**International Journal of Thesis Projects and Dissertations (IJTPD)**
Vol. 2, Issue 4, pp: (43-56), Month: October - December 2014, Available at: www.researchpublish.com

# Process Validation for Aceclofenac 100mg and Paracetamol 500mg Tablets

[1]Shahin.Mohammad, [2]K.Ayeshabegum, [3]P.Sandhya

[1,2,3] Shadan Womens College of Pharmacy Hyderabad, Telangana, India.

***Abstract:*** **The purpose of research was to study prospective process validation for Aceclofenac 100 mg and paracetamol 500mg tablets dosage formulation. The critical process parameters were identified with the help of process capability and evaluated by challenging its lower & upper release specification. Three initial process validation batches (I, II & III) of same size, method, equipment & validation criteria was taken. The critical parameter involved in sifting, dry mixing, preparation of granulating agent, wet mixing, wet milling, drying, sizing, lubrication, compression stages & coating were identified and evaluated as per validation master plan. The outcome indicated that this process validation data provides high degree of assurance that manufacturing process produces product meeting its predetermined specifications and quality attributes.**

***Keywords*****: Aceclofenac, Paracetamol, Prospective Process Validation, Validation.**

## I. INTRODUCTION

According to Indian GMP validation study is essential part of GMP. Those required to be done as per predetermined protocols. Prospective process validation[1], [2] is carried out during the development stage by means of risk analysis of the production process which is broken down into individual steps. These are then evaluated on basis of past experience to determine whether they might lead to critical[3],[4] situation are identified, the risk is evaluated, the potential cause are investigated and assessed for probability & extent, the teal plan are drawn up, & priorities are set The trial are then performed and evaluated & overall assessment is made. If at the end results[5] are acceptable the process is satisfactory. Unsatisfactory processes must be modified & improved until a validation exercise proves them to be satisfactory this form of validation is essential in order to limit the risk of error occurring on the production scale. This present work deals with identification of critical stage and their consequent evaluation by challenging its upper and lower specifications.

## II. MATERIALS AND METHODS

Paracetamol**,** aceclofenac**,** starch**,** microcrystalline cellulose**,** starch (for binding)**,** povidone(k-30)**,** methylparaben sodium**,** Propylparaben Sodium**,** Purified Water **,** Sodium Starch Glycollate**,** Sodium Lauryl Sulphate**,** Colloidal Silicon Dioxide**,** Magnesium Stearate**,** Talc **,** Wincoat WT white ready mix**,** Isopropyl Alcohol**,** Methylene Chloride.was used for this Formulation. All raw material used of IP grade and chemicals used in the analysis in the study were of analytical grade.

## III. MACHINERIES

Vibrosifter (50 to 300k, Saral-engineering), multimill (50 to 200kg, saral engineering), rapid mixing granulator [RMG] (150lts Saral engineering), fluid bed drier [FBD] (60kg,saral engineering), Mechanical Stirrer (Winmax enterprises), Conta Blender (200lts & 300lts bins, Saral engineering), compression machine (52,200 tab/hr for bi-layer tablets , Gaylord, 29 stations, double rotator, automatic & continuous), disintegration and friability test apparatus (Electo lab), Auto coater (SCS 1050 – 80 to 110 kg/batch & SCS 750 – 30 to 45 kg/ batch, Saral engineering), Analytical Balance(Sartorius), Hardness, Thickness & Diameter test apparatus (Pharma test), Friabilator(USP) (Electrolab), LOD Instrument(Ohaus).

## IV. MANUFACTURING FORMULAE

### FOR GRANULATION AND COMPRESSION

| | RAW MATERIALS | SPECIFICATION | UNITS | STANDARD QUANTITY |
|---|---|---|---|---|
| 1 | Paracetamol | IP | Kg | X |
| 2 | Aceclofenac | IP | Kg | X |
| 3 | Starch | IP | Kg | X |
| 4 | Microcrystalline cellulose | IP | Kg | X |
| 5 | Starch ( for binding) | IP | Kg | X |
| 6 | Povidone ( K-30) | IP | Kg | X |
| 7 | Methylparaben Sodium | IP | Kg | X |
| 8 | Propylparaben Sodium | IP | Kg | X |
| 9 | Purified Water | IP | Kg | X |
| 10 | Sodium Starch Glycollate | IP | Kg | X |
| 11 | Sodium Lauryl Sulphate | IP | Kg | X |
| 12 | Colloidal Silicon Dioxide | IP | Kg | X |
| 13 | Magnesium Stearate | IP | Kg | X |
| 14 | Talc | IP | Kg | X |

### FOR COATING SOLUTION MATERIALS

| S.NO | RAW MATERIALS | SPECIFICATION | UNITS | STANDARD QUANTITY |
|---|---|---|---|---|
| 15 | Wincoat WT white ready mix | IP | Kg | X |
| 16 | Isopropyl Alcohol | IP | Kg | X |
| 17 | Methylene Chloride | IP | Kg | X |

## V. PROCEDURE

**PREPARATION OF TABLETS:**

**1 GRANULATION:**

***1. A. Paste Preparation:***

1. To a suitable jacketed s.s vessel with stirrer charge 18 L Purified Water (Part of Item 09), heat to boiling. Charge the following in the order and stir to dissolve:

a. Sodium Methylparaben (Item 7)

b. Sodium Propylparaben (Item 8)

c. Polyvinylpyrrolidone (PVP K-30) (Item 6)

Check for clarity and completeness of the solution after each addition. Filter the solution, if necessary through mesh 100 s.s screen, Stop heating and keep the vessel covered.

