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GUANIDINE HYDROCHLORIDE 6M SOLUTION 2022
MAJESTIC
LONG TERM STABILITY REPORT

TABLE OF CONTENTS

1. OVERVIEW:.....	3
TABLE 1: STABILITY SPECIFICATIONS	3
2. REFERENCES:	3
3. SAMPLE DESIGNATION:.....	4
TABLE 2: PACKAGING DETAILS.....	4
4. STORAGE:.....	4
TABLE 3: PACKAGING DETAILS.....	4
5. INVESTIGATIONS	4
6. LOT EVALUATION:.....	5
TABLE 4: GHCL-0122-00184 BLACK BOTTLE WITH BLACK CAP.....	5
TABLE 5: GHCL-0122-00184 NATURAL WHITE HDPE BOTTLE.....	6
GRAPH 1: ABSORBANCE @ 280 NM	7
GRAPH 2: ABSORBANCE @ 260 NM	8
GRAPH 3: MOLARITY	9
7. CONCLUSION:.....	10
8. STATEMENT OF COMMITMENT	10

1. OVERVIEW:

The purpose of this report is to analyze and conclude on the data obtained from the Long-Term Stability Study of Guanidine Hydrochloride 6M Solution manufactured at the Bangor, PA facility. Testing intervals are designated by T_n , where n = the number of months on stability. Testing is performed every three months for the first year, every six months for the second year and annually for each subsequent year in order to maintain that the manufactured product remains stable under the specified conditions and for the specified interval of time. The analysis of the compiled data may also aid in a re-evaluation of the retest date for the finished good product.

This Long-Term stability analysis will assess the stability of Guanidine Hydrochloride 6M Solution lot GHCL-0122-00184 that completed thirty-six (36) months of long-term stability in December 2025. This study includes the analyses listed in Table 1 below. Results from all analyses are summarized in Tables 4 and 5.

Table 1: Stability Specifications

Analysis	Specifications
Absorbance	0.05 max @ 260nm
	0.05 max @ 280nm
Appearance and Color	Clear Colorless Liquid
Identity (IR)	Passes Test
Melamine	Report
Molarity	5.8 – 6.2M
Solutions Test	Passes Test

The data was analyzed utilizing a shelf-life plot, which determines the point in time at which the slope would exceed the acceptance criteria. As long as the slope has a statistically significant difference from zero using a 95% confidence limit, an estimated time in months can be established at which the acceptance criteria will no longer be met, i.e. the shelf life. This allows BioSpectra to ensure that the product is stable over the time period in which it is part of the stability program. All quantitative data was analyzed using these methods.

The stability program is designed to analyze for the stability indicating analyses established for a product in accordance with the Stability Testing Program, BSI-SOP-0136. The study is used to trend the data to determine if there is any significant change over the course of the study to establish the shelf life of the product. This study will be used to establish shelf life for all product codes for Guanidine Hydrochloride 6M Solution. The following product codes are commercially available:

- GHCL-3101

2. REFERENCES:

- 2.1. BSI-SOP-0136, Stability Testing Program
- 2.2. BSI-SOP-0146, Stability Inventory
- 2.3. Current USP
- 2.4. ICH Q1E

3. SAMPLE DESIGNATION:

- 3.1. The samples placed on the stability testing program consisted of one lot of Guanidine Hydrochloride 6M Solution. Stability samples from this lot were put in Black Bottle and Natural White Bottle packaging configurations. The samples were packaged in accordance with the Stability Inventory Procedure. Reference Table 2 for packaging configurations and descriptions. The type of packaging utilized in this stability study was based on BioSpectra's packaging configurations offered to the customer.

