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Puducherry.

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Product Name	Ibuprofen and Paracetamol Tablets	Product ID No.	977
Protocol Number	PVP/21/020	MFC No.	ST/MFC/118/R0
Effective Date	01/06/21	Market	EXPORT

PROCESS VALIDATION PROTOCOL

IBUPROFEN BP 400mg AND PARACETAMOL

BP 500mg TABLETS



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1.0 APPROVAL

Prepared By	Name	Designation	Signature	Date
QUALITY ASSURANCE	P. Vadivel	Sr. Executive QA	P. Vadivel	31/05/21

Reviewed By	Name	Designation	Signature	Date
PRODUCTION	V. Dharambadi	Sr. Gm	[Signature]	31/05/21
QUALITY CONTROL	V. Vijayaraj Kumar	AGM.	[Signature]	01/06/21

Approved By	Name	Designation	Signature	Date
QUALITY ASSURANCE	K. Chandrasekar	AGM.	[Signature]	01/06/21



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2.0 SCOPE:

This protocol is applicable for the manufacturing and sampling of Validation batches of **IBUPROFEN BP 400mg and PARACETAMOL BP 500mg** tablets with a batch size of 8.0 Lac tablets. In case data obtained from validation batches seem to be inadequate, further extension of the validation batches shall be done. For further confidence of efficacy and fitness till its assigned shelf life, this batch shall be charged for stability studies.

3.0 OBJECTIVE:

The objective of this protocol is to validate the process by establishing documented evidence for **IBUPROFEN BP 400mg and PARACETAMOL BP 500mg** tablets, to be manufactured at Safetab Life Science, Plot No: A-67-72, PIPDIC Electronic Park, Thirubuvanai, Puducherry, so that this will provide sufficient data there by the process will produce the product meeting its pre-determined specification and quality attributes in a reproducible manner.

4.0 INTRODUCTION:

IBUPROFEN BP 400mg and PARACETAMOL BP 500mg tablets is a solid dosage which contains Ibuprofen BP and Paracetamol BP as active ingredient. This is being manufactured at Safetab Life Science, Puducherry, with the batch size of 8.0 lac tablets as per Master Formula Card (MFC).

5.0 PROCESS VALIDATION APPROACH:

Prospective type of validation [Process Performance Qualification (PPQ)] approach will be adopted and the batches will be released for after verifying the compliance of validation acceptance criteria. During this validation the below mentioned process stages shall be evaluated for the controlling parameters, sequence, criticality to product quality and performance:

Note: PPQ batch will be released on concurrent approach through an interim process validation report.

- Dry Mixing
- Wet Granulation
- Drying
- Sizing
- Blending
- Compression

Data shall be collected from executed batch manufacturing record, IPQA test data sheets and in-process/ validation sample analysis reports, for the compilation of report.



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6.0 RESPONSIBILITY:

Validation Team	Responsibilities
Quality Assurance	1) Defining the manufacturing process and process parameters that impact the quality, safety, purity and efficacy of the product based on the knowledge gained through process validation.
	2) To ensure pre-requisite requirements are completed before proceeding for Process validation.
	3) Preparation of Process validation Protocol and Report.
	4) In-process monitoring and assurance of quality. Withdrawal of samples as per the sampling plan defined in this protocol.
	5) Review of batch records, analytical reports, compilation of data, evaluation of results and Process validation report.
	6) Reviewing and approving investigations and CAPA for deviations from defined manufacturing process and Process Validation protocol.
Production	1) Review of Process Validation protocol and Report.
	2) Execution of process as per the batch record and Process validation protocol and relevant operating procedures.
	3) Co-ordination with Quality Assurance for sampling.
	4) Investigating any deviations from defined manufacturing process and Process Validation protocol and identifying CAPA.
Quality Control	1) Review of Process validation protocol and report.
	2) Testing the samples drawn during Process validation study and compilation of results.
Engineering	1) Providing necessary utility as per the product requirement.
	2) Ensuring calibration of measuring devices available on process equipment and utilities and maintenance of processing equipments.
Head Quality Assurance	1) Approval of Protocol and Report.
	2) To review and approve the investigations and CAPA for deviations From defined manufacturing process and protocol.
	3) To take decision on further release and distribution of validation batches.



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7.0 PRODUCT DETAILS:

Product Name	Ibuprofen and Paracetamol Tablets
Label Claim	Each Uncoated tablet contains: Ibuprofen BP 400mg Paracetamol BP 500mg Colour: Approved Colour used
Overages (% w/w)	NA
Shelf life	36 Months
Storage Condition	Store at a temperature below 30°C. Protect from light.
Batch Size	800000 Tablets
Therapeutic Use	For the treatment of Patient with NSAIDs work by reducing pain, reducing swelling and lowering high temperatures. Paracetamol is an analgesic which works in a different way from ibuprofen to relieve pain and fever. Of non-serious arthritis, cold and flu symptoms, sore throat and fever.
Product Pack	Printed Foil: 172X0.04 mm sales printed foil. Base Foil: 176mm PVC Clear film.
Pack Style	Sales: (1X10)x10 Tablets

PRECAUTIONS:

Maintain temperature between 23°C to 27°C and relative humidity between 45% to 55% throughout the manufacturing process. Blended material and compressed tablets should be stored in HDPE container with double lined poly bags with lids securing on and labeled accordingly.



