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GUANIDINE HYDROCHLORIDE 6M SOLUTION

2016 - 2017

LONG TERM STABILITY REPORT

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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 Stroudsburg 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.

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 Testing Program. All quantitative data was analyzed using these methods. The data can be found in the Guanidine Hydrochloride 6M Solution Real Time Stability Program binders.

This Long Term Stability analysis will assess the stability of 3 lots of Guanidine Hydrochloride 6M Solution. Two lots were placed on stability in 2013, concluding the stability studies in 2016. One lot was place on stability in 2014, concluding the stability study in 2017.

2. DEFINITIONS:

CL: Control Limit, the average

UCL: Upper control limit, 3 sigma above the CL

LCL: Lower control limit, 3 sigma below the CL

OOT: Out Of Trend, this means that the material still meets control limits but was not in trend with the rest of the material.

OOS: Out of Specification, for the purpose of this stability analysis, OOS will mean that there is a point(s) that fall outside of the UCL or LCL.

3. SAMPLE DESIGNATION:

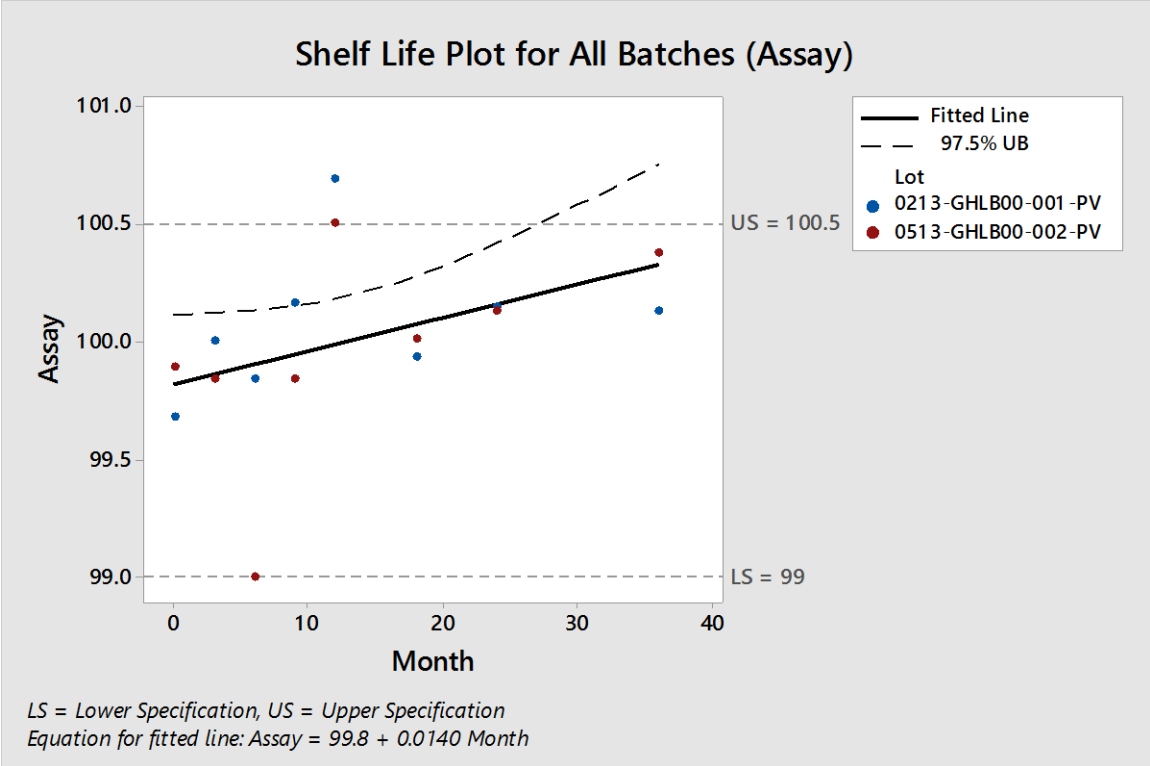
Samples initially placed on the Stability Testing Program consisted of all process validation batches and one lot per year. Stability samples from each of these batches were packaged in bottles representative of Finished Good lots that are packed out in totes. Samples were placed in the Long Term Stability area located in the Stroudsburg, PA BioSpectra facility.

