BIOSPECTRA
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DEGRADATION AND IMPURITY PROFILE REPORT: 2-MEA

TABLE OF CONTENTS

1. PURPOSE AND SCOPE:

1.1. The impurity profiling of 2-MEA was intended to identify and possibly quantify impurities found in the 2-MEA product manufactured at BioSpectra, in the Bangor, PA facility.

1.1.1. In the case where an impurity was found, a limit was set to the maximum allowable present without measurable compromise to predetermined critical quality attributes or toxicity. In the case where a limit could not be set, a procedure was written and followed,to identify if the possible impurity was present or not (i.e. an identity test, which is qualitative and not quantitative.)

1.1.2. The profiling results and data allowed BioSpectra to further understand the purity and characteristics of 2-MEA.

1.1.3. The four stages of 2-MEA that were tested are Raw Material (2-MEA), Mother Liquor, Wet Crystals, and Finished Goods.

1.1.4. The tests that were used to determine the presence of impurities and degradation products were as follows:

1.1.4.1. Appearance and Color

1.1.4.1.1. RM (each lot), FG Beginning Drum Batch 1

1.1.4.2. Appearance of Solution

1.1.4.2.1. RM (each lot), FG Beginning Drum Batch 1

1.1.4.3. HPLC Purity

1.1.4.3.1. RM (each lot), ML, WC Batch 1, FG Beginning Drum Batch 1

1.1.4.4. Identification (IR)

1.1.4.4.1. RM (each lot), WC Batch 1, FG Beginning Drum Batch 1

1.1.4.5. Loss on Drying

1.1.4.5.1. RM (each lot), WC Batch 1, FG Beginning Drum Batch 1

1.1.4.6. Residual Solvents

1.1.4.6.1. RM (each lot), FG Beginning Drum Batch 1

1.1.4.7. Trace Elements / Elemental Impurities

1.1.4.7.1. RM (each lot), ML, WC Batch 1, FG Beginning Drum Batch 1

2. RESPONSIBILITIES:

2.1. Quality Control Management was responsible for control, implementation, training, and maintenance of this procedure.

2.2. The QC Analysts were responsible for performing the testing stated in this Protocol and recording all results in the appropriate laboratory documentation.

2.3. The QC Compliance team, or qualified designee, were responsible for completing the degradation and impurity testing report.

3. REFERENCES:

3.1. BSI-ATM-0024, 2-MEA Testing Methods

3.2. BSI-ATM-0061, Method of Analysis: Determination of Elemental Impurities by ICP-MS in 2-MEA

3.3. BSI-PRL-0403, Analytical Method Validation Protocol: Aqueous Soluble Residual Solvents (2-MEA)

3.4. BSI-PRL-0415, Degradation and Impurity Profile Protocol: 2-MEA

3.5. BSI-RPT-1064, Elemental Impurity Assessment: Cysteamine HCl (2-MEA) 2022 Validation

3.6. BSI-SPC-0259, CSMH-3250 Cysteamine HCl (2-MEA) Bio Excipient Specifications

3.7. BSI-SOP-0102, Degradation and Impurity Profiling SOP

4. PROCEDURE:

4.1. APPEARANCE AND COLOR:

4.1.1. Refer to the Degradation and Impurity Profile Protocol: 2-MEA for testing methods and requirements. The results of the appearance and color testing are detailed in the table below.

TABLE 1: APPEARANCE AND COLOR

Lot	Stage	Specification	Result
RMAT-0222-0099	Raw Material	Monitor	White, Crystals
CSMH-0122-00033-PV Drum 1	Finished Good	White or Colorless Crystals or Powder, may contain lumps	White or Colorless Crystals or Powder, may contain lumps

4.2. APPEARANCE OF SOLUTION:

4.2.1. Refer to the Degradation and Impurity Profile Protocol: 2-MEA for testing methods and requirements. The results of the appearance of solution testing are detailed in the table below.

