	Safetab Life Science Puducherry			MASTER COPY
	PRODUCT SPECIFICATION			**Market** Export
Name of Product	**GRIPEX** (Paracetamol, Phenylephrine Hydrochloride, Chlorphenamine Maleate and Ascorbic Acid Sachet)			
Specification No.	SPEC-1048-00	**Revision No.**	00	**Product Code:**1048
Supersedes	FGSSSG001-00	**Effective Date:**	04/08/2023	**Page No.:** 1 of 7

S.NO	GENERAL SPECIFICATION (s)	
1	Pharmacopoeial Reference	In-House
2	Label claim	Each 4.5gm Sachet contains: Paracetamol BP---------- 650mg Phenylephrine Hydrochloride BP---------- 10mg Chlorphenamine Maleate BP ---------- 20mg Ascorbic acid BP---------- 50mg
3	Standard packing	10x4.5g's Sachets
4	Shelf Life	36 Months
5	In-Process Sample Quantity	a) In-process Intermediate – Blend, 50g. c) Intermediate- Filled sachets – 20 sachets
6	Finished Product sample quantity	For Microbial contamination Test : 3 sachets For Chemical Analysis : 20 sachets For Control sample : 46 sachets
7	Stability studies sample quantity	For Accelerated study : 63 sachets For Long term study : 212 sachets For Annual study : 172 sachets For Intermediate study : 63 sachets
8	Storage condition	Store in cool and dry place protect from light.
9	Destructions Instructions	Follow the Standard Operating Procedure: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

RELEASE SPECIFICATION FOR INTERMEDIATE – BLEND
SPECIFICATION CODE: SPEC-1048-BLD

S.NO	TEST (s)	SPECIFICATION (s)
1.0	Description	Light brown colored, free flowing powder, with lemon flavour.
2.0	**Identification**	
	a) Paracetamol (By HPLC)	The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Paracetamol in the standard preparation as obtained in assay.
	b) Phenylephrine Hydrochloride (By HPLC)	The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Phenylephrine Hydrochloride in the standard preparation as obtained in assay.
	c) Chlorphenamine Maleate (By HPLC)	The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Chlorphenamine Maleate in the standard preparation as obtained in assay.
	d) Ascorbic acid (By Chemical)	A deep violet colour is produced and deep violet colour disappears on add about 5mL of dilute Sulfuric acid.
3.0	Water Content by (KF)	Not more than 5.0 %

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

S.NO	TEST (s)	SPECIFICATION (s)
4.0	**Related Substances (By HPLC)**	
	Single maximum unknown impurity	Not more than 0.5%
	Total unknown impurities	Not more than 1.0%
5.0	**Assay: Each 4.5gm blend contains:**	
	Paracetamol BP 650mg	617.5mg to 715.0mg (95.0% to 110.0% of the labeled claim)
	Phenylephrine Hydrochloride BP 10mg	9.5 to 11.0mg (95.0% to 110.0% of the labeled claim)
	Chlorphenamine Maleate BP 20mg	19.0 to 22.0mg (95.0% to 110.0% of the labeled claim)
	Ascorbic acid BP 50mg	47.5mg to 55.0mg (95.0% to 110.0% of the labeled claim)

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

RELEASE SPECIFICATION – FINISHED PRODUCT
SPECIFICATION CODE: SPEC-1048-FP

S.NO	TEST (s)	SPECIFICATION (s)
1.0	Description	Light brown colored, free flowing powder, with lemon flavour.
2.0	**Identification***	
	b) Paracetamol (By HPLC)	The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Paracetamol in the standard preparation as obtained in assay.
	b) Phenylephrine Hydrochloride (By HPLC)	The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Phenylephrine Hydrochloride in the standard preparation as obtained in assay.
	c) Chlorphenamine Maleate (By HPLC)	The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Chlorphenamine Maleate in the standard preparation as obtained in assay.
	d) Ascorbic acid (By Chemical)	A deep violet colour is produced and deep violet colour disappears on add about 5mL of dilute Sulfuric acid.
3.0	Average net content weight	4.5000 g ± 5.0% (4.2750g to 4.7250g)
4.0	Uniformity of content weight	Individual content weight of sachet does not deviate by ±7.5% from the average net content weight.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