Table 2: Packaging Details

Packaging Configuration	Packaging Description
Black Bottle	The liquid sample is stored directly in the black HDPE container with the corresponding black lid
Natural White Bottle	The liquid sample is stored directly in the natural white HDPE container with the corresponding lid

4. STORAGE:

- 4.1. The Packaging and Storage requirements for Guanidine Hydrochloride 6M Solution are to be in tightly closed container in a dry and well-ventilated place. For this study, samples were stored in the Long-Term Stability Chamber at the Bangor, PA facility. For the time period of December 2022 to December 2025 the samples were located in the Real Time Stability Chamber, and all future time point samples remain at this condition. Storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}$), mean kinetic temperature (monitor) and relative humidity ($60\% \pm 5\%$). The storage conditions for the time period of this study are detailed in Table 3. Maximum and minimum values that are outside limits for temperature and humidity are due to opening the door of the chamber as explained in Temperature and Humidity Monitoring Assessments for the chambers. Section 5 will include any excursions from these conditions that resulted in an investigation.

Table 3: Packaging Details

Condition	Specification	Value
Minimum Temperature	$25^{\circ}\text{C} \pm 2^{\circ}\text{C}$	20.58°C
Maximum Temperature		25.73°C
Average Temperature		25.37°C
Mean Kinetic Temperature	Monitor	25.37°C
Minimum Humidity	60% RH \pm 5% RH	43.6%
Maximum Humidity		80.5%
Average Humidity		61.3%

5. INVESTIGATIONS

- 5.1. BDI24-13: Out of range humidity for the Real Time Stability Chamber H03SC01 caused by improper work order completion to prevent water leaking from the stability chamber. On 1/15/24 while conducting a maintenance walkthrough of the Bangor facility water was observed on the floor of room H03RM01. The issue was found to be a faulty pump and later repaired. There was no impact to the current list of materials in the stability chamber.

- 5.2. BDI24-126: Out of specification temperature and humidity for Real Time Stability Chamber H03SC01 occurred on 8/15/24. It was found that a fuse had blown which led to the decrease in humidity. The fuse was replaced and by 8/16/24, both temperature and humidity met specification. Total OOS time was 10 hours and 30 minutes. There was no impact to the material stored in this chamber.
- 5.3. BDI24-142: Melamine analysis was performed in duplicate for GHCL-0122-00184 t=12 Black Bottle with Black Cap. No Checklist was issued for this during review. There is no impact to the stability study as both packaging configurations at the t=12 time point had melamine results to report.
- 5.4. BSI-LI25-0019: Out of specification absorbance results at 260nm were obtained for GHCL-0122-00184 t=36 Natural White HDPE bottle. The investigation retests confirmed the initial out of specification result. There is no impact due to the absorbance failure as GHCL-0122-00184 was released with a 24-month retest date.

6. LOT EVALUATION:

Table 4: GHCL-0122-00184 Black Bottle with Black Cap

Time Point	Analyses/Specifications						
	Absorbance		Appearance and Color	Identity (IR)	Melamine	Molarity	Solutions Test
	0.05 max @ 260nm	0.05 max @ 280nm	Clear Colorless Liquid	Passes Test	Report	5.8 – 6.2M	Passes Test
T ₀	0.0140	<0.003	Clear Colorless Liquid	Passes Test	Passes Test	5.86M	Passes Test
T ₃	0.0214	0.0036	Clear Colorless Liquid	Passes Test	Passes Test	5.88M	Passes Test
T ₆	0.0229	0.0046	Clear Colorless Liquid	Passes Test	Passes Test	5.90M	Passes Test
T ₉	0.0232	0.0051	Clear Colorless Liquid	Passes Test	Passes Test	5.91M	Passes Test
T ₁₂	0.0248	0.0056	Clear Colorless Liquid	Passes Test	Passes Test	5.92M	Passes Test
T ₁₈	0.0267	0.0076	Clear Colorless Liquid	Passes Test	Passes Test	5.89M	Passes Test
T ₂₄	0.0285	0.0107	Clear Colorless Liquid	Passes Test	Passes Test	5.93M	Passes Test
T ₃₆	0.0331	0.0167	Clear Colorless Liquid	Passes Test	Passes Test	5.89M	Passes Test

