	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	CHLORPHENAMINE MALEATE BP			
Specification No.	RMASC0064-01	**Revision No.**	01	**Item Code.:** RMAC0064
Supersedes	RMASC0064-00	**Effective Date**	20/02/2023	**Page No.:** 1 of 3

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$C_{20}H_{23}ClN_2O_4$
2	Molecular weight	390.9
3	Storage conditions	Protected from light.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	6 g
6	Quantity of reserve sample	12 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	15/02/2023	16/02/2023	17/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	CHLORPHENAMINE MALEATE BP			
Specification No.	RMASC0064-01	**Revision No.**	01	**Item Code.:** RMAC0064
Supersedes	RMASC0064-00	**Effective Date**	20/02/2023	**Page No.:** 2 of 3

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, crystalline powder.
2.	*Solubility	Freely soluble in water, soluble in ethanol (96 per cent).
3.	*Identification **A.** By Melting point **B.** By IR **C.** Optical rotation	 Between 130 °C to 135 °C. The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Chlorphenamine Maleate WS. Between -0.10° to + 0.10°
4.	Appearance of solution	Solution S is clear and not more intensely coloured than reference solution BY_6.
5.	Optical rotation	Between -0.10° to + 0.10°
6.	*Related substances (By HPLC) (i) Impurity A (ii) Impurity B (iii) Impurity C (iv) Impurity D (v) Unspecified impurities (vi) Total impurities	 Not more than 0.2% Not more than 0.1% Not more than 0.1% Not more than 0.1% Not more than 0.1% Not more than 0.5%

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	15/02/2023	16/02/2023	17/02/2023

S.NO	TEST (s)	SPECIFICATION (s)
7.	Sulphated Ash	Not more than 0.1% w/w
8.	*Loss on drying	Not more than 0.5% w/w
9.	*Assay By Titration (On dried basis)	Not less than 98.0% and not more than 101.0% w/w.

Remarks: The above * Marked tests are to be performed while retesting the material.

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
RMASC0064-01	Periodic review.	NA	20/02/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	15/02/2023	16/02/2023	17/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	CHLORPHENAMINE MALEATE BP			
STP No.	RMATC0064-01	**Revision No.**	01	**Item Code.:** RMAC0064
Supersedes	RMATC0064-00	**Effective Date**	20/02/2023	**Page No.:** 1 of 8

1. DESCRIPTION: < REFER GAM 001>

White or almost white, crystalline powder.

2. SOLUBILITY: < REFER GAM 002>

100mg of sample + 1mL of Water	Freely soluble if the material dissolves.
100mg of sample + 3mL of Ethanol (96%)	Soluble if the material dissolves.

3. IDENTIFICATION:

A. By Melting point: < REFER GAM 028>

Between 130°C to 135°C.

B. By IR: < REFER GAM 003>

The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Chlorphenamine Maleate WS.

C. By Optical rotation:

Between -0.10° to + 0.10°.

4. APPEARANCE OF SOLUTION:

Solution S:

Dissolve 2.0 g in water and dilute to 20.0 mL with the same solvent.

Solution S is clear and not more intensely coloured than reference solution BY_6.

5. OPTICAL ROTATION:

Between -0.10° to + 0.10°, determined on solution S.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	15/02/2023	16/02/2023	17/02/2023

6. RELATED SUBSTANCES: (BY HPLC)

Chemicals/Reagents/Standards:

Chlorphenamine maleate	:	Working standard
Impurity A	:	Reference standard
Impurity B	:	Reference standard
Impurity C	:	Reference standard
Ammonium dihydrogen phosphate	:	AR grade
Phosphoric acid	:	AR grade
Acetonitrile	:	HPLC grade

Chromatographic Conditions:

Column	:	µ-BondaPak C18, 300mm x 3.9mm, (10µm) or equivalent.
Flow Rate	:	1.2ml/min
Wavelength	:	225nm
Injection volume	:	20µl
Run time	:	3.5 times the retention time of Chlorphenamine and relative retention time for maleic acid = about 0.2; impurity A = about 0.3; impurity B = about 0.4; impurity C = about 0.9; impurity D = about 3.0
Retention time	:	Retention time of Chlorphenamine peak is at about 11.0 minutes

Mobile phase:

Mix 20 volumes of acetonitrile and 80 volumes of a 8.57 g/L solution of ammonium dihydrogen phosphate previously adjusted to pH 3.0 with phosphoric acid.

Test solution:

Weigh accurately and dissolve about 0.100 g of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a):

Dilute 1.0 mL of the test solution to 200.0 mL with the mobile phase.

Reference solution (b):

Dilute 1.0 mL of reference solution (a) to 10.0 mL with the mobile phase.

Reference solution (c):

Weigh accurately and dissolve about 5 mg of chlorphenamine impurity C RS in 5 mL of the test solution and dilute to 50.0 mL with the mobile phase. Dilute 2 mL of this solution to 20 mL with the mobile phase.

Reference solution (d):

Weigh accurately and dissolve about 5 mg of 2,2′-dipyridylamine (impurity B) in the mobile phase and dilute to 100 mL with the mobile phase.

Reference solution (e):

Dissolve the contents of a vial of Chlorphenamine impurity A RS in 2 mL of the test solution. Sonicate for 5 min

System suitability Reference solution (c):

— **resolution:** minimum 1.5 between the peaks due to impurity C and chlorphenamine.

Limits:

— **correction factors:** for the calculation of contents, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 1.5; impurity B = 1.4;

— **impurity A:** not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

— **impurities B, C, D:** for each impurity, not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

— **unspecified impurities:** for each impurity, not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— **total:** not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

— **disregard limit:** the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard the peak due to maleic acid

Inject 20µl of the above solution as per following sequence.

Injection sequence:

S. No	Sample Name	No. of injections
1	Mobile phase (Blank)	1
2	System suitability (Reference solution (c))	1
3	Reference solution (a)	1
4	Reference solution (b)	1
5	Reference solution (d)	1
6	Blank	1
7	Test solution	1

Calculations:

Impurity A : (NMT 0.2%)

$$= \frac{ATA}{AS} \times \frac{WT}{100} \times \frac{1}{200} \times \frac{100}{WT} \times 1.5 \times 100$$

Where,

ATA = Area of Impurity A peak in Test solution.

AS = Area of the Principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Impurity B: (NMT 0.1%)

$$= \frac{ATB}{AS} \times \frac{WT}{100} \times \frac{1}{200} \times \frac{100}{WT} \times 1.4 \times 100$$

Where,

ATB = Area of Impurity B peak in Test solution.

AS = Area of the Principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Impurity C: (NMT 0.1%)

$$= \frac{ATC}{AS} \times \frac{WT}{100} \times \frac{1}{200} \times \frac{100}{WT} \times 100$$

Where,

AT_C = Area of Impurity C peak in Test solution.

AS = Area of the Principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Impurity D: (NMT 0.1%)

$$= \frac{AT_D}{AS} \times \frac{WT}{100} \times \frac{1}{200} \times \frac{100}{WT} \times 100$$

Where,

AT_D = Area of Impurity D peak in Test solution.

AS = Area of the Principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Unspecified impurity: (NMT 0.10%)

$$= \frac{AT_I}{AS} \times \frac{WT}{100} \times \frac{1}{200} \times \frac{100}{WT} \times 100$$

Where,

AT_I = Area of Unspecified impurity peak in Test solution.

AS = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Total impurities: (NMT 0.5%)

$$= \frac{AT_T}{AS} \times \frac{WT}{100} \times \frac{1}{200} \times \frac{100}{WT} \times 100$$

Where,

AT_T = Area of All impurities peak in Test solution.

AS = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Note: Calculate the content of Impurity A and Impurity B areas with multiply the respective correction factor.

7. SULPHATED ASH: < REFER GAM 032>

Maximum 0.1%. Determine on 1.0g of sample.

8. LOSS ON DRYING: < REFER GAM 026>

Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 4h.

9. ASSAY: (By Titration)

Weigh accurately and dissolve about 0.150g in 25 mL of anhydrous acetic acid. Titrate with 0.1M perchloric acid, determining the end-point potentiometrically.

1 mL of 0.1 M perchloric acid is equivalent to 19.54 mg of $C_{20}H_{23}ClN_2O_4$.

Calculation:

$$= \frac{\text{Titer value} \times \text{Molarity of 0.1M Perchloric acid} \times 0.01954 \times 100 \times 100}{\text{Sample weight in (g)} \times (100 - \text{Sample LOD}) \times 0.1}$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	15/02/2023	16/02/2023	17/02/2023

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
RMATC0064-01	Periodic review.	NA	20/02/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	15/02/2023	16/02/2023	17/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	PHENYLEPHRINE HYDROCHLORIDE BP			
Specification No.	RMASP0031-01	**Revision No.**	01	**Item Code.:** RMAP0031
Supersedes	RMASP0031-00	**Effective Date**	20/02/2023	**Page No.:** 1 of 4

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$C_9H_{14}ClNO_2$
2	Molecular weight	203.7
3	Storage conditions	Protected from light
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	6 g
6	Quantity of reserve sample	12 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	PHENYLEPHRINE HYDROCHLORIDE BP			
Specification No.	RMASP0031-01	**Revision No.**	01	**Item Code.:** RMAP0031
Supersedes	RMASP0031-00	**Effective Date**	20/02/2023	**Page No.:** 2 of 4

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, crystalline powder.
2.	*Solubility	Freely soluble in water and in ethanol (96 per cent).
3.	*Identification **A.** By Specific optical rotation	Between -43° to -47° (dried substance)
	B. By Melting point	Between 171°C to 176°C.
	C. By IR	The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Phenylephrine Hydrochloride RS.
	D. By Chemical test	The upper layer remains colourless.
	E. By Chlorides	A curdled, white precipitate is formed
4.	Appearance of solution	Solution S is clear and colourless
5.	Acidity or alkalinity	The solution is yellow. Not more than 0.4 mL of 0.01 M hydrochloric acid is required to change the colour of the indicator to red.
6.	*Specific optical rotation	-43° to -47° (dried substance)

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	PHENYLEPHRINE HYDROCHLORIDE BP			
Specification No.	RMASP0031-01	**Revision No.**	01	**Item Code.:** RMAP0031
Supersedes	RMASP0031-00	**Effective Date**	20/02/2023	**Page No.:** 3 of 4

S.NO	TEST (s)	SPECIFICATION (s)
7.	*Related substances (By HPLC) (i) Impurity C (ii) Impurity E (iii) Unspecified impurity (iv) Total impurities	 Not more than 0.1% Not more than 0.1% Not more than 0.1% Not more than 0.2%
8.	Sulfates	Maximum 500ppm
9.	Sulfated ash	Not more than 0.1%
10.	*Loss on drying	Not more than 1.0%
11.	*Assay (By Titration) (On dried basis)	Not more than 98.5% and not more than 101.0% w/w

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	PHENYLEPHRINE HYDROCHLORIDE BP			
Specification No.	RMASP0031-01	**Revision No.**	01	**Item Code.:** RMAP0031
Supersedes	RMASP0031-00	**Effective Date**	20/02/2023	**Page No.:** 4 of 4

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
RMASP0031-01	Periodic review.	NA	20/02/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	PHENYLEPHRINE HYDROCHLORIDE BP			
STP No.	RMATP0031-01	**Revision No.**	01	**Item Code.:** RMAP0031
Supersedes	RMATP0031-00	**Effective Date**	20/2/2023	**Page No.:** 1 of 9

1. DESCRIPTION: < REFER GAM 001>

White or almost white, crystalline powder.

2. SOLUBILITY: < REFER GAM 002>

100mg of sample + 1mL of Water	Freely soluble if the material dissolves.
100mg of sample + 1mL of Ethanol (96%)	Freely soluble if the material dissolves.

3. IDENTIFICATION:

First identification: A, C, E

Second identification: A, B, D, E

A. By Specific optical rotation: < REFER GAM 029>

Between -43° to -47° (dried substance)

B. By Melting point: < REFER GAM 028>

Between 171°C to 176°C.

Dissolve 0.3 g in 3 mL of water, add 1 mL of dilute ammonia and initiate crystallisation by scratching the wall of the tube with a glass rod. Wash the crystals with iced water and dry at 105 °C for 2 h.

C. By IR: < REFER GAM 003>

The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Phenylephrine Hydrochloride RS.

D. By Chemical test:

Dissolve about 10 mg in 1 mL of water and add 0.05 mL of a 125 g/L solution of copper sulfate pentahydrate and 1 mL of a 200 g/L solution of sodium hydroxide. A violet colour is produced. Add 1 mL of ether and shake; the upper layer remains colourless.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

E. By Chlorides: < REFER GAM 003>

Dissolve in 2 mL of water a quantity of the substance to be examined equivalent to about 2 mg of chloride Acidify with dilute nitric acid and add 0.4 mL of silver nitrate solution. Shake and allow to stand. A curdled, white precipitate is formed.

Centrifuge and wash the precipitate with three quantities, each of 1 mL, of water. Carry out this operation rapidly in subdued light, disregarding the fact that the supernatant solution may not become perfectly clear. Suspend the precipitate in 2 mL of water and add 1.5 mL of ammonia. The precipitate dissolves easily with the possible exception of a few large particles which dissolve slowly.

4. APPEARANCE OF SOLUTION:

Solution S:

Dissolve 2.00 g in carbon dioxide-free water prepared from distilled water and dilute to 100.0 mL with the same solvent.

Solution S is clear and colourless.

5. ACIDITY OR ALKALINITY:

To 10 mL of solution S add 0.1 mL of methyl red solution and 0.2 mL of 0.01 M sodium hydroxide. The solution is yellow. Not more than 0.4 mL of 0.01 M hydrochloric acid is required to change the colour of the indicator to red.

6. SPECIFIC OPTICAL ROTATION: < REFER GAM 029>

Between -43º to -47º (dried substance), determined on solution S.

7. RELATED SUBSTANCES: (BY HPLC)

Chemicals/Reagents/Standards:

Phenylephrine Hydrochloride : Working standard

Phenylephrine Hydrochloride for peak identification	:	Reference standard
Sodium octanesulfonate monohydrate	:	AR grade
Phosphoric acid	:	AR grade
Purified Water	:	Milli-Q water (or) equivalent
Acetonitrile	:	HPLC grade

Chromatographic Conditions:

Column	:	Purospher STAR RP-18 endcapped, 55mm x 4.0mm, (3.0µm) or equivalent.
Column Temperature	:	45°C
Flow Rate	:	1.5ml/min
Wavelength	:	215nm
Injection volume	:	10µl
Retention time	:	Retention time of Phenylephrine hydrochloride peak is at about 2.8 minutes

Buffer solution pH 2.8:

Dissolve 3.25 g of Sodium octanesulfonate monohydrate in 1000 mL of water by stirring for 30 min and adjust to pH 2.8 with dilute phosphoric acid.

Mobile phase A:

Acetonitrile, buffer solution pH 2.8 (10:90 V/V);

Mobile phase B:

Buffer solution pH 2.8, Acetonitrile(10:90 V/V);

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

Gradient program:

Time (min)	Mobile phase A (per cent V/V)	Mobile phase B (per cent V/V)
0 - 3	93	7
3 - 13	93 → 70	7 → 30
13 - 14	70 → 93	30 → 7

Solvent mixture:

Mobile phase B, mobile phase A (20:80 V/V).

Test solution:

Weigh accurately about 50.0 mg of the substance to be examined in the solvent mixture and dilute to 50.0 mL with the solvent mixture.

Reference solution (a):

Dilute 5.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 2.0 mL of this solution to 100.0 mL with the solvent mixture.

Reference solution (b):

Dissolve the contents of a vial of phenylephrine hydrochloride for peak identification RS (containing impurities C and E) in 2.0 mL of the solvent mixture.

Relative retention With reference to phenylephrine (retention time = about 2.8 min): impurity C = about 1.3; impurity E = about 3.6.

System suitability:

— **Symmetry factor:** maximum 1.9 for the principal peak in the chromatogram obtained with the test solution;

— **Peak-to-valley ratio:** minimum 5, where H_p = height above the baseline of the peak due to impurity C and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to phenylephrine in the chromatogram obtained with reference solution (b).

Limits:

— **Correction factors:** for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity C = 0.5; impurity E = 0.5;

— **impurities C, E:** for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

— **unspecified impurities:** for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— **total:** not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

— **disregard limit:** 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Inject 10µl of the above solution as per following sequence.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

Injection sequence:

S. No	Sample Name	No. of injections
1	Solvent mixture (Blank)	1
2	System suitability (Reference solution (b))	1
3	Reference solution (a)	1
4	Blank	1
5	Test solution	1

Calculations:

Impurity C: (NMT 0.1%)

$$= \frac{A_{TC}}{A_{SC}} \times \frac{WT}{50} \times \frac{5}{100} \times \frac{2}{100} \times \frac{50}{WT} \times 0.5 \times 100$$

Where,

A_{TC} = Area of Impurity C peak in Test solution.

A_{SC} = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Impurity E: (NMT 0.1%)

$$= \frac{A_{TE}}{A_{SE}} \times \frac{WT}{50} \times \frac{5}{100} \times \frac{2}{100} \times \frac{50}{WT} \times 0.5 \times 100$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

Where,

ATE = Area of Impurity E peak in Test solution.

ASE = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Unspecified impurity: (NMT 0.1%)

$$= \frac{AT_I}{AS_I} \times \frac{WS}{50} \times \frac{5}{100} \times \frac{2}{100} \times \frac{50}{WT} \times 100$$

Where,

ATI = Area of Unspecified impurity peak in Test solution.

ASI = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Total impurities: (NMT 0.2%)

$$= \frac{AT_T}{AS_T} \times \frac{WS}{50} \times \frac{5}{100} \times \frac{2}{100} \times \frac{50}{WT} \times 100$$

Where,

ATT = Area of All impurities peak in Test solution.

AST = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

Note: Calculate the content of Impurity C and Impurity E areas with multiply the respective correction factor.

8. SULFATES: < REFER GAM 009>

Maximum 500 ppm, determined on solution S.

9. SULPHATED ASH: < REFER GAM 032>

Maximum 0.1%. Determine on 1.0g of sample.

10. LOSS ON DRYING: < REFER GAM 026>

Maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

11. ASSAY: (By Titration)

Weigh accurately and dissolve about 0.150 g in a mixture of 0.5 mL of 0.1 M hydrochloric acid and 80 mL of ethanol (96 per cent). Carry out a potentiometric titration using 0.1M ethanolic sodium hydroxide. Read the volume added between the 2 points of inflexion.

1 mL of 0.1M ethanolic sodium hydroxide is equivalent to 0.02037g of $C_9H_{14}ClNO_2$.

Calculation:

$$= \frac{\text{Titer value x 0.1M ethanolic sodium hydroxide x 0.02037g x100 x 100}}{\text{Sample weight in (g) X (100 – Sample LOD) x 0.1}}$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
RMATP0031-01	Periodic review.	NA	20/02/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	16/02/2023	17/02/2023	18/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	CAFFEINE ANHYDROUS BP			
Specification No.	RMASC0065-01	**Revision No.**	01	**Item Code.:** RMAC0065
Supersedes	RMASC0065-00	**Effective Date**	14/02/2023	**Page No.:** 1 of 4

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$C_8H_{10}N_4O_2$
2	Molecular weight	194.2
3	Storage conditions	NA
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	6 g
6	Quantity of reserve sample	12 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	CAFFEINE ANHYDROUS BP			
Specification No.	RMASC0065-01	**Revision No.**	01	**Item Code.:** RMAC0065
Supersedes	RMASC0065-00	**Effective Date**	14/02/2023	**Page No.:** 2 of 4

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, crystalline powder or silky crystals.
2.	*Solubility	Sparingly soluble in water, freely soluble in boiling water, slightly soluble in ethanol (96 per cent). It dissolves in concentrated solutions of alkali benzoates or salicylates. It sublimes readily.
3.	*Identification **A.** By Melting point **B.** By IR **C.** By Chemical test **D.** By Chemical test **E.** Loss on drying **F.** Xanthines	 **A.** 234 °C to 239 °C. **B.** The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Caffeine WS. **C.** A brown precipitate is formed **D.** An intense blue colour develops. **E.** Not more than 0.5 per cent **F.** The colour of the residue changes to violet-red.
4.	Appearance of solution	Solution S is clear and colourless
5.	Acidity	The solution is green or yellow. Not more than 0.2 mL of 0.01 M sodium hydroxide is required to change the colour of the indicator to blue

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	CAFFEINE ANHYDROUS BP			
Specification No.	RMASC0065-01	**Revision No.**	01	**Item Code.:** RMAC0065
Supersedes	RMASC0065-00	**Effective Date**	14/02/2023	**Page No.:** 3 of 4

S.NO	TEST (s)	SPECIFICATION (s)
6.	*Related substances (By HPLC) (i) Unspecified impurity (ii) Total impurities	 Not more than 0.1% Not more than 0.1%
7.	Sulfates	Maximum 500 ppm
8.	Sulphated Ash	Not more than 0.1% w/w
9.	*Loss on drying	Not more than 0.5% w/w
10.	*Assay By Titration (On dried basis)	Not less than 98.5% and not more than 101.5% w/w.