	Safetab Life Science Puducherry			MASTER COPY
	PRODUCT SPECIFICATION			**Market** Export
Name of Product	**GRIPEX** (Paracetamol, Phenylephrine Hydrochloride, Chlorphenamine Maleate and Ascorbic Acid Sachet)			
Specification No.	SPEC-1048-00	**Revision No.**	00	**Product Code:**1048
Supersedes	FGSSSG001-00	**Effective Date:**	04/08/2023	**Page No.:** 5 of 7

S.NO	TEST (s)	SPECIFICATION (s)
5.0	Water Content by (KF) *	Not more than 5.0 %
6.0	**Related Substances (By HPLC)***	
	Single maximum unknown impurity	Not more than 0.5%
	Total unknown impurities	Not more than 1.0%
7.0	**Assay: Each 4.5gm sachet contains*:**	
	Paracetamol BP 650mg	617.5mg to 715.0mg (95.0% to 110.0% of the labeled claim)
	Phenylephrine Hydrochloride BP 10mg	9.5 to 11.0mg (95.0% to 110.0% of the labeled claim)
	Chlorphenamine Maleate BP 20mg	19.0 to 22.0mg (95.0% to 110.0% of the labeled claim)
	Ascorbic acid BP 50mg	47.5mg to 55.0mg (95.0% to 110.0% of the labeled claim)
8.0	**Microbial contamination**	
	i)Total viable aerobic count	
	a) Total aerobic microbial count	Not more than 1000 cfu/g
	b) Total yeast and mould count	Not more than 100 cfu/g
	ii) Escherichia coli	Should be absent/g
	iii) Salmonella Species	Should be absent/10g
	iv) Pseudomonas aeruginosa	Should be absent/g
	v) Staphylococcus aureus	Should be absent/g

Note: * Marked test results shall be taken from Blend.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

	Safetab Life Science Puducherry			MASTER COPY
	PRODUCT SPECIFICATION			**Market** Export
Name of Product	**GRIPEX** (Paracetamol, Phenylephrine Hydrochloride, Chlorphenamine Maleate and Ascorbic Acid Sachet)			
Specification No.	SPEC-1048-00	**Revision No.**	00	**Product Code:**1048
Supersedes	FGSSSG001-00	**Effective Date:**	04/08/2023	**Page No.:** 6 of 7

STABILITY SPECIFICATION
SPECIFICATION CODE: SPEC-1048-ST

S.NO	TEST (s)	SPECIFICATION (s)
1.0	Description	Light brown colored, free flowing powder, with lemon flavour.
2.0	Average net fill weight	4.5000 g ± 5.0% (4.2750g to 4.7250g)
3.0	Water Content by (KF)	Not more than 5.0 %
4.0	**Related Substances (By HPLC)**	
	Single maximum unknown impurity	Not more than 0.5%
	Total unknown impurities	Not more than 1.0%
5.0	**Assay: Each 4.5gm sachet contains:**	
	Paracetamol BP 650mg	585.0mg to 715.0mg (90.0% to 110.0% of the labeled claim)
	Phenylephrine Hydrochloride BP 10mg	9.0 to 11.0mg (90.0% to 110.0% of the labeled claim)
	Chlorphenamine Maleate BP 20mg	18.0 to 22.0mg (90.0% to 110.0% of the labeled claim)
	Ascorbic acid BP 50mg	45.0mg to 55.0mg (90.0% to 110.0% of the labeled claim)

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

	Safetab Life Science Puducherry			MASTER COPY
	PRODUCT SPECIFICATION			**Market** Export
Name of Product	**GRIPEX** (Paracetamol, Phenylephrine Hydrochloride, Chlorphenamine Maleate and Ascorbic Acid Sachet)			
Specification No.	SPEC-1048-00	**Revision No.**	00	**Product Code:**1048
Supersedes	FGSSSG001-00	**Effective Date:**	04/08/2023	**Page No.:** 7 of 7

S.NO	TEST (s)	SPECIFICATION (s)
6.0	**Microbial contamination#**	
	i) Total viable aerobic count	
	a) Total aerobic microbial count	Not more than 1000 cfu/g
	b) Total yeast and mould count	Not more than 100 cfu/g
	ii) Escherichia coli	Should be absent/g
	iii) Salmonella Species	Should be absent/10g
	iv) Pseudomonas aeruginosa	Should be absent/g
	v) Staphylococcus aureus	Should be absent/g

Mark test will performed on 6th month of Accelerated stability and every 12th month of Long term stability.

