PROCESS VALIDATION PROTOCOL CUM REPORT

FOR

PARACETAMOL, PHENYLEPHRINE HYDROCHLORIDE,

CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER

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1.0 PROTOCOL APPROVAL :

1.1 Prepared By :

Dept.	Name	Designation	Signature	Date
Quality Assurance	P. Vadivel	Sr. Executive QA	P. Vad	18/04/22

1.2 Verified By:

Dept.	Name	Designation	Signature	Date
Head-Production	G. Vijayalakshmi	Sr. Manager Production	Vijayalakshmi	19/04/22
Head-Quality Control	M. Vijayakumar	AGM-QC		19/04/22

1.3 Approved By:

Dept.	Name	Designation	Signature	Date
Head-Quality Assurance	A. G. Ramesh	GM - QA	A. G. R	19/04/22

2.0 PURPOSE:

To establish that the manufacturing process (blending, Filling stage) of Paracetamol, Phenylephrine Hydrochloride, Chlorphenamine Maleate and Ascorbic Acid Powder will meet the predetermined specifications and quality attributes consistently.

3.0 SCOPE:

This protocol is applicable for the manufacturing and sampling of validation batches of Paracetamol, Phenylephrine Hydrochloride, Chlorphenamine Maleate and Ascorbic Acid Powder with a batch size of 200000 Sachets. 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, these three batches shall be charged for both Long term and Accelerated stability study.

4.0 RESPONSIBILITIES OF VALIDATION TEAM:

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.

5.0 ACCEPTANCE CRITERIA:

All the product quality parameters must comply within the acceptance criteria as specified in this protocol.

6.0 PROCEDURE:

Execute three batches as per Master Formula Record and Batch Manufacturing Record. Record the critical parameters of the manufacturing unit operations as described in this protocol and compile subsequent test report. Raise deviation as per ST/QA/005. if any abnormalities found during the process validation. Necessary corrective actions and preventive actions if required shall be documented.

7.0 PRODUCT DETAILS:

Product Name	PARACETAMOL, PHENYLEPHRINE HYDROCHLORIDE, CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER
Label Claim	Each 4.5g sachet contains: Paracetamol BP 650mg Phenylephrine Hydrochloride BP 10mg Chlorphenamine Maleate BP 20mg Ascorbic Acid BP 50mg Flavour: Lemon flavour used.
Shelf life	36 Months
Storage Condition	**Store in cool and dry place. Protect from light.**
Batch Size	200000 sachets
Therapeutic Use	Used to temporarily relieve symptoms caused by the common cold, Flu, Allergies or other breathing illness. Antihistamines help to relieve watery eyes, runny nose, Sneezing.
Product Pack	120mm,4 colours-PET :12µ,Aluminium:9µ,LDPE:65µ
Pack Style	10 X 4.5g sachets

Product Name : PARACETAMOL, PHENYLEPHRINE HYDROCHLORIDE, CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER			
BRAND NAME:			
Batch No :			
Batch Size :			
Mfg. Date :			
Expiry Date :			

8.0 REFERENCE DOCUMENTS FOR METHOD OF MANUFACTURING AND TESTING:

S.No.	NAME OF THE DOCUMENT	DOCUMENT NUMBER
1	Batch Manufacturing Record	BMR:134/01
2	Product specifications and Test Procedure	IMSG00137-00 IMTG00137-00

9.0 REASON FOR VALIDATION:

Reasons	Tick in the appropriate row	Reasons	Tick in the appropriate row
New formulation		Significant changes in process	
Change in formulation		Change/modification in equipment	
Change in location		Change in batch size	
Change in vendor of API		Any other reasons (specify)	

10.0 BILL OF RAW MATERIALS

Material code	Name of the Ingredient	Specification	Mg/ Sachet	Std.Qty.per batch (kg)	Approved Vendor
RMAP0030	Paracetamol*	BP	650.000	130.000	Valiant Laboratories LTD
RMAP0031	Phenylephrine Hydrochloride*	BP	10.000	2.000	Divis Laboratories
RMAC0064	Chlorphenamine Maleate*	BP	20.000	4.000	Supriya Life Science
RMAA0029	Ascorbic Acid*	BP	50.000	10.000	Bajaj Health Care
RMAM0044	Maltodextrin #	BP	2215.000	443.000	Roquette India PVT .Ltd
RMEC0017	Hydrophobic colloidal anhydrous silica	BP	30.000	6.000	Wacker
RMEC0020	Citric Acid Monohydrate	BP	50.000	10.000	Sunil Chemicals
RMEO0027	Orange Pekoe Extract	IHS	1200.000	240.000	Omni Active Health Technologies
RMES0034	Sucralose	BP	25.000	5.000	Shangdong kanbo Bio chemical
RMEL0025	Lemon lime Premaseal (75412-71)	IHS	250.000	50.000	Givaudan India Pvt.Ltd
Total			4500.000	900.000	

