min 22 sec |
| **Batch Y**   |                                                                                     |      |      |      |      |
| Description   | White circular tablets debossed with GL/2.5 on one side                              | Complies | Complies | Complies | Complies |
| Average Weight| 80.0 mg ± 5 % (76.0 to 84.0 mg)                                                     | 82.8 mg | 83.5 mg | 81.8 mg | 84.2 mg |
| Uniformity Weight| NMT 2 tablets deviate by more than ±10 % from the average weight and none deviate by ±20 % from the average weight. | -2.04 to +1.52 % | -1.55 % to +2.09 % | -2.28 % to +2.59 % | -3.33 % to +5.36 % |
| Hardness      | 19.6 N to 49.0 N                                                                   | Min – 33 | Max - 42 | Min – 31 | Max - 36 | Min – 32 | Max – 39 |
| Thickness     | 2.50 to 3.00 mm                                                                     | Min – 2.55 | Max – 2.86 | Min – 2.64 | Max – 2.78 | Min – 2.76 | Max – 2.98 |
| Friability    | Not more than 1 % w/w                                                                | 0.31 % | 0.29 % | 0.28 % | 0.26 % |
| Disintegration| Not more than 8 minutes                                                              | 01 min 38 sec | 01 min 02 sec | 01 min 18 sec | 01 min 22 sec |
| **Batch Z**   |                                                                                     |      |      |      |      |
| Description   | White circular tablets debossed with GL/2.5 on one side                              | Complies | Complies | Complies | Complies |
| Average Weight| 80.0 mg ± 5 % (76.0 to 84.0 mg)                                                     | 84.6 mg | 82.8 mg | 82.8 mg | 83.8 mg |
| Uniformity Weight| NMT 2 tablets deviate by more than ±10 % from the average weight and none deviate by ±20 % from the average weight. | -2.11 to +1.53 % | -1.49 % to +2.07 % | -2.25 % to +2.60 % | -3.34 % to +5.34 % |
| Hardness      | 19.6 N to 49.0 N                                                                   | Min – 35 | Max - 41 | Min – 31 | Max - 39 | Min – 29 | Max – 36 |
| Thickness     | 2.50 to 3.00 mm                                                                     | Min – 2.54 | Max – 2.76 | Min – 2.70 | Max – 2.83 | Min – 2.66 | Max – 2.86 |
Friability | Not more than 1 % w/w | 0.33 % | 0.27 % | 0.29 % | 0.25 %
Disintegration | Not more than 8 minutes | 01 min 33 sec | 01 min 29 sec | 01 min 21 sec | 01 min 26 sec

Table 10. Compression stage analytical results

| Test                        | Acceptance Criteria | Batch X | Batch Y | Batch Z | Min Speed | Max Speed | Min Speed | Max Speed | Min Speed | Max Speed |
|-----------------------------|---------------------|---------|---------|---------|-----------|-----------|-----------|-----------|-----------|-----------|
| Uniformity of dosage        | Less than or equal to 15.0 | 4.6     | 4.3     | 4.8     | 4.2       | 5.1       | 4.9       |
| (by content uniformity)     |                      |         |         |         |           |           |           |
| Assay (By HPLC)             | 95.0 % to 105.0 % of label amount of glibenclamide | 97.6 %  | 97.0 %  | 97.2 %  | 96.0 %    | 98.8 %    | 98.6 %    |
| Dissolution Profile in %    | Limit between 45 % to 70 % after 30 mins | Min 54 | 55      | 56      | Max 58    | 59        | 60        |
|                            | Avg 56               | 57      | 59      | 57      |           |           |           |

Table 11. Results of analysis of compressed tablet

| Parameter                  | Acceptance limit                  | Observation |
|----------------------------|-----------------------------------|-------------|
|                            |                                   | Batch X     | Batch Y     | Batch Z     |
| Assay (HPLC)               | Glibenclamide 2.38 to 2.63 mg/tablets | 2.44 mg/tablets | 2.49 mg/tablets | 2.48 mg/tablets |
| Content Uniformity         | Less than or equal to 15.0        | 4.7         | 4.8         | 4.7         |
| Dissolution                | 45 to 70 % after 30 mins          | Min – 58 %  | Min – 59 %  | Min – 58 %  |
|                            | Max – 62 %                       | Max – 62 %  | Max – 63 %  | Max – 63 %  |
|                            | Avg – 60 %                       | Avg – 61 %  | Avg – 60 %  | Avg – 60 %  |

*Min: Minimum, Max: Maximum, Avg: Average
Fig 1. Manufacturing process flow chart of Glibenclamide 2.5 mg tablet

REFERENCES
1. Manohar A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Second Edition, Dec. 2007: 8.1 - 8.6.
2. Food and Drug Administration’s Guidance for Industry Process Validation: General Principles and Practices, Revision I, January 2011: 8-14.
3. Prashant B P, Rupesh K, Zamir G K. Process Validation of Bethanechol Chloride Tablet 25 mg. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2016 Apr 1; 6(2): 167-181.
4. Agalloco J. Validation: an unconventional review and reinvention. PDA journal of pharmaceutical science and technology. 1995 Jul 1; 49 (4):175-9.
5. Global Harmonization Task Force (GHTF), Quality Management System, Process Validation Guidance, Study Group – 3, January 2004: 6-7.
6. Vinod J. Process Validation of Atrovastatin Tablet 1 mg. Indo American Jour of Pharma Res. 2013; 3(12):1438-50.
7. “Guidance for Industry Process Validation: General Principles and Practices” (PDF). Food and Drug Administration. Retrieved 16 December 2014.
8. Bahri-Najafi R, Tavakoli N, Senemar M, Peikanpour M. Preparation and pharmaceutical evaluation of glibenclamide slow release mucoadhesive buccal film. Research in pharmaceutical sciences. 2014 May; 9(3):213.
9. Patil Prashant B, Nandwalkar Rahul K, Khan Zamir G. Prospective Process Validation Study of Nifedipine Extended Release Tablets. Inveniti Rapid: Pharm Analysis & Quality Assurance, 2016(3): 1-7.
10. Kour G. Process Validation of Metered Dose Inhaler, Inter. Jour of Res Pharm. 2012; 3(3): 55 – 59.
11. Patil Prashant B, Nandre Atul N, Bari Sanjay B, Zamir, G. Khan, Concurrent Process Validation Study of Cilnidipine and Chlorthalidone Tablets, Inveniti Rapid: Pharm Analysis & Quality Assurance, 2016(4):1-7, 2016.