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8.0 RAW MATERIAL COMPONENTS:

Material Code	Ingredient	Grade	FUNCTION	Mg/Tablet	Quantity Kg/Batch 8.0 L	Vendor
Dry Mixing and Granulation:						
RMAP0030	Paracetamol ***	BP	Pain killer	500.000	400.000	Bharat Chemicals
RMAI0015	Ibuprofen ***	BP	NSAID	400.000	320.000	IOL Chemicals and Pharmaceuticals Pvt Ltd.
RMEM0034	Maize Starch ***	BP	Diluent	55.920	44.736	Roquette, Riddhi Siddhi
RMEP0044	Povidone K 90	BP	Binder	26.000	20.800	Haungshan Bonsun Pharmaceuticals
RMEP0048	Sodium Propyl Hydroxybenzoate	BP	Preservative	0.440	0.352	Rasula Pharmaceuticals and Fine Chemicals
RMES0030	Sunset Yellow supra	INH	Colourant	0.140	0.112	Neelkanth
RMEP0033	Purified Water @	BP	vehicle	175.000	140.000	Inhouse
RMEP0032	Pregelatinized Starch 1500	BP	Diluent	40.000	32.000	Colorcon
RMES0029	Sodium Starch Glycolate	BP	Disintegrant	15.000	12.000	Roquette Riddhi Siddhi
RMEM0033	Magnesium Stearate	BP	Lubricant	2.500	2.000	Nitika
Total				1040	832.000	-----

***Refer Calculation**

@ Does not appear in final product, Evaporate during the processing.

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9.0 CALCULATIONS:

9.1 Potency calculation for Paracetamol:

* The given quantity is based on 100% Assay on dried basis and without LOD.

Actual quantity to be added is calculated as:

$$500 \times 100 \times 100$$

$$\text{Actual quantity of Paracetamol} = \frac{\text{-----}}{\% \text{ Assay of Paracetamol on dried basis} \times (100 - \% \text{ LOD})} \text{ mg/tablet}$$

9.2 Potency calculation for Ibuprofen:

*The given quantity is based on 100% assay on dried basis, and without LOD.

Actual quantity to be added is calculated as:

$$400 \times 100 \times 100$$

$$\text{Actual quantity of Ibuprofen} = \frac{\text{-----}}{\% \text{ Assay of Ibuprofen on dried basis} \times (100 - \% \text{ LOD})} \text{ mg/tablet}$$

** Quantity Maize starch varies based on assay content of Paracetamol and Ibuprofen for keeping the core tablet weight constant.

Note: If the assay of Paracetamol and Ibuprofen more than 100 %, calculation has to be done only for 100%.



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10.0 PACKING MATERIAL COMPONENTS:

Material code	Components	Vendor
PMG00067	172x0.04mm printed Aluminum blister foil	Daga Poly Laminators PVT Ltd.
PMPV0036	176mm PVC clear back foil	ICM plastic PVT Ltd.

11.0 EQUIPMENT DETAILS:

Table 1: List of major process equipment to be used in the manufacturing:

Sr. No.	Equipment	Make	Equipment No.
1.0	Weighing Balances	Essae Teraoka	ST/WB/189 ST/SRWB/001 ST/SRWB/002 ST/PRWB/001 ST/PRWB/002
2.0	Vibratory Sifter	GEM Pharma	ST/PRVS/001 or ST/PRVS/002 or ST/PRVS/003 or ST/PRVS/004
3.0	Fluid bed drier(250kg)	GEM Pharma	ST/PRFD/003
4.0	Rapid mixer granulator(600L)	GEM Pharma	ST/PRRG/005
5.0	Multimill	GEM Pharma	ST/PRG/009
6.0	Octagonal Blender (2200L)	SRI KARPAGA VINAYAGAR	ST/PROB/001
7.0	Compression Machine 27 stn.	CADMECH	ST/PRCM/001 or ST/PRCM/003 or ST/PRC/004 or ST/PRCM/004
8.0	Blister packing machine	Rapid pack Rapid pack-240	ST/PPB/001 ST/PPB2/001