2. To a separate s.s vessel, charge q.s.Purified Water (Part of Item 09). To it add Maize Starch (Item 5) (previously sifted through mesh 40) under stirring. Stir to form uniform lump free slurry.

Charge the Starch slurry briskly to the solution in Step.1.A-1, under stirring. Continue stirring at temp. 80°C to 90°C and stir to form characteristic lump free, gelatinous, translucent paste. Rinse the starch slurry container with q.s of Purified Water (Part of Item 11) and add to the paste. Cool the paste to about 40°C. Keep covered until used in Step.1.B-4. Record the weight and temperature of the paste.

***1. B. Blending and Wet Granulation:***

1) Pass Aceclofenac xx kg (Item 2) & Maize Starch xx kg (Item 3) through mesh 100 s.s screen fitted onto a vibratory sifter and collect in double PE lined bags. Store in controlled area until taken for further use.

2) Sift the following through mesh 40 fitted on to a vibratory sifter.

Paracetamol xxkg (Item 1)

Microcrystalline Cellulose xxkg (Item 4)

3) Charge the sifted materials from Step 4.18.1.1.B-1 & 4.18.1.1.B-2 in the mixer e. g. RMG. Mix for about 10 minutes to attain uniformity.

4) Charge 3/4$^{th}$ of the Starch – PVP paste from Step 4.18.1.1.A-3, while slow mixing the powders, after uniform mixing add remaining quantity of the paste, rinse the container with q.s Purified Water (Part of Item 9) and add to the wet mass. Use additional Purified Water (Part of Item 11) if required. Continue mixing until characteristic granular mass is obtained. Record the quantity of Purified Water required in ml.

5) Semidry the wet mass from Step 1.B-4 in FBD for 15 minutes at temperature **NMT 60°C**.

6) Pass the semi dried granules through mesh 16 s.s screen fitted on to a vibratory sifter and Mill coarse granules retained on the sieve if any, through 2 mm screen in Multimill, using knives forward, medium speed (KFMS). **Note:** Avoid excessive generation of fines. Pass the milled granules through mesh 16 s.s screen fitted onto a vibratory sifter. Collect the sifted material in FBD bowl.

7) Finally dry the semidried granules suitably in FBD at temperature **NMT 60°C**, until LOD is between 3.0 % and 3.5 % on IR moisture balance at 105°C for 5 minutes.

8) Pass the dried granules through mesh 16 s.s screen fitted on to a vibratory sifter. Mill coarse granules retained on the sieve if any, through 2.5 mm screen in Multimill, using knives forward, medium speed (KFMS). **Note:** Avoid excessive generation of fines. Pass the milled coarse granules through mesh 20 s.s screen fitted onto a vibratory sifter.

9) Collect sized dried granules in double PE lined air tight containers close securely, appropriately label and store in RH controlled area (RH NMT 40% at temperature NMT 27°C) until taken for lubrication.

**1.2. LUBRICATION:**

- **Record RH of Drying area every hour until process is complete (Limit: NMT 40%):**
- **Record RH of Lubrication area every hour until process is complete (Limit: NMT 40%):**

1) Sift the following through mesh 60 s.s screen fitted on to a vibratory sifter.

a. Sodium Starch Glycollate) (Item 10)

b. Sodium Lauryl Sulphate (Item 11)

c. Colloidal Silicon Dioxide (Item 12)

Collect in a double PE lined air tight container securely closed until taken for further use.

2) Sift separately Purified Talc (Item 14) and Magnesium Stearate (Item 13) through mesh 60 s.s screen fitted on to a vibratory sifter. Collect into double PE lined containers closed securely until taken for further use.

3) In a suitable blender e. g. Conta Blender, charge the following in the order:

a. ½ quantity of Dried sifted granules from Step.1.B-10.

b. Sifted material from 1.2-1.

c. Remainder quantity of Dried sifted granules from Step 1.B-10.

Blend for about 10 minutes to uniformity.

4) Take out about Xg of blend from Step 1.2-3 and mix suitably with sifted Purified Talc and Magnesium Stearate from Step 1.2-2. Spread uniformly onto the contents of blender and further mix for 2 minutes to attain uniformity.

5) Unload the lubricated granules in double PE lined airtight containers, appropriately label, securely close and store in RH controlled area (RH NMT 50% at temperature NMT 27°C), until taken for compression.

**1.3. COMPRESSION:**

- **Record RH of Compression area every hour until process is complete (Limit: NMT 45%):**

1) Compress the granules using 19 mm mm x 9.1 mm; capsule shaped punch sets and suitable dies.