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	CAFFEINE ANHYDROUS BP			
Specification No.	RMASC0065-01	**Revision No.**	01	**Item Code.:** RMAC0065
Supersedes	RMASC0065-00	**Effective Date**	14/02/2023	**Page No.:** 4 of 4

REVISION HISTORY:

Specification No.	Effective Date	Reason for Review
RMASC0065-00	14-02-2023	New specification prepared
RMASC0065-01	14/02/2023	Periodic review.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	CAFFEINE ANHYDROUS BP			
STP No.	RMATC0065-01	**Revision No.**	01	**Item Code.:** RMAC0065
Supersedes	RMATC0065-00	**Effective Date**	14/02/2023	**Page No.:** 1 of 7

1. DESCRIPTION: < REFER GAM 001>

White or almost white, crystalline powder or silky crystals.

2. SOLUBILITY: < REFER GAM 002>

100mg of sample + 10mL of Water	Sparingly soluble if the material dissolves.
100mg of sample + 1mL of Boiling Water	Freely soluble if the material dissolves.
10mg of sample + 10mL of Ethanol (96%)	Slightly soluble if the material dissolves.

It dissolves in concentrated solutions of alkali benzoates or salicylates. It sublimes readily.

3. IDENTIFICATION:

First identification: A, B, E

Second identification: A, C, D, E, F

A. By Melting point: < REFER GAM 028>

234 °C to 239 °C.

B. By IR: < REFER GAM 003>

The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Caffeine WS.

C. By Chemical test:

To 2mL of a saturated solution add 0.05mL of iodinated potassium iodide solution. The solution remains clear. Add 0.1mL of dilute hydrochloric acid; a brown precipitate is formed. Neutralise with dilute sodium hydroxide solution; the precipitate dissolves.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

D. By Chemical test:

In a ground-glass-stoppered tube, dissolve about 10mg in 0.25mL of a mixture of 0.5mL of acetylacetone and 5mL of dilute sodium hydroxide solution. Heat in a water-bath at 80°C for 7 min. Cool and add 0.5mL of dimethylaminobenzaldehyde solution. Heat again in a water-bath at 80°C for 7 min. Allow to cool and add 10mL of water; an intense blue colour develops.

E. By Loss on drying : < REFER GAM 026>

Loss on drying (see Tests).

F. By xanthines: < REFER GAM 003>

To a few milligrams of the substance to be examined add 0.1mL of strong hydrogen peroxide solution and 0.3mL of dilute hydrochloric acid. Heat to dryness on a water-bath until a yellowish-red residue is obtained. Add 0.1mL of dilute ammonia. The colour of the residue changes to violet-red.

Solution S:

Dissolve 0.5g with heating in 30mL of carbon dioxide-free water prepared from distilled water, cool and dilute to 50mL with the same solvent.

4. APPEARANCE OF SOLUTION:

Solution S is clear and colourless.

5. ACIDITY:

To 10mL of solution S add 0.05mL of bromothymol blue solution; the solution is green or yellow. Not more than 0.2mL of 0.01M sodium hydroxide is required to change the colour of the indicator to blue.

6. RELATED SUBSTANCES: (BY HPLC)

Chemicals/Reagents/Standards:

Caffeine	:	Working standard
Tetrahydrofuran	:	AR grade
Acetonitrile	:	AR grade
Anhydrous sodium acetate	:	AR grade
Glacial acetic acid	:	AR grade

Chromatographic Conditions:

Column	:	Waters Xterra, 150mm x 4.6mm, (5µm) or equivalent.
Flow Rate	:	1.0ml/min
Wavelength	:	275nm
Injection volume	:	10µl
Run time	:	15 minutes
Retention time	:	Retention time of Caffeine peak is at about 8.0 minutes

Mobile phase:

A Mixture 20 volumes of tetrahydrofuran, 25 volumes of acetonitrile and 955 volumes of a solution containing 0.82g/L of anhydrous sodium acetate previously adjusted to pH 4.5±0.05 with glacial acetic acid.

Test solution:

Weigh accurately about 0.100g of the substance to be examined in the mobile phase and dilute to 50.0mL with the mobile phase. Dilute 1.0mL of this solution to 10.0mL with the mobile phase.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

Reference solution (a):

Dilute 2.0mL of the test solution to 100.0mL with the mobile phase. Dilute 1.0mL of this solution to 10.0mL with the mobile phase.

Reference solution (b):

Weigh accurately about 5mg of caffeine for system suitability CRS (containing impurities A, C, D and F) in the mobile phase and dilute to 5mL with the mobile phase. Dilute 2mL of this solution to 10mL with the mobile phase.

Identification of impurities: Use the chromatogram supplied with caffeine for system suitability CRS and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, C, D and F.

Relative retention:

With reference to caffeine (retention time = about 8 min): impurity C =about 0.38; impurity D = about 0.42; impurity F = about 0.6, impurity A =about 0.7.

System suitability Reference solution (b):

Resolution: minimum 2.0 between the peaks due to impurities C and D and minimum 2.5 between the peaks due to impurities F and A.

Limits:

Unspecified impurities: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

Total: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

Disregard limit: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Inject 10µl of the above solution as per following sequence.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

Injection sequence:

S. No	Sample Name	No. of injections
1	Mobile phase (Blank)	1
2	Reference solution (a)	1
3	Reference solution (b)	1
4	Mobile phase (Blank)	1
5	Test solution	1

Calculations:

Unspecified impurity: (NMT 0.10%)

$$= \frac{AT_I}{AS_I} \times \frac{WT}{50} \times \frac{1}{10} \times \frac{2}{100} \times \frac{1}{10} \times \frac{50}{WT} \times \frac{10}{1} \times 100$$

Where,

AT_I = Area of unspecified impurity peak in Test solution.

AS_I = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Total impurities: (NMT 0.1%)

$$= \frac{AT_T}{AS_T} \times \frac{WT}{50} \times \frac{1}{10} \times \frac{2}{100} \times \frac{1}{10} \times \frac{50}{WT} \times \frac{10}{1} \times 100$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

Where,

AT_T = Area of Total impurities peak in Test solution.

AS_T = Area of the principal peak in the Reference solution (a)

WT = Weight of the Test solution in mg.

7. SULFATES: < REFER GAM 009>

Maximum 500 ppm, determined on 15 mL of solution S.

Prepare the standard using a mixture of 7.5 mL of sulfate standard solution (10 ppm SO_4) and 7.5 mL of distilled water.

8. SULPHATED ASH: < REFER GAM 032>

Maximum 0.1%. Determine on 1.0g of sample.

9. LOSS ON DRYING: < REFER GAM 026>

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 1 h.

10. ASSAY: (By Titration)

Weigh accurately about 0.170 g with heating in 5 mL of anhydrous acetic acid. Allow to cool, add 10 mL of acetic anhydride and 20 mL of toluene. Titrate with 0.1 M perchloric acid, determining the end-point potentiometrically.

1 mL of 0.1 M perchloric acid is equivalent to 19.42 mg of $C_8H_{10}N_4O_2$.

Calculation:

$$= \frac{\text{Titer value x Molarity of 0.1M Perchloric acid x 0.01942 x 100 x100}}{\text{Sample weight in (g) X (100 – Sample LOD) x 0.1}}$$

REVISION HISTORY:

STP No.	Effective Date	Reason for Review
RMATC0065-00	14-02-2020	New STP prepared
RMATC0065-01	14/02/2023	Periodic review.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	PARACETAMOL BP			
Specification No.	SPEC-RMAP0030-02	**Revision No.**	02	**Item Code.:** RMAP0030
Supersedes	RMASP0030-01	**Effective Date**	08/06/2023	**Page No.:** 1 of 3

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$C_8H_9NO_2$
2	Molecular weight	151.2
3	Storage conditions	Protected from light.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	3 g
6	Quantity of reserve sample	6 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	06/06/2023	07/06/2023	07/06/2023

	Safetab Life Science Puducherry			
	RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	PARACETAMOL BP			
Specification No.	SPEC-RMAP0030-02	**Revision No.**	02	**Item Code.:** RMAP0030
Supersedes	RMASP0030-01	**Effective Date**	08/06/2023	**Page No.:** 2 of 3

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, crystalline powder.
2.	*Solubility	Sparingly soluble in water, freely soluble in ethanol (96 per cent), very slightly soluble in methylene chloride.
3.	*Identification **A.** By Melting point **B.** By IR	**Result A:** 168°C to 172°C. **Result B:** The absolute difference between the melting point of the mixture and the value obtained in determination A is not greater than 2°C. The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Paracetamol RS.
4.	*Related substances (By HPLC) (i) Impurity K (ii) Impurity J (iii) Unspecified impurity (iv) Total impurities	 Not more than 50 ppm Not more than 10 ppm Not more than 0.05% Not more than 0.2%
5.	Sulphated Ash	Not more than 0.1% w/w
6.	*Loss on drying	Not more than 0.5% w/w

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	06/06/2023	07/06/2023	07/06/2023

S.NO	TEST (s)	SPECIFICATION (s)
7.	*Assay By Titration (On dried basis)	Not less than 99.0% and not more than 101.0% w/w.

Remarks: The above * Marked tests are to be performed while retesting the material.

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-RMAP0030-02	(i) There is no changes in Specification. (ii) Specification number has been changed as per ERP. This changes captured as per change control number.	ST/CC/23/063	08/06/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	06/06/2023	07/06/2023	07/06/2023

	Safetab Life Science Puducherry STANDARD TESTING PROCEDURE			MASTER COPY
Name of Product	PARACETAMOL BP			
STP No.	STP-RMAP0030-02	**Revision No.**	02	**Item Code.:** RMAP0030
Supersedes	RMATP0030-01	**Effective Date**	08/06/2023	**Page No.:** 1 of 8

1. DESCRIPTION: < REFER GAM 001>

White or almost white, crystalline powder.

2. SOLUBILITY: < REFER GAM 002>

100mg of sample + 10mL of Water	Sparingly soluble if the material dissolves.
100mg of sample + 1mL of Ethanol (96%)	Freely soluble if the material dissolves.
10mg of sample + 100mL of methylene chloride	Very slightly soluble if the material dissolves.

3. IDENTIFICATION: < REFER GAM 003>

First identification: B.

Second identification: A.

A. By Melting point:

Determination A:

Determine the melting point of the substance to be examined.

Result A: 168 °C to 172 °C.

Determination B:

Mix equal parts of the substance to be examined and Paracetamol RS and determine the melting point of the mixture.

Result B: The absolute difference between the melting point of the mixture and the value obtained in determination A is not greater than 2°C.

B. By IR:

The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Paracetamol RS.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	06/06/2023	07/06/2023	07/06/2023

4. RELATED SUBSTANCES: (BY HPLC)

Chemicals/Reagents/Standards:

Paracetamol Impurity K	:	Reference standard
Paracetamol Impurity J	:	Reference standard
Potassium dihydrogen phosphate	:	AR grade
Dipotassium hydrogen phosphate	:	AR grade
Purified Water	:	Milli-Q water (or) equivalent
Methanol	:	HPLC grade

Chromatographic Conditions:

Column	:	150mm x 4.6mm, end-capped solid core Octadecylsilyl silica, (5µm).
Column Temperature	:	30°C
Auto sampler temperature	:	5°C
Flow Rate	:	1.5ml/min
Wavelength	:	254nm
Injection volume	:	50µl
Retention time	:	Retention time of Paracetamol peak is at about 4.0 minutes

Mobile phase A:

Dissolve 1.7g of Potassium dihydrogen phosphate and 1.8 g of Dipotassium hydrogen phosphate in water for chromatography and dilute to 1000 mL with the same solvent.

Mobile phase B: Methanol

Gradient program:

Time (min)	Mobile phase A (per cent V/V)	Mobile phase B (per cent V/V)
0 – 1.5	95	5
1.5 – 14.4	95 → 90	5 → 10
14.4 – 28.8	90	10
28.8 – 57.6	90 → 66	10 → 34
57.6 - 60	66	34

Solvent mixture:

A mixture of 15 volumes of Methanol and 85 volumes of water.

Test solution:

Weigh accurately and dissolve about 50.0mg of the substance to be examined in 0.75ml of methanol and dilute to 5.0ml with water.

Reference solution (a):

Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 20.0 mL with the solvent mixture.

Reference solution (b):

Dissolve 5.0mg of Paracetamol impurity J RS in 25ml of methanol and dilute to 250.0 mL with the solvent mixture. Dilute 1.0 mL of the solution to 200.0 mL with the solvent mixture.

Reference solution (c):

Weigh accurately about 5.0mg of Paracetamol impurity K RS in the solvent mixture and dilute to 100.0 mL with the solvent mixture. Dilute 1.0 mL of the solution to 10.0 mL with the solvent mixture.

Reference solution (d):

Dilute 1.0 mL of the reference solution (c) to 10.0 mL with the solvent mixture.

Reference solution (e):

Mix 1.0 mL of the reference solution (a) and 1ml of reference solution (c) and dilute to 10.0 mL with the solvent mixture.

Procedure:

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity J; use the chromatogram obtained with reference solution (d) to identify the peak due to impurity K.

Relative retention With reference to Paracetamol (retention time = about 4 min): impurity K = about 0.4; impurity J = about 10.1.

System suitability Reference solution (e):

— **Resolution**: minimum 5.0 between the peaks due to impurity K and Paracetamol.

Calculation of percentage contents:

— for impurity J, use the concentration of impurity J in reference solution (b);

— for impurity K, use the concentration of impurity K in reference solution (d);

— for impurities other than J and K, use the concentration of Paracetamol in reference solution (a).

Limits:

— impurity K: maximum 50 ppm;

— impurity J: maximum 10 ppm;

— unspecified impurities: for each impurity, maximum 0.05 per cent;

— total: maximum 0.2 per cent;

— reporting threshold: 0.03 per cent, except for impurities J and K.

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

Injection sequence:

S. No	Sample Name	No. of injections
1	Solvent mixture (Blank)	1
2	System suitability (Reference solution (e))	1
3	Reference solution (b)	1
4	Reference solution (d)	1
5	Reference solution (a)	1
6	Blank	1
7	Test solution	1

Calculations:

Impurity K : (NMT 50ppm)

$$= \frac{AT_K}{AS_K} \times \frac{RS}{100} \times \frac{1}{10} \times \frac{1}{10} \times \frac{5}{WT} \times \frac{P_K}{100} \times 1000 \times 1000$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	06/06/2023	07/06/2023	07/06/2023

Where,

AT_K = Area of Impurity K peak in Test solution.

AS_K = Area of the Impurity K peak in the Reference solution (d)

RS = Weight of the Impurity K Reference standard in mg.

WT = Weight of the sample taken in mg.

P = Potency of Impurity K Reference standard in % (as such basis).

Impurity J : (NMT 10ppm)

$$= \frac{AT_J}{AS_J} \times \frac{RS}{250} \times \frac{1}{200} \times \frac{5}{WT} \times \frac{P_J}{100} \times 1000 \times 1000$$

Where,

AT_J = Area of Impurity J peak in Test solution.

AS_J = Area of the Impurity J peak in the Reference solution (b)

RS = Weight of the Impurity J Reference standard in mg.

WT = Weight of the sample taken in mg.

P = Potency of Impurity J Reference standard in % (as such basis).

Unspecified impurity: (NMT 0.05%)

$$= \frac{AT_I}{AS} \times \frac{WT}{5} \times \frac{1}{100} \times \frac{1}{20} \times \frac{5}{WT} \times 100$$

Where,

AT_I = Area of Unspecified impurity peak in Test solution.

AS = Area of the principal peak in the Reference solution (a)

WT = Weight of the sample taken in mg.

Total impurities: (NMT 0.2%)

$$= \frac{AT_T}{AS} \times \frac{WT}{5} \times \frac{1}{100} \times \frac{1}{20} \times \frac{5}{WT} \times 100$$

Where,

AT_T = Area of Total impurities peak in Test solution.

AS = Area of the principal peak in the Reference solution (a)

WT = Weight of the Test solution in mg.

5. SULPHATED ASH: < REFER GAM 032>

Not more than 0.1% w/w. Determine on 1.0g of sample.

6. LOSS ON DRYING: < REFER GAM 026>

Not more than 0.5% w/w, determined on 1.0g of sample by drying in an oven at 105°C.

7. ASSAY: (By Titration)

Weigh accurately about 0.300g of sample in a mixture of 10mL of water and 30mL of dilute sulfuric acid. Boil under a reflux condenser for 1 h, cool and dilute to 100.0mL with water. To 20.0mL of the solution add 40mL of water, 40g of ice, 15mL of dilute hydrochloric acid and 0.1mL of ferroin. Titrate with 0.1M cerium sulfate until a greenish-yellow colour is obtained. Carry out a blank titration

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	06/06/2023	07/06/2023	07/06/2023

1ml of 0.1M Cerium sulphate is equivalent to 0.00756g of Paracetamol.

Calculation:

$$= \frac{\text{Blank-Titer value} \times \text{Molarity of 0.1M Cerium sulphate} \times 0.00756 \times 100 \times 100 \times 100}{20 \times \text{Sample weight in (g)} \times (100 - \text{Sample LOD}) \times 0.1}$$

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-RMAP0030-02	(i) Related substance test procedure has been changed as per BP 2023 (ii) STP numbering procedure revised as per SOP No. ST/QC/058.	ST/CC/23/084 ST/CC/23/063	08/06/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	06/06/2023	07/06/2023	07/06/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	PREGELATINISED STARCH BP (STARCH 1500)			
Specification No.	RMESP0046-01	**Revision No.**	01	**Item Code.:** RMEP0046
Supersedes	RMESP0046-00	**Effective Date**	14/02/2023	**Page No.:** 1 of 3

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	NA
2	Molecular weight	NA
3	Storage conditions	Store protected from moisture.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	50 g
6	Quantity of reserve sample	100 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	PREGELATINISED STARCH BP (STARCH 1500)			
Specification No.	RMESP0046-01	**Revision No.**	01	**Item Code.:** RMEP0046
Supersedes	RMESP0046-00	**Effective Date**	14/02/2023	**Page No.:** 2 of 3

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or yellowish-white powder. It swells in cold water.
2.	*Identification **A.** Microscopic **B.** By Chemical test	 **A.** The starch granules with a distinct black cross intersecting at the hilum may be seen. **B.** A reddish-violet or blue colour is produced.
3.	*pH	Between 4.5 to 7.0
4.	Oxidising substances	Not more than 0.002%
5.	Sulphur dioxide	Not more than 50ppm
6.	Iron	Not more than 20ppm
7.	Foreign matter	Not more than traces of matter other than starch granules are present.
8.	*Loss on drying	Not more than 15.0% w/w.
9.	Sulfated ash	Not more than 0.6% w/w.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	PREGELATINISED STARCH BP (STARCH 1500)			
Specification No.	RMESP0046-01	**Revision No.**	01	**Item Code.:** RMEP0046
Supersedes	RMESP0046-00	**Effective Date**	14/02/2023	**Page No.:** 3 of 3

S.NO	TEST (s)	SPECIFICATION (s)
10.	*Microbial contamination	
	(i) Total aerobic microbial count	Not more than 1000 cfu/g
	(ii) Total yeast and mold count	Not more than 100 cfu/g
	iii) Escherichia coli	Should be absent/g
	iv) Salmonella species	Should be absent/10g

Remarks: The above * Marked tests are to be performed while retesting the material.

REVISION HISTORY:

Specification No.	Effective Date	Reason for Review
RMESP0046-00	14-02-2020	New specification prepared
RMESP0046-01	14/02/2023	Periodic review.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	PREGELATINIZED STARCH BP (STARCH 1500)			
STP No.	RMETP0046-01	**Revision No.**	01	**Item Code.:** RMEP0046
Supersedes	RMETP0046-00	**Effective Date**	14/02/2023	**Page No.:** 1 of 4

1. DESCRIPTION: < REFER GAM 001>

White or yellowish-white powder. It swells in cold water.

2. IDENTIFICATION: < REFER GAM 003>

A. Microscopic:

Examined under a microscope using a mixture of equal volumes of glycerol and water it presents irregular, translucent, white or yellowish-white flakes or pieces with an uneven surface. Under polarised light (between crossed nicol prisms), starch granules with a distinct black cross intersecting at the hilum may be seen.

B. By Chemical test:

Disperse 0.5 g in 2 mL of water without heating and add 0.05 mL of iodine solution. A reddish-violet or blue colour is produced.

3. pH: < REFER GAM 030>

Between 4.5 to 7.0

Weigh accurately about 3.0g of sample dissolved in 100ml carbon dioxide free water and stirring continuously. Determine the pH when a homogeneous solution is obtained.

Rinse the electrodes with distilled water and wipe dry with tissue paper. Set the instrument using buffer solution pH 6.87 by following instrument Operating Procedure. Clean the electrode. Immerse the electrode in the solution being examined and measure the pH.