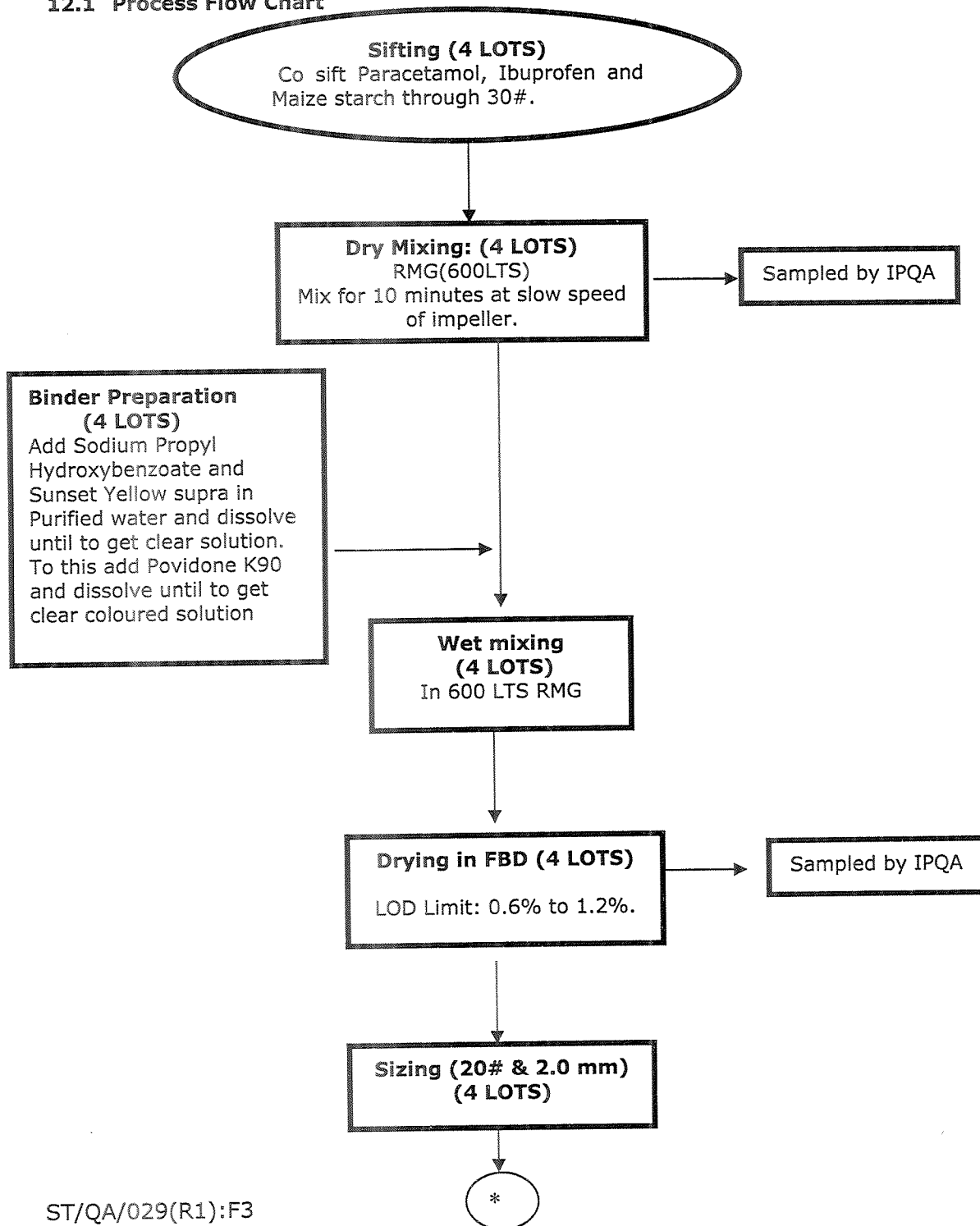
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12.0 PROCESS DESCRIPTION:

12.1 Process Flow Chart

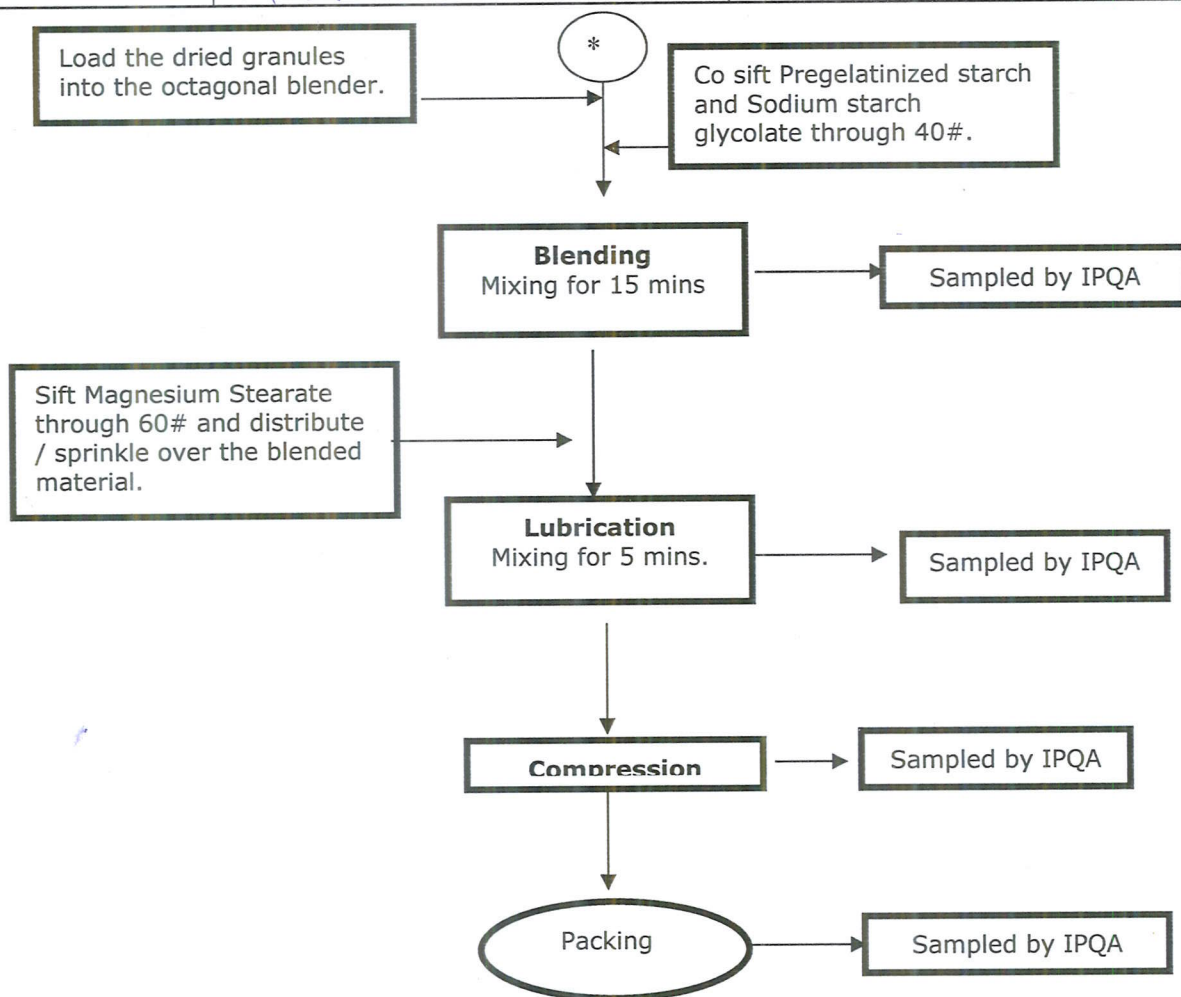




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12.2 Brief Explanation of manufacturing process:

The steps in the manufacturing process shall be followed as per the approved batch manufacturing record. Process parameters during each unit operation shall be monitored to demonstrate that product meets the Acceptance Criteria.

The processing of Paracetamol and Ibuprofen tablets comprises of following stages:

Stage	Manufacturing Procedure
1 Dispensing	Dispense the raw material as per the standard operating procedure.
2. Sifting	Co sift equal amount Paracetamol, Ibuprofen and Maize starch through 30#.
3.Dry Mixing	Load sifted materials into RMG and mix for 10 minutes at slow speed of impeller and chopper off.
4. Binder Preparation	Add Sodium Propyl Hydroxybenzoate and Sunset Yellow supra in Purified water and dissolve until to get clear solution. To this add Povidone K90 and dissolve until to get clear coloured solution.
5. Granulation	Granulation:(Wet mixing) Binder addition: 3-5 minutes mixing at slow/fast speed impeller/chopper ON at slow/fast speed. Kneading: Mixing: 2-5 minutes mixing at fast/slow speed impeller/chopper ON at fast/slow speed. If required add additional Purified water and mix for 2-3minutes to form a required granules.



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Stage	Manufacturing Procedure
6. Drying and Sizing	Load the wet granules into FBD and air drying for 10-15 minutes with intermittent racking. Continue the drying at the temperature of $50^{\circ}\text{C} \pm 5^{\circ}\text{C}$ until LOD reaches the limit 0.6% to 1.2%. Sift the dried granules through 16#. Mill the retained granules through 2.0mm screen and pass through 20#. NOTE: Dispensing, Sifting, Dry Mixing, Binder Preparation, Granulation, Drying and Sizing 4 Lots.
7. Blending and Lubrication	Load the dried granules into the octagonal blender. Co sift Pregelatinized starch and Sodium starch glycolate through 40#. Mix for 15minutes. Sift the Magnesium Stearate through 60# and distribute / sprinkle over the blended material Mix for 5 minutes. Unload the final lubricated granules into the suitable container lined with double poly bag with proper status label.



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Stage	Manufacturing Procedure	
8.0 Compression	Compress the blend as single layer tablet by using Upper Punch: 19.3x9.0mm oval shape biconcave with break line. Lower punch: 19.3x9.0mm oval shape biconcave plain. Dies : 19.3x9.0mm. Pass the compressed tablets through deduster to remove powder particles.	
	Description	Light orange coloured oval shape biconvex uncoated tablets with half break line on one side and plain on another side.
	Average Weight per tablet	1040mg± 3.00% (1008.800mg-1071.200mg)
	Weight of 20 tablets	20.800±3.00% (20.176g to 21.424g)
	Uniformity of weight	Average weight ± 5% (988.000mg to 1092.000mg)
	Thickness	7.90± 0.3mm (7.60 to 8.20 mm) ***
	Hardness	160 N to 230 N ***
	Friability	NMT 1.0%w/w
	Disintegration Time	NMT 15 mins at 37°C±2°C
NOTE: ***Test shall be monitored to first 3 batches.		



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Stage	Manufacturing Procedure
9.0 Inspection	Inspect the tablets visually for removing defected tablets.
10.0 Metal detector	Tablets pass through the metal detector.