2) Compress the lubricated granules to the following parameters:

a. Theoretical Compression Weight : 900 mg / tab

b. Weight of 20 tablets : 18 g per 20 tablets

c. Variation from Average Weight : ± 3 % (16.296 g to 17.304 g)

d. Weight Variation : NMT 2 tablets differ by ± 5 % & none differs by ± 10 % from average weight.

e. Hardness : NLT 5 kg

f. Thickness : 5.8 mm (Limit 5.6 mm to 6 mm)

g. Friability : NMT 1 % (Action limit: 0.3%)

h. Disintegration time : NMT 15minutes (Action:10 minutes)

i. Appea :White coloured elongated and film coated tablets free from loose dust.

3) Collect the on line de-dusted compressed tablets in double PE lined containers, appropriately label.

4) Close the containers securely and store in RH controlled (RH NMT 45% at temperature NMT27°C) area until taken for coating.

**1.4. COLOUR COATING:**

**CAUTION:** Organic solvent based coating to be done in spark proof area.

- **Record RH of Coating area every hour until process is complete (Limit: NMT 50%):**

***NOTE:*** *Instructions (given only as guidelines)*

a. Ensure coating pan is dry and clean

b. Adjust R.P.M of coating pan between 3 to 5

c. Set the blower temperature at 60°C.

d. Adjust atomizing pressure at 2.5 – 3 $kg/cm^2$

1) Charge 60% of Methylene Chloride (Part of Item 17) and Isopropyl Alcohol (Item 16) in s.s tank, mix and charge under stirring Wincoat WT Readymix (Item 15) until uniform suspension is obtained. Add the remainder Methylene Chloride (Balance part of Item 17), q.s. to make up the volume. Mix until uniformity is obtained.

2) Filter the colour suspension through mesh 200 nylon cloth, Store in airtight container, until taken for spraying.

3) Charge de-dusted tablets from Step 1.3-4 to the clean and dry coating pan.

4) Warm the tablet bed to about 35 $^oC$ to 40 $^oC$, by flipping the tablets intermittently.

5) Arrange the spray gun in such a way, that the spray droplets just touch the tablet bed on upper rim. The spray should not fall on the wall of the pan. Start rolling the tablets and simultaneously spraying.

**6) Note:** Following coating parameters are given as guidelines.

a. Pan load : Suitable to the pan dimensions. The cores should roll and not fall freely from the top edge.

b. Pan Speed : 5 to 7 r.p.m (Ideal 5 rpm)

c. Atomizing pressure : 2 $Kg/cm^2$

d. Solution Tank Pressure : Gravity or NMT 0.5 Kg / $cm^2$

e. Spray rate : Commensurate with the pan load,exhaust cfm etc. (200 ml / minute, 2 Guns)

f. Tablet bed temperature : 35 $^oC$ to 40 $^oC$

g. Average weight gain : 2.5- 3.0 % over average weight of Protective coated tablets.

Total solution required: in L. Average Weight gain obtained: in %

7) Dry the tablets at temperature NMT 50$^0$C for 1-2 hours in tray dryer or by hot air in the pan by intermittently flipping the tablet bed for 1 hour. Cool the tablets to room temperature in controlled room condition (RH NMT 50%)

**Caution:** Ensure the bed temperature does not rise excessively. Cool to room temperature.

8) Record LOD of Coated (powdered) tablets (Limit NMT 2.0 %) (For Monitoring Purpose only) Found LOD: _____%.

Appearance: Coloured, capsule shaped, film coated tablets with smooth surface.

Thickness: in mm (Limit: 6.2 ± 0.2 mm)

Monitor the Disintegration time of coated (powdered) tablets. (Limit: NMT 20 minutes.)Found Disintegration Time: in minutes.

9) Unload the coated tablets in a double PE lined airtight container and store securely in Controlled RH area (NMT 50% at temperature NMT 27°C), until taken for Inspection.

### 1.5. INSPECTION AND PACKAGING:

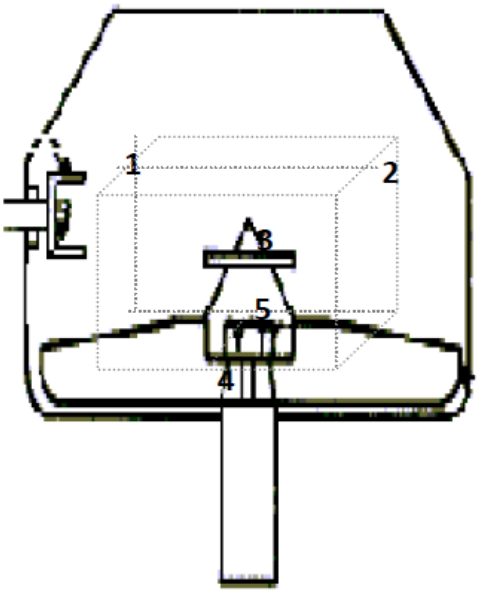
- **Record RH of Primary Packaging area every hour until process is complete (Limit: NMT 50%):**

1. Inspect individual tablets and collect good tablets in a double PE lined airtight containers.
2. Request QA to collect the Sample.
3. Store the inspected tablets securely in a controlled RH area (NMT 50%), until approved for packaging.
4. Fill the approved inspected tablets into approved primary containers and appropriately label with all required details. Pack as per the current packaging specification.

Note: Packed goods must be handled in well ventilated, dry and cool place away from direct sunlight and strong odour.