REMAINING TESTING INTERVAL PULL DATES

T = 48; Scheduled for December 21, 2026

T = 60; Scheduled for December 21, 2027

Table 5: GHCL-0122-00184 Natural White HDPE Bottle

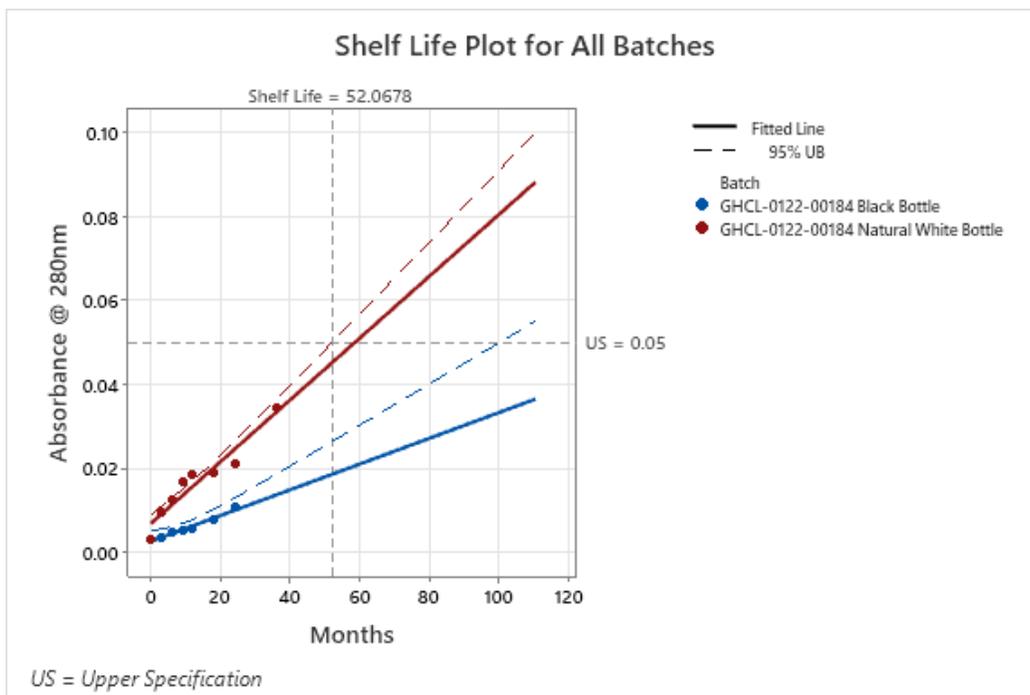
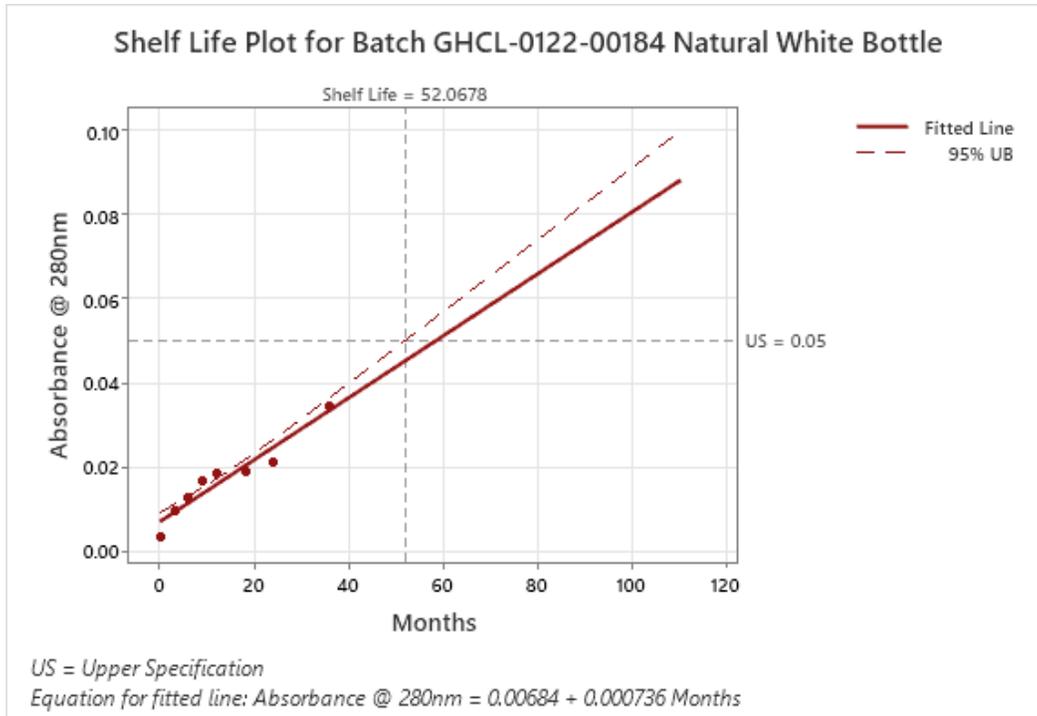
Time Point	Analyses/Specifications						
	Absorbance		Appearance and Color	Identity (IR)	Melamine	Molarity	Solutions Test
	0.05 max @ 260nm	0.05 max @ 280nm	Clear Colorless Liquid	Passes Test	Report	5.8 – 6.2M	Passes Test
T ₀	0.0140	<0.003	Clear Colorless Liquid	Passes Test	Passes Test	5.86M	Passes Test
T ₃	0.0346	0.0095	Clear Colorless Liquid	Passes Test	Passes Test	5.90M	Passes Test
T ₆	0.0391	0.0124	Clear Colorless Liquid	Passes Test	Passes Test	5.90M	Passes Test
T ₉	0.0444	0.0167	Clear Colorless Liquid	Passes Test	Passes Test	5.89M	Passes Test
T ₁₂	0.0470	0.0184	Clear Colorless Liquid	Passes Test	Passes Test	5.91M	Passes Test
T ₁₈	0.0464	0.0188	Clear Colorless Liquid	Passes Test	Passes Test	5.86M	Passes Test
T ₂₄	0.0497	0.0211	Clear Colorless Liquid	Passes Test	Passes Test	5.91M	Passes Test
T ₃₆	0.0667 ¹	0.0343	Clear Colorless Liquid	Passes Test	Passes Test	5.87M	Passes Test