4. OXIDISING SUBSTANCES:

Weigh accurately about 4.0g of sample to a glass-stoppered, 125ml conical flask and add 50.0ml water. Insert the stopper and swirl for 5 minutes. Transfer to a glass-stoppered 50ml centrifuge tube and centrifuge. Transfer 30.0ml of the clear supernatant liquid to a glass-stoppered 125-ml conical flask. Add 1ml of glacial acetic acid and 0.5g to 1.0g of potassium iodide. Insert the stopper, swirl, and allow to stand for 25 to 30 minutes in the dark. Add 1ml of starch solution and titrate with 0.002M sodium thiosulphate until the starch-iodine colour disappears. Carry out a blank titration. Not more than 1.4ml of 0. 002M sodium thiosulphate is required (0.002 per cent, calculated as H_2O_2).

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

1 ml of 0.002M sodium thiosulphate is equivalent to 0.034mg of oxidising substances, calculated as H_2O_2.

Calculation:

$$= \frac{\text{Titer value x Molarity of 0.002M sodium thiosulphate x 0.034 x 100}}{\text{Sample weight in mg x 0.002}}$$

5. SULPHUR DIOXIDE:

Maximum 50 ppm.

Method II:

Introduce 150 mL of water into the flask (*A*) and pass carbon dioxide through the whole system for 15 min at a rate of 100 ± 5 mL/min. To 10 mL of dilute hydrogen peroxide solution add 0.15 mL of a 1 g/L solution of bromophenol blue in ethanol (20 per cent *V/V*). Add 0.1 M sodium hydroxide until a violet-blue colour is obtained, without exceeding the end-point. Place the solution in the test-tube (*D*). Without interrupting the stream of carbon dioxide, remove the funnel (*B*) and introduce through the opening into the flask (*A*) 25.0 g (*m*) of the substance to be examined with the aid of 100 mL of water. Replace the funnel. Close the tap of the funnel and add 80 mL of dilute hydrochloric acid to the funnel. Open the tap of the funnel to allow the hydrochloric acid solution to flow into the flask, making sure that no sulphur dioxide escapes into the funnel by closing the tap before the last few millilitres of hydrochloric acid solution drain out. Boil for 1 h. Open the tap of the funnel and stop the flow of carbon dioxide and also the heating and the cooling water. Transfer the contents of the test-tube with the aid of a little water to a 200 mL wide-necked, conical flask. Heat on a water-bath for 15 min and allow to cool. Add 0.1 mL of a 1 g/L solution of bromophenol blue in ethanol (20 per cent *V/V*) and titrate with 0.1 M sodium hydroxide until the colour changes from yellow to violet-blue (V_1 mL). Carry out a blank titration (V_2 mL).

6. IRON: < REFER GAM 007>

Maximum 20 ppm.

Dissolve the residue obtained in the test for sulfated ash in 20 mL of dilute hydrochloric acid. Filter. The filtrate complies with the test.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

7. FOREIGN MATTER:

Examined under a microscope using a mixture of equal volumes of glycerol and water, not more than traces of matter other than starch granules are present.

8. LOSS ON DRYING: < REFER GAM 026>

Not more than 15.0% w/w, Determined on 1.0g of sample by drying in an oven at 130°C for 90 minutes.

9. SULFATED ASH: < REFER GAM 032>

Maximum 0.6 per cent, determined on 1.0 g.

10. MICROBIAL CONTAMINATION:

Use 11.0g of sample for Total Microbial count and pathogen test.

Total Aerobic microbial count:

Procedure: Proceed as per the current general testing procedure GAM-035.

Total Yeast and mold count:

Procedure: Proceed as per the current general testing procedure GAM-036.

Escherichia Coli:

Procedure: Proceed as per the current general testing procedure GAM-037.

Salmonella species:

Procedure: Proceed as per the current general testing procedure GAM-038.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

REVISION HISTORY:

STP No.	Effective Date	Reason for Review
RMETP0046-00	14-02-2023	New STP prepared.
RMETP0046-01	14/02/2023	Periodic review.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	09/02/2023	10/02/2023	11/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	MICROCRYSTALLINE CELLULOSE PH 101 BP			
Specification No.	RMESM0031-01	**Revision No.**	01	**Item Code.:** RMEM0031
Supersedes	RMESM0031-00	**Effective Date**	17/02/2023	**Page No.:** 1 of 4

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$C_6nH_{10}n_{+2}O_5n_{+1}$
2	Molecular weight	NA
3	Storage conditions	NA
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	36 g
6	Quantity of reserve sample	72 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	13/02/2023	14/02/2023	15/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	MICROCRYSTALLINE CELLULOSE PH 101 BP			
Specification No.	RMESM0031-01	**Revision No.**	01	**Item Code.:** RMEM0031
Supersedes	RMESM0031-00	**Effective Date**	14/02/2023	**Page No.:** 2 of 4

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, fine or granular, slightly hygroscopic powder.
2.	*Solubility	Practically insoluble in water, in acetone, in anhydrous ethanol, in toluene, in dilute acids and in a 50 g/L solution of sodium hydroxide
3.	*Identification **A.** By IR **B.** By Chemical test **C.** By degree of polymerisation	 **A.** The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Microcrystalline Cellulose WS. **B.** The substance becomes violet-blue. **C.** The degree of polymerisation is not more than 350
4.	Solubility (Ammoniacal copper tetrammine)	It dissolves completely, leaving no residue
5.	*pH	Between 5.0 to 7.5
6.	*Conductivity	Not more than 75 $\mu S \cdot cm^{-1}$
7.	Ether-soluble substances	Not more than 0.05%
8.	Water-soluble substances	Not more than 0.25%

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	13/02/2023	14/02/2023	15/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	MICROCRYSTALLINE CELLULOSE PH 101 BP			
Specification No.	RMESM0031-01	**Revision No.**	01	**Item Code.:** RMEM0031
Supersedes	RMESM0031-00	**Effective Date**	17/02/2023	**Page No.:** 3 of 4

S.NO	TEST (s)	SPECIFICATION (s)
9.	Sulphated Ash	Not more than 0.1% w/w
10.	*Loss on drying	Not more than 7.0% w/w
11.	***Microbial contamination**	
	i) Total aerobic microbial count	Not more than 1000 cfu/g
	ii) Total yeast and mould count	Not more than 100 cfu/g
	iii) Esherichia Coli	Should be absent/g
	iv) Pseudomonas aeruginosa	Should be absent/10g
	v) Staphylococcus aureus	Should be absent/g
	vi) Salmonella Species	Should be absent/g

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	13/02/2023	14/02/2023	15/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	MICROCRYSTALLINE CELLULOSE PH 101 BP			
Specification No.	RMESM0031-01	**Revision No.**	01	**Item Code.:** RMEM0031
Supersedes	RMESM0031-00	**Effective Date**	17/02/2023	**Page No.:** 4 of 4

REVISION HISTORY:

Specification No.	Effective Date	Reason for Review
RMESM0031-00	17/02/2020	New specification prepared
RMESM0031-01	17/02/2023	Periodic review.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	13/02/2023	14/02/2023	15/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	MICROCRYSTALLINE CELLULOSE PH 101 BP			
STP No.	RMETM0031-01	**Revision No.**	01	**Item Code.:** RMEM0031
Supersedes	RMETM0031-00	**Effective Date**	17/02/2023	**Page No.:** 1 of 5

1. DESCRIPTION: < REFER GAM 001>

White or almost white, fine or granular, slightly hygroscopic powder.

2. SOLUBILITY: < REFER GAM 002>

10mg of sample + 100mL of Water	Practically insoluble if the material not dissolves.
10mg of sample + 100mL of Acetone	Practically insoluble if the material not dissolves.
10mg of sample + 100mL of Anhydrous ethanol	Practically insoluble if the material not dissolves.
10mg of sample + 100mL of toluene	Practically insoluble if the material not dissolves.
10mg of sample + 100mL of Dilute acids	Practically insoluble if the material not dissolves.
10mg of sample + 100mL of Sodium hydroxide	Practically insoluble if the material not dissolves.

3. IDENTIFICATION:

A. By IR: < REFER GAM 003>

The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Microcrystalline Cellulose WS.

Disregard any band between 800 cm^{-1} and 825 cm^{-1} or between 950 cm^{-1} and 1000 cm^{-1}.

B. By Chemical test:

Place about 10 mg on a watch-glass and disperse in 2 mL of iodinated zinc chloride solution. The substance becomes violet-blue.

C. By Degree of polymerisation:

The degree of polymerisation is not more than 350.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	13/02/2023	14/02/2023	15/02/2023

Transfer 1.300g to a 125 mL conical flask. Add 25.0 mL of water and 25.0 mL of cupriethylenediamine hydroxide solution. Immediately purge the solution with nitrogen, insert the stopper and shake until completely dissolved. Transfer an appropriate volume of the solution to a suitable capillary viscometer.

Equilibrate the solution at 25 ± 0.1 °C for at least 5 min. Record the flow time (t_1) in seconds between the 2 marks on the viscometer. Calculate the kinematic viscosity (v_1) of the solution using the following expression:

$$t1(k1)$$

k_1 = viscometer constant.

Dilute a suitable volume of cupriethylenediamine hydroxide solution with an equal volume of water and measure the flow time (t_2) using a suitable capillary viscometer. Calculate the kinematic viscosity (v_2) of the solvent using the following expression:

$$t2(k2)$$

k_2 = viscometer constant.

Determine the relative viscosity (η_{rel}) of the substance to be examined using the following expression:

$$v1/v2$$

Determine the intrinsic viscosity ($[\eta]_c$) by interpolation, using the intrinsic viscosity table (Table 0316.-1).

Calculate the degree of polymerisation (P) using the following expression:

$$95[\eta]cm[(100-b)/100]$$

m = mass of the substance to be examined, in grams;
b = loss on drying, in per cent.

4. SOLUBILITY:

Dissolve 50 mg in 10 mL of ammoniacal solution of copper tetrammine. It dissolves completely, leaving no residue.

5. pH: < REFER GAM 030>

5.0 to 7.5 for the supernatant.

Shake 5g with 40 mL of carbon dioxide-free water for 20 min and centrifuge.

6. CONDUCTIVITY:

The conductivity of the test solution does not exceed the conductivity of the water by more than 75 $\mu S \cdot cm^{-1}$.

Use as test solution the supernatant obtained in the test for pH. Measure the conductivity of the supernatant after a stable reading has been obtained and measure the conductivity of the water used to prepare the test solution.

7. ETHER-SOLUBLE SUBSTANCES:

Maximum 0.05 per cent (5.0 mg) for the difference between the mass of the residue and the mass obtained from a blank determination.

Place 10.0g in a chromatography column about 20 mm in internal diameter and pass 50 mL of peroxide-free ether through the column. Evaporate the eluate to dryness in a previously dried and tared evaporating dish, with the aid of a current of air in a fume cupboard. After all ether has evaporated, dry the residue at 105 °C for 30 min, allow to cool in a desiccator and weigh. Carry out a blank determination.

8. WATER-SOLUBLE SUBSTANCES:

Maximum 0.25 per cent (12.5 mg) for the difference between the mass of the residue and the mass obtained from a blank determination.

Shake 5.0 g with 80 mL of water for 10 min. Filter through a filter paper with the aid of vacuum into a tared flask. Evaporate to dryness on a water-bath avoiding charring. Dry at 105 °C for 1 h, allow to cool in a desiccator and weigh. Carry out a blank determination.

9. SULPHATED ASH: < REFER GAM 032>

Maximum 0.1%. Determine on 1.0g of sample.

10. LOSS ON DRYING: < REFER GAM 026>

Maximum 7.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

11. MICROBIAL CONTAMINATION:

a. Total aerobic microbial count:

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

b. Total yeast and Moulds count:

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

c. Esherichia Coli:

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

d. Salmonella Species:

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

e. Pseudomonas aeruginosa:

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

f. Staphylococcus aureus:

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	13/02/2023	14/02/2023	15/02/2023

REVISION HISTORY:

STP No.	Effective Date	Reason for Review
RMETM0031-00	17-02-2020	New STP prepared
RMETM0031-01	17/02/2023	Periodic review.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	13/02/2023	14/02/2023	15/02/2023

	Safetab Life Science Puducherry			
	RAW MATERIAL SPECIFICATION MASTER COPY			
Name of Product	POVIDONE K 90 BP (BOVIDONE K 90)			
Specification No.	SPEC-RMEP0045-00	**Revision No.**	00	**Item Code.:** RMEP0045
Supersedes	RMESP0045-00	**Effective Date**	25/08/2023	**Page No.:** 1 of 4

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$(C_6H_9NO)_n$
2	Molecular weight	NA
3	Storage conditions	Store in well-closed, air-tight containers.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	25 g
6	Quantity of reserve sample	50 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: 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	21/08/2023	22/08/2023	22/08/23

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	POVIDONE K 90 BP (BOVIDONE K 90)			
Specification No.	SPEC-RMEP0045-00	**Revision No.**	00	**Item Code.:** RMEP0045
Supersedes	RMESP0045-00	**Effective Date**	25/08/2023	**Page No.:** 2 of 4

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or yellowish-white, hygroscopic powder or flakes.
2.	*Solubility	Freely soluble in water, in ethanol (96%) and in methanol, very slightly soluble in acetone.
3.	*Identification **A.** By IR **B.** By Chemical test **C.** By Chemical test **D.** By Chemical test	 The infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Povidone K 25. A pink colour is produced. A red colour is produced. The substance dissolves.
4.	Appearance of solution	Solution S is clear, and not more intensely coloured than reference solution B_6, BY_6 or R_6.
5.	*pH	Between 4.0 to 7.0
6.	Viscosity (Expressed as K- value)	Between 81.0 to 96.3
7.	Aldehydes (Expressed as Acetaldehyde)	Not more than 500ppm

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

	Safetab Life Science Puducherry			
	RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	POVIDONE K 90 BP (BOVIDONE K 90)			
Specification No.	SPEC-RMEP0045-00	**Revision No.**	00	**Item Code.:** RMEP0045
Supersedes	RMESP0045-00	**Effective Date**	25/08/2023	**Page No.:** 3 of 4

S.NO	TEST (s)	SPECIFICATION (s)
8.	Peroxides	Not more than 400 ppm
9.	Formic Acid	Not more than 0.5%
10.	Limit of Hydrazine	Not more than 1ppm.
11.	Impurity A	Not more than 10ppm.
12.	Impurity B	Not more than 3.0%
13.	*Water content (By KFR)	Not more than 5.0%
14.	Sulphated ash	Not more than 0.1%
15.	*Assay on anhydrous basis	Not less than 11.5% and not more than 12.8% of Nitrogen content.

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	POVIDONE K 90 BP (BOVIDONE K 90)			
Specification No.	SPEC-RMEP0045-00	**Revision No.**	00	**Item Code.:** RMEP0045
Supersedes	RMESP0045-00	**Effective Date**	25/08/2023	**Page No.:** 4 of 4

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-RMEP0045-00	(i) Periodic review. (ii) Specification numbering procedure revised as per SOP No. ST/QC/058.	ST/CC/23/016	25/08/2023

**** 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	21/08/2023	22/08/2023	22/08/23

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	POVIDONE K 90 BP (BOVIDONE K 90)			
STP No.	STP-RMEP0045-00	**Revision No.**	00	**Item Code.:** RMEP0045
Supersedes	RMETP0045-00	**Effective Date**	25/08/2023	**Page No.:** 1 of 12

1. DESCRIPTION: < REFER GAM 001>

White or yellowish-white, hygroscopic powder or flakes.

2. SOLUBILITY: < REFER GAM 002>

100mg of sample + 1ml of Water	Freely soluble if the material dissolves.
100mg of sample + 1ml of Ethanol (96%)	Freely soluble if the material dissolves.
100mg of sample + 1ml of Methanol	Freely soluble if the material dissolves.
10mg of sample + 100ml of Acetone	Very slightly soluble if the material dissolves.

3. IDENTIFICATION: < REFER GAM 003>

First identification test: A and D.

Second identification test: B,C and D

Solution S1: Dissolve 2.5g of sample in carbon dioxide-free water and dilute to 25ml with the same solvent. Add the substance to be examined to the water in small portions, stirring using a magnetic stirrer. **Note:** Solution S1 will be used in Identification B & C tests.

A. By IR:

Previously dried at 105°C for 6 hour.

The infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Povidone K 25 WS.

B. By Chemical test:

To 1ml of Solution S1, add 0.2ml of dimethylaminobenzaldehyde solution and 0.1ml of sulfuric acid. A pink colour is produced.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

C. By Chemical test:

To 0.1ml of Solution S1, add 5ml of water and 0.2ml of 0.05M iodine. A red colour is produced.

D. By Chemical test:

Weigh about 0.5g of sample dissolved in 10ml of water and shake. The substances dissolves.

SOLUTION S:

Dissolve 1.0g of sample in carbon dioxide free water and dilute to 20ml with the same solvent. Add the substance to be examined to the water in small portions, stirring using a magnetic stirrer.

4. APPEARANCE OF SOLUTION:

Solution S is clear and not more intensely coloured than reference solution B_6, BY_6 or R_6.

5. pH: < REFER GAM 030>

Between 4.0 to 7.0 for Solution S.

6. VISCOSITY (EXPRESSED AS K-VALUE):

Procedure:

Dissolve a 1.0 g of substance in 100 ml of water. Allow to stand for 1 hr. and determine the viscosity of the solution at 25°C, using viscometer no.1 with a minimum flow time of 100 s.

The time required for the level of the liquid to drop from one mark to the other is measured with a stop-watch to the nearest one-fifth of a second. The result is valid only if two consecutive readings do not differ by more than 1 per cent. The average of not fewer than three readings gives the flow time of the liquid to be examined.

Calculate the K-value using the following expression:

$$1.5\log v_{rel} - 10.15 + 0.003c + 300c\log v_{rel} + (c + 1.5c\log v_{rel})2\sqrt{0.15c + 0.003c^2}$$

Where,

c = concentration of the substance to be examined (anhydrous substance, in grams per 100 ml.

v_{rel} = kinematic viscosity of the solution relative to that of water.

Acceptance criteria:

Between 81.0 to 96.3.

7. ALDEHYDES:

Test solution:

Dissolve a quantity of the substance to be examined equivalent to 1.0g of the anhydrous substance to be examined in phosphate buffer solution pH 9.0 and dilute to 100.0ml with the same solvent. Stopper the flask tightly and heat at 60°C for 1 hrs. Allow to cool to room temperature.

Reference solution:

Dissolve 0.140g of acetaldehyde ammonia trimer trihydrate in water and dilute to 200.0ml with the same solvent. Dilute 1.0ml of this solution to 100.0ml with phosphate buffer solution pH 9.0.

Into 3 identical spectrophotometric cells with a path length of 1 cm, introduce separately 0.5 ml of the test solution, 0.5 ml of the reference solution and 0.5 ml of water (blank). To each cell, add 2.5 ml of phosphate buffer solution pH 9.0 and 0.2 ml of nicotinamide-adenine dinucleotide solution. Mix and stopper tightly. Allow to stand at 22 ± 2°C for 5 min. measure the absorbance of each solution at 340 nm using water as the compensation liquid. To each cell add 0.05 mL of aldehyde dehydrogenase solution, mix and stopper tightly. Allow to stand at 22 ± 2 °C for 5 min. Measure the absorbance of each solution at 340 nm using water as the compensation liquid.

Calculate the content of using the following expression:

$$= \frac{(A_{t2} - A_{t1}) - (A_{b2} - A_{b1})}{(A_{s2} - A_{s1}) - (A_{b2} - A_{b1})} \times 100000 \times Cm$$

Where,

A_{t1} = absorbance of the test solution before the addition of aldehyde dehydrogenase.

A_{t2} = absorbance of the test solution after the addition of aldehyde dehydrogenase.

A_{s1} = absorbance of the reference solution before the addition of aldehyde dehydrogenase.

A_{s2} = absorbance of the reference solution after the addition of aldehyde dehydrogenase.

A_{b1} = absorbance of the blank solution before the addition of aldehyde dehydrogenase.

A_{b2} = absorbance of the blank solution after the addition of aldehyde dehydrogenase.

m = mass of the substance to be examined (anhydrous substance) in the test solution, in grams

C = concentration of acetaldehyde in the reference solution, calculated from the weight of the acetaldehyde ammonia trimer trihydrate with the factor 0.72, in milligrams per millimeter.

Acceptance criteria: Not more than 500ppm, expressed as acetaldehyde.

8. PEROXIDES:

Dissolve a quantity of the substance to be examined equivalent to 4.0g of the anhydrous substance in 100ml of water. To 25ml of this solution, add 2ml of titanium trichloride-sulfuric acid reagent. Allow to stand for 30 min. The absorbance of the solution, measured at 405 nm using a mixture of 25ml of the stock solution and 2ml of a 13% V/V solution of sulfuric acid as the compensation liquid, is not greater than 0.35.