## VI. SAMPLING POINTS IN RAPID MXER GRANULATER

i. Top left
ii. Top right
iii. Middle
iv. Bottom front
v. Bottom rear

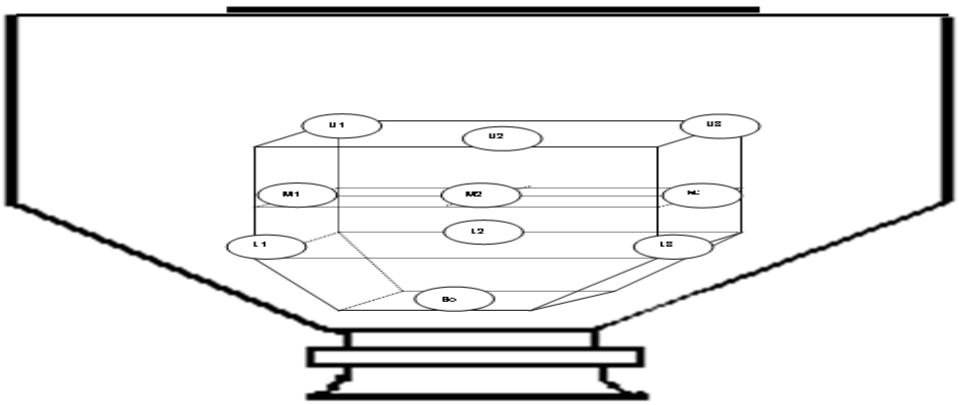


## VII. SAMPLING POINTS IN CONTA BLENDER

U1: Upper - Left – Rear. U2: Upper - Center – Front. U3: Upper - Right – Rear

M1: Middle - Left – Center. M2: Middle - Center – Center M3: Middle - Right – Center.

L1: Lower - Left – Front. L2: Lower - Center – Rear. L3: Lower - Right – Front.



Bo: Bottom – Center

## VIII. TEST PROGRAM AND ACCEPTANCE CRITERIA

**UN-COATED TABLETS SPECIFICATION**

| PARAMETER | SPECIFIED LIMIT |
|---|---|
| Theoretical Compression Weight | 900 mg / tab |
| Weight of 20 tablets | 18 g per 20 tablets |
| Variation from Average Weight | ± 3 % (16.296 g to 17.304 g) |
| Weight Variation | NMT 2 tablets differ by + 5 % &None differs by + 10 % from average weight. |
| Hardness | NLT 5 kg |
| Thickness | 5.8 mm (Limit 5.6 mm to 6 mm) |
| Friability | NMT 1 % (Action limit: 0.3%) |
| Disintegration time | NMT 15minutes(Action:10 minutes) |
| Appearance | White coloured elongated and film coated tablets free from loose dust. |
| Size Of Upper Punch | 19 mm |
| Size Of Lower Punch | 9.1mm |
| Shape Of Upper Punch | capsule |
| Shape Of Lower Punch | capsule |

# IX. RESULTS AND DISCUSSION

## 1. DESCRIPTION:

**ACECLOFENAC 100 mg and PARACETEMOL 500 mg tablets** stage prospective validation was carriedout with the input batch size of 150000 tablets, as per process validation protocol. Three batches wrere considered for process validation and batch numbers are I, II and III[7].

## 2. PRODUCT DETAILS

| **Product Name** | **ACECLOFENAC 100 mg and PARACETEMOL 500 mg tablets** | | |
|---|---|---|---|
| **Generic Name** | **ACECLOFENAC 100 mg and PARACETEMOL 500 mg tablets** | | |
| **Batch No.** | **I** | **II** | **III** |
| **Batch Size** | 150000 tablets | 150000 tablets | 150000 tablets |

## 3. PREPARATION OF LUBRICATED BLEND

### 3.1: Observations during Sifting

**EQUIPMENT NAME:** Vibrosifter

| **Batch No** | | **I** | **II** | **III** |
|---|---|---|---|---|
| **Control variables** | **Acceptance Criteria** | | | |
| **Sieve integrity before sifting** | Should not be Damaged | Complies | Complies | Complies |
| **Sieve integrity after sifting** | Should not be Damaged | Complies | Complies | Complies |