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-1408-00	(i) Specification numbering system has revised as per SOP No.ST/QC/058. (ii) Related substances test has been incorporated.	ST/CC/23/063 ST/CC/23/149	04/08/2023

**** END OF THE DOCUMENT ****

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

1.0 DESCRIPTION: (By Visual Inspection)

Blend: Spread about 1 to 2 g of sample on a white surface and note the observation.

2.0 IDENTIFICATION:

a) Paracetamol: (By HPLC)

The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Paracetamol in the standard preparation as obtained in assay.

b) Phenylephrine Hydrochloride: (By HPLC)

The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Phenylephrine Hydrochloride in the standard preparation as obtained in assay.

c) Chlorphenamine Maleate: (By HPLC)

The retention time of one of major peak in the chromatogram of the sample preparation corresponds to the peak due to Chlorphenamine Maleate in the standard preparation as obtained in assay.

d) Ascorbic acid (By Chemical):

Dilute Sulfuric acid:

Add carefully drop wise 5.5 mL of Conc. Sulfuric acid to 100 mL volumetric flask containing 80 mL of purified water. Dilute to volume with purified water and mix.

Procedure:

Transfer about 500 mg of sample powder into a test tube, add 5 mL of purified water and sonicate to dissolve. Add about 150 mg of sodium bicarbonate and 20 mg of ferrous sulphate. Shake vigorously and allow to stand. A deep violet colour is produced. Add about 5 mL of dilute Sulfuric acid; deep violet colour disappears.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	07/08/23

3.0 AVERAGE NET FILL WEIGHT OF SACHET:

Weigh 10 intact sachets. Open each sachet carefully without loosing any part of the sachet and remove the content as completely as possible. Wash the sachet with suitable solvents and dry weigh the empty sachet. Determine the filled weight by substracting the weight of empty sachet from the weight of intact sachet and calculate the average net weight.

$$\text{Average net filled content(in g)} = \frac{(W1-W2)}{10}$$

Where ,

W1= Total weight of 10 intact sachets, in g.
W2= Total weight of 10 empty sachets, in g.

4.0 UNIFORMITY OF FILL WEIGHT:

Weigh 10 sachets at random and calculate the average net weight of content is not less than 4.1625 g and not more than 4.8735 g.

Calculate the percentage deviation for the highest individual weight of content in sachets as follows:

$$\left[\frac{\text{Highest individual net weight of content in sachets (in g)}}{\text{Average net weight of content in sachets (in g)}} \times 100\right] - 100$$

Calculate the percentage deviation for the lowest individual weight of content in sachets as follows:

$$\left[\frac{\text{Lowest individual net weight of content in sachets (in g)}}{\text{Average net weight of content in sachets (in g)}} \times 100\right] - 100$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

5.0 WATER CONTENT BY KF:

Add about 20 mL of anhydrous methanol in to the titration vessel to ampherometric end-point with Karl-fisher reagent. Crush the sample in to fine power, weigh and quickly transfer about 500 mg of sample to the titration vessel. Stir well and titrate against to the ampherometric end-point using Karl-fisher reagent. Calculate and report.

Calculation:

$$\% \text{ Water} = \frac{\text{Titer value (mL) x Kf factor x 100}}{\text{Weight of sample taken (mg)}}$$

6.0 RELATED SUBSTANCES:

Reference: In-House
Procedure: By HPLC

Chemicals/Reagents/Standards:

Paracetamol	:	Working standard
Ascorbic acid	:	Working standard
Chlorphenamine Maleate	:	Working standard
Phenylephrine HCL	:	Working standard
Potassium dihydrogen orthophosphate	:	AR grade
Orthophosphate	:	AR grade
Methanol	:	HPLC grade
Purified Water	:	Milli-Q water (or) equivalent

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

Chromatographic condition:

Column description	:	C8 4.6mmx250mm, 5µ (Kromasil column is suitable)
Flow rate	:	1.0ml/min
Detector	:	220nm
Column temperature	:	30°C
Injection volume	:	10µl

Preparation of Buffer solution:

Weigh accurately and transfer about 6.8g of Potassium dihydrogen orthophosphate to 1000ml glass beaker. Add about 500ml of water, shake and sonicate to dissolve completely and finally make the solution to 1000ml with water. Adjust the pH to 3.0±0.05 with Orthophosphoric acid.

Preparation of Mobile phase:

Mix 860ml of butter solution and 140ml Methanol. Filter through 0.20µ membrane filter and degas.

