



100 Majestic Way, Bangor, PA 18013 / www.biospectra.us

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
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 - 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

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- 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 |

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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% |

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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 ICHQ3DOption 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.

Signature Manifest

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