**Results:** Parameters were well within the specification.

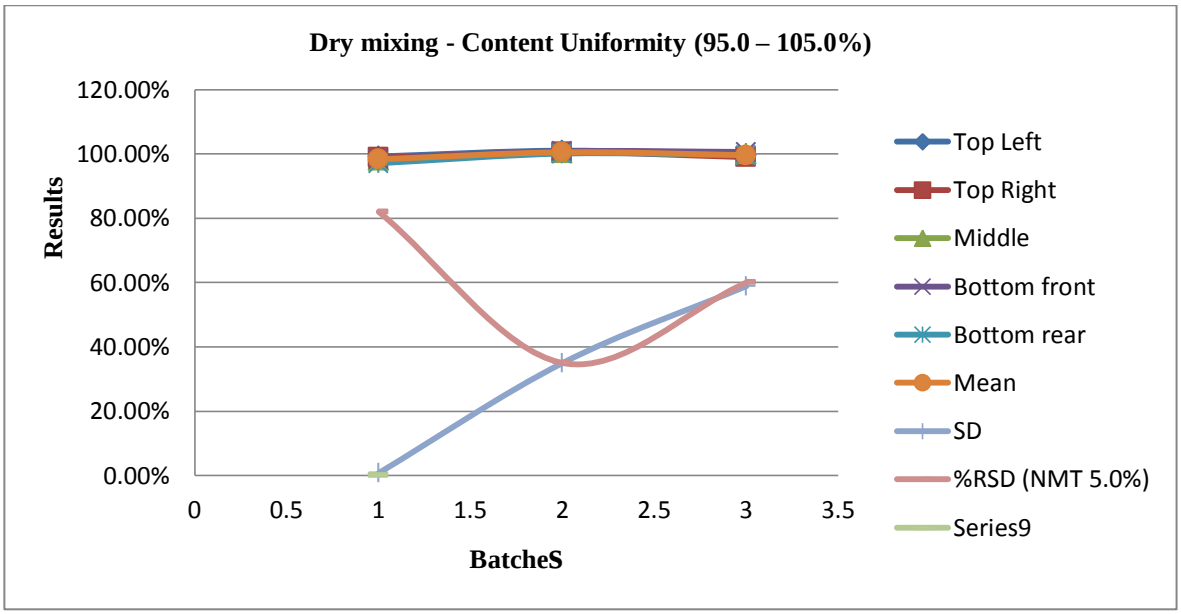
### 3.2: Observations during Dry Mixing

**EQUIPMENT NAME: RAPID MIXER GRANULATOR**

| **Batch No.** | | **I** | **II** | **III** |
|---|---|---|---|---|
| **Parameters** | **Acceptance criteria** | | | |
| **Impeller speed** | 70±5% RPM | 70 RPM | 70 RPM | 70 RPM |
| **Chopper speed** | NA | NA | NA | NA |
| **Time** | 5 min | 5 min | 5 min | 5 min |

| Sample location | Dry mixing - Content Uniformity (95.0 – 105.0%) | | |
|---|---|---|---|
| **Batch No:** | **I** | **II** | **III** |
| **Top Left** | 99.2% | 101.0% | 99.6% |
| **Top Right** | 98.8% | 100.5% | 99.0% |
| **Middle** | 98.0% | 100.4% | 100.0% |
| **Bottom front** | 98.4% | 100.8% | 100.6% |
| **Bottom rear** | 97.1% | 100.1% | 99.6% |
| **Mean** | 98.3% | 100.5% | 99.6% |
| **SD** | 0.0080 | 0.350 | 0.589 |
| **%RSD (NMT 5.0%)** | **0.82** | **0.35** | **0.60** |

**LUBRICATION BLEND**




**GRAPH .DRY MIXING – CONTENT UNIFORMITY**

**Results:** Parameters were well within the specification.

**WET GRANULATION:**

| **Batch No.** | **Acceptance criteria** | **I** | **II** | **III** |
|---|---|---|---|---|
| **End point Amperage** | 10.5-13.0 | 10.8 | 12.5 | 11.1 |
| **Addition of Isopropyl Alcohol** | 7.380 Kg | 7.380 Kg | 7.380 Kg | 7.380 Kg |

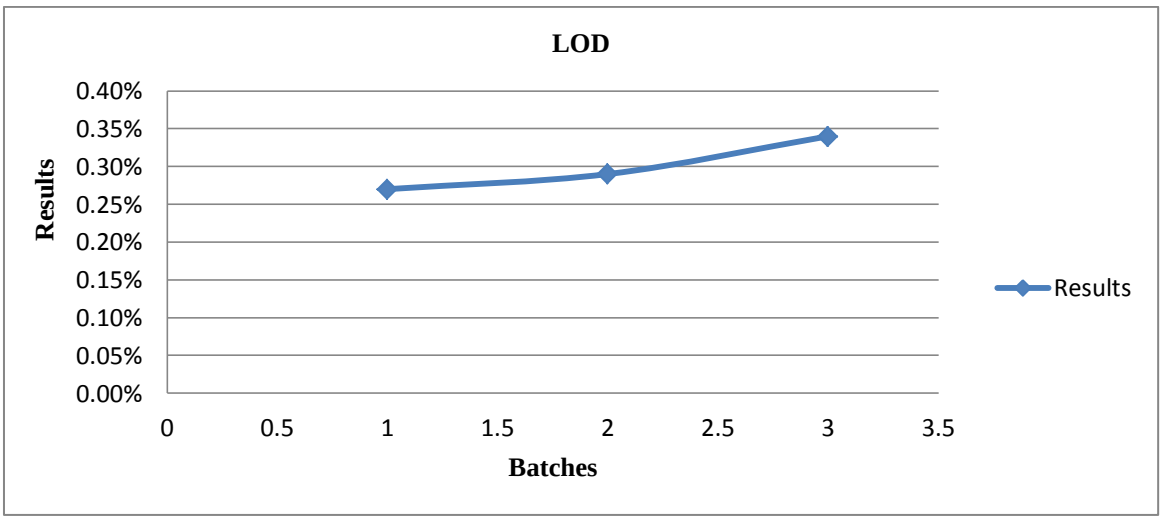
**Results:** Parameters were well within the specification.