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13.0 SAMPLING PLAN AND ACCEPTANCE CRITERIA:

13.1 CRITICAL PROCESS STAGES TO BE VALIDATED:

13.1.1 DRY MIXING STAGE

DRY MIXING PROCEDURE (Refer MFR/BMR more details)	CRITICAL PARAMETER TO BE VALIDATED	SAMPLING PROCEDURE
Co sift equal amount Paracetamol, Ibuprofen and Maize starch through 30#. Load sifted materials into RMG and mix for 10 minutes at slow speed of impeller and chopper off.	MIXING TIME	Samples shall be withdrawn from 10 different locations Collect approximately 2gm of Dry mixing powder sample. Location each in duplicate from top, middle and bottom level of the RMG (as per 18.1) separately using sampling thief after 10 minutes mixing. Use these samples for blend uniformity test as per 13.2.1.1 Note: Duplicate samples to be retained for contingency.

13.1.2 DRYING

DRYING PROCEDURE (Refer MFR/BMR more details)	CRITICAL PARAMETER TO BE VALIDATED	SAMPLING PROCEDURE
Loss on drying of dried granules to be evaluated using Moisture balance.	DRYING	Samples of the dried granules shall be withdrawn from FBD bowl from 5 random locations (As per 18.2).



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13.1.3 BLENDING AND LUBRICATION STAGE

BLENDING AND LUBRICATION PROCEDURE (Refer MFR/BMR more details)	CRITICAL PARAMETER TO BE VALIDATED	SAMPLING PROCEDURE
Step-1: Dried granules shall be loaded into Octagonal blender and Co sift Pregelatinized starch and Sodium starch glycolate through 40#. Mix for 15 minutes. Step - 2 Sift the Magnesium Stearate through 60# and distribute / sprinkle over the blended material Mix for 5 minutes.	<u>1. Mixing time (Pre-lubricated blend uniformity)</u> <u>2. Mixing time (Lubricated blend uniformity)</u>	<u>Step- 1: PRE - LUBRICATION:</u> Samples shall be withdrawn from 10 different locations Collect approximately 2 g of blend sample. Location each in duplicate from top, middle and bottom level of the Octagonal blender (as per 18.2) separately into the tarred using sampling thief after 15 minutes mixing. Use these samples for blend uniformity test as per 13.2.2.1 <u>Step- 2: AFTER LUBRICATION:</u> Samples shall be withdrawn from 10 different locations Collect approximately 2 g of lubrication blend sample. Location each in duplicate from top, middle and bottom level of the Octagonal blender (as per 18.2) separately into the tarred vials using sampling thief after 5 minutes mixing. Use these samples for blend uniformity test as per 13.2.2.2 For first batch only: After 3 minutes mixing of lubricated blend, collect a pooled sample – about 250g total from three different sampling locations viz; top, middle and bottom of the Octagonal blender. Use this pooled sample for evaluation of physical parameters as per 13.2.2.2



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13.2 TEST PROGRAM AND ACCEPTANCE CRITERIA FOR VALIDATION:

S.No.	MEASURED PARAMETERS	ACCEPTANCE CRITERIA	TEST PROCEDURE
13.2.1	GRANULATION PROCESS :		
13.2.1.1	Dry Mixing:		
1	Blend uniformity: (Paracetamol and Ibuprofen)	Individual sample values between 85% to 115% & RSD: NMT 5 % Average value between 90% to 110%.	Specification and test procedure no: IMSG00121-00 IMTG00121-00
13.2.2	BLENDING & LUBRICATION PROCESS:		
13.2.2.1	BLENDING – PRE LUBRICATION:		
1	Blend uniformity: (Paracetamol and Ibuprofen)	Individual sample values between 85% to 115% & RSD: NMT 5 % Average value between 90% to 110%.	Specification and test procedure no: IMSG00121-00 IMTG00121-00
13.2.2.2	LUBRICATION:		
1	Appearance (pooled sample)	Light orange colour powder	Specification and test procedure no: IMSG00121-00 IMTG00121-00
2	Blend uniformity: (Paracetamol and Ibuprofen)	Individual sample values between 85% to 115% & RSD: NMT 5 % Average value between 90% to 110%.	
3	Bulk density (Weight of 100 ml -pooled sample)	For information only	NA
4	Tap density (pooled sample)	For information only	



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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
13.2.3	COMPRESSION PROCESS:			
13.2.3.1	COMPRESSION FORCE To find out the hardness range, the following procedure to be adopted. To fix minimum compression force: Adjust the compression force to achieve the thickness at higher limit 8.20mm and run the machine. Record the minimum compression force. Collect about 100 tablets and perform tests as per Specification and Test Procedure given at right side. To fix standard compression force: Adjust the compression force to achieve the thickness at standard limit 7.90mm and run the machine. Record the optimum compression force. Collect about 100 tablets and perform tests as per Specification and Test Procedure given at right side.	i) Appearance ii) Average weight (20 tablets) iii) Weight Variation (20 tablets) iv) Thickness (Average 10 tablets) v) Friability	Light orange coloured oval shape biconvex uncoated tablets with half break line on one side and plain on another side. 1040mg± 3.00% (1008.800mg-1071.200mg) Not more than 2 of the individual masses deviate from the average mass by more than ±5%. 7.90mm± 0.3mm (7.60mm to 8.20 mm) Not more than 1.0% w/w	Specification and test procedure no: IMSG00122-00 IMTG00122-00