9. FORMIC ACID: (By HPLC)

Chromatographic Condition:

Columns : 30-cm x 7.8-mm; 9-µm

Detector	:	UV 210 nm
Columns temperature	:	35°C
Flow rate	:	1.0 ml/min
Injection Volume	:	50µl
Retention time	:	About 8 minutes

Mobile phase:

Dilute 1.0ml of perchloric acid to 700ml with water.

Test solution:

Dissolve a quantity of the substance to examined equivalent to 2.0g of the anhydrous substance in water and dilute to 100.0ml with the same solvent (Test stock solution). Transfer a suspension of strongly acidic ion exchange resin for column chromatography in water to a to a column of about 0.8cm in internal diameter to give a packing of about 20 mm in length and keep the strongly acidic ion exchange resin layer constantly immersed in water. Pour 5ml of water and adjust the flow rate to about 1ml/min. When the level of the water comes down to near the top of the strongly acidic ion exchange resin layer, introduce the stock solution into the column.

Discard the first 2ml of the eluate, then collect 1.5ml of the solution and use this solution as the test solution.

Reference solution:

Dissolve 0.100g of anhydrous formic acid in water and dilute to 100ml with same solvent. Dilute 1.0ml of this solution to 100ml with water.

Suitability requirements:

Repeatability: maximum relative standard deviation of 2.0 per cent determined on 6 injections.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

Column efficiency:

NLT 1000 theoretical plates for the formic acid peak

Symmetry factor:

0.5-1.5 for the formic acid for six injections

Calculate the percentage of formic acid using the following expression:

$$\text{Result} = A_1A_2 \times Mm$$

A_1 = Area of the peak due to formic acid in the chromatogram obtained with the Test solution.

A_2 = Area of the peak due to formic acid in the chromatogram obtained with the Reference solution.

m = Mass of the substance to be examined (anhydrous substances) in the test solution, in grams.

M = Mass of anhydrous formic acid in the reference solution, in grams.

Acceptance criteria:

Not more than 0.5%

10. HYDRAZINE: (By Thin-layer chromatography)

Chromatographic conditions:

Plate	:	TLC silanised silica gel plate. F_{254}.
Mobile phase	:	Water and methanol (1:2 V/V).
Application	:	10µl
Development	:	Over 3/4 of the plate.
Drying	:	In air

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

	Detection	:	Examine in ultraviolet light at 365 nm.
	Retardation factor	:	salicylaldehyde azine = about 0.3

Note: Use freshly prepared solutions.

Test solution:

Dissolve a quantity of the substance to examined equivalent 2.5 g of the anhydrous substance in 25 ml of water. Add 0.5 ml of a 50g /L solution of salicylaldehyde in methanol, mix and heat in a water-bath at 60 °C for 15 min. Allow to cool, add 2.0 ml of toluene, shake for 2 min. and centrifuge. Use the upper layer of the mixture.

Reference solution:

Dissolve 90 mg of salicylaldehyde azine in toluene and dilute to 100 ml with the same solvent. Dilute 1 ml of the solution to 100 ml with toluene.

Limit:

Any spot corresponding to salicylaldehyde azine obtained with the test solution is not more intense than the spot obtained with the reference solution (Not more than 1ppm).

11. IMPURITY A: (By HPLC)

Chromatographic conditions:

Precolumn	:	Size: l = 10mm, Ø = 4.0 mm
Stationary phase	:	Base deactivated end capped octadecylsilyl silica gel for chromatography (5 µm).
Column	:	Size: l = 150mm, Ø = 4.6 mm
Stationary phase	:	Base deactivated end capped octadecylsilyl silica gel for chromatography (5 µm).
Temperature	:	40°C.
Detection	:	UV at 235 nm.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

Injection : 20µl.

Flow rate : 1.0ml /min.

Mobile phase : Acetonitrile, Water (10:90 V/V).

Test solution:

Dissolve a quantity of the substance to be examined equivalent to 0.250g of the anhydrous substance in the mobile phase and dilute to 10.0ml with the mobile phase.

Reference solution (a):

Dissolve 50mg of 1-vinylpyrrolidin-2-one in mobile phase and dilute to 100.0ml with the mobile phase. Dilute 1.0ml of the solution to 100.0ml with mobile phase. Dilute 5.0ml of this solution to 100.0ml with mobile phase.

Reference solution (b):

Dissolve 10mg of 1-vinylpyrrolidin-2-one and 0.5g of vinyl acetate in methanol and dilute to 100.0ml with the same solvent. Dilute 1.0ml of the solution to 100.0ml with mobile phase.

* **Note:** After injection of the test solution, wait for about 2 min and wash the precolumn by passing the mobile phase backwards, at the same flow rate applied in the test, for 30 min.

Relative retention time with reference to vinyl acetate (retention time = about 14 min.) impurity A = about 0.6 min.

System suitability:

In the chromatogram obtained with reference solution (b), Resolution: minimum 2.0 between the peaks due to impurity A and to vinyl acetate.

In the chromatogram obtained with reference solution (a), Repeatability: maximum relative standard deviation of 2.0 %.

In the chromatogram obtained with reference solution (a), the symmetry factor for peak due to 1-vinylpyrrolidin-2-one (impurity A) is between 0.8 to 1.5.

Calculate the percentage of content of impurity A in parts per million using the following expression:

$$\text{Result} = A_1 A_2 \times 2.5m$$

Where,

A_1 = area of the peak due to impurity A in the chromatogram obtained with the test solution.

A_2 = area of the peak due to impurity A in the chromatogram obtained with the reference solution (a).

m = mass of the substance to be examined (anhydrous substance) in the test solution in grams.

Acceptance criteria: Not more than 10ppm.

12. IMPURITY B: (By HPLC)

Chromatographic conditions:

Precolumn	:	Size: l = 10mm, Ø = 3 mm
Stationary phase	:	Base deactivated end capped octadecylsilyl silica gel for chromatography (5 µm).
Column	:	Size: l = 150mm, Ø = 4.6 mm
Stationary phase	:	Base deactivated end capped octadecylsilyl silica gel for chromatography (5 µm).
Temperature	:	40°C.
Detection	:	UV Spectrophotometer at 205 nm.
Flow rate	:	0.8 ml / min.
Injection	:	50 µl.
Retention time	:	Impurity B about 7 minutes.
Mobile phase	:	Methanol and water in the ratio (5:95 V/V)

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

Test solution:

Dissolve a quantity of the substance to be examined equivalent to 0.500 g of the anhydrous substance in the mobile phase and dilute to 100.0 ml with the mobile phases.

Reference solution:

Dissolve 0.150 g of 2-pyrrolidone in mobile phase and dilute to 100.0 ml with the mobile phase. Dilute 2.0 ml of the solution to 100.0 ml with the mobile phase.

* **Note:** After each injection of the test solution, wait for about 2 min. and wash the precolumn by passing the mobile phase through the column backward for about 30 min. at the same flow rate as applied in the test.

System suitability: Reference solution:

Repeatability: maximum relative standard deviation of 2.0%.

The symmetry factor for peak due to 2-pyrrolidone (impurity B) is between 0.8 to 1.5.

Calculate the percentage of content of impurity B using the following expression:

$$\text{Result} = A_1A_2 \times 0.3m$$

Where,

A_1 = area of the peak due to impurity B in the chromatogram obtained with the test solution

A_2 = area of the peak due to impurity B in the chromatogram obtained with the reference solution

m = mass of the substance to be examined (anhydrous substance) in the test solution in grams

Acceptance criteria: Not more than 3.0%.

13. WATER: < REFER GAM 010>

Not more than 5.0%, determined on 0.5g of sample.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

14. SULFATED ASH: < REFER GAM 032>

Not more than 0.1% w/w, determined on 1.0g of sample.

15. ASSAY: (Nitrogen Determination)

Place 100.0mg of the substance to be examined (m mg) in a combustion flask, add 5g of a mixture of 1g of copper sulfate pentahydrate, 1g of titanium dioxide and 33g of dipotassium sulfate, and 3 glass beads. Wash any adhering particles from the neck into the flask with a small quantity of water. Add 7ml of sulfuric acid, allowing it to run down the insides of the flask. Heat the flask gradually until the solution has a clear, yellowish-green colour, and the insides wall of the flask is free from a carbonized material and then heat for a further 45 min. after cooling, and cautiously 20ml of water, and connects the flask to the distillation apparatus previously washed by passing steam through it. To the absorption flask add 30ml of a 40 g / L solution of boric acid, 3 drops of bromocresol green-methyl red solution and sufficient water to immerse the lower end of the condenser tube. Add 30ml of strong sodium hydroxide solution through the lower the funnel, rinse the funnel cautiously with 10 ml of water, immediately close the clamp on the rubber tube, and then start distillation with steam to obtain 80 to 100ml of distillate. Remove the absorption flask from the lower end of the condenser tube, rinsing the end part with a small quantity of water and titrate the distillate with 0.025M Sulfuric acid until the colour of the solution changes from green through pale greyish blue to pale greyish reddish-purple. Carry out a blank determination.

1 ml of 0.025 M Sulfuric acid is equivalent to 0.700 mg of Nitrogen.

Calculation:

$$= \frac{\text{Titer value} \times \text{Molarity of 1ml 0.025N sulphuric acid} \times 0.700 \times 100 \times 100}{\text{Sample weight in mg} \times 0.025 \times (100 - \%\ \text{of LOD})}$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/08/2023	22/08/2023	22/08/23

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-RMEP0045-00	(i) Periodic review. (ii) STP numbering procedure revised as per SOP No. ST/QC/058.	ST/CC/23/016	25/08/2023

****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	21/08/2023	22/08/2023	22/08/23

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Material	PURIFIED WATER			
Specification No.	SPEC-RMEP0033-01	**Revision No.**	01	**Item Code.:** RMEP0033
Supersedes	SPEC-RMEP0033-00	**Effective Date**	17/07/2025	**Page No.:** 1 of 4

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	H_2O
2	Molecular weight	18.02
3	Storage conditions	Not applicable
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	1000 ml for chemical Analysis 500 ml for Microbial analysis
6	Quantity of reserve sample	Nil
7	Retest period	Not applicable
9	Reference	IP/BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	C.K.SARAVANAN	S.PALANICHAMY	S.MARAN
Designation	Asst. Manager-QC	Asst. Manager-QC	AGM-QA
Signature			
Date	14/07/2025	15/07/2025	16/07/2025

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Material	PURIFIED WATER			
Specification No.	SPEC-RMEP0033-01	**Revision No.**	01	**Item Code.:** RMEP0033
Supersedes	SPEC-RMEP0033-00	**Effective Date**	17/07/2025	**Page No.:** 2 of 4

S.NO	TEST (s)	SPECIFICATION (s)
1.	Description	A Clear, colourless and odourless liquid.
2.	Acidity or alkalinity **A.** Methyl Red **B.** Bromothymol Blue	 The resulting solution is not red. The resulting solution is not blue.
3.	Heavy metals	Not more than 0.1ppm.
4.	Nitrates	Not more than 0.2ppm.
5.	Oxidisable substances	The solution remains faintly pink.
6.	pH at 25°C	Between 5.0 and 7.0
7.	Conductivity at 25°C	Not more than 2.1µS.cm^{-1}

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	C.K.SARAVANAN	S.PALANICHAMY	S.MARAN
Designation	Asst. Manager-QC	Asst. Manager-QC	AGM-QA
Signature			
Date	14/07/2025	15/07/2025	16/07/2025

S.NO	TEST (s)	SPECIFICATION (s)
8.	Microbial contamination	
	Total aerobic microbial count	Not more than 100 cfu /ml
	Pathogen tests:	
	(i) E. Coli	Should be absent/ml
	(ii) Salmonella species	Should be absent/10ml
	(iii) Pseudomonas	Should be absent/ml
	(iv) Staphylococcus aureus	Should be absent/ml

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	C.K.SARAVANAN	S.PALANICHAMY	S.MARAN
Designation	Asst. Manager-QC	Asst. Manager-QC	AGM-QA
Signature			
Date	14/07/2025	15/07/2025	16/07/2025

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-RMEP0033-00	(i) Specification numbering procedure revised as per SOP No. ST/QC/058. (ii) There is no changes in specification as per current monographs.	ST/CC/23/063 ST/CC/24/067	15-03-2024
SPEC-RMEP0033-01	Ammonium, Calcium and Magnesium, Chlorides, Sulphates and Residue on evaporation specification has been removed as per current monographs (IP/BP).	ST/CC/25/162	17/07/2025

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	C.K.SARAVANAN	S.PALANICHAMY	S.MARAN
Designation	Asst. Manager-QC	Asst. Manager-QC	AGM-QA
Signature			
Date	14/07/2025	15/07/2025	16/07/2025

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Material	PURIFIED WATER			
STP No.	STP-RMEP0033-01	**Revision No.**	01	**Item Code.:** RMEP0033
Supersedes	STP-RMEP0033-00	**Effective Date**	17/07/2025	**Page No.:** 1 of 4

1. DESCRIPTION: < REFER GAM 001>

A clear, colourless and odourless liquid.

2. ACIDITY OR ALKALINITY:

Acidity: Take about 50 ml of the sample in clean dry glass flask, boil and cool. Pipette out 10 ml of sample and add 0.05 ml of methyl red solution. Check the colour of the solution. The solution should not become red coloured.

Alkalinity: Take about 50 ml of the sample in clean dry glass flask, boil and cool .Pipette out 10 ml of sample and add 0.1 ml of bromothymol blue solution. Check the colour of the solution. The solution should not become blue coloured.

3. HEAVY METALS: < REFER GAM 006>

Sample preparation:

Transfer 200ml sample in a evaporating dish. Add 0.15mL of 0.1 nitric acid Heat on water-bath until the volume is reduced to 20ml. Take 12mL of the concentrated solution.

Standard preparation:

Take 10ml of Lead standard solution (1 ppm Pb), adding 0.075mL of 0.1M nitric acid and add 2ml of concentrated sample in a test-tube.

Blank preparation:

Take 10ml of Distilled water, add 0.075mL of 0.1M nitric acid and mix 2ml of concentrated sample.

Procedure:

To each of the above solutions, add 2ml of acetate buffer pH 3.5, and add the mixtures to 1.2ml of thioacetamide reagent separately and allow to stand for 2 minutes.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	C.K.SARAVANAN	S.PALANICHAMY	S.MARAN
Designation	Asst. Manager-QC	Asst. Manager-QC	AGM-QA
Signature			
Date	14/07/2025	15/07/2025	16/07/2025

Observation:

After 2 minutes, any brown colour produced by the sample is not more intense than that the standard solution.

4. **NITRATES:**

Sample preparation:

Take 5ml of sample in a test-tube and immersed in ice water. Add 0.4ml of Potassium Chloride solution (10g of Potassium chloride in 100ml of water), 0.1ml of diphenylamine solution and add 5ml of nitrogen-free sulphuric acid drop wise with shaking. Transfer the tube to water bath at 50°C and keep it for 15 minutes.

Standard preparation:

Take 4.5ml of nitrate free water and 0.5ml Nitrate standard solution (2 ppm NO_3) in test tube. Add 0.4ml of potassium chloride solution (10g of Potassium chloride in 100ml of water), 0.1ml of diphenylamine solution and add 5ml of nitrogen-free sulphuric acid drop wise with shaking. Transfer the tube to water bath at 50°C and keep it for 15 minutes.

Observation:

After 15 minutes, Any blue colour produced by the sample is not more intense than the standard solution.

5. **OXIDISABLE SUBSTANCES:**

Take 100 ml of sample in a conical flask, add 10 ml of dilute sulphuric acid and 0.1ml of 0.02M potassium permanganate and boil for 5 minutes. The solution remains faintly pink.

6. **pH: < REFER GAM 030>**

Between 5.0 and 7.0

Take 100ml of sample in a clean dry beaker and measure the pH by calibrated pH meter at 25°C as per operating procedure No: ST/QC/085.

7. CONDUCTIVITY:

Not more than 2.1 $\mu S.cm^{-1}$

Rinse the conductivity electrode two to three times with purified water and wipe dry with tissue paper. Take 100ml of sample in a clean dry beaker and measure the conductivity by calibrated Conductivity meter at 25°C as per operating procedure No: ST/QC/086.

8. MICROBIAL CONTAMINATION:

Total Viable aerobic count and Pathogen test refer as per the current SOP No: ST/MB/011.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	C.K.SARAVANAN	S.PALANICHAMY	S.MARAN
Designation	Asst. Manager-QC	Asst. Manager-QC	AGM-QA
Signature			
Date	14/07/2025	15/07/2025	16/07/2025

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-RMEP0033-00	(i) STP numbering procedure revised as per SOP No. ST/QC/058. (ii) Testing procedure for ammonium has been changed as per current monograph.	ST/CC/23/063 ST/CC/24/067	15-03-2024
STP-RMEP0033-01	Ammonium, Calcium and Magnesium, Chlorides, Sulphates and Residue on evaporation testing procedure has been removed as per current monographs (IP/BP).	ST/CC/25/162	17/07/2025

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	C.K.SARAVANAN	S.PALANICHAMY	S.MARAN
Designation	Asst. Manager-QC	Asst. Manager-QC	AGM-QA
Signature			
Date	14/07/2025	15/07/2025	16/07/2025

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	TARTRAZINE SUPRA (E102)			
Specification No.	SPEC-RMET0011-00	**Revision No.**	00	**Item Code.:** RMET0011
Supersedes	RMEST0011-00	**Effective Date**	26/09/2023	**Page No.:** 1 of 3

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	NA
2	Molecular weight	NA
3	Storage conditions	NA
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	32g
6	Quantity of reserve sample	64g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	IHS
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	TARTRAZINE SUPRA (E102)			
Specification No.	SPEC-RMET0011-00	**Revision No.**	00	**Item Code.:** RMET0011
Supersedes	RMEST0011-00	**Effective Date**	26/09/2023	**Page No.:** 2 of 3

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	Orange yellow powder.
2.	*Total dye content	Not Less than 87.0%
3.	Loss on drying at 135°C & Chlorides & Sulphates expressed as sodium salt	Not more than 13.0%
4.	Water insoluble matter	Not more than 0.2%
5.	Combined ether extracts	Not more than 0.2%
6.	Subsidiary Dyes	Not more than 1.0%
7.	Dye Intermediates	Not more than 0.5%
8.	Lead	Not more than 10mg/kg

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

S.NO	TEST (s)	SPECIFICATION (s)
9.	Arsenic	Not more than 3mg/kg
10.	Heavy metals	Not more than 40mg/kg

Remarks: The above * Marked tests are to be performed while retesting the material.

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-RMET0011-00	(i) Periodic review. (ii) Specification numbering procedure revised as per SOP No. ST/QC/058.	ST/CC/23/063	26/09/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	TARTRAZINE SUPRA (E102)			
STP No.	STP-RMET0011-00	**Revision No.**	00	**Item Code.:** RMET0011
Supersedes	RMETT0011-00	**Effective Date**	26/09/2023	**Page No.:** 1 of 15

1. DESCRIPTION: < REFER GAM 001>

Orange yellow powder.

2. TOTAL DYE CONTENT:

Weigh accurately 0.1gm of sample previously dried at 110°C for 2 hrs in a 100ml volumetric flask. Add 20ml of 0.1N hydrochloric acid (HCL)* and shake until the solution is clear. Dilute to volume with 0.1N HCL and mix well. Pipette 1ml into a 100ml volumetric flask and again dilute to volume with 0.1N HCl and mix well. Measure the extinction of resulting solution in 1cm cell at 428nm in Spectrophotometer.

Using 485 as 'E'-value

Calculations:

$$= \frac{Abs}{485} \times \frac{100}{WT} \times \frac{100}{1} \times 10 \times 100$$

Where,

Abs = Absorbance of sample

WT = Weight of sample taken

3. LOSS ON DRYING AT 135ºC & CHLORIDES & SULPHATES EXPRESSED AS SODIUM SALT:

a) LOSS ON DRYING:

Weigh 2.0gm of the sample in a petri dish and dry for 3 hours at 135°C. Find out the loss in weight after drying and calculate the percentage loss.

b) Determination of chloride as sodium chloride:

Weigh 0.5 to 1.0gm of sample in a 250ml beaker, dissolve in 100ml of distilled water and acidify with 5 ml of 1.5 N nitric acid solution. Perform potentiometric titration i.e. Place Ag & calomel electrode to solution & connect it to pH meter.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

Determine the chloride content of the solution by titration against the 0.1N silver nitrate solution (AgN03) and calculate the result as sodium chloride.

[1 ml of 0.1 N silver nitrate solution= 0.00585 gm of sodium chloride (NaCl)] Express the result as a percentage of the mass of sample taken.

F = 0.00585gm of NaCl

$$\% \text{ of Chloride content} = \frac{TR \times N \times F \times 100}{\text{Sample taken} \times 0.1}$$

N = Normality of 0.1N AgNO3

c) Determination of Sulphate as sodium sulphate:

Weigh 5.0 gm of the sample, transfer it to a 250 ml conical flask and dissolve in about 100 ml of water by heating on a water bath . Add 35 gm of sulphate free sodium chloride, stopper the flask, and swirl at frequent intervals during 1 hour.