¹Refer to BSI-LI25-0019

REMAINING TESTING INTERVAL PULL DATES

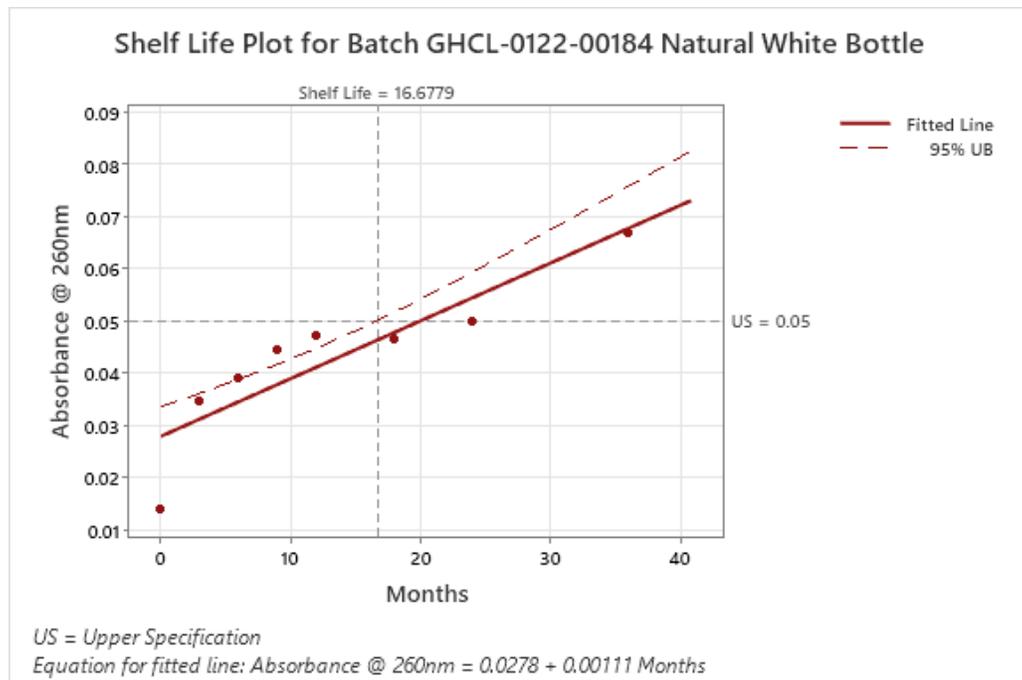
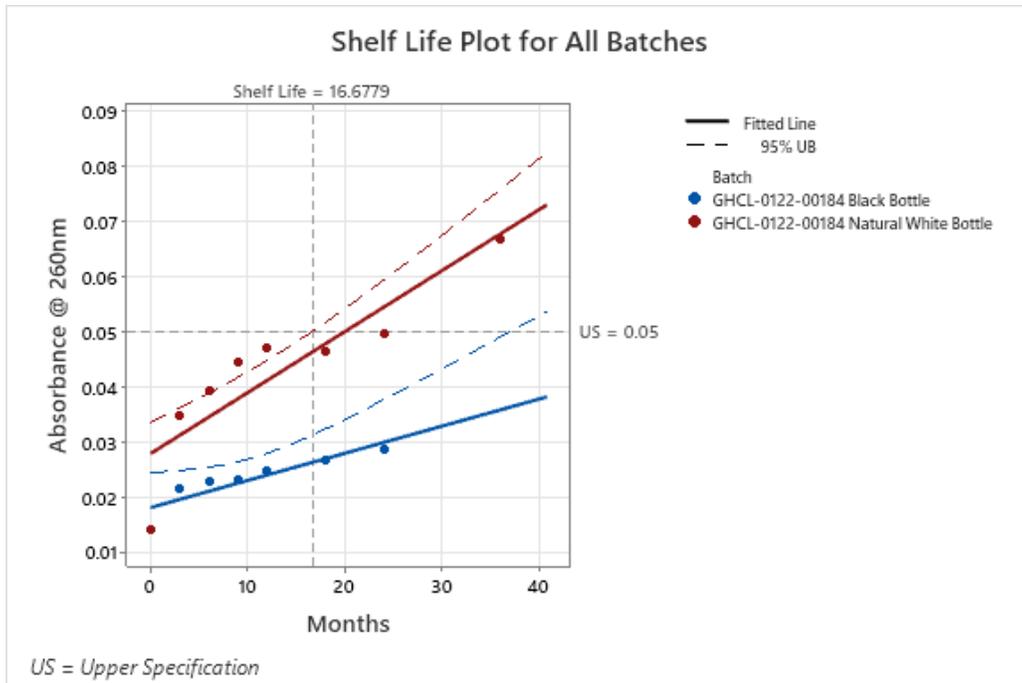
T = 48; Scheduled for December 21, 2026

