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DEGRADATION AND IMPURITY PROFILE REPORT:
GUANIDINE THIOCYANATE 2022
PROCESS VALIDATION: BSI-PRL-0551

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1. PURPOSE AND SCOPE:

- 1.1. The impurity profiling of Guanidine Thiocyanate was intended to identify and possibly quantify impurities found in the product manufactured and purified at BioSpectra.
 - 1.1.1. In the case where an impurity was found, a limit was set to the maximum allowable without measurable compromise to predetermined critical quality attributes. 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 Guanidine Thiocyanate.
 - 1.1.3. The four stages of Guanidine Thiocyanate that were tested are the raw material, the mother liquor, the wet crystals, and the finished goods. The stage analyzed was dictated by the analysis required.
 - 1.1.4. The tests that were used to determine the presence of impurities and degradation products were as follows:
 - 1.1.4.1. Absorbance (1.7M and 70%)
 - 1.1.4.6.1 Raw Material
 - 1.1.4.6.2 Wet Crystal
 - 1.1.4.6.3 Finished Good Beginning Drum
 - 1.1.4.2. Appearance and Color
 - 1.1.4.6.4 Raw Material
 - 1.1.4.6.5 Finished Good Beginning Drum
 - 1.1.4.3. Assay
 - 1.1.4.6.6 Raw Material
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 - 1.1.4.4. Elemental Impurities with the addition of Ba, Fe, K, and Na
 - 1.1.4.6.9 Raw Material
 - 1.1.4.6.10 Mother Liquor
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 - 1.1.4.6.12 Finished Good Beginning Drum
 - 1.1.4.5. Identification (IR)
 - 1.1.4.6.13 Raw Material
 - 1.1.4.6.14 Finished Good Beginning Drum
 - 1.1.4.6. pH (5%)
 - 1.1.4.6.15 Raw Material
 - 1.1.4.6.16 Finished Good Beginning Drum
 - 1.1.4.7. Loss on Drying
 - 1.1.4.7.1 Finished Good Beginning Drum
 - 1.1.4.7.2 Water is the only solvent used in the synthetic pathway for the Raw Material.
 - 1.1.4.8. Solubility 6M
 - 1.1.4.8.1 Raw Material
 - 1.1.4.8.2 Finished Good Beginning Drum

- 1.2. Only approved Raw Material was used in the manufacturing process during process validations. When Applicable, the Raw Material analysis was transcribed from the completed summary sheet.
- 1.3. All results were recorded in the appropriate laboratory documentation. The results were detailed and analyzed in this report. This report includes all relevant data as well as references to the initial documented results. This report discusses any impurities found in the product and includes a specification for any limits on the impurities found when applicable.

2. RESPONSIBILITIES:

- 2.1. The QC Lab Manager was responsible for control, implementation, training and maintenance of this procedure.
- 2.2. The QC Analysts were responsible for performing the testing stated in the protocol.
- 2.3. The QC Systems Team was responsible for completing the degradation and impurity testing report.

3. REFERENCES:

- 3.1. BSI-ATM-0003, Guanidine Thiocyanate Testing Methods
- 3.2. BSI-ATM-0073, Analytical Method of Analysis: Guanidine Thiocyanate, MOPS, and Urea via ICP-MS
- 3.3. BSI-SOP-0102, Degradation and Impurity Profiling SOP

4. PROCEDURE:

- 4.1 **ABSORBANCE (1.7M)** :
- 4.1.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Absorbance 1.7M testing are detailed in the table below.

TABLE 1: ABSORBANCE (1.7M)

Lot Number	Stage of Material	Specification	Result		
			280 nm	300 nm	340 nm
RMAT-0921-0062	Raw Material	0.3000 a.u. max @ 280 nm 0.0500 a.u. max @ 300 nm 0.0300 a.u. max @ 340 nm	0.1193	0.0171	0.0044
GTHI-0122-00008-PV WC Top	Wet Crystals	0.3000 a.u. max @ 280 nm 0.050 a.u. max @ 300 nm 0.030 a.u. max @ 340 nm	0.0941	0.0115	0.0026
GTHI-0122-00008-PV WC Bottom			0.0915	0.0096	0.0011
GTHI-0122-00008-PV Beginning Drum	Finished Goods	0.300 a.u. max @ 280 nm 0.050 a.u. max @ 300 nm 0.030 a.u. max @ 340 nm	0.0951	0.0103	0.0012

4.2. **ABSORBANCE (70%)** :

- 4.2.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Absorbance 70% testing are detailed in the table below.