*, # Quantity varies based on Potency Calculation

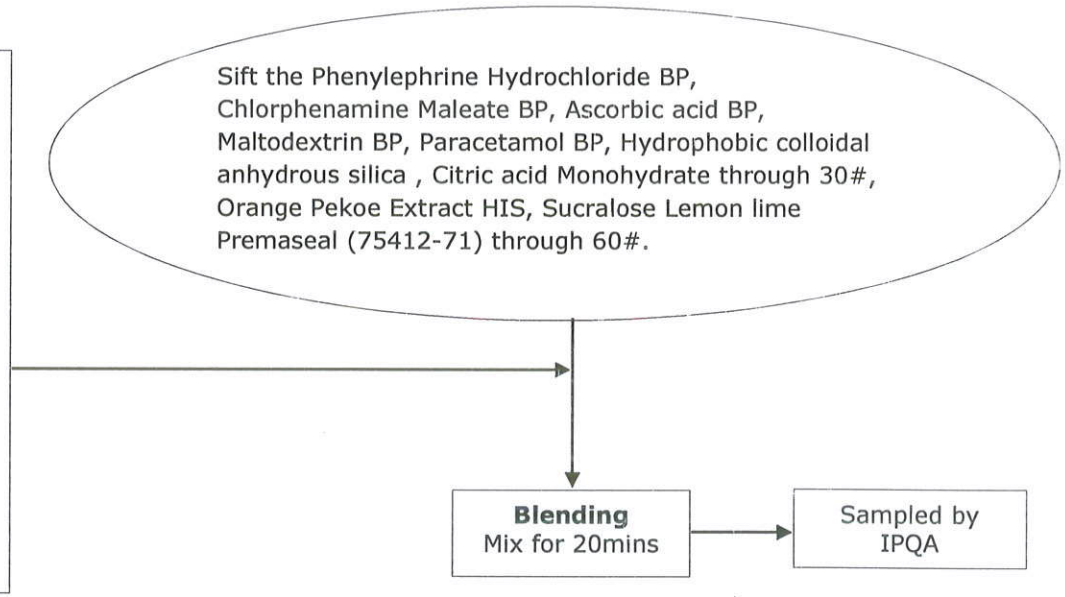
11.0 EQUIPMENT DETAILS:

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

SR.NO.	EQUIPMENT	MAKE	EQUIPMENT NO.
1.	WEIGHING BALANCE	ESSAE TERAOKA PVT LTD	ST/SRWB/001, ST/SRWB/002, ST/WB/189, ST/PRWB/002, ST/WB/202
2.	SIFTER	SARAL	☐ ST/PRVS/001, ☐ ST/PRVS/002, ☐ ST/PRVS/003 ☐ ST/PRVS/004
3.	BLENDER (2200 LTS)	SRI KARPAKA VINAYAKAR	ST/PROB/001
Note: Put tick mark (√) whichever is applicable			

12.0 PROCESS FLOW CHART :

Step 1. Co-sift Phenylephrine Hydrochloride, Chlorphenamine Maleate and ascorbic acid through 30#.
Step 2. Mix step (1) material with maltodextrin in geometrical dilution method by sifting through 30#.
Step 3. Co-sift with Paracetamol through 20#.
Step 4. Load the above sifted material into the octagonal blender and mix for 20 minutes and then sift through 20#.
Step 5. Hydrophobic colloidal anhydrous silica and Citric acid Monohydrate through 30#.
Step 6. Sift sucralose, lemon lime premaseal 75412-71 and Orange Pekoe Extract through 60#.
Transfer the sifted material step (4), step (5) and step (6) into the octagonal blender and mix for 20 minutes
Unload the final blend into double polybag lined container with Proper status label.