Preparation of diluent:

Use mobile phase as such.

Preparation of blank:

Inject mobile phase as such.

Preparation of placebo solution:

Weigh accurately and transfer about 0.348g Placebo powder into 100ml volumetric flask. Add about 20ml of diluent sonicate for 10 minutes with intermittent shaking to dissolve and dilute up to the volume with diluent. Filter sufficient quantity of this solution through 0.45µ syringe filter.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

Preparation of Resolution stock solution:

Weigh accurately and transfer about 116.0mg of Ascorbic acid Working standard, 46.0mg of Chlorphenamine Working standard and 23.0mg of Phenylephrine Hydrochloride into 50ml volumetric flask. Add about 20ml of diluent, sonicate for 10 minutes with intermittent shaking to dissolve and dilute up to the volume with diluent. Dilute 10ml of this solution to 50ml with diluent and mix well.

Preparation of Resolution solution:

Weigh accurately and transfer about 60.0mg of Paracetamol Working standard into 100ml volumetric flask. Add 10ml of Resolution stock solution and 50 ml of diluents, sonicate to dissolve and dilute up to mark with diluents mix well and inject.

Concentration of Ascorbic acid: 0.046 mg/ml , Chlorphenamine: 0.0184 mg/ml, Phenylephrine: 0.0092 mg/ml and Paracetamol: 0.6mg/ml)

Preparation of Standard low load solution:

Weigh accurately and transfer about 60.0mg of Paracetamol Working standard into 100ml volumetric flask. Add about 50ml of diluents, sonicate to dissolve and dilute upto mark with diluents. Dilute 5ml of this solution to 100ml with diluent and mix well. Further dilute 5ml of this solution 50ml with diluent. Mix well and inject. (Concentration of Paracetamol:0.003 mg/ml).

Preparation sample solution:

Weigh accurately and transfer about 0.415g of sample powder into 100ml volumetric flask. Add about 50ml of diluent, sonicate for 10 minutes with intermittent shaking to dissolve and dilute up to the volume with diluent. Filter sufficient quantity of this solution through 0.45µ syringe filter. (Concentration of Ascorbic acid:0.046 mg/ml, Chlorphenamine: 0.0184 mg/ml, Phenylephrine: 0.0092 mg/ml and Paracetamol: 0.6mg/ml)

Procedure:

Equilibrate the chromatographic system with mobile phase till a stable baseline is obtained. Separately inject equal volumes (10µl) of solutions as per sequence of injections in to the chromatograph and record the peak area responses for the major peaks and check for the system suitability requirements.

Injection sequence:

S. No	Sample Name	No. of injections
1	Diluent (Blank)	1
2	Resolution solution	1
3	Standard low load solution	6
4	Blank solution	1
5	Placebo solution	1
6	Sample solution	1
7	Bracketing standard low load solution	1 Each after every 6 sample injection

System suitability:

1) The Resolution between the peaks corresponding to

(i) Ascorbic acid and Chlorphenamine

(ii) Chlorphenamine and Phenylephrine

(iii) Phenylephrine and Paracetamol obtained with Resolution should not be less than 2.0.

2) The theoretical plates for the peaks of Paracetamol obtained with standard low load solution should not be less than 2000.

3) The symmetry factor for the peaks of Paracetamol obtained with standard low load solution should not be more than 2.0.

4) The %RSD for the retention time of peaks of Paracetamol obtained with replicate injection of standard low load solution should not be more than 1.0.

5) The %RSD of peak area response for the peaks of Paracetamol obtained with replicate injection of standard low load solution should not more than 5.0.

6) The %RSD for the retention time of peaks of Paracetamol obtained with replicate injection of standard low load solution and bracketing standard low load solution should not be more than 1.0.

7) The %RSD of peak area response for the peaks of Paracetamol obtained with replicate injection of standard low load solution and bracketing standard low load solution should not be more than 5.0.