Cool, transfer with saturated sodium chloride solution to a 250 ml measuring flask and dilute to the mark at 20°C. Shake the flask and filter the solution through a dry filter paper. Pipette 100 ml of the filtrate into a 500 ml beaker, dilute to 300 ml with water and acidify with hydrochloric acid, adding 1 ml in excess.

Heat the solution to boiling and add an excess of 0.25 N barium chloride solution, drop by drop with stirring. Allow the mixture to stand on a hot plate for 4 hours or leave it overnight at room temperature and then bring it to about 80°C and allow the precipitate to settle.

Filter off the precipitated barium sulphate, wash with hot water and ignite at a dull red heat in a tared crucible until a constant mass is obtained.

Carry out a blank determination, apply any necessary correction to the mass of barium sulphate found in the test and calculated the result as sodium sulphate.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

$$\text{Mass of sodium sulphate} = \frac{\text{Residue} \times 5 \times 2.5 \times 0.6086}{\text{Weight taken}}$$

Loss on drying at 135°C and chlorides and sulphates expressed as sodium salt = 3(a)+3(b)+3(c)

4. WATER INSOLUBLE MATTER:

Dissolve 5 gm of the material in 200 ml of hot water (80-90°C) and allow the solution to cool to room temperature. Filter through the tared gooch or sintered glass filter, wash with cold water until the washings are colourless. Dry at 135± 2°C for 3 hours. Cool on a desiccator and weigh.

5. COMBINED ETHER EXTRACTS:

Apparatus:

Separator or continuous extractor of 250 ml capacity.

Reagents:

(i) Isopropyl Ether - Wash one litre of isopropyl ether with (a) two 100 ml portions of sodium hydroxide (0.5 N), (b) saturated solution of ferrous sulphate, and (c) with three 100ml portions of water.

(ii) Sodium Hydroxide Solution - 10 percent (m/v).

(iii) Sodium Hydroxide Wash Solution - 0.1 N.

(iv) Dilute Hydrochloric Acid (1:1) Prepared by diluting hydrochloric acid, sp gr 1.16 With equal volume of water.

(v) Hydrochloric Acid wash solution - concentrated hydrochloric acid diluted 200 times

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

Procedure for Extraction in the Separator:

a) Neutral Ether Extract –

Place the aqueous, solution containing 10g of the material in a separator and dilute to 200 ml. Extract with two 100ml portions of the washed ether, shaking for one minute during each extraction. Decant ether into another clean separator and rinse the first separator with 10 ml of the ether, decanting into the second separator. Reserve the aqueous colour solution. Wash combined extracts with 20 ml portions of water until the washings are colourless. Decant the ether into a beaker. Place the beaker on a water bath or steam bath in dust free atmosphere and allow the ether to evaporate to a volume of 50 ml. Transfer to a previously weighed evaporating dish of 250 ml capacity. Rinse the beaker with 40 ml of ether and drain into the same dish. Evaporate the remaining ether, dry in a desiccator and weigh. Repeat the process of evaporating, drying and weighing till the difference between two successive weighings is less than a milligram. Note the lowest mass. Calculate the mass of the neutral ether extract.

Note - Do not fill the beaker or dish more than one third of the capacity and do not allow the ether to boil.

b) Alkaline Ether Extract:

To the reserved aqueous solution, add 2 ml of sodium hydrochloride solution and proceed in the same manner as in (a) except to wash the ether extract with sodium hydroxide wash solution instead of water. Reserve the aqueous solution for use in (c). Calculate the mass of the alkaline ether extract.

c) Acid Ether Extract:

To the reserved aqueous solution add 3 ml of dilute hydrochloric acid (1:1) and proceed in the same manner as in (a) except to wash the ether extract with hydrochloric acid wash solution instead of water. Discard the colour solution. Calculate the mass of the acid ether extract.

Procedure for Extraction in the Continuous Extractor

1) Neutral Ether Extract:

Dissolve 5g of the material in water and extract in the continuous extractor with about 100 ml of the ether for 5 hours. Transfer the extract to the separator, rinse the flask with 10 ml of ether and add the rinsing to the main extract. Proceed in the same manner as in (a) from the washing stage onwards.

2) Alkaline Ether Extract:

To the aqueous solution in the extractor add 2 ml of sodium hydroxide solution and proceed in the same manner as in (1) except to wash the ether extract with sodium hydroxide wash solution instead of water.

3) Acid Ether Extract:

Add 3 ml of dilute hydrochloric acid solution to the alkaline aqueous solution of the material in the extractor and proceed in the same manner as in (1) except to wash the ether extract with hydrochloric acid wash solution instead of water.

6. SUBSIDIARY DYES:

Principle:

The subsidiary dyes are separated from the main dye by ascending paper chromatography and are extracted separately from the paper. The optical densities of the extracts are measured at their wavelengths of maximum absorption in the visible spectrum and are used to calculate the content of subsidiary dyes as percentage by mass of the sample.

Apparatus:

1. Chromatography tank and ancillary equipment

(i) A glass tank and glass cover

(ii) A supporting frame for the chromatography grade paper sheets

(iii) A tray for developing solvent

(iv) A secondary frame supporting drapes of filter paper

(v) Sheets of chromatography grade paper , not less than 200mm x 200mm (whatman no. 1 chromatography grade is suitable)

2. Microsyringe:

Capable of delivering 0.1 ml with a tolerance of ±0.002 ml

3. Spectrophotometer

Reagents:

Chromatography solvents

(i) Water: Ammonia (sp. gravity 0.880): trisodium citrate (95 ml: 5 ml: 2 gm)

(ii) n-butanol : water: ethanol : ammonia (sp. gravity 0.880) (600ml: 264ml: 135ml: 6 ml)

(iii) butan-2-one : acetone : water (7: 3: 3)

(iv) butan-2-one : acetone : water : ammonia (sp. gravity 0.880) (700ml: 300ml: 300ml: 2ml)

(v) butan-2-one : acetone : water : ammonia (sp. gravity 0.880) (700ml: 160ml: 300ml: 2 ml)

(vi) n-butanol : glacial acetic acid : water (4:1:5)

Shake for 2 minutes, allow layers to separate. Use the upper layer as the chromatography solvent. The particular solvent to be used as given in individual specifications.

Extracting solvent:

A mixture of equal volumes of acetone and water.

Sodium bicarbonate - 0.05N

Procedure:

(i) Not less than 2 hours before carrying out the determination, arrange the filter paper drapes in the glass tank and pour over the drapes and into the bottom of the tank sufficient of the atmosphere saturating solvent to cover the bottom of the tank to a depth of approximately 1 cm. Place the solvent tray in position and fit the cover to the tank.

(ii) Mark out a sheet of chromatography grade paper. Apply 0.1ml of 1.0 percent aqueous solution of the dye as uniformly as possible within the confines of the 180 mm x 7 mm rectangle, holding the nozzle of the microsyringe steadily in contact with the paper. Allow the paper to dry at room temperature for 1 to 2 hours or at 50°C for 5 minutes followed by 15 minutes at room temperature. Mount the sheet, together with a plain sheet to act as a blank. Pour sufficient of the chromatography solvent into the tray to bring the surface of the solvent about 1cm below the baseline of the sheet of chromatography paper. The volume necessary will depend on the dimensions of the apparatus and should be predetermined. Put the frame into position and replace the cover.

Allow the solvent front to ascent the full height of paper, development being continued for 1hour afterwards, then remove the frame and transfer it to a drying cabinet at 50° to 60° C for 10 to 15 minutes. Remove the sheets from frame.

Note: If required, several chromatograms may be developed simultaneously.

(iii) Cut each subsidiary band from the sheet as a strip and cut an equivalent strip from the corresponding position of the plain sheet. Place each strip, subdivided into a suitable number of approximately equal portions, in a separate test-tube, swirl for 2 to 3 minutes, add 15 ml of the sodium bicarbonate solution and shake the tube to ensure mixing. Filter the coloured extracts and blanks through a 9 cm filter paper of open texture and determine wavelengths of maximum absorption, using cells of suitable light path, against a filtered mixture of 5ml of extracting solvent and 15 ml of the sodium bicarbonate solution. Measure the optical densities of the extract of the blank strips at the wavelengths at which those of the corresponding coloured extracts were measured.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

Calculation:

The content of the subsidiary dye, expressed as a percentage (S) of the sample, is given by:
S= F [(D1 + D2+ ....)- (b1 + b2.....)]

Where,

F is the mean conversion factor and is equal to 11.4

D1, D2 etc are the optical densities of the subsidiary dye extracts and

b1, b2 etc are the optical densities of the extracts of the corresponding blanks

The conversion factor F in the above expression is derived from the extraction coefficient of the main colour, not that of the subsidiaries and from the other constants of the determination.

7. DYE INTERMEDIATES:

Apparatus:

(i) Chromatographic tube

(ii) Suitable spectrophotometer for use in the ultra-violet range

(iii) Column preparation

Prepare a slurry of whatman powdered cellulose (or equivalent) in a 25 percent ammonium sulphate (very low in iron) solution. If other cellulose is used, the iron content should be very low. Prepare the column and pass 200 ml of 25 percent ammonium sulphate solution through it. The ultra- violet absorption of the solution shall be sufficiently low to avoid interference with the intended analysis. Use about 75 gm of cellulose to 500 ml of liquid. Place a small disc of stainless steel gauze in the constriction above the tip of the tube. Pour sufficient slurry into the tube to give a column to height of about 5 cm in the mouth of the tube. Tap the tube occasionally to ensure a well packed column. Wash the column with 200 ml of the eluent.

Procedure:

Place 0.200 gm of the dye sample in a beaker and dissolve in 20ml of water. Add approximately 5 gm of powdered cellulose. Add 50 gm of ammonium sulphate to the dye.

Transfer the mixture to the column, rinse the beaker with 25 percent ammonium sulphate solution and add washings to the tube. Allow the column to drain until flow ceases or nearly so. Add the ammonium sulphate solution to the column at a rate equivalent to the rate of flow through the column. Collect the effluent in 100 ml fractions. Continue until 12 fractions have been collected. Reserve the column and contents until the last fractions have been examined Mix each fraction well and obtain the ultra-violet absorption spectra of each solution from 200 to 400 nm. The specific spectra may be chosen depending on the nature of the dyes. If the spectrum of the twelfth fraction shows the presence of any intermediate, continue collecting fractions until the intermediates present are eluted. Usually only one intermediate is encountered. Identification and quantitative determination shall be accomplished by comparison of the absorption spectra of the eluted material with the spectra of solutions of the pure intermediate in the same solvent. When more than one intermediate is present in significant quantities in any fractions, the spectrophotometric data shall indicate this. In such cases, the amounts of the various intermediates should be determined by the procedure customarily used in spectrophotometric analysis of mixture of absorbing materials.

(ii) Some samples contain small amounts of various materials, particularly inorganic salts that contribute 'background absorption'. Correction for this is made as follows:

Determine the amount of such absorption of the fraction collected from the column immediately before and after the fraction immediately following those fractions in which the intermediates are encountered. Subtract one half of the sum of these two determinations from the observed absorbance of the fractions containing the intermediates. The remainder should be taken as the absorbance due to the intermediate present.

8. LEAD:

Reagents:

(1) Nitric acid - 65 percent

(2) Sulphuric acid - sp. gr 1.84

(3) Ammonium acetate- citrate solution -Dissolve 12.5gm of ammonium acetate and 12.5 gm of ammonium citrate in water add concentrated ammonia untill the solution is alkaline to thymol blue paper and add water to 100 ml.

Purify with 0.002 percent m/v solution of dithiozone in carbon tetrachloride and finally shake the solution with carbon tetrachloride to remove excess of dithiozone.

(4) Ammonia solution - 25 percent

(5) Carbon tetrachloride

(6) Ammonium hydroxide - 0.2 N

(7) Potassium cyanide- 10 percent

(8) Hydroxylamine hydrochloride solution - 10 percent

(9) Dithizone solution - 0.1 percent (m/v) purified by following procedure Dissolve the dithizone in chloroform and treat it with ammonia. Add mineral acid. Precipitate shall be pure dithizone. The aqueous ammoniacal solution obtained from chloroform solution of dithizone should be colourless; otherwise further purification as mentioned above should be carried out.

(10) Buffer pH2 - add 11.90 ml of 0.2M hydrochloric acid and 88.10 ml of 0.2M potassium chloride in a 200 ml volumetric flask and add water to volume.

Procedure:

The limit test described for lead is designed to show if a sample contains more than 10mg/kg or 20mg/kg of lead. The sample is digested with nitric acid and sulphuric acid and a clear solution of the digest is prepared.

Digestion:

Weigh 1.0gm of sample for substances with 10mg/kg limit or 0.5gm for those with 20mg/kg limit. Place with 5ml of water, 5ml of 65 percent nitric acid and 5ml of sulphuric acid in a digestion flask. Warm slightly. If foaming becomes excessive, add a little water. Evaporate the mixture. Maintain strongly oxidizing condition in the flask during digestion by adding cautiously small quantities of nitric acid whenever the mixture begins to turn brown or dark. Continue digestion untill organic matter is destroyed and sulphuric trioxide fumes are copiously evolved. The final solution should be colourless or at most slight straw colour.

To remove nitrosylsulphuric acid, after partial cooling transfer the residue to a dish, rinse with 25 ml of water, evaporate and heat again to fuming point. Add 25 ml of water and evaporate and heat again.

Solution of digest - Allow to cool add 20ml of ammonium acetate - citrate solution and allow again to cool, neutralize to about pH 7 with 25 percent ammonia and boil if necessary to dissolve calcium sulphate. Cool the clear solution. Shake the solution with 10ml of carbon tetrachloride and discard the lower layer.

Test with dithiozone - To a 100ml separatory funnel add 10ml of 0.2N ammonium hydroxide , 2ml of 10 percent potassium cyanide, 2ml of 10 percent of hydroxylamine hydrochloride solution and 2ml of 20 mg per litre solution of dithiozone in carbon tetrachloride. Shake the separatory funnel for few minutes and discard the carbon tetrachloride layer. Add 2ml of carbon tetrachloride, shake and discard again the carbon tetrachloride layer. Add the solution of digest to the separatory funnel. Again add 5ml of dithiozone solution in carbon tetrachloride and shake vigorously for a few minutes. The carbon tetrachloride layer becomes red according to the amount of lead present.

Treat simultaneously a standard solution containing 10 µg of lead in the same manner as the solution of the digest. Evaluate the quantity of lead in the digest by comparing the colour of the carbon tetrachloride layers.

Ensure that the red colour is due to lead by shaking the carbon tetrachloride layer obtained from the digest solution with 10 ml of a buffer pH 2. The red colour will turn green if it is due to lead.

9. ARSENIC:

Reagents:

1. Nitric acid (sp. gravity 1.4)

2. Sulphuric acid (sp. gravity 1.84)

3. HCL (sp. gravity 1.16)

4. Brominated HCL (0.03% KBr in HCL)

5. Stannous chloride (2% in 10% HCL)

6. Cotton gauze (soaked in 5% lead acetate solution and dry it)

7. Test paper (soak strips of filter paper in saturated ethanolic solution of mercuric bromide and dry)

8. Std. arsenic solution- Dissolve 0.330 gm of arsenic trioxide in 5 ml of 2M NaOH and dilute it to 250 ml in distilled water. Further dilute 1 ml of above solution to 100 ml with distilled water. (y) 1 ml= 10 ppm

9. Zn-metal

Weigh 1.0gm of the sample; transfer it to Kjeldhl's flask. Add 5ml of water, 5ml of Nitric Acid and 5ml of Sulphuric Acid. Warm gently. If foaming becomes excessive, add a little water. Evaporate the mixture. Maintain strongly oxidizing condition in the flask during digestion by adding cautiously small quantity of Nitric Acid whenever the mixture begins to turn brown or dark. Continue digestion until organic matter is destroyed and sulphuric trioxide fumes are continuously evolved. The final solution should be colourless or at the most straw colour.

To remove nitrosyl sulphuric acid after partial cooling, transfer the residue to an evaporating dish. Wash the flask twice with 10ml water. Collect the washing with residue in an evaporating dish, heat again to fuming point. Add 25ml of water and evaporate.

Add 20ml Brominated Hydrochloric Acid and 10ml of water and boil for 2 to 3 minutes. Cool it. Remove the excess of Bromine with a few drops of stannous chloride solutions. Transfer to a wide mouthed bottle of arsenic apparatus. Add 5ml of IM KI & 10gm Zn metal. Tube is placed quickly in position.

(For checking Arsenic< y ppm)

Standard stain is produced by taking 'y/10' ml of std. diluted arsenic solution in a wide mouthed bottle with 20 ml Brominated Hydrochloric Acid and a few drops of stannous chloride solutions, operating in a similar manner as sample.

The reaction is allowed to proceed for 40 minutes. If arsenic is present, the yellow stain is produced on the mercuric bromide paper, which is compared by daylight with the standard stains.

10. HEAVY METALS:

Reagents:

Lead Nitrate Stock solution:

Dissolve 0.1598 gm of Lead Nitrate in 100 ml of distilled water to which add 1ml of Nitric acid & then dilute with distilled water to 1000 ml.

Ammonia solution - dilute 400 ml of ammonium hydroxide (28%) to 1 lit. with distilled water HCl 10%

Nitric acid (sp. gravity 1.4)

Sulphuric acid (sp. gravity 1.84)

Hydrogen sulphide - saturated solution of hydrogen sulphide made by passing hydrogen sulphide gas through cold water.

Acetic acid (10%)

Standard solution (for checking heavy metal< x ppm)

On the day of use, dilute 'x' ml of lead nitrate stock solution to 100 ml with distilled water. This solution contains ' x' mg of lead per ml solution (x ppm)

Standard preparation (Solution A)

Into a 50 ml nessler cylinder, pipette out 2 ml of standard lead solution, dilute with water to 25 ml. Adjust with dilute acetic acid or dilute ammonia solution to a pH between 3.0 - 4.0 Dilute further with water to about 35 ml.

Test solution

Weigh 1.0gm of sample in a suitable crucible. Add sufficient sulphuric acid to moisten the sample and ignite carefully at low temperature until thoroughly charred. Add to this charred mass, 2ml of Nitric Acid and 5 drops of Sulphuric Acid. Heat continuously until white fumes is no longer evolved. Ignite preferably in a muffle furnace at 600°C to 700° C until the carbon is burnt off. Cool, add 4 ml of HCL. Cover and digest it on water bath for 15 min. Uncover & slowly evaporate to dryness on a water bath.

Moisten the residue with few drops of HCl, add 10 ml of hot water and digest for 2 min. Add ammonia solution drop wise till solution is just alkaline to litmus paper. Dilute with water to 25 ml and adjust with dilute acetic acid to a pH between 3.0- 4.0.

Filter if necessary, rinse the crucible with 10 ml of water and filter. Combine the filtrate and washings in a Nessler's Cylinder, dilute with water to about 35 ml.

To each of the cylinder (one containing the standard solution & other test solution), add 10 ml of freshly prepared hydrogen sulphide solution, mix and dilute with water to 50 ml. Allow it to stand for 5 min. and then view downwards over the white surface.

The colour produced in test solution should not be darker than that of solution A.

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-RMET0011-00	(i) Periodic review. (ii) STP numbering procedure revised as per SOP No. ST/QC/058.	ST/CC/23/063	26/09/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.SANTHI	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/23	22/09/2023	22/09/23

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	SODIUM METHYL HYDROXYBENZOATE BP			
Specification No.	RMESM0032-01	**Revision No.**	01	**Page No.:** 1 of 4
Supersedes	RMESM0032-00	**Effective Date**	03/09/2022	**Review Period:** 3 years

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$C_8H_7NaO_3$
2	Molecular weight	174.1
3	Storage conditions	In an airtight container.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	8g
6	Quantity of reserve sample	16g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

	PREPARED BY	REVIEWED BY	APPROVED BY
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	29/08/2022	30/08/2022	01/09/22

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	SODIUM METHYL HYDROXYBENZOATE BP			
Specification No.	RMESM0032-01	**Revision No.**	01	**Page No.:** 2 of 4
Supersedes	RMESM0032-00	**Effective Date**	03/09/2022	**Review Period:** 3 years

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, hygroscopic, crystalline powder.
2.	*Solubility	Freely soluble in water, sparingly soluble in ethanol (96 per cent), practically insoluble in methylene chloride.
3.	*Identification **A.** By Melting point **B.** By IR **C.** By Thin-layer chromatography **D.** By Sodium Salts	 **A.** The precipitate melts at 125 °C to 128 °C. **B.** The Infrared absorption spectrum of sample should be concordant with that of reference spectrum of Methyl parahydroxybenzoate RS. **C.** The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a). **D.** A dense white precipitate is formed.
4.	Appearance of solution	Solution S examined immediately after preparation is clear and not more intensely coloured than reference solution BY_6.
5.	*pH	Between 9.5 to 10.5
6.	*Related substances (i) Impurity A (ii) Unspecified impurities (iii) Total impurities (Excluding impurity A)	 Not more than 3.0% Not more than 0.5% Not more than 1.0%

	PREPARED BY	REVIEWED BY	APPROVED BY
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	29/08/2022	30/08/2022	01/09/22

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	SODIUM METHYL HYDROXYBENZOATE BP			
Specification No.	RMESM0032-01	**Revision No.**	01	**Page No.:** 3 of 4
Supersedes	RMESM0032-00	**Effective Date**	03/09/2022	**Review Period:** 3 years

S.NO	TEST (s)	SPECIFICATION (s)
7.	Chlorides	Not more than 350ppm
8.	Sulfates	Not more than 300ppm
9.	*Water content	Not more than 5.0%
10.	*Assay by HPLC (anhydrous basis)	Not less than 95.0% and Not more than 102.0% w/w.