T = 60; Scheduled for December 21, 2027



Graph 1: Absorbance @ 280 nm

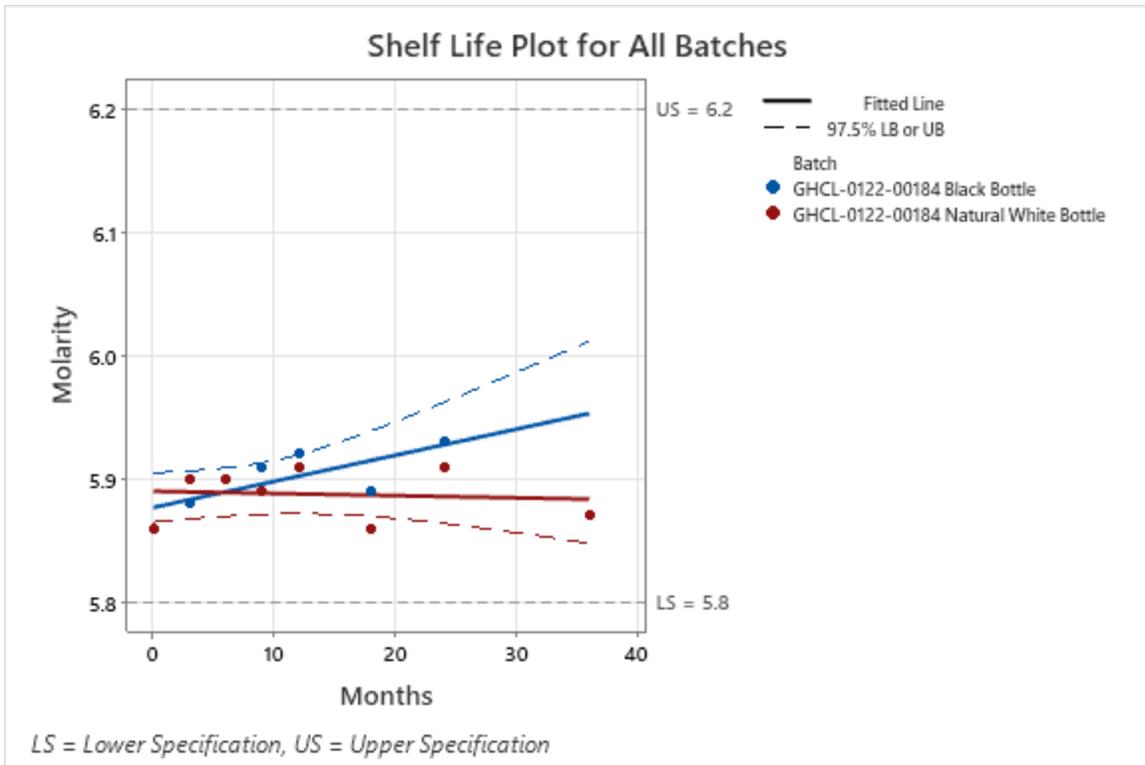
The predicted shelf-life of the batches tested for Absorbance at 280 nm was determined to be 52.0678 months as of the T=36-month time interval. There is no impact to the product or currently assigned retest period of this material.



Graph 2: Absorbance @ 260 nm

The predicted shelf-life for Absorbance at 260 nm was determined to be 16.6779 months as of the T=36-month time interval for batch GHCL-0122-00184 packaged in Natural White Bottles. The shelf-life is defined as the time period in which you may be 95% confident that at least 50% of the response is within the required limits of specifications. All data up to the 24-month time point met the required specification. The material was out of specification in the Natural White Bottle for absorbance at 260nm at t=36 time point, however, remained passing in the Black Bottle. There is no impact as this is outside of the assigned 24-month retest date.

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Graph 3: Molarity

No shelf-life was able to be determined for Molarity at the 36-month time point, as the mean response slope is not significantly different from zero using 95% confidence. There is no impact to the product or currently assigned retest period of this material.

7. CONCLUSION:

In regards to the long-term stability study, all data met the specifications set forth in the stability testing program for one lot of Guanidine Hydrochloride 6M solution stored at the recommended long-term condition. In accordance with ICH Q1E, the retest date may be proposed for up to 2x, where x is the period covered by long-term stability data, but should be no more than 12 months beyond for real time conditions. Long-Term stability data displayed in this report up to 36 months of testing of Guanidine Hydrochloride 6M Solution manufactured at BioSpectra in the Bangor, PA facility, support a retest date of 24 months for Guanidine Hydrochloride 6M Solution.

8. STATEMENT OF COMMITMENT

- 8.1. BioSpectra is responsible for the following regarding stability data in this report:
 - 8.1.1. In the event that any real time stability analysis produces results found to be out of specification, the batch produced immediately before and after will be tested in full and analyzed in comparison with the batch in question.
 - 8.1.2. This will serve to provide information to effectively ensure that the root cause of the investigation has not impacted the batch manufactured before or after the batch in question.
 - 8.1.3. If a stability analysis is found to be out of specification and the product has an established shelf life, the batch will be withdrawn from the market through communication with any customer. Additionally, an investigation will be conducted to determine the possible withdrawal of the batches produced before and after the batch in question.
 - 8.1.4. In the event that any out of specification results are confirmed, all authorized users of the material will be notified.