Calculation:

Calculate the % content of single maximum impurity by following formula:

$$= \frac{AT_I}{AS} \times \frac{WS}{100} \times \frac{5}{100} \times \frac{5}{50} \times \frac{100}{WT} \times \frac{P}{100} \times \frac{AFW}{LC} \times 100$$

Calculate the % content of total unknown impurities by following formula:

$$= \frac{AT_T}{AS} \times \frac{WS}{100} \times \frac{5}{100} \times \frac{5}{50} \times \frac{100}{WT} \times \frac{P}{100} \times \frac{AFW}{LC} \times 100$$

Where,

AT_I	=	Peak area response of single maximum impurity obtained with sample solution.
AT_T	=	Peak area response of total unknown impurities obtained with sample solution.
AS	=	Average peak area response of Paracetamol peak obtained with replicate injections of standard low load solution
WS	=	Weight of Paracetamol Working standard in mg.
WT	=	Weight of Sample taken in mg.
P	=	Potency of Paracetamol working standard (on % as is basis).
AFW	=	Average fill weight of sachet in mg.
LC	=	Label claim of Paracetamol in mg.

7.0 **ASSAY:**

For Paracetamol, Phenylephrine Hydrochloride and Chlorphenamine maleate:

Reference: In House
Procedure: By HPLC

Chemicals/Reagents/Standards:

Paracetamol	:	Working standard
Phenylephrine Hydrochloride	:	Working standard
Chlorphenamine Maleate	:	Working standard
1-Heptanesulphonic acid sodium salt	:	AR grade
Orthophosphoric acid	:	AR grade

Methanol	:	HPLC grade
Acetonitrile	:	HPLC grade
Purified Water	:	Milli-Q water (or) equivalent

Preparation of Buffer solution:

Weigh and dissolve about 2.0g of 1-heptane sulphonic acid sodium salt in 1000 mL of Milli-Q water. And adjust pH to 3.0±0.05 with Orthophosphoric acid. Filter through 0.45µ membrane filter and degas.

Preparation of Mobile Phase A:

Use buffer solution as mobile phase A.

Preparation of Mobile Phase B:

Use acetonitrile as mobile phase B.

Preparation of Diluent:

Prepare a degassed mixture of buffer and methanol in the ratio of 50:50 *v/v*.

Chromatographic Conditions:

Column	:	Zodiac C18, 250 mm X 4.6 mm, 5µm (or) equivalent
Wave length	:	UV at 220 nm
Column Temperature	:	30°C
Flow Rate	:	1.2 mL/min
Injection Volume	:	50 µL
Run time	:	20 Minutes

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

Preparation of Blank Solution:

Use diluent as blank.

Note: Keep all the prepared standard and sample solutions on bench top for 10minutes before further using for dilution / filtration.

Gradient Program:

Time	Mobile phase A %	Mobile phase B%
0.01	80	20
5.0	80	20
8.0	50	50
14.0	50	50
14.01	80	20
20.0	80	20

Preparation of Standard Stock Solution-1:

Weigh and transfer accurately about 40 mg of Phenylephrine hydrochloride WS into a 200 mL clean, dry volumetric flask. Add 140 mL of diluent and sonicate to dissolve. Dilute up to the volume with diluent and mix.

Preparation of Standard Stock Solution-2:

Weigh and transfer accurately about 40 mg of Chlorphenamine maleate WS into a 100 mL clean dry volumetric flask. Add 70 mL of diluent and sonicate to dissolve. Dilute up to the volume with diluent and mix.

Preparation of Standard Stock Solution-3:

Weigh and transfer accurately about 65 mg of Paracetamol WS into a 100 mL clean dry volumetric flask. Add 70 mL of diluent and sonicate to dissolve. Dilute up to the volume with diluent and mix.

Preparation of Standard Solution:

Transfer each 5 mL of standard stock solution-1, standard stock solution-2 and standard stock solution-3 and into a 50 mL volumetric flask. Dilute up to the volume with diluent and mix.

Preparation of Sample solution-A (For Phenylephrine & Chlorphenamine maleate):

Transfer and mix the contents of not less than 5 sachets. Weigh and transfer the sample equivalent to 650mg of Paracetamol into a 500 mL volumetric flask add about 340 mL of diluent and sonicate for 30 minutes with intermittent shaking. Cool to room temperature and dilute up to the volume with diluent and mix. Filter through 0.45µm PVDF filter.

Preparation of Sample solution-B (For Paracetamol):

Transfer 5 mL of above Sample solution-A in to a 100 mL volumetric flask and dilute up to the volume with diluent and mix.

Procedure:

Inject diluent as blank solution. Inject Standard solution in five replicates, Inject Sample solution-A and Sample solution-B in duplicates into the chromatograph. Record the chromatograms and measure the responses for the major peaks.

The retention times for Paracetamol, Phenylephrine and Chlorphenamine were about 4.0 minutes, 6.7 minutes and 10.4minutes respectively and it's for information purpose only.