13.0 CRITICAL PROCESS STAGES TO BE VALIDATED:

13.1 BLENDING STAGE:

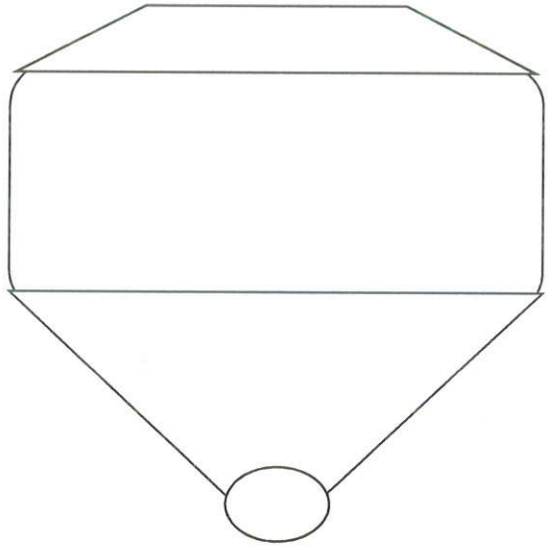
BLENDING AND LUBRICATION PROCEDURE (Refer MFR/BMR more details)	**CRITICAL PARAMETER TO BE VALIDATED**	**SAMPLING PROCEDURE**
Step 1. Co-sift Phenylephrine Hydrochloride, Chlorphenamine Maleate and ascorbic acid through 30#. **Step 2.** Mix step (1) material with maltodextrin in geometrical dilution method by sifting through 30#. **Step 3.**Co-sift with Paracetamol through 20#. **Step 4.**Load the above sifted material into the octagonal blender and mix for 20 minutes and then sift through 20#. **Step 5.**Hydrophobic colloidal anhydrous silica and Citric acid Monohydrate through 30#. **Step 6.**Sift sucralose, lemon lime premaseal 75412-71 and Orange Pekoe Extract through 60#. Transfer the sifted material step (4), step (5) and step (6) into the octagonal blender and mix for 20 minutes Unload the final blend into double polybag lined container with Proper status label.	1. Mixing time **(Blend uniformity)**	**BLENDING:** Samples shall be withdrawn from 10 different locations Collect approximately 20 g of blend sample each location from top, middle and bottom level of the Octagonal blender (as per sampling diagram 13.2) separately by using sampling thief after **20 minutes** mixing. Use these samples for blend uniformity test as per 14.1.1

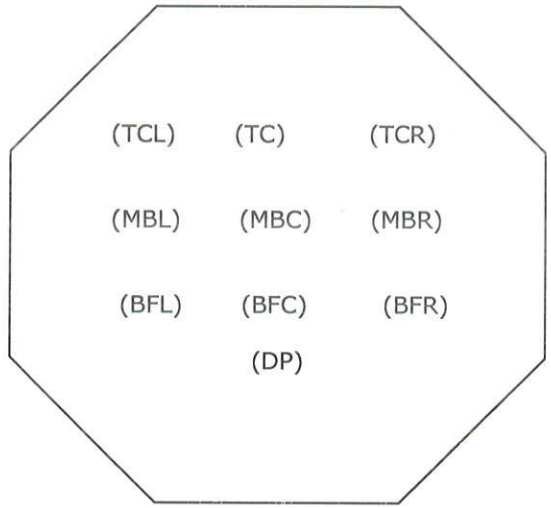
13.2 SAMPLING LOCATIONS IN OCTAGONAL BLENDER:

SIDE VIEW

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





14.0 TEST PROGRAM AND ACCEPTANCE CRITERIA FOR VALIDATION:

14.1 GRANULATION PROCESS:

S.No.	MEASURED PARAMETERS	ACCEPTANCE CRITERIA	TEST PROCEDURE
14.1.1	**BLENDING:**		
1	**Description**	Light brown colored, free flowing powder, with lemon flavour.	Specification and test procedure no: IMSG00137-00 IMTG00137-00
2	**Blend uniformity:**	Individual sample values between (85.0% to 115.0%) of label claim & RSD: NMT 6.0 % and Average value between (95.0% to 110.0%).	
3	**Bulk density** (pooled sample)	For information only	NA
4	**Tap density** (pooled sample)	For information only	
5	**Particle size distribution**	For information only	