TABLE 2: ABSORBANCE 70%

Lot Number	Stage of Material	Specification	Result
			280 nm
RMAT-0921-0062	Raw Material	0.8000 a.u. max @ 280 nm	0.4661
GTHI-0122-00008-PV WC Top	Wet Crystals	Monitor	0.3416
GTHI-0122-00008-PV WC Bottom			0.3397
GTHI-0122-00008-PV Beginning Drum	Finished Goods	0.8000 a.u. max @ 280 nm	0.3485

4.3. **APPEARANCE AND COLOR** :

- 4.3.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Appearance and Color testing are detailed in the table below.

TABLE 3: APPEARANCE AND COLOR

Lot Number	Stage of Material	Specification	Result
RMAT-0921-0062	Raw Material	White/Crystals	White/Crystals
GTHI-0122-00008-PV Beginning Drum	Finished Goods	White/Crystals	White/Crystals

4.4. **ASSAY** :

- 4.4.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Assay testing are detailed in the table below.

TABLE 4: ASSAY

Lot Number	Stage of Material	Specification	Result
RMAT-0921-0062	Raw Material	99.0% min (As-Is)	99.8%
PMAT-0622-00613	Mother Liquor	Monitor	60.27%
GTHI-0122-00008-PV Beginning Drum	Finished Goods	99.5% min (Dried)	99.9%

4.5. **ELEMENTAL IMPURITIES W/ADDITION OF Ba, Fe, K, AND Na** :

- 4.5.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Elemental Impurities w/ addition of Ba, Fe, K, and Na testing are detailed in the table below.
- 4.5.2. Finished Good EI analysis was in accordance with USP<232><233> and ICHQ3D Option 1:10gram MDD.

TABLE 5: ELEMENTAL IMPURITIES W/ ADDITION OF BA, FE, K, AND NA

Lot Number	Stage of Material	Specification	Result
RMAT-0921-0062	Raw Material	Monitor	Refer to BSI-RPT-1053 for Elemental Impurity Assessment
PMAT-0622-00613	Mother Liquor		
GTHI-0122-00008-PV WC Top	Wet Crystal		
GTHI-0122-00008-PV WC Bottom	Wet Crystal		
GTHI-0122-00008-PV Beginning Drum	Finished Good	<5ppm Ba <5ppm Fe <50ppm K <5000ppm Na	

4.6. **IDENTITY (IR)** :

- 4.6.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Identity (IR) testing are detailed in the table below.

TABLE 6: IDENTITY (IR)

Lot Number	Stage of Material	Specification	Result
RMAT-0921-0062	Raw Material	Passes Test	Passes Test; 0.995097
GTHI-0122-00008-PV Beginning Drum	Finished Goods	Passes Test	Passes Test; 0.985957

4.7. **pH (5%)** :

- 4.7.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the pH (5%) testing are detailed in the table below.

TABLE 7: PH (5%)

Lot Number	Stage of Material	Specification	Result
RMAT-0921-0062	Raw Material	Monitor	5.52 @ 23.1°C
GTHI-0122-00008-PV Beginning Drum	Finished Good	5.0-6.5	5.6 @ 23.2°C

4.8. **LOSS ON DRYING** :

4.8.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Loss on Drying testing are detailed in the table below.

TABLE 8: LOSS ON DRYING

Lot Number	Stage of Material	Specification	Result
GTHI-0122-00008-PV Beginning Drum	Finished Good	0.5% max	0.2%

4.9. **SOLUBILITY 6M** :

4.9.1. Refer to Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022 for testing methods and requirements. The results of the Solubility 6M testing are detailed in the table below.

TABLE 9: SOLUBILITY 6M

Lot Number	Stage of Material	Specification	Result
RMAT-0921-0062	Raw Material	Monitor	Passes Test
GTHI-0122-00008-PV Beginning Drum	Finished Good	Clear	Clear

5. CONCLUSION

- 5.1. All samples met the specifications for the required analyses as dictated in the Degradation and Impurity Profile Protocol: Guanidine Thiocyanate 2022.
- 5.2. It can be concluded that there are no additional identifiable impurities present in the Guanidine Thiocyanate material at any stage of the process at this time.