System suitability:

Theoretical plate	: NLT 2000 for Paracetamol, Phenylephrine and Chlorphenamine peak.
Tailing factor	: NMT 2.0 for Paracetamol, Phenylephrine and Chlorphenamine peak.
Relative standard Deviation	: NMT 2.0% for five replicate standard injection of Paracetamol, Phenylephrine and Chlorphenamine.

Inject 50µl of the above solution as per following sequence.

Injection sequence:

S. No	Sample Name	No. of injections
1	Diluent (Blank)	1
2	Standard preparation	5
3	Sample preparation-A	2
4	Sample preparation-B	2
5	Bracketing standard	1 Each after every 6 sample injection

Calculate the assay of Paracetamol in mg/sachet as follows:

$$= \frac{AT}{AS} \times \frac{WS}{100} \times \frac{5}{50} \times \frac{500}{WT} \times \frac{100}{5} \times \frac{P}{100} \times AFW$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

Where,

AT = Average area of peak due to Paracetamol in Sample solution B.
AS = Average area of peak due to Paracetamol in standard preparation.
WS = Weight of Paracetamol working standard in mg.
WT = Weight of sample taken in mg.
AFW = Average fill weight of sachet in mg.
P = Potency of Paracetamol working standard in % on as such basis.

Calculate the assay of Paracetamol in % as follows:

$$= \frac{\text{mg/sachet}}{\text{LC}} \times 100$$

LC = Label claim of Paracetamol in mg/sachet.

Calculate the assay of Phenylephrine Hydrochloride in mg/sachet as follows:

$$= \frac{AT}{AS} \times \frac{WS}{200} \times \frac{5}{50} \times \frac{500}{WT} \times \frac{P}{100} \times AFW$$

Where,

AT = Average area of peak due to Phenylephrine Hydrochloride in Sample solution A.
AS = Average area of peak due to Phenylephrine Hydrochloride in standard preparation.
WS = Weight of Phenylephrine Hydrochloride working standard in mg.
WT = Weight of sample taken in mg.
AFW = Average fill weight of sachet in mg.
P = Potency of Phenylephrine Hydrochloride working standard in % on as such basis.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

Calculate the assay of Phenylephrine Hydrochloride in % as follows:

$$= \frac{\text{mg/sachet}}{\text{LC}} \times 100$$

LC = Label claim of Phenylephrine Hydrochloride in mg/sachet.

Calculate the assay of Chlorphenamine maleate in mg/sachet as follows:

$$= \frac{AT}{AS} \times \frac{WS}{100} \times \frac{5}{50} \times \frac{500}{WT} \times \frac{P}{100} \times AFW$$

Where,

AT	=	Average area of peak due to Chlorphenamine maleate in Sample solution A.
AS	=	Average area of peak due to Chlorphenamine maleate in standard preparation.
WS	=	Weight of Chlorphenamine maleate working standard in mg.
WT	=	Weight of sample taken in mg.
AFW	=	Average fill weight of sachet in mg.
P	=	Potency of Chlorphenamine maleate working standard in % on as such basis.

Calculate the assay of Chlorphenamine maleate in % as follows:

$$= \frac{\text{mg/sachet}}{\text{LC}} \times 100$$

LC = Label claim of Chlorphenamine maleate in mg/sachet.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

FOR ASCORBIC ACID (BY TITRIMETRY):

Chemicals/Reagents/Standards:

Potassium iodide	: AR grade
Sodium carbonate	: AR grade
Hydrochloric acid	: AR grade
Starch	: AR grade
Potassium bromate	: Primary standard
Iodine	: AR grade
Glacial acetic acid	: AR grade
Sulfuric acid	: AR grade
Sodium thiosulphate	: AR grade
Water	: Purified

Preparation of 0.1M sodium thiosulfate solution:

Weigh and transfer accurately 25.0 g of potassium iodide and 0.2 g of sodium carbonate into 1000 mL volumetric flask. Add about 400 mL of purified water and sonicate to dissolve. Make up to the volume with purified water and mix.

Preparation of 2M hydrochloric acid solution:

Transfer accurately 17 mL of hydrochloric acid and dilute to 100 mL with purified water.

Preparation of starch solution:

Weigh and transfer accurately 1 g of starch into a 200 mL beaker, add 100 mL of boiling water, and dissolve.

Use freshly prepared starch solution.