15.0 TEST DATA FOR VALIDATION OF BLENDING : 1ST ,2ND & 3RD BATCHES

15.1 TEST DATA FOR VALIDATION OF BLENDING STAGE: 1st Batch No.:

S.No	MEASURED PARAMETERS	ACCEPTANCE CRITERIA	TEST RESULTS				
			Mixing time (20 minutes)				
			Sample Location	Paracetamol	Phenylephrine Hydrochloride	Chlorphenamine Maleate	Ascorbic Acid
1	**Blend uniformity:**	Individual sample values between (85.0% to 115.0%) of label claim & RSD: NMT 6.0 % and Average value between (95.0% to 110.0%).	**TCL**				
			TC				
			TCR				
			MBL				
			MBC				
			MBR				
			BFL				
			BFC				
			BFR				
			DP				
			Avg.				
			RSD				
			Composite				
All the validation test results of blending stage are found to be **satisfactory/not satisfactory.**			**QA-Sign & Date:**				

15.2 TEST DATA FOR VALIDATION OF BLENDING STAGE: **2nd Batch No.:**

S.No	MEASURED PARAMETERS	ACCEPTANCE CRITERIA	TEST RESULTS				
			Mixing time (20 minutes)				
			Sample Location	Paracetamol	Phenylephrine Hydrochloride	Chlorphenamine Maleate	Ascorbic Acid
1	**Blend uniformity:**	Individual sample values between (85.0% to 115.0%) of label claim & RSD: NMT 6.0 % and Average value between (95.0% to 110.0%).	**TCL**				
			TC				
			TCR				
			MBL				
			MBC				
			MBR				
			BFL				
			BFC				
			BFR				
			DP				
			Avg.				
			RSD				
			Composite				
All the validation test results of blending stage are found to be **satisfactory/not satisfactory.**			**QA-Sign & Date:**				

15.3 TEST DATA FOR VALIDATION OF BLENDING STAGE: **3rd Batch No.:**

S.No	MEASURED PARAMETERS	ACCEPTANCE CRITERIA	TEST RESULTS				
			Mixing time (20 minutes)				
			Sample Location	Paracetamol	Phenylephrine Hydrochloride	Chlorphenamine Maleate	Ascorbic Acid
1	**Blend uniformity:**	Individual sample values between (85.0% to 115.0%) of label claim & RSD: NMT 6.0 % and Average value between (95.0% to 110.0%).	**TCL**				
			TC				
			TCR				
			MBL				
			MBC				
			MBR				
			BFL				
			BFC				
			BFR				
			DP				
			Avg.				
			RSD				
			Composite				
All the validation test results of blending stage are found to be **satisfactory/not satisfactory.**			**QA-Sign & Date:**				

15.4 TEST DATA FOR BLENDING STAGE :

S. No		ON POOLED SAMPLE			
		ACCEPTANCE CRITERIA	TEST RESULTS		
			1ST B.No:	2ND B.No:	3RD B.No:
1	**Description**	Light brown colored, free flowing powder, with lemon flavour			
2	**Bulk Density**	For information only			
3	**Tapped Density**	For information only			
4	**Particle size of retains (cumulative %)** #20,30,40,60,80 and 100 Mesh. **Passing** # 100 mesh	For information only			
QA-Sign & Date:					

15.4 CONCLUSION ON VALIDATION OF BLENDING STAGE OF : 1ST ,2ND & 3RD BATCHES

All the validation test results of Blending stage of Paracetamol, Phenylephrine Hydrochloride, Chlorphenamine Maleate and Ascorbic acid powder are found to be **Satisfactory/Not Satisfactory** after **20 Minutes** Mixing.

S.No	Process stage	Equipment	Fixed Standard (minutes)
1.	Blending stage	Octagonal Blender	

Head-Quality Assurance:_____
(Sign & Date)

16.0 PROCESS PARAMETERS :

Manufacturing Process Stages	Critical Process Parameters	Set-Point
Blending	Mixing Time	20 minutes

17.0 DEVIATIONS:

18.0 EVALUATION OF RESULTS,CONCLUSION AND RECOMMENDATIONS:

Head-Quality Assurance:_____
(Sign & Date)

19.0 REPORT APPROVAL

19.1 Compiled By :

Dept.	Name	Designation	Signature	Date
Quality Assurance				

19.2 Verified By:

Dept.	Name	Designation	Signature	Date
Head-Production				
Head-Quality Control				

19.3 Approved By:

Dept.	Name	Designation	Signature	Date
Head-Quality Assurance				