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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
	To fix maximum compression force: Adjust the compression force to achieve the thickness at lower limit 7.60mm and run the machine. Record the maximum compression Force. Collect about 100 tablets and perform tests as per Specification and Test Procedure given at right side. This challenge study is applicable for first validation batch only. Fixed compression forces shall be verified in next two consecutive validation batches.	vi)Hardness (Average of 10 tablets) vii)Disintegration time	160 N to 230 N Not more than 15 minutes	Specification and test procedure no: IMSG00122-00 IMTG00122-00



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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
13.2.3.2	Compression Rate (RPM -Challenge)			
	<u>For first batch only:</u> Start compressing the lubricated blend at constant optimum compression force parameters, hopper level – (not at nearly-empty) and at minimum to maximum compression speeds starting from 10rpm, 15 rpm, 20rpm, 25rpm, 30rpm, & 35rpm , Collect about 100 tablets during each speed individually. To fix the Minimum Speed: Initially check the physical parameters of the tablets collected at 10 rpm. If all the physical parameters comply with the acceptance criteria, fix 10rpm as the minimum speed. If any physical parameter does not comply with the acceptance criteria, repeat the same procedure to the next sample collected at 12rpm.	i) Appearance ii) Average weight (20 tablets) iii) Weight Variation (20 tablets) iv) Thickness (Average 10 tablets) v) Friability	Light orange coloured oval shape biconvex uncoated tablets with half break line on one side and plain on another side. 1040mg± 3.00% (1008.800mg-1071.200mg) Not more than 2 of the individual masses deviate from the average mass by more than ±5%. 7.90mm± 0.3mm (7.60mm to 8.20 mm) Not more than 1.0% w/w	Specification and test procedure no: IMSG00122-00 IMTG00122-00



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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
	Repeat this procedure at different speeds as mentioned above (in an increasing order) and fix the minimum speed on which all the test results are satisfactory. To fix the Maximum Speed: Similarly check on the last sample collected at 35 rpm. If all the results are satisfactory fix the same as the maximum speed. If not, check on the previous sample collected at 18rpm. Repeat this procedure at different speeds as mentioned above (in a decreasing order) and fix the maximum speed on which all the test results are satisfactory. This challenge study is applicable for first validation batch. Fixed compression machine speeds shall be verified in next two consecutive validation batches.	vi)Hardness (Average of 10 tablets) vii)Disintegration time	160 N to 230 N Not more than 15 minutes	Specification and test procedure no: IMSG00122-00 IMTG00122-00

ST/QA/029(R1):F3



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Title	PROCESS VALIDATION PROTOCOL		Page No.: 23 of 32
Product Name	Ibuprofen and Paracetamol Tablets	Product ID No.	977
Protocol Number	PVP/21/020	MFC No.	ST/MFC/118/R0
Effective Date	01/06/21	Market	EXPORT

S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
13.2.3.3	Hopper Level (Hopper level - Challenge)			
	<u>For first batch only:</u> Collect about 100 tablets while running the machine at optimum setting parameters and at three different levels of blend in the hopper. (Full, Half-full and Nearly -empty) Initially check the physical parameters (other than assay and dissolution) for all the samples collected at three different hopper levels. If any physical parameter does not comply with the acceptance criteria for any sample, raise an unplanned deviation report as per ST/QA/005(R2):F3. If all the test results are well within the acceptance criteria for all the hopper levels, perform the assay and dissolution for the samples collected at nearly-empty level.	i) Appearance ii) Average weight (20 tablets) iii) Weight Variation (20 tablets) iv) Thickness (Average 10 tablets)	Light orange coloured oval shape biconvex uncoated tablets with half break line on one side and plain on another side. 1040mg± 3.00% (1008.800mg-1071.200mg) Not more than 2 of the individual masses deviate from the average mass by more than ±5%. 7.90mm± 0.3mm (7.60mm to 8.20 mm)	Specification and test procedure no: IMSG00122-00 IMTG00122-00



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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
	If assay and dissolution tests also comply with the acceptance criteria, conclude that process complies at all the blend levels in the hopper. If assay and / or dissolution test for the samples collected at nearly-empty level does not comply to the acceptance criteria, raise an unplanned Deviation report as per ST/QA/005(R2):F3 and perform the assay and dissolution tests on the samples collected at half-full hopper level.	v) Friability vi) Hardness (Average of 10 tablets) vii) Disintegration time viii) Assay: i) Ibuprofen BP 400mg ii) Paracetamol BP 500mg	Not more than 1.0% w/w 160 N to 230 N Not more than 15 minutes 90.0% - 110.0% of the labeled claim 90.0% - 110.0% of the labeled claim	Specification and test procedure no: IMSG00122-00 IMTG00122-00



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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
	If the results are not satisfactory, repeat the same with samples collected at full hopper level also. If assay and dissolution tests for the samples collected at half -full hopper level comply with the acceptance criteria, the assay and dissolution tests are not necessarily to be carried out for the Samples at full hopper level. This challenge study is applicable for first validation batch. Near empty level shall be verified in next two consecutive validation batches	ix) Dissolution i) Ibuprofen BP ii) Paracetamol BP	Not less than 80% of stated amount ibuprofen dissolved in 60 minutes Not less than 80% of stated amount paracetamol dissolved in 60 minutes	Specification and test procedure no: IMSG00122-00 IMTG00122-00