Standardization of 0.1M sodium thiosulfate solution:

Weigh accurately 0.200 g of potassium bromate, transfer into a 250 mL of volumetric flask add 50 mL of purified water swirl to dissolve and make up to the volume with purified water. Transfer 50 mL of above solution to a 250 mL conical flask. Add 2 g of potassium iodide and 3 mL of 2 M hydrochloric acid solution.

Titrate with 0.1 M sodium thiosulfate solution using starch solution, added towards the end point of the titration, as indicator until the blue colour is discharged.

1 mL of 0.1 M sodium thiosulfate solution is equivalent to 0.002784 g of $KBrO_3$.

Calculation:

Calculate the actual molarity of 0.1 M Sodium thiosulfate as follows,

$$\text{Actual Molarity} = \frac{\text{Weight of Potassium bromate(g)} \times 50}{\text{Titer value} \times 0.002784 \times 250}$$

Preparation of 0.05 M Iodine:

Weigh and transfer accurately 20.0 g of potassium iodide and 12.6 g of Iodine into 1000 mL volumetric flask. Add about 700 mL of purified water and sonicate for 30 minutes with intermittent shaking (ensure iodine balls dissolved completely). And make up to the volume with Purified water and mix.

Preparation of dilute acetic acid solution:

Transfer accurately about 5.7 mL of glacial acetic acid and dilute to 100 mL with purified water and mix.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

Standardization of 0.05 M Iodine:

Transfer accurately 10 mL of 0.05M Iodine solution into a conical flask, add 1 mL of dilute acetic acid, 40 mL of purified water and 1 mL of starch solution and titrate against 0.1 M sodium thiosulfate solution until the appearance of violet blue color. Perform a blank determination for correction.

Calculation:

Calculate the actual molarity of 0.05 M iodine as follows,

$$\text{Actual Molarity} = \frac{M_1 \times V_1 \times 0.05}{V_2 \times 0.1}$$

Where,

M_1 : Molarity of titrant

V_1 : Volume of 0.05 M Iodine taken (mL)

V_2 : Titer volume (mL)

Preparation of dilute sulfuric acid solution:

Transfer accurately about 5.7 mL of sulfuric acid and dilute to 100 mL with purified water and mix well.

Procedure:

Transfer the contents of not less than 10 sachets. Weigh accurately and transfer sample equivalent to 100 mg of ascorbic acid into a 250 mL conical flask. Add 10 mL of dilute sulfuric acid and sonicate for 15 minutes with intermittent shaking. Ensure to disperse sample completely. Add 80 mL of purified water and sonicate for 15 minutes with intermittent shaking add 1.0 mL of starch solution as indicator. Titrate against 0.05M iodine solution until the appearance of dark violet blue color as end point. Perform a blank determination for correction.

Each mL of 0.05 M iodine equivalent to 8.81 mg of ascorbic acid.

Calculation:

Calculate the content of Ascorbic acid (mg) as follows,

$$\text{Ascorbic acid (mg) per sachet} = \frac{\text{Titer value} \times \text{Actual strength of Iodine} \times 8.81 \times \text{Avg fill Wt. (mg)}}{\text{Weight of the sample taken (mg)} \times 0.05}$$

$$\text{Ascorbic acid (\%) per sachet} = \frac{\text{Content in of Ascorbic acid (mg/Sachet)}}{\text{Label claim of Ascorbic acid (mg/sachet)}} \times 100$$

8.0 **MICROBIAL CONTAMINATION:**

i) Total Viable aerobic count

a. Total aerobic microbial count:

Procedure: Proceed as per the current General Analytical Method GAM-035.

b. Total yeast and mould count:

Procedure: Proceed as per the current General Analytical Method GAM-036.

Pathogens:

ii) Escherichia Coli:

Procedure: Proceed as per the current General Analytical Method GAM-037.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23

iii) Salmonella Species:

Procedure: Proceed as per the current General Analytical Method GAM-038.

iv) Pseudomonas aeruginosa:

Procedure: Proceed as per the current General Analytical Method GAM-039.

v) Staphylococcus aureus:

Procedure: Proceed as per the current General Analytical Method GAM-040.

EVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-1048-00	(i) STP numbering system has revised as per SOP No.ST/QC/058. (ii) Related substances test has been incorporated.	ST/CC/23/063 ST/CC/23/149	04/08/2023

****END OF THE DOCUMENT****

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	03/08/2023	03/08/2023	03/08/23