### 3.3. Observations During Drying

**EQUIPMENT NAME: FLUID BED DRYER**

| Batch No | | I | II | III |
|---|---|---|---|---|
| **Control variables** | **Acceptance criteria** | | | |
| **Inlet temperature** | 45± 5°C | 47.7°C | 46.9°C | 48.1°C |
| **Outlet temperature** | 35±5°C | 37.9°C | 39.4°C | 38.5°C |

| Batch No. | I | II | III |
|---|---|---|---|
| **LOD** (NMT 1.0% w/w) | 0.27% | 0.29% | 0.34% |




**GRAPH .LOD%**

**Results:** Parameters were well within the specification

### 3.4 Observations During Sizing Of Granules

**EQUIPMENT NAME: MULTI MILL**

| Batch No | | I | II | III |
|---|---|---|---|---|
| **Control variables** | **Acceptance criteria** | | | |
| **Screen integrity before milling** | Should not be damaged | Complies | Complies | Complies |
| **Screen integrity after milling** | Should not be damaged | Complies | Complies | Complies |

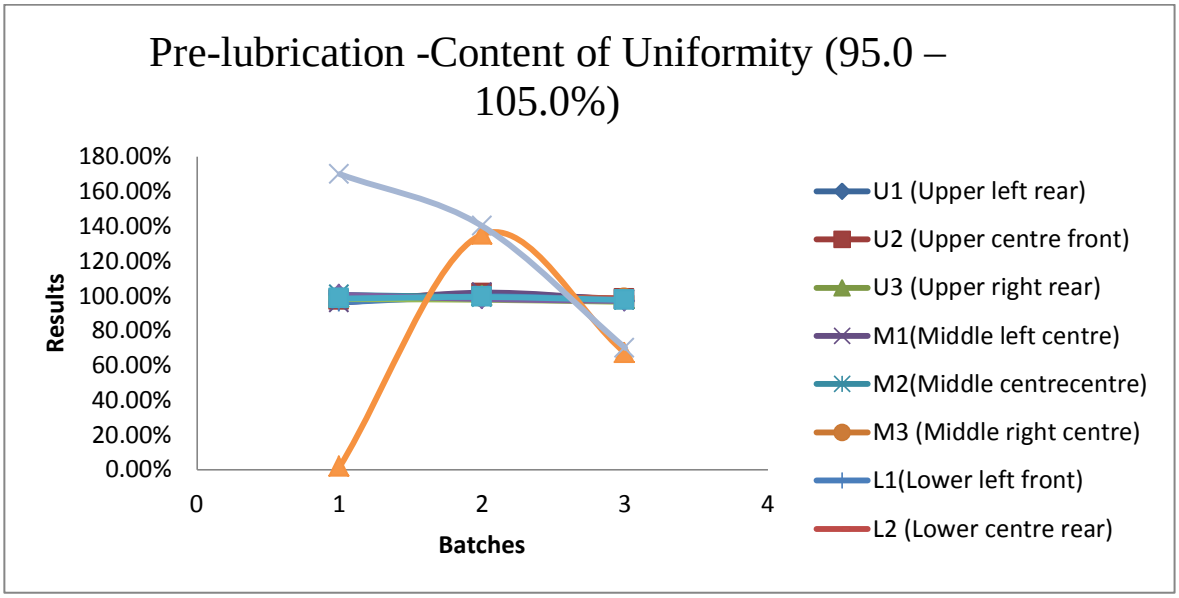
**Results:** Parameters were well within the specification.

**3.5 Observations during Pre-Lubrication & Lubrication**

**EQUIPMENT NAME: CONTA BLENDER**

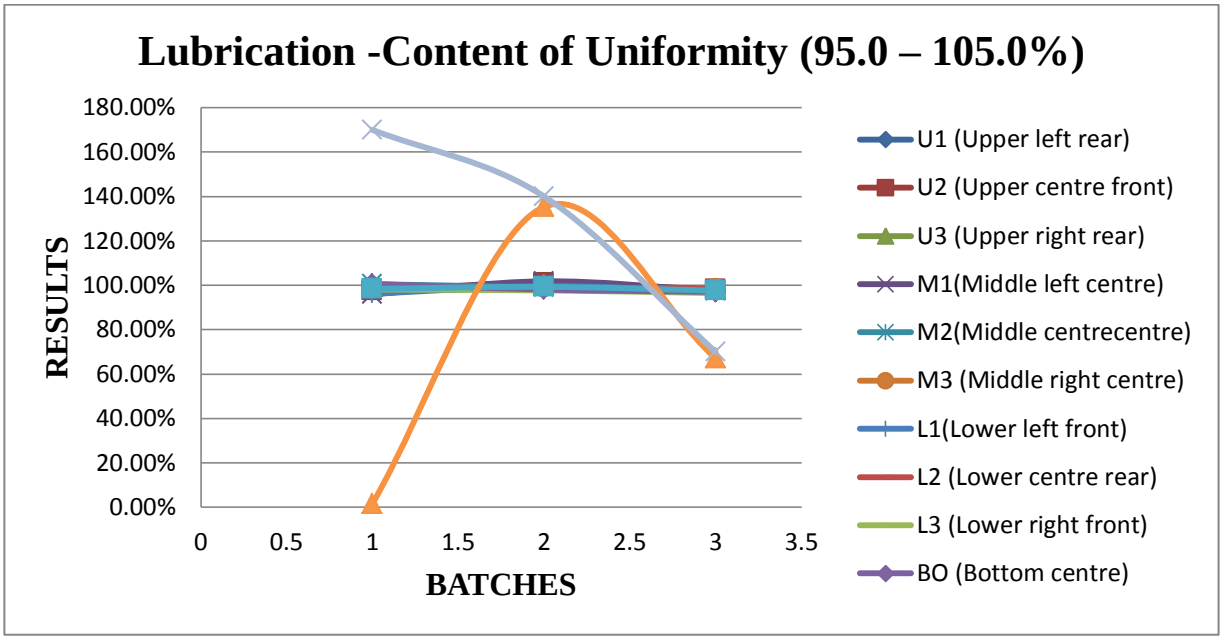
| **Pre lubrication:** | | | | |
|---|---|---|---|---|
| **Parameters** | **Acceptance criteria** | **I** | **II** | **III** |
| **Pre lubrication time** | 5 min | 5 min | 5 min | 5 min |
| **Pre lubrication RPM** | 10 | 10 | 10 | 10 |
| **Lubrication :** | | | | |
| **Lubrication time** | 2 min | 2 min | 2 min | 2 min |
| **Lubrication RPM** | 10 | 10 | 10 | 10 |