Remarks: The above * Marked tests are to be performed while retesting the material.

	PREPARED BY	REVIEWED BY	APPROVED BY
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	29/08/2022	30/08/2022	01/09/22

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	SODIUM METHYL HYDROXYBENZOATE BP			
Specification No.	RMESM0032-01	**Revision No.**	01	**Page No.:** 4 of 4
Supersedes	RMESM0032-00	**Effective Date**	03/09/2022	**Review Period:** 3 years

REVISION HISTORY:

Specification No.	Effective Date	Reason for Review
RMESM0032-00	21-02-2020	New specification prepared
RMESM0032-01	03/09/2022	Name of the product in Specification has been changed to Sodium methyl hydroxybenzoate as per BP monograph. This changes captured as per Change Control number ST/CC/22/164.

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

	PREPARED BY	REVIEWED BY	APPROVED BY
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	29/08/2022	30/08/2022	01/09/22

1. DESCRIPTION: < REFER GAM 001>

White or almost white, hygroscopic, crystalline powder.

2. SOLUBILITY: < REFER GAM 002>

100mg of sample + 1mL of water	Freely soluble if the material dissolves.
100mg of sample + 10mL of ethanol (96%)	Sparingly soluble if the material dissolves.
10mg of sample + 100mL of methylene chloride	Practically insoluble if the material does not dissolves.

3. IDENTIFICATION:

First identification: B, D

Second identification: A, C, D

A) By Melting point:

Dissolve 0.5g of sample in 50mL of water. Immediately add 5mL of hydrochloric acid. Filter and wash the precipitate with water. Dry in vacuo at 80°C for 2 h. The precipitate melts at 125°C to 128°C.

B) By IR: < REFER GAM 003>

The Infrared absorption spectrum of sample should be concordant with that of reference spectrum of Methyl parahydroxybenzoate RS.

C) By Thin-layer chromatography:

Test solution (a):

Dissolve 0.10g of the substance to be examined in 10mL of water. Immediately add 2 mL of hydrochloric acid and shake with 50mL of 1,1-dimethylethyl methyl ether. Evaporate the upper layer to dryness and take up the residue with 10mL of acetone.

Test solution (b):

Dilute 1mL of test solution (a) to 10ml with acetone.

Reference solution (a):

Dissolve 10mg of Methyl parahydroxybenzoate RS in acetone and dilute to 10mL with the same solvent.

Reference solution (b):

Dissolve 10mg of Ethyl parahydroxybenzoate RS in 1mL of test solution (a) and dilute to 10mL with acetone.

Plate: TLC octadecylsilyl silica gel F_{254} plate.

Mobile phase:

A mixture of 1 volumes of glacial acetic acid, 30 volumes of water and 70 volumes of methanol.

Application: 5 µL of test solution (b) and reference solutions (a) and (b).

Development: Over 2/3 of the plate.

Drying: In air.

Detection: Examine in ultraviolet light at 254 nm.

System suitability Reference solution (b):

The chromatogram shows 2 clearly separated principal spots.

Results:

The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

D. By Sodium Salts:

To 1ml solution S and add 1ml of water mix and Add 2 mL of a 150 g/L solution of potassium carbonate and heat to boiling. No precipitate is formed. Add 4 mL of potassium pyroantimonate solution and heat to boiling. Allow to cool in iced water and if necessary rub the inside of the test-tube with a glass rod. A dense white precipitate is formed.

Solution S

Dissolve 5.0 g in carbon dioxide-free water prepared from distilled water, and dilute to 50 mL with the same solvent.

4. APPEARANCE OF SOLUTION: <REFER GAM 024>

Solution S examined immediately after preparation is clear and not more intensely coloured than reference solution BY_6.

5. pH: <REFER GAM 030>

Dilute 1 mL of solution S to 100 mL with carbon dioxide-free water. The pH of the solution is 9.5 to 10.5.

6. RELATED SUSTANCES: (determined by liquid chromatography)

Chemicals/Reagents/Standards:

Methyl parahydroxybenzoate	:	Reference standard
4-Hydroxybenzoic acid (Impurity A)	:	Reference standard
Potassium dihydrogen phosphate	:	AR grade
Methanol	:	HPLC grade
Purified Water	:	Milli-Q water (or) Equivalent

Chromatographic Condition:

Column	:	Waters Xterra C18, (150 X 4.6mm), 5µm or equivalent
Flow rate	:	1.3 mL / minute
Detector wavelength	:	UV at 272 nm
Injection Volume	:	10µl
Run time	:	5 times the retention time of Methyl parahydroxybenzoate.
Retention time	:	Retention time of Methyl parahydroxybenzoate peak is at about 2.3 minutes

Mobile phase preparation:

A mixture of 35 volumes 6.8g/L solution of potassium dihydrogen phosphate and 65 volumes of methanol.

Test solution:

Weigh accurately about 50mg of the substance to be examined in 2.5ml of methanol and dilute to 50.0ml with the mobile phase. Dilute 10.0ml of this solution to 100.0ml with the mobile phase.

Reference solution (a):

Dissolve 5 mg of 4-hydroxybenzoic acid (impurity A) RS and 5 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 10.0 mL with the mobile phase.

Reference solution (b):

Dissolve 50mg of Methyl parahydroxybenzoate RS in 2.5ml of methanol and dilute to 50.0ml with the mobile phase. Dilute 10.0ml of this solution to 100.0ml with the mobile phase.

Reference solution (c):

Dilute 1.0ml of the test solution to 20.0ml with the mobile phase. Dilute 1.0ml of this solution to 10.0ml with the mobile phase.

Relative retention:

With reference to Methyl parahydroxybenzoate (retention time = about 2.3 min): impurity A = about 0.6.

System suitability: Reference solution (a):

resolution:

Minimum 2.0 between the peaks due to impurity A and Methyl parahydroxybenzoate.

Inject 10µl of the above solution as per following sequence.

Injection sequence:

S. No	Sample Name	No. of injections
1	Blank	1
2	Reference solution (a)	1
3	Reference solution (c)	1
4	Blank	1
5	Test solution	1

Impurity A: (NMT 3.0%)

$$= \frac{AT_A}{AS} \times \frac{WT}{50} \times \frac{10}{100} \times \frac{1}{20} \times \frac{1}{10} \times \frac{50}{WT} \times \frac{100}{10} \times 100 \times 1.4$$

Where,

AT_A = Area of impurity A peak in Test preparation.

AS =Area of the principal peak in the reference solution (c)

WT = Weight of the sample taken in mg.

1.4 = Correction factor

Unspecified Impurity: (NMT 0.5%)

$$= \frac{AT_I}{AS} \times \frac{WT}{50} \times \frac{10}{100} \times \frac{1}{20} \times \frac{1}{10} \times \frac{50}{WT} \times \frac{100}{10} \times 100$$

Where,

AT_I = Area of Unspecified Impurity peak in Test preparation.

AS =Area of the principal peak in the reference solution (c)

WT = Weight of the sample taken in mg.

Total Impurities (Excluding Impurity A): (NMT 1.0%)

$$= \frac{AT_T}{AS} \times \frac{WT}{50} \times \frac{10}{100} \times \frac{1}{20} \times \frac{1}{10} \times \frac{50}{WT} \times \frac{100}{10} \times 100$$

Where,

AT_T = Area of Total Impurities peak in Test preparation.

AS =Area of the principal peak in the reference solution (c)

WT = Weight of the sample taken in mg.

Limits:

Correction factor:

For the calculation of content, multiply the peak area of impurity A by 1.4

Impurity A:

Not more than 6 times the area of the principal peak in the chromatogram obtained with reference solution (c) (3.0 per cent)

Unspecified impurities:

For each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent)

Total Impurities(Excluding Impurity A):

Not more than twice the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent)

Disregard limit:

0.2 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent).

7. CHLORIDE:<REFER GAM 008>

Maximum 350 ppm.

To 10 mL of solution S, add 1 mL of nitric acid and 30 mL of water and dilute to 50 mL with water. Shake and filter. Dilute 10 mL of the filtrate to 15 mL with water. Prepare the standard using 14 mL of chloride standard solution (5 ppm Cl) to which 1 mL of water has been added.

8. SULPHATE: <REFER GAM 009>

Maximum 300 ppm.

To 25 mL of solution S, add 5 mL of distilled water and 10 mL of hydrochloric acid and dilute to 50 mL with distilled. Shake and filter. Dilute 10 mL of the filtrate to 15 mL with distilled water.

9. WATER: <REFER GAM 010>

Not more than 5.0% w/w, determined on 0.500g of sample.

10. ASSAY:

Determine by liquid chromatography as described in the related substances.

Inject reference solution (b) and the test solution.

Calculate the content of $C_8H_7NaO_3$, from the declared content of Methyl parahydroxybenzoate RS multiplied by a correction factor of 1.145.

Inject the reference solution (b). The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent

Inject 10µl of the above solution as per following sequence.

Injection sequence:

S. No	Sample Name	No. of injections
1	Blank	1
2	Reference solution (b)	5
3	Test solution (PPN-1)	2
4	Test solution (PPN-2)	1

Calculations:

Calculate the assay in % of Sodium Methyl hydroxybenzoate as such basis of the sample as below.

$$= \frac{AT}{AS} \times \frac{WS}{50} \times \frac{10}{100} \times \frac{50}{WT} \times \frac{100}{10} \times \frac{P}{100} \times 1.145 \times 100$$

Where,

AT = Average area of the principal peak in Test solution.

AS = Average area of the principal peak in the Reference solution (b).

WS = Weight of the Methyl parahydroxybenzoate Reference standard in mg.

WT = Weight of the sample taken in mg.

P = Potency of the Methyl parahydroxybenzoate Working standard in % on as such basis.

1.145 = Correction factor.

Calculate the assay in % of Sodium Methyl hydroxybenzoate on anhydrous basis of the sample as below.

$$= \frac{\text{Assay as such basis}}{(100 - \%\ \text{Water})} \times 100$$

11. REVISION HISTORY:

STP No.	Effective Date	Reason for Review
RMETM0032-00	21-02-2020	New specification prepared
RMETM0032-01	03/09/2022	Name of the product in Specification has been changed to Sodium methyl hydroxybenzoate as per BP monograph. This changes captured as per Change Control number ST/CC/22/164.

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

	Safetab Life Science Puducherry RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	SODIUM STARCH GLYCOLATE (TYPE A) BP			
Specification No.	RMESS0029-01	**Revision No.**	01	**Item Code.:** RMAS0029
Supersedes	RMESS0029-00	**Effective Date**	28/09/2022	**Page No.:** 1 of 4

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	NA
2	Molecular weight	NA
3	Storage conditions	In an airtight container, protected from light.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	23 g
6	Quantity of reserve sample	46 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

	Safetab Life Science Puducherry RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	SODIUM STARCH GLYCOLATE (TYPE A) BP			
Specification No.	RMESS0029-01	**Revision No.**	01	**Item Code.:** RMAS0029
Supersedes	RMESS0029-00	**Effective Date**	28/09/2022	**Page No.:** 2 of 4

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, fine, free-flowing powder, very hygroscopic.
2.	*Solubility	Practically insoluble in methylene chloride. It gives a translucent suspension in water.
3.	*Identification **A.** By pH **B.** By Chemical test **C.** By Chemical test **D.** By Sodium salts	 **A.** Between 5.5 to 7.5 **B.** A suspension forms that settles after standing. **C.** The solution becomes blue or violet. **D.** A dense white precipitate is formed.
4.	Appearance of solution	Solution S1 is clear and colourless
5.	*pH	Between 5.5 to 7.5
6.	Sodium glycolate	Not more than 2.0%.
7.	Sodium chloride	Not more than 7.0%.
8.	Iron.	Not more than 20ppm.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

S.NO	TEST (s)	SPECIFICATION (s)
9.	*Loss on drying	Not more than 10.0% w/w.
10.	*Assay (On dried basis)	Not less than 2.8% and not more than 4.2% w/w of Sodium. Calculated on the material washed with ethanol (80%) and dried as described under assay.
11.	*Microbial contamination Escherichia coli Salmonella Species	 Should be absent/1gm Should be absent/10gm

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

	Safetab Life Science Puducherry			
	RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	SODIUM STARCH GLYCOLATE (TYPE A) BP			
Specification No.	RMESS0029-01	**Revision No.**	01	**Item Code.:** RMAS0029
Supersedes	RMESS0029-00	**Effective Date**	28/09/2022	**Page No.:** 4 of 4

REVISION HISTORY:

Specification No.	Effective Date	Reason for Review
RMESS0029-00	17-02-2020	New specification prepared
RMESS0029-01	28/09/2022	Title name has been changed from Sodium starch glycolate to Sodium starch glycolate (Type A) as per BP monograph. This changes captured as per Change Control number ST/CC/22/189.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

	Safetab Life Science Puducherry			
	STANDARD TESTING PROCEDURE			MASTER COPY
Name of Product	SODIUM STARCH GLYCOLATE (TYPE A) BP			
STP No.	RMETS0029-01	**Revision No.**	01	**Item Code.:** RMAS0029
Supersedes	RMETS0029-00	**Effective Date**	28/09/2022	**Page No.:** 1 of 5

1. DESCRIPTION: < REFER GAM 001>

White or almost white, fine, free-flowing powder, very hygroscopic.

2. SOLUBILITY: < REFER GAM 002>

10mg of sample + 100mL of Methylene chloride	Practically insoluble if the material does not dissolves.

It gives a translucent suspension in water.

3. IDENTIFICATION:

A. By pH: < REFER GAM 030>

Between 5.5 to 7.5

B. By Chemical test:

Prepare with shaking and without heating a mixture of 4.0 g of the substance to be examined and 20 mL of carbon dioxide-free water. The mixture has the appearance of a gel. Add 100 mL of carbon dioxide-free water and shake. A suspension forms that settles after standing.

C. By Chemical test:

To an acidified solution, add iodinated potassium iodide solution. The solution becomes blue or violet.

D. Sodium salts:

a) Pipette 2ml of solution S2 and Add 2 mL of a 150 g/L solution of potassium carbonate and heat to boiling. No precipitate is formed. Add 4 mL of potassium pyroantimonate solution and heat to boiling. Allow to cool in iced water and if necessary rub the inside of the test-tube with a glass rod. A dense white precipitate is formed.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

4. APPEARANCE OF SOLUTION:

Solution S1:

Centrifuge the suspension obtained in identification test B at 2500RPM for 10 min. Collect carefully the supernatant.

Solution S2:

Place 2.5g in a silica or platinum crucible and add 2 mL of a 500 g/L solution of sulfuric acid. Heat on a water-bath, then cautiously over a naked flame, raising the temperature progressively, then incinerate in a muffle furnace at 600 ± 25 °C. Continue heating until all black particles have disappeared. Allow to cool, add a few drops of dilute sulfuric acid, heat and incinerate as above. Allow to cool, add a few drops of ammonium carbonate solution, evaporate to dryness and incinerate cautiously. Allow to cool and dissolve the residue in 50 mL of water.

5. pH: < REFER GAM 030>

Between 5.5 to 7.5, Disperse 1.0 g in 30 mL of carbon dioxide-free water.

6. SODIUM GLYCOLATE:

Maximum 2.0 per cent. Carry out the test protected from light. Test solution Place 0.20 g in a beaker. Add 5 mL of acetic acid and 5 mL of water. Stir until dissolution is complete (about 10 min). Add 50 mL of acetone and 1 g of sodium chloride. Filter through a fast filter paper impregnated with acetone, rinse the beaker and filter with acetone. Combine the filtrate and washings and dilute to 100.0 mL with acetone. Allow to stand for 24 h without shaking. Use the clear supernatant.

Reference solution:

Dissolve 0.310 g of glycollic acid previously dried in vacuo over diphosphorus pentoxide at room temperature overnight, in water and dilute to 500.0 mL with the same solvent. To 5.0 mL of this solution add 5 mL of acetic acid and allow to stand for about 30 min. Add 50 mL of acetone Rand 1 g of sodium chloride . Filter through a fast filter paper impregnated with acetone, rinse the beaker and filter with acetone.

Combine the filtrate and washings and dilute to 100.0 mL with acetone. Allow to stand for 24 h without shaking. Use the clear supernatant. Heat 2.0 mL of the test solution on a water-bath for 20 min. Cool to room temperature and add 20.0 mL of 2, 7-dihydroxynaphthalene solution. Shake and heat in a water-bath for 20 min. Cool under running water, transfer to a volumetric flask and dilute to 25.0 mL with sulfuric acid, maintaining the flask under running water.

Within 10 min, measure the absorbance at 540 nm using water as the compensation liquid. The absorbance of the solution prepared with the test solution is not greater than that of a solution prepared at the same time and in the same manner with 2.0 mL of the reference solution.

7. SODIUM CHLORIDE:

Maximum 7.0 per cent. Place 0.500 g in a beaker and suspend in 100 mL of water. Add 1 mL of nitric acid. Titrate with 0.1 M silver nitrate, determining the end-point potentiometrically using a silver-based indicator electrode and a double-junction reference electrode containing a 100 g/L solution of potassium nitrate in the outer jacket and a standard filling solution in the inner jacket.1 mL of 0.1 M silver nitrate is equivalent to 5.844 mg of NaCl.

Calculation:

$$= \frac{\text{Titer value} \times \text{Molarity of 0.1 M silver nitrate} \times 0.005844\ \text{g} \times 100}{\text{Sample weight in gx0.1}}$$

8. IRON: < REFER GAM 007>

Maximum 20 ppm, determined on 10 mL of solution S2.

9. LOSS ON DRYING: < REFER GAM 026>

Not more than 10.0 per cent, determined on 1.000 g by drying in an oven at 130 °C for 1.5 h.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

10. ASSAY :

Shake about 1 g with 20 mL of ethanol (80 per cent V/V), stir for 10 min and filter. Repeat the operation until chloride has been completely extracted and verify the absence of chloride using silver nitrate solution. Dry the residue at 105 °C to constant mass. To 0.700 g of the dried residue, add 80 mL of glacial acetic acid and heat under a reflux condenser for 2 h. Cool the solution to room temperature. Titrate with 0.1 M perchloric acid, determining the end-point potentiometric ally. Carry out a blank titration.

1 mL of 0.1 M perchloric acid is equivalent to 2.299 mg of Na.

Calculation:

$$= \frac{\text{Titer value} - \text{Blank value} \times \text{Molarity of 0.1M perchloric acid} \times 0.002299 \times 100}{0.1 \times \text{Sample weight in g}}$$

11. MICROBIAL CONTAMINATION:

a. Esherichia Coli:

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

b. Salmonella Species:

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

12. REVISION HISTORY:

STP No.	Effective Date	Reason for Review
RMETS0029-00	17-02-2020	New STP prepared
RMETS0029-01	28/09/2022	Title name has been changed from Sodium starch glycolate to Sodium starch glycolate (Type A) as per BP monograph. This changes captured as per Change Control number ST/CC/22/189.

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	A.G.KANNAN
Designation	Asst. Manager-QC	AGM-QC	GM-QA
Signature			
Date	26/09/2022	27/09/2022	27/09/2022

	Safetab Life Science Puducherry			
	RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	PURIFIED TALC BP			
Specification No.	RMEST0012-01	**Revision No.**	01	**Item Code.:** RMET0012
Supersedes	RMEST0012-00	**Effective Date**	24/02/2023	**Page No.:** 1 of 3

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$Mg_3Si_4O_{10}(OH)_2$
2	Molecular weight	379.26
3	Storage conditions	Store protected from Moisture
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	27 g
6	Quantity of reserve sample	54 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	20/02/2023	21/02/2023	22/02/2023

	Safetab Life Science Puducherry			
	RAW MATERIAL SPECIFICATION			MASTER COPY
Name of Product	PURIFIED TALC BP			
Specification No.	RMEST0012-01	**Revision No.**	01	**Item Code.:** RMET0012
Supersedes	RMEST0012-00	**Effective Date**	24/02/2023	**Page No.:** 2 of 3

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	Light, homogeneous, white or almost white powder, greasy to the touch (non abrasive).
2.	*Solubility	Practically insoluble in water, in ethanol (96 per cent) and in dilute solutions of acids and alkali hydroxides.
3.	*Identification **A.** By IR **B.** By Chemical test **C.** By Silicates	 The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Purified Talc WS. A white crystalline precipitate is formed. Within a short time a white ring is rapidly formed around the drop of water.
4.	Acidity or alkalinity	Not more than 0.4 mL of 0.01M Hydrochloric acid is required to change the colour of the indicator to green. Not more than 0.3 mL of Sodium hydroxide is required to change the colour of the indicator to pink.
5.	Water soluble substance	Not more than 0.2%
6.	Aluminium	Not more than 2.0%
7.	Calcium	Not more than 0.9%

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	20/02/2023	21/02/2023	22/02/2023

S.NO	TEST (s)	SPECIFICATION (s)
8.	Iron	Not more than 0.25%.
9.	Lead	Not more than 10 ppm.
10.	Magnesium	Between 17.0% to 19.5%
11.	*Loss on ignition	Not more than 7.0% w/w.
12.	*Microbial contamination i) Total aerobic microbial count ii) Total yeast and mould count	 Not more than 1000 cfu/g Not more than 100 cfu/g

Remarks: The above * Marked tests are to be performed while retesting the material.

