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	PROCESS VALIDATION PROTOCOL CUM REPORT		
GENERIC NAME	PARACETAMOL, PHENYLEPHRINE HYDROCHLORIDE, CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER		Page 1 of 15 Protocol No.: PVP/22/016-01 Revision no.:00 Effective date: 19/04/2022

PROCESS VALIDATION PROTOCOL CUM REPORT
FOR
PARACETAMOL, PHENYLEPHRINE HYDROCHLORIDE,
CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER



Safetab Life Science,

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CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER

Effective date: 19/04/2022

1.0 PROTOCOL APPROVAL :**1.1 Prepared By :**

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

1.2 Verified By:

Dept.	Name	Designation	Signature	Date
Head-Production	G. Vijayalakshy	Sr. Manager Production	Vijayalakshy	19/04/22
Head-Quality Control	P. S. Srinivas Kumar	Asst. M. Coe	P. S. Srinivas Kumar	19/04/22

1.3 Approved By:

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

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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.

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CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER

Effective date: 19/04/2022

Product Name : PARACETAMOL, PHENYLEPHRINE HYDROCHLORIDE, CHLORPHENAMINE MALEATE AND ASCORBIC ACID POWDER

BRAND NAME:	GRIPRX	GRIPRX	GRIPRX
Batch No :	U1722056	U1722057	U1722062
Batch Size :	2.0L	2.0L	2.0L
Mfg. Date :	04/2022	04/2022	05/2022
Expiry Date :	03/2025	03/2025	04/2025

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	NA
Change in formulation	NA	Change/modification in equipment	NA
Change in location	NA	Change in batch size	NA
Change in vendor of API	NA	Any other reasons (specify)	NA

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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
RME00027	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



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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.

Sift the Phenylephrine Hydrochloride BP, Chlorphenamine Maleate BP, Ascorbic acid BP, Maltodextrin BP, Paracetamol BP, Hydrophobic colloidal anhydrous silica, Citric acid Monohydrate through 30#, Orange Pekoe Extract HIS, Sucralose Lemon lime Premaseal (75412-71) through 60#.

Blending
Mix for 20mins

Sampled by
IPQA

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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.	<u>1. Mixing time</u> (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



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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

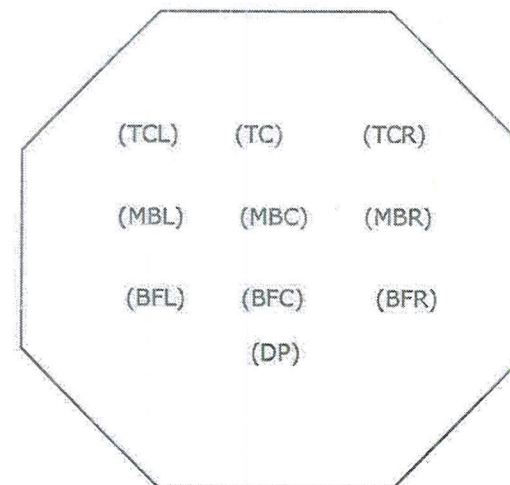
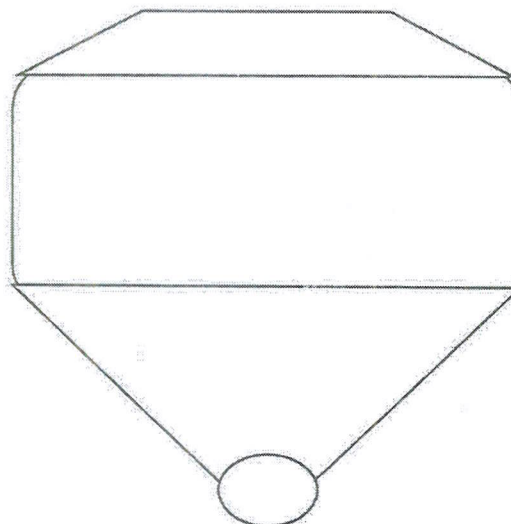
MBR – Middle back right

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	
4	Tap density (pooled sample)	For information only	NA
5	Particle size distribution	For information only	



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

15.1 TEST DATA FOR VALIDATION OF BLENDING STAGE:

1st Batch No.: 611722056

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	98.1%.	100.0%.	98.8%.	103.8%.
			TC	98.5%.	97.4%.	99.4%.	102.9%.
			TCR	97.9%.	97.7%.	103.1%.	103.1%.
			MBL	98.0%.	99.2%.	96.4%.	103.8%.
			MBC	97.8%.	98.0%.	101.4%.	103.1%.
			MBR	98.0	96.4%.	99.9%.	103.8%.
			BFL	98.3%.	98.0%.	99.9%.	102.9%.
			BFC	97.4%.	101.0%.	95.9%.	102.2%.
			BFR	97.2%.	101.1%.	96.7%.	102.9%.
			DP	96.7%.	99.3%.	99.9%.	102.2%.
			Avg.	97.8%.	98.8%.	99.1%.	103.2%.
			RSD	0.6%.	1.6%.	2.3%.	0.53%.
			Composite	99.5%.	98.4%.	101.4%.	103.1%.
All the validation test results of blending stage are found to be satisfactory/not satisfactory.			QA-Sign & Date: P. Val 03/06/22				



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15.2 TEST DATA FOR VALIDATION OF BLENDING STAGE:

2nd Batch No.: 61722057

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	113.0%.	108.3%.	114.6%.	102.9%.
			TC	104.8%.	100.2%.	104.1%.	103.8%.
			TCR	97.1%.	98.2%.	95.9%.	108.8%.
			MBL	99.4%.	94.7%.	100.2%.	103.8%.
			MBC	108.6%.	108.5%.	110.3%.	102.9%.
			MBR	113.8%.	108.6%.	113.7%.	103.8%.
			BFL	101.7%.	99.1%.	105.6%.	102.9%.
			BFC	103.8%.	99.7%.	104.6%.	103.8%.
			BFR	112.2%.	109.7%.	111.4%.	103.8%.
			DP	109.7%.	108.4%.	109.5%.	102.9%.
			Avg.	106.2%.	103.3%.	107.0%.	103.5%.
			RSD	5.6%.	5.8%.	5.6%.	0.43%.
			Composite	108.2%.	100.9%.	106.3%.	102.9%.
All the validation test results of blending stage are found to be satisfactory/not satisfactory.			QA-Sign & Date: P. val / 03/06/22				

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15.3 TEST DATA FOR VALIDATION OF BLENDING STAGE:3rd Batch No.: 61722062

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	100.1%	102.0%	105.7%	104.4%
			TC	99.4%	99.9%	101.3%	104.4%
			TCR	107.4%	111.5%	111.7%	105.2%
			MBL	101.8%	101.7%	99.9%	105.2%
			MBC	107.0%	110.3%	110.2%	103.5%
			MBR	103.8%	108.9%	106.5%	104.8%
			BFL	106.3%	107.0%	107.0%	104.4%
			BFC	100.0%	103.5%	103.1%	104.4%
			BFR	108.8%	112.8%	107.7%	104.4%
			DP	108.4%	110.6%	111.2%	103.5%
			Avg.	104.1%	106.8%	106.2%	104.5%
			RSD	3.9%	4.4%	4.2%	0.49%
			Composite	98.6%	99.4%	103.6%	104.4%
All the validation test results of blending stage are found to be satisfactory/not satisfactory.			QA-Sign & Date: P. Val P 03/06/22				

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15.4 TEST DATA FOR BLENDING STAGE :

S. No		ACCEPTANCE CRITERIA	ON POOLED SAMPLE		
			TEST RESULTS		
			1 ST B.No: 611722056	2 ND B.No: 611722057	3 RD B.No: 611722062
1	Description	Light brown colored, free flowing powder, with lemon flavour	Light brown colored free flowing powder with lemon flavour	Light brown colored free flowing powder with lemon flavour	Light brown colored free flowing powder with lemon flavour
2	Bulk Density	For information only	0.53 g/ml	0.50 g/ml	0.59 g/ml
3	Tapped Density	For information only	0.77 g/ml	0.77 g/ml	0.78 g/ml
4	Particle size of retains (cumulative %) #20,30,40,60,80 and 100 Mesh. Passing # 100 mesh	For information only	#20 - 0.17%, #100 - 27.45%, #30 - 0.71%, passing #40 - 1.69%, #100 - #60 - 5.39%, 71.81%, #80 - 17.37%	#20 - 0.00%, #100 - 37.82%, #30 - 0.49%, passing #40 - 1.31%, #100 - #60 - 5.20%, #100 - #80 - 20.21%, 64.37%	#20 - 0.03%, #100 - 24.74%, #30 - 0.20%, 24.74%, #40 - 0.45%, passing #60 - 3.57%, #100 - #80 - 16.71%, 74.22%
QA-Sign & Date: P. V. 03/06/22					

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	20 minutes

Head-Quality Assurance: A. G. 03/06/22

(Sign & Date)

ST/QA/029 (R2):F4

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16.0 PROCESS PARAMETERS :

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

17.0 DEVIATIONS:

Blend Mixing time is increase to 25 minutes from 20 minutes due to improper mixing of granules observed when checked visually. So for all the validation batches blend mixing time shall be followed as 25 minutes instead of 20 minutes.

18.0 EVALUATION OF RESULTS, CONCLUSION AND RECOMMENDATIONS:

Blending for sized granules has been carried out according to the RMP procedure for three commercial batches. Batch no: 011762056, 011722057, 011722062 blending has been carried out 25 minutes mixing at 18 RPM. Samples were collected from 10 different locations by covering top, middle and bottom of octagonal blender. The sample has been tested for all locations of blend for uniformity of Paracetamol, phenylephrine hydrochloride, chlorphenamine maleate and ascorbic acid content and composite sample as per specification.

All three batches results were found well with in the acceptance criteria and consistent.

No deviation or abnormalities observed in validation sample results. Hence the blending results are evidenced that the process is under state of control, so the manufacturing process the product Paracetamol, phenylephrine hydrochloride, chlorphenamine maleate and ascorbic acid powder is

Head-Quality Assurance:

(Sign & Date)

ST/QA/029 (R2):F4

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19.0 REPORT APPROVAL

19.1 Compiled By :

Dept.	Name	Designation	Signature	Date
Quality Assurance	T. Vadivel	Sr. Executive QA	T. Vadivel	03/06/22

19.2 Verified By:

Dept.	Name	Designation	Signature	Date
Head-Production	V. Dharabai	Sr. GM	V. Dharabai	04/06/22
Head-Quality Control	P. Vijayakumar	Phm	P. Vijayakumar	04/06/22

19.3 Approved By:

Dept.	Name	Designation	Signature	Date
Head-Quality Assurance	A. G. Kannan	GM-QA	A. G. Kannan	04/06/22