| **Sample location** | **Pre-lubrication -Content of Uniformity (95.0 – 105.0%)** | | |
|---|---|---|---|
| **Batch No:** | **I** | **III** | **III** |
| **U1** (Upper left rear) | 99.5% | 100.6% | 100.0% |
| **U2** (Upper centre front) | 99.4% | 99.6% | 100.4% |
| **U3** (Upper right rear) | 96.6% | 95.8% | 100.3% |
| **M1**(Middle left centre) | 98.7% | 98.7% | 103.2% |
| **M2**(Middle centrecentre) | 98.4% | 98.5% | 99.2% |
| **M3** (Middle right centre) | 98.9% | 98.6% | 101.3% |
| **L1**(Lower left front) | 99.7% | 101.8% | 101.0% |
| **L2** (Lower centre rear) | 98.5% | 98.6% | 102.9% |
| **L3** (Lower right front) | 97.9% | 98.9% | 101.2% |
| **BO** (Bottom centre) | 98.1% | 100.3% | 100.2% |
| **Mean** | 98.6% | 99.1% | 100.9% |
| **SD** | 0.91 | 1.604 | 1.260 |
| **%RSD (NMT 5.0%)** | **0.9** | **1.6** | **1.2** |




**GRAPH: PRE-LUBRICATION CONTENT UNIFORMITY.**

| Sample location | Lubrication- Content of Uniformity (95.0 – 105.0%) | | |
|---|---|---|---|
| **Batch No:** | **I** | **II** | **III** |
| U1 (Upper left rear) | 97.6% | 98.3% | 97.0% |
| **U2** (Upper centre front) | 97.6% | 101.1% | 98.1% |
| **U3** (Upper right rear) | 99.1% | 100.0% | 98.0% |
| **M1**(Middle left centre) | 95.9% | 101.8% | 97.6% |
| **M2**(Middle centrecentre) | 100.5% | 99.1% | 97.4% |
| **M3** (Middle right centre) | 98.7% | 98.9% | 98.4% |
| **L1**(Lower left front) | 96.2% | 99.6% | 97.4% |
| **L2** (Lower centre rear) | 100.0% | 98.2% | 98.6% |
| **L3** (Lower right front) | 98.1% | 97.7% | 96.5% |
| **BO** (Bottom centre) | 100.6% | 98.1% | 97.0% |
| **Mean** | 98.4% | 99.3% | 97.6% |
| **SD** | 1.66% | 1.353 | 0.671 |
| %RSD (NMT 5.0%) | 1.7 | 1.4 | 0.7 |




**GRAPH: LUBRICATION- CONTENT OF UNIFORMITY**

### 3.6 Blend Analysis: (Composite Sample)

| Test | Specification | Batch No | | |
|---|---|---|---|---|
| | | I | II | III |
| **Water by KF** | NMT 5% | 0.69% | 0.57% | 0.85% |
| **Bulk density** | 0.30 to 0.50 gm/ml | 0.47 gm/ml | 0.44 gm/ml | 0.42gm/ml |
| **Tapped density** | 0.50 to 0.70 gm/ml | 0.55 gm/ml | 0.58 gm/ml | 0.57 gm/ml |
| **Assay** | 95.0 to 105.0% on label claim | 97.1% | 96.2% | 97.9% |