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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
13.2.3.4	Composite Sample (100 NO'S) to be collected to represent entire batch.	i) Appearance ii) Average weight (20 tablets) iii) Weight Variation (20 tablets) iv) Thickness (Average 10 tablets) v) Friability vi) Hardness (Average of 10 tablets) vii) Disintegration time	Light orange coloured oval shape biconvex uncoated tablets with half break line on one side and plain on another side. 1040mg± 3.00% (1008.800mg-1071.200mg) Not more than 2 of the individual masses deviate from the average mass by more than ±5%. 7.90mm± 0.3mm (7.60mm to 8.20 mm) Not more than 1.0% w/w 160 N to 230 N Not more than 15 minutes	Specification and test procedure no: IMSG00122-00 IMTG00122-00

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Title	PROCESS VALIDATION PROTOCOL		Page No.: 27 of 32
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S.NO	SAMPLING LOCATION	MEASURED PARAMETER	ACCEPTANCE CRITERIA	TEST PROCEDURE
	Composite Sample (100 NO'S) to be collected to represent entire batch.	viii) Assay: i) Ibuprofen BP 400mg ii) Paracetamol BP 500mg ix) Dissolution i) Ibuprofen BP ii) Paracetamol BP x) Related Substances i) Single maximum unknown purity. ii) Total impurities.	90.0% - 110.0% of the labeled claim 90.0% - 110.0% of the labeled claim Not less than 80% of stated amount ibuprofen dissolved in 60 minutes Not less than 80% of stated amount paracetamol dissolved in 60 minutes Not more than 0.20%. Not more than 0.50%	Specification and test procedure no: IMSG00122-00 IMTG00122-00



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14.0 PROCESS PARAMETERS:

Manufacturing Process Stages	Critical Process Parameters	Set-Point
Dry Mixing	Mixing Time	10 min
Drying	LOD	0.6 to 1.2%
Sizing	Sifter Screen	16#
	Miller Screen	2.0mm
Blending	Mixing Time	15 min
Lubrication	Mesh size	60#
	Lubrication Time	5 min
Compression	Compression Machine Speed	10 – 35 rotation/min ***
	Hardness	160 N to 230 N ***
Packing	Sealing temperature	190°C to 205°C ***
	Speed of blister packing machine	30-40 strokes/min ***

NOTE: *Test shall be monitored to first 3 batches.**



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15.0 YIELD (%):

Yield details shall be captured in process validation report as per the batch record.

16.0 DEVIATIONS:

Any deviation from the protocol related to manufacturing process, raw materials, equipments used, sampling, in-process controls and analytical methods should be authorized and documented in the batch manufacturing record as well as the validation report.

17.0 EVALUATION OF RESULTS AND CONCLUSION:

A Process validation report shall be prepared to summarise the results of the batch validation studies and process parameters shall be established and reflected in the validation summary sheet which shall be attached to the protocol after the completion of validation batches. On the basis of evaluation of results, a conclusion shall be drawn to state the adequacy of the process to carry out the manufacturing of Ibuprofen and Paracetamol Tablets.



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18.0 SAMPLING LOCATION DIAGRAM:

18.1 Sampling Plan Diagram of RMG:

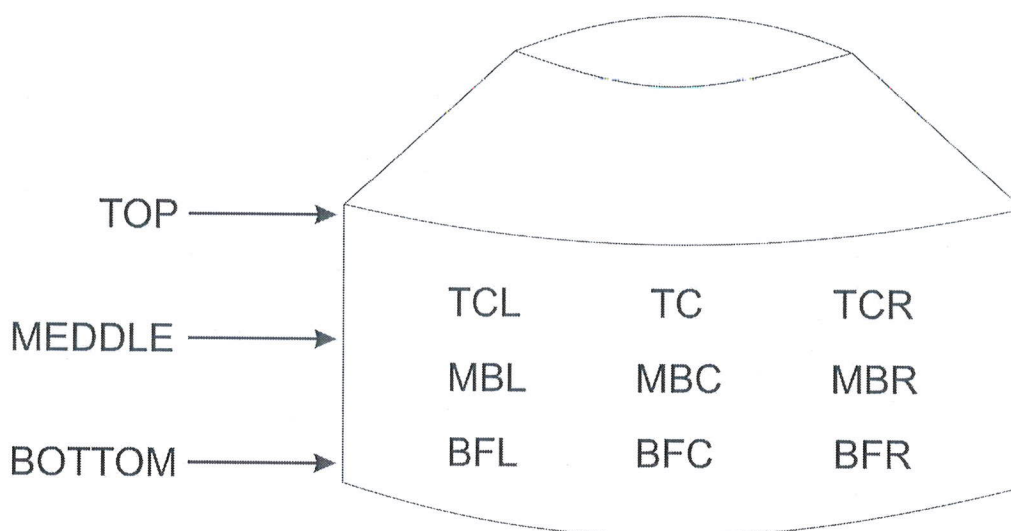


Fig. No.1

- TCL - Top center left
- TC - Top center
- TCR - Top center right
- MBL - Middle back left
- MBC - Middle back center
- MBR - Middle back right
- BFL - Bottom front left
- BFC - Bottom front center
- BFR - Bottom front right