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
RMEST0012-01	Periodic review.	NA	24/02/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	20/02/2023	21/02/2023	22/02/2023

	Safetab Life Science Puducherry			
	STANDARD TESTING PROCEDURE			MASTER COPY
Name of Product	PURIFIED TALC BP			
STP No.	RMETT0012-01	**Revision No.**	01	**Item Code.:** RMET0012
Supersedes	RMETT0012-00	**Effective Date**	24/02/2023	**Page No.:** 1 of 6

1. DESCRIPTION: < REFER GAM 001>

Light, homogeneous, white or almost white powder, greasy to the touch (non abrasive).

2. SOLUBILITY: < REFER GAM 002>

10mg of sample + 100mL of water	Practically insoluble if the material does not dissolves.
10mg of sample + 100mL of Ethanol (96%)	Practically insoluble if the material does not dissolves.
10mg of sample + 100mL of dilute acids	Practically insoluble if the material does not dissolves.
10mg of sample + 100mL of dilute alkali hydroxides	Practically insoluble if the material does not dissolves.

3. IDENTIFICATION:

A) By IR: < REFER GAM 003>

The Infrared absorption spectrum of sample should be concordant with that of reference spectrum or with the spectrum obtained from Purified Talc WS.

B) By Chemical test:

In a platinum crucible, melt a mixture of 0.2g of anhydrous sodium carbonate and 2.0g of potassium carbonate. To the melted mass add 0.1g of the substance under examined and heat until the mixture is completely melted. Allow to cool and transfer the melted mass into an evaporating dish with 50ml of hot water. Add hydrochloric acid until effervescence ceases. Add 10ml of hydrochloric acid and evaporate to dryness on a water-bath. Allow to cool. Add 20ml of water, heat to boiling and filter (the residue is used for identification test C). To 5ml of the filtrate add 1ml of ammonia and 1ml of ammonium chloride solution and filter. To the filtrate add 1ml of disodium hydrogen phosphate solution. A white, crystalline precipitate is formed.

C) By Silicates:

Mix the residue obtained from Identification test B in a lead or platinum crucible mix by means of a copper wire with about 10 mg of sodium fluoride and a few drops of sulfuric acid to give a thin slurry.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	20/02/2023	21/02/2023	22/02/2023

Cover the crucible with a thin, transparent plate of plastic under which a drop of water is suspended and warm gently. Within a short time a white ring is rapidly formed around the drop of water.

Solution S1:

Weigh 10.0 g into a conical flask fitted with a reflux condenser, gradually add 50 mL of 0.5 M hydrochloric acid while stirring and heat on a water-bath for 30 min. Allow to cool. Transfer the mixture to a beaker and allow the undissolved material to settle. Filter the supernatant through medium-speed filter paper into a 100 mL volumetric flask, retaining as much as possible of the insoluble material in the beaker. Wash the residue and the beaker with 3 quantities, each of 10 mL, of hot water. Wash the filter with 15 mL of hot water, allow the filtrate to cool and dilute to 100.0 mL with the same solvent.

Solution S2:

Perchlorates mixed with heavy metals are known to be explosive. Take proper precautions while performing this procedure Weigh 0.5 g in a 100 mL polytetrafluoroethylene dish, add 5 mL of hydrochloric acid , 5 mL of lead-free nitric acid and 5 mL of perchloric acid. Stir gently then add 35 mL of hydrofluoric acid and evaporate slowly to dryness on a hot plate. To the residue, add 5 mL of hydrochloric acid, cover with a watch-glass, heat to boiling and allow to cool. Rinse the watch-glass and the dish with water. Transfer into a volumetric flask, rinse the dish with water and dilute to 50.0 mL with the same solvent.

4. ACIDITY OR ALKALINITY:

Boil 2.5 g with 50 mL of carbon dioxide-free water under reflux. Filter in vacuo. To 10 mL of the filtrate add 0.1 mL of bromothymol blue solution; not more than 0.4 mL of 0.01 M hydrochloric acid is required to change the colour of the indicator to green. To 10 mL of the filtrate add 0.1 mL of phenolphthalein solution; not more than 0.3 mL of 0.01 M sodium hydroxide is required to change the colour of the indicator to pink.

5. WATER SOLUBLE SUBSTANCES:

Not more than 0.2%. To 10.0 g add 50 mL of carbon dioxide-free water, heat to boiling and maintain boiling under a reflux condenser for 30 min. Allow to cool, filter through a medium-speed filter paper and dilute to 50.0 mL with water.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	20/02/2023	21/02/2023	22/02/2023

Take 25.0 mL of the filtrate, evaporate to dryness and heat 105 °C for 1h. The residue weighs a maximum of 10 mg.

6. ALUMINIUM: (ATOMIC ABSORPTION SPECTROMETRY)

Not more than 2.0%

Test solution:

To 5.0 mL of solution S2 add 10 mL of a 25.34 g/L solution of caesium chloride, 10.0 mL of hydrochloric and dilute to 100.0 mL with water.

Reference solutions:

Into 4 identical volumetric flasks, each containing 10.0 mL of hydrochloric acid and 10 mL of a 25.34 g/L solution of caesium chloride, introduce respectively 5.0 mL, 10.0 mL, 15.0 mL and 20.0 mL of aluminium standard solution (100 ppm Al) and dilute to 100.0 mL with water.

Source: Aluminium hollow-cathode lamp.

Wavelength: 309.3 nm.

Atomization device: Nitrous oxide-acetylene flame.

7. CALCIUM: (ATOMIC ABSORPTION SPECTROMETRY)

Not more than 0.9 per cent.

Test solution:

To 5.0 mL of solution S2 add 10.0 mL of hydrochloric acid, 10 mL of lanthanum chloride solution and dilute to 100.0 mL with water.

Reference solutions :

Into 4 identical volumetric flasks, each containing 10.0 mL of hydrochloric acid and 10 mL of lanthanum chloride solution, introduce respectively 1.0 mL, 2.0 mL, 3.0 mL and 5.0 mL of calcium standard solution (100 ppm Ca) and dilute to 100.0 mL with water.

Source: Calcium hollow-cathode lamp.

Wavelength:422.7 nm.

Atomisation device: Nitrous oxide-acetylene flame.

8. IRON: < REFER GAM 007> (ATOMIC ABSORPTION SPECTROMETRY)

Not more than 0.25 percent.

Test solution:

To 2.5 mL of solution S1, add 50.0 mL of 0.5 M hydrochloric acid and dilute to 100.0 mL with water.

Reference solutions:

Into 4 identical volumetric flasks, each containing 50.0 mL of 0.5 M hydrochloric acid, introduce respectively 2.0 mL, 2.5 mL, 3.0 mL and 4.0 mL of iron standard solution (250 ppm Fe) and dilute to 100.0 mL with water.

Source: Iron hollow-cathode lamp.

Wavelength: 248.3 nm.

Atomization device: Air-acetylene flame. Correction Deuterium lamp.

9. LEAD: (ATOMIC ABSORPTION SPECTROMETRY)

Not more than 10 ppm.

Test solution: Use solution S1.

Reference solutions:

Into 4 identical volumetric flasks, each containing 50.0 mL of 0.5 M hydrochloric acid, introduce respectively 5.0 mL, 7.5 mL, 10.0 mL and 12.5 mL of lead standard solution (10 ppm Pb) and dilute to 100.0 mL with water.

Source: Lead hollow-cathode lamp.

Wavelength: 217.0 nm.

Atomisation device: Air-acetylene flame.

10. MAGNESIUM: (ATOMIC ABSORPTION SPECTROMETRY)

17.0 per cent to 19.5 per cent.

Test solution:

Dilute 0.5 mL of solution S2 to 100.0 mL with water. To 4.0 mL of the solution, add 10.0 mL of hydrochloric acid, 10 mL of lanthanum chloride solution and dilute to 100.0 mL with water.

Reference solutions:

Into 4 identical volumetric flasks, each containing 10.0 mL of hydrochloric acid and 10 mL of lanthanum chloride solution, introduce respectively 2.5 mL, 3.0 mL, 4.0 mL and 5.0 mL of magnesium standard solution (10 ppm Mg) and dilute to 100.0 mL with water.

Source: Magnesium hollow-cathode lamp.

Wavelength: 285.2 nm.

Atomisation device: Air-acetylene flame.

11. LOSS ON IGNITION: < REFER GAM 027>

Maximum 7.0 per cent, determined on 1.00 g by ignition to constant weight at 1050-1100°C.

12. MICROBIAL CONTAMINATION:

Use 1.0g of sample for Total Microbial count.

Total Aerobic microbial count:

Procedure: Proceed as per the current general testing procedure GAM-035.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	20/02/2023	21/02/2023	22/02/2023

Total Yeast and mold count:

Procedure: Proceed as per the current general testing procedure GAM-036

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
RMETT0012-01	Periodic review.	NA	24/02/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	K.JAYARAJ
Designation	Asst. Manager-QC	AGM-QC	Asst. Manager-QA
Signature			
Date	20/02/2023	21/02/2023	22/02/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	COLLOIDAL ANHYDROUS SILICA BP			
Specification No.	SPEC-RMEC0017-00	**Revision No.**	00	**Item Code.:** RMEC0017
Supersedes	RMESC0017-01	**Effective Date**	18/11/2023	**Page No.:** 1 of 3

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	SiO_2
2	Molecular weight	60.1
3	Storage conditions	Store protected from light.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	5 g
6	Quantity of reserve sample	10 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	14/11/2023	15/11/2023	17/11/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	COLLOIDAL ANHYDROUS SILICA BP			
Specification No.	SPEC-RMEC0017-00	**Revision No.**	00	**Item Code.:** RMEC0017
Supersedes	RMESC0017-01	**Effective Date**	18/11/2023	**Page No.:** 2 of 3

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	White or almost white, light, fine, amorphous powder, with a particle size of about 15nm.
2.	*Solubility	Practically insoluble in water and in mineral acids except hydrofluoric acid. It dissolves in hot solutions of alkali hydroxides.
3.	*Identification By Silicates	Within a short time a white ring is rapidly formed around the drop of water.
4.	*pH	Between 3.5 to 5.5
5.	Chlorides	Not more than 250ppm.
6.	*Loss on ignition	Not more than 5.0% w/w.
7.	*Assay (On ignited basis)	Not less than 99.0% and not more than 100.5% w/w.

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	14/11/2023	15/11/2023	17/11/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	COLLOIDAL ANHYDROUS SILICA BP			
Specification No.	SPEC-RMEC0017-00	**Revision No.**	00	**Item Code.:** RMEC0017
Supersedes	RMESC0017-01	**Effective Date**	18/11/2023	**Page No.:** 3 of 3

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-RMEC0017-00	(i) The Product name has been corrected as per BP monograph. (ii) Specification format revised as per SOP No. ST/QC/058.	ST/CC/23/243 ST/CC/23/063	18/11/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	14/11/2023	15/11/2023	17/11/2023

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	COLLOIDAL ANHYDROUS SILICA BP			
STP No.	STP-RMEC0017-00	**Revision No.**	00	**Item Code.:** RMEC0017
Supersedes	RMETC0017-01	**Effective Date**	18/11/2023	**Page No.:** 1 of 3

1. DESCRIPTION: < REFER GAM 001>

White or almost white, light, fine, amorphous powder, with a particle size of about 15nm.

2. SOLUBILITY: < REFER GAM 002>

10mg of sample + 100mL of Water	Practically insoluble if the material does not dissolves.
10mg of sample + 100mL of Mineral acids except hydrofluoric acid.	Practically insoluble if the material does not dissolves.

It dissolves in hot solutions of alkali hydroxides.

3. IDENTIFICATION: < REFER GAM 003>

By Silicates:

About 25mg of sample ignited in a platinum crucible at 900±50ºC for 2hour, cool and add about 10 mg of sodium fluoride and a few drops of sulfuric acid to give a thin slurry. Cover the crucible with a thin, transparent plate of plastic under which a drop of water is suspended and warm gently. Within a short time a white ring is rapidly formed around the drop of water.

4. pH: < REFER GAM 030>

Between 3.5 to 5.5

Weigh accurately about 1.0g of sample dissolved in 100ml carbon dioxide free water and stirring continuously. Determine the pH when a homogeneous solution is obtained.

Rinse the electrodes with distilled water and wipe dry with tissue paper. Set the instrument using buffer solution pH 6.87 by following instrument Operating Procedure. Clean the electrode. Immerse the electrode in the solution being examined and measure the pH.

5. CHLORIDES: <REFER GAM 008>

Not more than 250 ppm.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	14/11/2023	15/11/2023	17/11/2023

To 1.0 g add 30 mL of methanol and 20 mL of dilute nitric acid, Heat on a water-bath for 15 min stirring frequently. Cool, dilute to 50 mL with water and filter. Dilute 10 mL of the filtrate to 15 mL with water.

6. LOSS ON IGNITION: <REFER GAM 027>

Not more than 5.0 per cent, determined on 0.200 g by ignition in a platinum crucible at 900 ± 50 °C for 2 h. It is advisable to place the crucible in a cold oven and then to heat up the oven. Allow to cool in a desiccator before weighing.

7. ASSAY (ON IGNITED BASIS):

To the residue obtained in the test for loss on ignition add 0.2ml of sulphuric acid and sufficient ethanol (96 per cent) to moisten the residue completely. Add 6 mL of hydrofluoric acid and evaporate to dryness on a hot-plate at 95-105 °C, taking care to avoid loss from sputtering. Wash down the sides of the platinum crucible with 6 mL of hydrofluoric acid and evaporate to dryness. Ignite at 900 ± 50 °C, allow to cool in a desiccator and weigh.

The difference between the mass of the residue and the mass of the final residue obtained in the test for loss on ignition gives the amount of SiO_2 in the quantity of the substance to be examined.

Calculation:

Calculate the silicon dioxide % w/w on ignited basis.

$$\frac{(LR - AR) \times 100 \times 100}{WT \times (100 - \%\ LOI)}$$

Where,

LR = Weight of residue from loss on ignition.
AR = Weight of residue from assay.
LOI = Loss on ignition.
WT = Weight of sample taken for Loss on ignition.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	14/11/2023	15/11/2023	17/11/2023

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-RMEC0017-00	(i) The Product name has been corrected as per BP monograph. (ii) STP format revised as per SOP No. ST/QC/058.	ST/CC/23/243 ST/CC/23/063	18/11/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	14/11/2023	15/11/2023	17/11/2023

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	TARTRAZINE LAKE (E102 LAKE)			
Specification No.	SPEC-RMET0013-00	**Revision No.**	00	**Item Code.:** RMET0013
Supersedes	RMEST0013-00	**Effective Date**	25/09/2023	**Page No.:** 1 of 3

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	NA
2	Molecular weight	NA
3	Storage conditions	NA
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	25g
6	Quantity of reserve sample	50g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	IHS
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.PALANICHAMY	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/2023	22/09/2023	22/09/23

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	TARTRAZINE LAKE (E102 LAKE)			
Specification No.	SPEC-RMET0013-00	**Revision No.**	00	**Item Code.:** RMET0013
Supersedes	RMEST0013-00	**Effective Date**	25/09/2023	**Page No.:** 2 of 3

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	Yellow powder
2.	*Total dye content on dry basis	Between 4.0 to 45.0%
3.	*Loss on drying at 110°C	Not more than 17.0%
4.	*pH	Between 3.5 to 7.0
5.	Bleeding (or) free dye content	Not more than 0.4%
6.	Sieve Analysis 325 mesh	Not less than 85.0%
7.	Bulk Density	Not more than 0.4 gm/ml
8.	Lead & Heavy metals	Not more than 20ppm
9.	Arsenic	Not more than 2 ppm

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.PALANICHAMY	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/2023	22/09/2023	22/09/23

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-RMET0013-00	(i) Periodic review. (ii) Specification numbering procedure revised as per SOP No. ST/QC/058.	ST/CC/23/063	25/09/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.PALANICHAMY	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/2023	22/09/2023	22/09/23

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	TARTRAZINE LAKE (E102 LAKE)			
STP No.	STP-RMET0013-00	**Revision No.**	00	**Item Code.:** RMET0013
Supersedes	RMETT0013-00	**Effective Date**	25/09/2023	**Page No.:** 1 of 6

1. DESCRIPTION: < REFER GAM 001>

Yellow powder.

2. TOTAL DYE CONTENT:

Weigh accurately 0.2gm of sample in a 100ml volumetric flask. Add 20ml of concentrated Hydrochloric Acid and shake until the solution is clear. Boil the Solution if required to dissolve it completely. Dilute to volume with water and mix well. Cool the above solution. Pipette 5ml into a 100ml volumetric flask and again dilute to volume with water and mix well. Measure the extinction of resulting solution in 1cm cell at 428nm in a spectrophotometer.

Using 485 as 'E'-value

Calculations:

$$\text{Total dye content on as is basis (\%)} = \frac{Abs}{485} \times \frac{100}{WT} \times \frac{100}{5} \times 10 \times 100$$

Where,

Abs = Absorbance of sample

WT = Weight of sample taken

$$\text{Total dye content on dry basis (\%)} = \frac{\text{as is basis}}{(100 - \text{Loss on drying})} \times 100$$

3. LOSS ON DRYING:

Weigh 2 gm of the sample in a petri dish and dry for 2 hours at 110° C. Find out the loss in weight after drying and calculate the percentage loss.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.PALANICHAMY	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/2023	22/09/2023	22/09/23

4. pH: < REFER GAM 030>

Take 2.0gm of the lake colour, add 100 ml distilled water and stir for 10 to 15 minutes. Find its pH value.

5. BLEEDING (OR) FREE DYE CONTENT:

Shake 2.0gm of the sample with 100ml of water for about 10 minutes, filter through Whatman no.41 filter paper, reject the first few ml of filtrate. If filtrate is colourless, that means there is no bleeding, if it is coloured, measure the extinction of the resulting solution in 1cms cell at 428nm in a spectrophotometer.

Using 485 as 'E' Value

Calculations:

$$= \frac{Abs}{485} \times \frac{100}{WT} \times 10 \times 100$$

Where,

Abs = Absorbance of sample

WT = Weight of sample taken

6. SIEVE ANALYSIS, PASSING THROUGH 325 MESH:

Weigh 5.0gm lake colour and transfer it to 325-mesh sieve, run under tap water and brush it Transfer residual lake colour on filter paper, dry at 110°C for 30 min. and weigh the residual mass. Calculate the percentage of retained mass.

Calculations:

$$\text{Retained mass (\%)} = \frac{\text{residual mass} \times 100}{5\ gm} = X$$

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.PALANICHAMY	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/2023	22/09/2023	22/09/23

Material passing through 325 mesh (%) = 100-X

7. BULK DENSITY:

Weigh exactly 10gms of powder fill it up in a 100ml graduated cylinder. Tap it 100 times. Note down the volume (A) of the powder set in the gradated cylinder.

Calculations:

$$B.D. = \frac{\text{Weight of the powder}}{\text{Volume}} = \frac{10}{A}$$

8. LEAD & HEAVY METAL:

Reagents

Lead Nitrate Stock solution

(i) Dissolve 0.1598 gm of Lead Nitrate in 100 ml of distilled water to which add 1 ml of Nitric acid & then dilute with distilled water to 1000ml.

(ii) Ammonia solution - dilute 400ml of ammonium hydroxide (28%) to 1 lit. with distilled water.

(iii) HCL 10%

(iv) Nitric acid (sp. gravity 1.4)

(v) Sulphuric acid (sp. gravity 1.84)

(vi) Hydrogen sulphide - saturated solution of hydrogen sulphide made by passing hydrogen sulphide gas through cold water.

(vii) Acetic acid (10%)

Standard solution (for checking heavy metal < x ppm):

On the day of use, dilute 'x' ml of lead nitrate stock solution to 100 ml with distilled water. This solution contains 'x' mg of lead per ml solution (x ppm)

Standard preparation (Solution A):

Into a 50 ml nessler cylinder, pipette out 2 ml of standard lead solution (10 ppm pb), dilute with water to 25 ml. Adjust with dilute acetic acid or dilute ammonia solution to a pH between 3.0 - 4.0 Dilute further with water to about 35 ml.