**Results:** Parameters were well within the specification.

### 3.7 Tablet Compression

**EQUIPMENT NAME: TABLET COMPRESSION MACHINE**

| SR. NO. | TEST | SPECIFICATION | RESULT | | |
|---|---|---|---|---|---|
| **Batch No** | | | **I** | **II** | **III** |
| 1 | **Appearance** | White coloured elongated and film coated tablets free from loose dust. | Complies | Complies | Complies |
| 2 | **TheoreticalCompression Weight** | 900 mg / tab | Complies | Complies | Complies |
| 3 | **Weight of 20 tabl ts** | 18 g per 20 tablets | Complies | Complies | Complies |

| | | | | | |
|---|---|---|---|---|---|
| 4 | **Variation from Average Weight** | ± 3 % (16.296 g to 17.304 g) | ± 3 % (16.296 g to 17.304 g) | ± 3 % (16.296 g to 17.304 g) | ± 3 % (16.296 g to 17.304 g |
| 5 | **Dimensions** | | | | |
| | Length | 19.0 mm | 19.0mm | 19.0mm | 19.0 mm |
| | Thickness | 5.8 mm (Limit 5.6 mm to 6 mm) | 5.8mm | 5.8mm | 5.8mm |
| | Width | 9.1mm | 9.1mm | 9.1mm | 9.1mm |
| 6 | **Weight Variation** | NMT 2 tablets differ by + 5 % &None differs by + 10 % from average weight. | Complies | Complies | Complies |
| 7 | **Disintegration time** | NMT 15 minutes | 7 min 6 Sec | 7min 4 sec | 7min 30 Sec |
| 8 | **Hardness** | NLT 5 kg | NLT 5 kg | NLT 5 kg | NLT 5 kg |
| 9 | **Friability** | NMT 1 % (Action limit: 0.3%) | NMT 1% (Action limit:0.3% | NMT 1 % (Action limit:0.3%) | NMT 1 % (Action limit:0.3%) |
| 10 | **Shape Of Upper& lower Punch** | capsule | capsule | capsule | capsule |

## X. CONCLUSION

Aceclofenac 100mg & paracetamol 500 mg tablets B.No: I, II and III parameters at the Initial stage of Compression,& during compression at middle stage ,&at the end of the compression & composite parameters & composite sample analysis results (after coating) were found complies and well within the specification limits.

## XI. SUMMARY AND CONCLUSION

Based on the data obtained from the process validation batches of aceclofenac 100mg and paracetamol 500mg tablets, it is observed that,

- The results of the process validation batches at different manufacturing stages i.e. dry mixing, Wet granulation, Drying, Pre-lubrication and Lubrication are found satisfactory and well within the specification limits.
- The raw materials (API & Excipients) which were used were taken from the approved vendor source.
- The equipments which were used at various stages of the manufacturing are already been qualified and validated as per the respective validation master plan and other standard operating procedures.
- The critical process parameters and critical process steps which were identified at various stages of the manufacturing were found well within the specification limits. Hence, it can be recommended that, the same parameters shall be considered as final for the further commercial production batches of aceclofenac 100mg and paracetemol 500mg tablets.

- The process which is adopted for the following stages is considered as validated and the same process can be used further without any changes.
  - Dry Mixing
  - Wet Granulation
  - Drying
  - Pre-Lubrication
  - Lubrication

**Conclusion**

Aceclofenac 100mg and paracetamol 500mg tablets were considered for the process validation batches of manufacturing process. Based on the above summary and evaluation of data, it can be concluded that, the process adopted for the manufacturing of aceclofenac 100mg and paracetamol 500mg tablets is considered as validated for dry mixing, wet granulation, drying, pre-lubrication and lubrication.

**REFERENCES**

[1] P.P.Sharma, validation in pharmaceutical industry, concepts, approaches& guidelines, vandana publications pvt ltd.

[2] An Overview Of Pharmaceutical Validation And Process Controls In Drug Development, www.ajol.info /index. php/ tjpr/article/view/14592/16163

[3] Quality Management System Process Validation System, www.ghtf.org/documents/sg3/sg3_fd_n99-10_edition2.pdf

[4] Concept of Process Validation For Pharmaceutical Industry http://eziniearticles.com/?Concept-of-Process-Validation-For-Pharmaceutical-Industry&id=2404112

[5] A Practical Roadmap To Pharmaceutical Process Validation, http://www.pharmaqbd.com/a-practical-roadmap-to-pharmaceutical-process-validation/

[6] QA and R&D Department of Sun rise international labs Ltd.

[7] Validation Protocol, Reports of Sun rise international labs Ltd.

[8] PIC/S Pharmaceutical Inspection Co Operation Scheme, http://www.picscheme.org/

[9] "Guidelines On General Principles Of Process Validation'', EMEA, www.ema.europa.eu/ ema/pages/includes/ document/open_document.jsp?...(EMEA)

[10] Preparation of validation master plan, www.hsa.gov.sg/publish/etc/...1.../GUIDE-MQA-005-006-web.pdf

[11] Equipment Qualification, www.analytik-jena.de/files_db/1246610013_1148__22.pdf

[12] Lachman, Liberman. H.A, Kanig.J.L. The Theory and Practice of Industrial Pharmacy, Third Edition. IC/S Pharmaceutical inspection Cooperation Scheme, http://www.picscheme.org/

[13] "Guidelines on general principles of process validation'', fda, www.pharmamanufacturing.com /industrynews/ 2011/012.html(FDA)

[14] A WHO guide to good manufacturing practice (GMP) requirements whqlibdoc.who.int /hq/ 1997/ WHO_ VSQ_97.02.pdf

[15] General consideration about the process validation, http://en.wikipedia.org/wiki/Validation, http://en.wikipedia. org/wiki/ Validation_%28drug_manufacture%29 http://en.wikipedia.org/wiki/Verification_and_validation.