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18.2 Sampling Plan Diagram of FBD:

SIDE VIEW

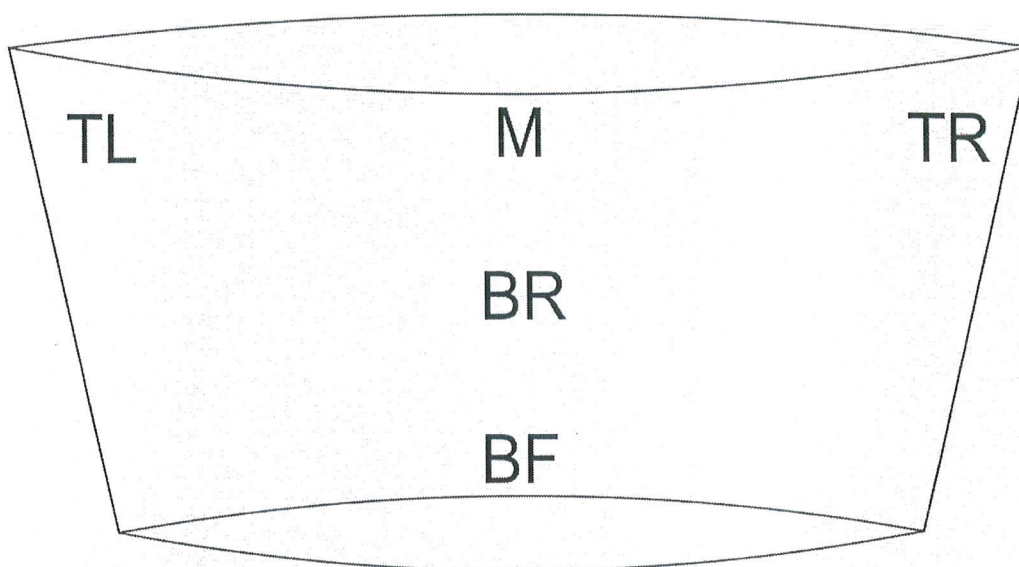


Fig. No.2

TL – Top Left
TR – Top Right
M – Middle
BF – Bottom Front
BR – Bottom Rear



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18.3 Sampling Plan Diagram of Octagonal Blender:

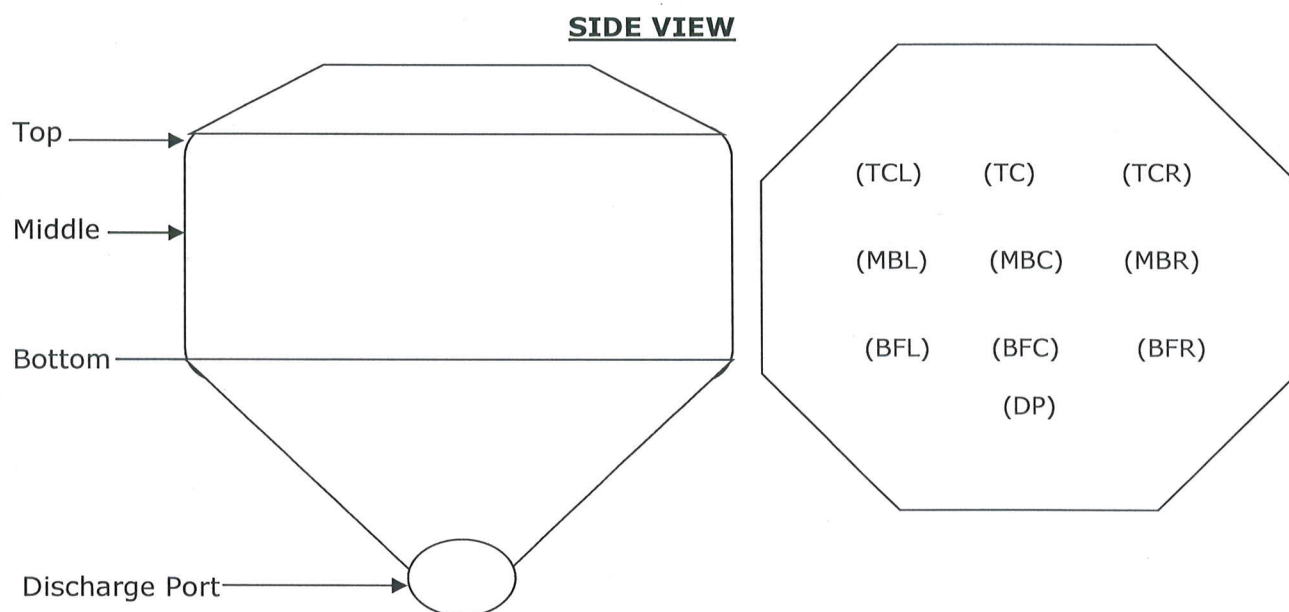


Fig-3

Samples are to be drawn from 10 different positions as follows:

- TCL – Top center left
- TC – Top center
- TCR – Top center right
- MBL – Middle back left
- MBC – Middle back center
- MBR – Middle back right
- BFL – Bottom front left
- BFC – Bottom front center
- BFR – Bottom front right
- DP – Discharge port