Test solution:

Weigh 1gm of sample in a suitable crucible. Add sufficient sulphuric acid to moisten the sample and ignite carefully at low temperature until thoroughly charred. Add to this charred mass, 2 ml of Nitric Acid and 5 drops of Sulphuric Acid. Heat continuously until white fumes is no longer evolved. Ignite preferably in a muffle furnace at 600° C to 700° C until the carbon is burnt off. Cool, add 4 ml of HCL. Cover and digest it on water bath for 15 min. Uncover & slowly evaporate to dryness on a water bath.

Moisten the residue with few drops of HCL, add 10 ml of hot water and digest for 2 min. Add ammonia solution drop wise till solution is just alkaline to litmus paper. Dilute with water to 25 ml and adjust with dilute acetic acid to a pH between 3.0- 4.0

Filter if necessary, rinse the crucible with 10 ml of water and filter. Combine the filtrate and washings in a Nessler's Cylinder, dilute with water to about 35 ml.

To each of the cylinder (one containing the standard solution & other test solution), add 10 ml of freshly prepared hydrogen sulphide solution, mix and dilute with water to 50 ml. Allow it to stand for 5 min. and then view downwards over the white surface.

The colour produced in test solution should not be darker than that of solution A.

9. ARSENIC:

Reagents

(i) Nitric acid (sp. gravity 1.4)

(ii) Sulphuric acid (sp. gravity 1.84)

(iii) HCl (sp. gravity 1.16)

(iv) Brominated HCl (0.03% KBr in HCl)

(v) Stannous chloride (2% in 10% HCl)

(vi) Cotton gauze (soaked in 5% lead acetate solution and dry it)

(vii)Test paper (soak strips of filter paper in saturated ethanolic solution of mercuric bromide and dry)

(viii)Standard arsenic solution- Dissolve 0.330 gm of arsenic trioxide in 5 ml of 2M NaOH and dilute it to 250 ml in distilled water Further dilute 1 ml of above solution to 100 ml with distilled water. (y) 1ml=10ppm

(ix) Zn-metal

Weigh 1.0gm of the sample; transfer it to Kjeldhl's flask. Add 5ml of water, 5ml of Nitric Acid and 5ml of Sulphuric Acid. Warm gently. If foaming becomes excessive, add a little water. Evaporate the mixture. Maintain strongly oxidizing condition in the flask during digestion by adding cautiously small quantity of Nitric Acid whenever the mixture begins to turn brown or dark. Continue digestion until organic matter is destroyed and sulphuric trioxide fumes are continuously evolved. The final solution should be colourless or at the most straw colour.

To remove nitrosyl sulphuric acid after partial cooling, transfer the residue to an evaporating dish. Wash the flask twice with 10ml water. Collect the washing with residue in an evaporating dish, heat again to fuming point. Add 25ml of water and evaporate.

Add 20ml Brominated Hydrochloric Acid and 10ml of water and boil for 2 to 3 minutes. Cool it. Remove the excess of Bromine with a few drops of stannous chloride solutions. Transfer to a wide mouthed bottle of arsenic apparatus. Add 5 ml of 1M KI & 10 gm Zn metal. Tube is placed quickly in position.

(For checking Arsenic< y ppm)

Standard stain is produced by taking 'y/10' ml of std. diluted arsenic solution in a wide mouthed bottle with 20 ml Brominated Hydrochloric Acid and a few drops of stannous chloride solutions, operating in a similar manner as sample.

The reaction is allowed to proceed for 40 minutes. If arsenic is present, the yellow stain is produced on the mercuric bromide paper, which is compared by daylight with the standard stains.

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-RMET0013-00	(i) Periodic review. (ii) STP numbering procedure revised as per SOP No. ST/QC/058.	ST/CC/23/063	25/09/2023

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	S.PALANICHAMY	M.VIJAYAKUMAR	S.MARAN
Designation	Asst. Manager-QC	AGM-QC	AGM-QA
Signature			
Date	21/09/2023	22/09/2023	22/09/23

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	MAGNESIUM STEARATE BP			
Specification No.	SPEC-RMEM0033-00	**Revision No.**	00	**Item Code.:** RMEM0033
Supersedes	RMESM0033-01	**Effective Date**	14/03/2024	**Page No.:** 1 of 4

S.NO	RAW MATERIAL GENERAL SPECIFICATION (s)	
1	Molecular formula	$(C_{17}H_{35}CO_2)_2$ Mg
2	Molecular weight	591.27
3	Storage conditions	Store at ambient temperature.
4	Precautions & Special instructions for sampling	Use hand gloves and nose mask while sampling. Reseal the containers immediately after sampling. Avoid inhaling.
5	Quantity of sample required for analysis	20 g
6	Quantity of reserve sample	40 g
7	Retest period	12 months from the date of release
8	Re-test Parameter	As mentioned in Specification
9	Reference	BP
10	Sampling instruction	Follow the standard operating procedure No.: ST/QC/040.
11	Destructions instructions	Follow the standard operating procedure No.: ST/QC/032.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	MAGNESIUM STEARATE BP			
Specification No.	SPEC-RMEM0033-00	**Revision No.**	00	**Item Code.:** RMEM0033
Supersedes	RMESM0033-01	**Effective Date**	14/03/2024	**Page No.:** 2 of 4

S.NO	TEST (s)	SPECIFICATION (s)
1.	*Description	A white or almost white, very fine, light powder, greasy to the touch.
2.	*Solubility	Practically insoluble in water and in anhydrous ethanol.
3.	*Identification **A.** By Freezing point **B.** By Acid value **C.** By Fatty acid composition **D.** By Chemical test	 Not less than 53°. The acid value of the fatty acids is 195 to 210. The principle peaks in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution. A white crystalline precipitate is formed.
4.	Acidity or alkalinity	Not more than 0.05ml of 0.1M Hydrochloric acid or 0.1M Sodium hydroxide is required to change the colour of the indicator.
5.	Chlorides	Not more than 0.1%.
6.	Sulfates	Not more than 1.0%.
7.	Cadmium	Not more than 3 ppm

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024

	Safetab Life Science Puducherry			MASTER COPY
	RAW MATERIAL SPECIFICATION			
Name of Product	MAGNESIUM STEARATE BP			
Specification No.	SPEC-RMEM0033-00	**Revision No.**	00	**Item Code.:** RMEM0033
Supersedes	RMESM0033-01	**Effective Date**	14/03/2024	**Page No.:** 3 of 4

S.NO	TEST (s)	SPECIFICATION (s)
8.	Lead	Not more than 10 ppm
9.	Nickel	Not more than 5 ppm
10.	*Loss on drying	Not more than 6.0% w/w.
11.	*Assay for Magnesium (On dried basis)	Not less than 4.0% and not more than 5.0% w/w
12.	Stearic acid and Palmitic acid (i) Stearic acid (ii) Sum of Stearic acid and Palmitic acid	 Not less than 40.0% Not less than 90.0%
13.	*Microbial contamination (i) Total aerobic microbial count (ii) Total yeast and mold count iii) Escherichia coli iv) Salmonella species	 Not more than 1000 cfu/g Not more than 100 cfu/g Should be absent Should be absent

Remarks: The above * Marked tests are to be performed while retesting the material.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024

REVISION HISTORY:

Specification No.	Reason for Review	Change control No.	Effective Date
SPEC-RMEM0033-00	(i) Specification numbering procedure revised as per SOP No. ST/QC/058. (ii) There is no changes in specification as per current monograph.	ST/CC/23/063 ST/CC/24/067	14/03/2024

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024

	Safetab Life Science Puducherry			MASTER COPY
	STANDARD TESTING PROCEDURE			
Name of Product	MAGNESIUM STEARATE BP			
STP No.	STP-RMEM0033-00	**Revision No.**	00	**Item Code.:** RMEM0033
Supersedes	RMETM0033-01	**Effective Date**	14/03/2024	**Page No.:** 1 of 11

1. DESCRIPTION: < REFER GAM 001>

A white or almost white, very fine, light powder, greasy to the touch.

2. SOLUBILITY: < REFER GAM 002>

10mg of sample + 100mL of Water	Practically insoluble if the material does not dissolves.
10mg of sample + 100mL of Anhydrous ethanol	Practically insoluble if the material does not dissolves.

3. IDENTIFICATION: < REFER GAM 003>

First identification : C and D

Second identification: A, B and D

To 5.0g of sample add 50 ml of peroxide-free ether, 20ml of dilute nitric acid and 20ml of water and heat under a reflux condenser until dissolution is complete. Allow to cool. In a separating funnel, separate the aqueous layer and shake the ether layer with 2 quantities, each of 4ml of water. Combine the aqueous layers, wash with 15ml of peroxide-free ether and dilute to 50ml with water (Solution S). Evaporate the organic layer to dryness and dry the residue at 100-105°C. Keep the residue for identification tests A and B.

A. By Freezing point:

Determined on the residue obtained in the preparation of solution S has a freezing point not less than 53°C.

B. By Acid value:

The acid value of the fatty acids is 195 to 210, dissolved on 0.2g of the residue obtained in the preparation of solution S in 25ml of the mixture of equal volumes of ethanol (96 per cent) and light petroleum, previously neutralised with 0.1M potassium hydroxide or 0.1M sodium hydroxide, unless otherwise specified, using 0.5mL of phenolphthalein solution as indicator. If necessary, heat to about 90°C to dissolve the substance to be examined. When the substance to be examined has dissolved, titrate with 0.1M potassium hydroxide or 0.1M sodium hydroxide until the pink colour persists for at least 15s (n mL of titrant). When heating has been applied to aid dissolution maintain the temperature at about 90°C during the titration.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024

$$I_A = \frac{5.61n}{m}$$

C. By Fatty acid composition:

Examine the chromatograms obtained in the assay of stearic acid and palmitic acid.

The two principle peaks in the chromatogram obtained with the test solution are similar in retention time to the two principal peaks in the chromatogram obtained with the reference solution.

D. By Chemical test:

Take 1ml of Solution S, add 1ml of dilute ammonia; a white precipitate is formed that dissolves on addition 1ml of ammonium chloride solution. Add 1ml of 120g/L solution of disodium hydrogen phosphate dodecahydrate; a white crystalline precipitate is formed.

4. ACIDITY OR ALKALINITY:

To 1.0g of sample, add 20ml of carbon dioxide free water and boil for 1 minute with continuous shaking. Cool and filter. To 10ml of filtrate add 0.05ml of bromothymol blue solution. Not more than 0.05ml of 0.1M hydrochloric acid or 0.1M sodium hydroxide is required to change the colour of the indicator.

5. CHLORIDES: < REFER GAM 008>

Not more than 0.1%.

Dilute 10.0mL of Solution S to 40mL with water. Neutralise if necessary with nitric acid using litmus as indicator. Add 1mL of nitric acid and 1mL of 0.1M silver nitrate and dilute to 50mL with water. Mix and allow to stand for 5 min protected from light. The turbidity, if any, is not greater than that produced in a solution containing 1.4mL of 0.02M hydrochloric acid.

6. SULFATES: < REFER GAM 009>

Not more than 1.0%.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024

Dilute 6.0 ml of Solution S to 40.0 ml with water. Neutralise if necessary with hydrochloric acid using litmus as indicator. Add 1mL of 3M hydrochloric acid and 3mL of a 120g/L solution of barium chloride and dilute to 50mL with water. Mix and allow to stand for 10 min. The turbidity, if any, is not greater than that produced in a solution containing 3.0mL of 0.02M sulfuric acid.

7. CADMIUM: (ATOMIC ABSORPTION SPECTROMETRY)

Not more than 3ppm.

For the preparation of all aqueous solutions and for the rinsing of glassware before use, employ water that has been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin before use. Select all reagents to have as low a content of cadmium, lead and nickel as practicable and store all reagent solutions in containers of borosilicate glass. Clean glassware before use by soaking in warm 8M nitric acid for 30 min and by rinsing with deionised water.

Blank solution:

Dilute 25mL of cadmium and lead-free nitric acid to 100.0 mL with water.

Modifier solution:

Dissolve 20g of ammonium dihydrogen phosphate and 1g of magnesium nitrate in water and dilute to 100mL with the same solvent. Alternatively, use an appropriate matrix modifier as recommended by the graphite furnace atomic absorption (GFAA) spectrometer manufacturer.

Test solution:

Place 0.100g of the substance to be examined in a polytetrafluoroethylene digestion bomb and add 2.5mL of cadmium- and lead-free nitric acid. Close and seal the bomb according to the manufacturer's operating instructions (when using a digestion bomb, be thoroughly familiar with the safety and operating instructions. Carefully follow the bomb manufacturer's instructions regarding care and maintenance of these digestion bombs. Do not use metal jacketed bombs or liners which have been used with hydrochloric acid due to contamination from corrosion of the metal jacket by hydrochloric acid). Heat the bomb in an oven at 170°C for 3 h. Cool the bomb slowly in air to room temperature according to the bomb manufacturer's instructions.

Place the bomb in a fume cupboard and open carefully as corrosive gases may be expelled. Dissolve the residue in water R and dilute to 10.0 mL with the same solvent.

Reference solution:

Prepare a solution of 0.0030 µg/mL of Cd by suitable dilutions of a 0.00825 µg/mL solution of cadmium nitrate tetrahydrate in the blank solution.

Dilute 1.0mL of the test solution to 10.0mL with the blank solution. Prepare mixtures of this solution, the reference solution and the blank solution in the following proportions: (1.0:0:1.0 V/V/V), (1.0:0.5:0.5 V/V/V), (1.0:1.0:0 V/V/V).

To each mixture add 50µL of modifier solution and mix. These solutions contain respectively 0µg, 0.00075µg and 0.0015µg of cadmium per millilitre from the reference solution (keep the remaining test solution for use in the test for lead and nickel).

Source: Cadmium hollow-cathode lamp.

Wavelength: 228.8 nm.

Atomisation device: Furnace.

Platform: Pyrolytically coated with integrated tube.

Operating conditions:

Use the temperature programme recommended for cadmium by the GFAA spectrometer manufacturer. An example of temperature parameters for GFAA analysis of cadmium is shown below.

Stage	Final temperature (°C)	Ramp time (s)	Hold time (s)
Drying	110	10	20
Ashing	600	10	30
Atomisation	1800	0	5

8. LEAD: (ATOMIC ABSORPTION SPECTROMETRY)

Not more than 10 ppm.

For the preparation of all aqueous solutions and for the rinsing of glassware before use, employ water that has been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin before use.

Select all reagents to have as low a content of cadmium, lead and nickel as practicable and store all reagent solutions in containers of borosilicate glass. Clean glassware before use by soaking in warm 8M nitric acid for 30 min and by rinsing with deionised water.

Blank solution:

Use the solution described in the test for cadmium.

Modifier solution:

Use the solution described in the test for cadmium.

Test solution:

Use the solution described in the test for cadmium.

Reference solution:

Prepare a solution of 0.100 µg/mL of Pb by suitable dilutions of lead standard solution (100 ppm Pb) R with the blank solution.

Prepare mixtures of the test solution, the reference solution and the blank solution in the following proportions: (1.0:0:1.0 V/V/V), (1.0:0.5:0.5 V/V/V), (1.0:1.0:0 V/V/V). To each mixture add 50 µL of modifier solution and mix. These solutions contain respectively 0 µg, 0.025 µg and 0.05 µg of lead per millilitre from the reference solution.

Source: Lead hollow-cathode lamp.

Wavelength: 283.3 nm.

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024

Atomisation device: Furnace.

Platform: Pyrolytically coated with integrated tube.

Operating conditions:

Use the temperature programme recommended for lead by the GFAA spectrometer manufacturer. An example of temperature parameters for GFAA analysis of lead is shown below.

Stage	Final temperature (°C)	Ramp time (s)	Hold time (s)
Drying	110	10	20
Ashing	450	10	30
Atomisation	2000	0	5

9. NICKEL: (ATOMIC ABSORPTION SPECTROMETRY)

Not more than 5 ppm.

For the preparation of all aqueous solutions and for the rinsing of glassware before use, employ water that has been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin before use. Select all reagents to have as low a content of cadmium, lead and nickel as practicable and store all reagent solutions in containers of borosilicate glass. Clean glassware before use by soaking in warm 8M nitric acid for 30 min and by rinsing with deionised water.

Blank solution:

Use the solution described in the test for cadmium.

Modifier solution:

Dissolve 20g of ammonium dihydrogen phosphate in water R and dilute to 100mL with the same solvent.

Alternatively, use an appropriate matrix modifier as recommended by the GFAA spectrometer manufacturer.

Test solution:

Use the solution described in the test for cadmium.

Reference solution:

Prepare a solution of 0.050 µg/mL of Ni by suitable dilutions of a 0.2477 µg/mL solution of nickel nitrate hexahydrate in the blank solution.

Prepare mixtures of the test solution, the reference solution and the blank solution in the following proportions: (1.0:0:1.0 V/V/V), (1.0:0.5:0.5 V/V/V), (1.0:1.0:0 V/V/V). To each mixture add 50 µL of matrix modifier solution and mix. These reference solutions contain respectively 0 µg, 0.0125 µg and 0.025 µg of nickel per millilitre from the reference solution.

Source: Nickel hollow-cathode lamp.

Wavelength: 232.0 nm.

Atomisation device: Furnace.

Platform: Pyrolytically coated with integrated tube.

Operating conditions:

Use the temperature programme recommended for nickel by the GFAA spectrometer manufacturer. An example of temperature parameters for GFAA analysis of nickel is shown below.

Stage	Final temperature (°C)	Ramp time (s)	Hold time (s)
Drying	110	10	20
Ashing	1000	20	30
Atomisation	2300	0	5

10. LOSS ON DRYING: < REFER GAM 026>

Not more than 6.0 per cent, determined on 1.0g by drying in an oven at 105°C.

11. ASSAY:

Magnesium:

Weigh 0.5g of sample in a 250ml conical flask, add 50ml of a mixture of equal volumes of anhydrous ethanol and butanol, 5ml of concentrated ammonia, 3ml of ammonium chloride buffer solution pH 10.0, 30.0ml of 0.1M sodium edetate and 15mg of mordant black II triturate. Heat at 45°C to 50°C until the solution is clear and titrate with 0.1M zinc sulphate until the colour changes from blue to violet. Carry out a blank titration.

1ml of 0.1 M sodium edetate is equivalent to 2.431 g of Mg.

Calculation:

$$= \frac{\text{Titer value-Blank value x Molarity of 0.1M disodium edetate x 2.431 x 100 x 100}}{\text{0.1 x Sample weight in mg x (100 – Sample LOD)}}$$

12. STEARIC ACID AND PALMITIC ACID:

Determine by gas chromatography:

Test solution:

In a conical flask fitted with a reflux condenser, dissolve 0.10g of the substance to be examined in 5mL of boron trifluoride-methanol solution. Boil under a reflux condenser for 10 min. Add 4 mL of heptane through the condenser and boil again under a reflux condenser for 10 min. Allow to cool. Add 20 mL of saturated sodium chloride solution. Shake and allow the layers to separate. Dry the organic layer over 0.1g of anhydrous sodium sulfate (previously washed with heptane). Dilute 1.0mL of the solution to 10.0mL with heptane.

Reference solution:

Prepare the reference solution in the same manner as the test solution using 50.0 mg of palmitic acid CRS and 50.0mg of stearic acid CRS instead of the substance to be examined.

Chromatographic conditions:

Material	:	Fused silica;
Size	:	l = 30 m, Ø = 0.32 mm;
Stationary phase	:	Macrogol 20,000 (film thickness 0.5 µm).
Carrier gas	:	Helium for chromatography.
Flow rate	:	2.4 mL/min.
Detection	:	Flame ionisation.
Injection	:	1 µL.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 2	70
	2 - 36	70 → 240
	36 - 41	240
Injection port		220
Detector		260

Relative retention:

With reference to methyl stearate: methyl palmitate = about 0.9.

System suitability: Reference solution.

Resolution: Minimum 5.0 between the peaks due to methyl palmitate and methyl stearate;

Relative standard deviation:

Maximum 3.0 per cent for the areas of the peaks due to methyl palmitate and methyl stearate, determined on 6 injections; maximum 1.0 per cent for the ratio of the areas of the peaks due to methyl palmitate to the areas of the peaks due to methyl stearate, determined on 6 injections.

13. MICROBIAL CONTAMINATION:

Total Viable aerobic count and Pathogen test refer as per the current SOP No: ST/MB/011.

REVISION HISTORY:

STP No.	Reason for Review	Change control No.	Effective Date
STP-RMEM0033-00	(i) STP numbering procedure revised as per SOP No. ST/QC/058. (ii) Testing procedure for acid value has been incorporated in the identification test.	ST/CC/23/063 ST/CC/24/067	14/03/2024

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

Particulars	PREPARED BY	REVIEWED BY	APPROVED BY
Name	K.SARAVANAN	M.VIJAYAKUMAR	S.MARAN
Designation	Dy. Manager-QC	GM-QC	AGM-QA
Signature			
Date	12/03/2024	13/03/2024	13/03/2024