TABLE 2: APPEARANCE OF SOLUTION

Lot	Stage	Specification	Result
RMAT-0222-0099	Raw Material	Monitor	Colorless, Clear Solution
CSMH-0122-00033-PV Drum 1	Finished Good	Colorless, Clear Solution	Colorless, Clear Solution

4.3. HPLC PURITY:

4.3.1. Refer to the Degradation and Impurity Profile Protocol: 2-MEA for testing methods and requirements. The results of the HPLC Purity testing are detailed in the table below.

TABLE 3: HPLC PURITY

Lot	Stage	Specification	Result
RMAT-0222-0099	Raw Material	Monitor	99.7%
CSMH-0122-00033-PV ML	Mother Liquor		100.0%
CSMH-0122-00033-PV WC Basket 1	Wet Crystals		100.0%
CSMH-0122-00033-PV WC Basket 2			100.0%
CSMH-0122-00033-PV WC Basket 3			100.0%
CSMH-0122-00033-PV Drum 1	Finished Good	≥98%	100.0%

4.4. **IDENTIFICATION TEST (IR)** :

4.4.1. Refer to the Degradation and Impurity Profile Protocol: 2-MEA for testing methods and requirements. The results of the Identification IR testing are detailed in the table below.

TABLE 4: IDENTIFICATION (IR)

Lot	Stage	Specification	Result
RMAT-0222-0099	Raw Material	Monitor	Passes Test; 0.988599
CSMH-0122-00033-PV WC Basket 1	Wet Crystals		Passes Test; 0.969964
CSMH-0122-00033-PV WC Basket 2			Passes Test; 0.985509
CSMH-0122-00033-PV WC Basket 3			Passes Test; 0.968128
CSMH-0122-00033-PV Drum 1	Finished Good	Conforms to Reference Standard	Conforms to Reference; 0.988931

4.5. **LOSS ON DRYING** :

4.5.1. Refer to the Degradation and Impurity Profile Protocol: 2-MEA for testing methods and requirements. The results of the Loss on Drying testing are detailed in the table below.

TABLE 5: LOSS ON DRYING

Lot	Stage	Specification	Result
RMAT-0222-0099	Raw Material	Monitor	0.2802%
CSMH-0122-00033-PV WC Basket 1	Wet Crystals		2.5828%
CSMH-0122-00033-PV WC Basket 2			1.5004%
CSMH-0122-00033-PV WC Basket 3			2.5775%
CSMH-0122-00033-PV Drum 1	Finished Good	≤1.0%	0.5070%

4.6. **RESIDUAL SOLVENTS** :

4.6.1. Refer to the Degradation and Impurity Profile Protocol: 2-MEA for testing methods and requirements. The results of the residual solvents testing are detailed in the table below.

TABLE 6: RESIDUAL SOLVENTS

Lot	Stage	Specification	Result		
			Ethanol	IPA	TBME
RMAT-0222-0099	Raw Material	Monitor	<2380ppm	3340 ppm	ND[1]
CSMH-0122-00033-PV Drum 1	Finished Good	Conforms to USP <467><1467>	ND	<2640 ppm	ND[1]

[1]ND = None Detected

4.7. **TRACE ELEMENTS/ELEMENTAL IMPURITY :**

4.7.1. Refer to the Degradation and Impurity Profile Protocol: 2-MEA for testing methods and requirements. The results of the trace metal and elemental impurity testing are detailed in the table below.

TABLE 7: TRACE METALS/ELEMENTAL IMPURITY

Lot	Stage	Specification	Result
RMAT-0222-0099	Raw Material	Report	Refer to BSI-RPT-1064 for Elemental Impurity Assessment
CSMH-0122-00033-PV ML	Mother Liquor		
CSMH-0122-00033-PV WC Basket 1	Wet Crystals		
CSMH-0122-00033-PV WC Basket 2			
CSMH-0122-00033-PV WC Basket 3			
CSMH-0122-00033-PV Drum 1	Finished Good	Refer to BSI-SPC-0259	

5. CONCLUSION:

5.1. All samples met the specifications for the required analyses as dictated in the Degradation and Impurity Profile Protocol: 2-MEA.

5.2. It can be concluded that there are no additional identifiable impurities in the 2-MEA material at any stage of the process at this time.