4. STORAGE:

Although there is no storage conditions for Guanidine Hydrochloride 6M Solution, storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature (15-30°C) and humidity (monitor).

5. LOT ANALYSIS 2013 BATCHES:

Graph 1. Assay (%) For 2013



Results for assay showed no predictable shelf life as the mean response slope is not significantly different from zero. This is observed as there is negligible degradation of the product shown from these analyses in the 36 month analysis time frame.

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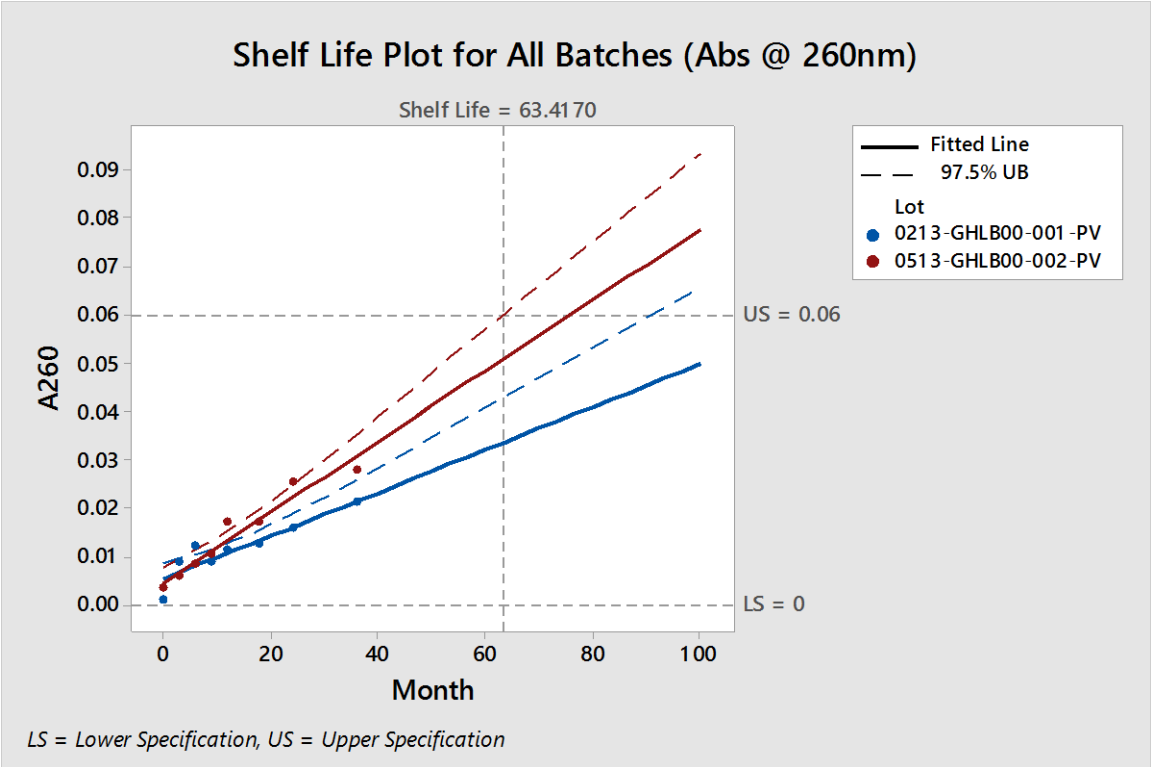
Graph 2. Abs @ 260nm for 2013



A Shelf life of 63.4170 months was predicted based on data for absorbance @ 260nm. The predicted shelf life exceeds the current 24 month retest date as well as the 36 month maximum expiration date assigned to this material.

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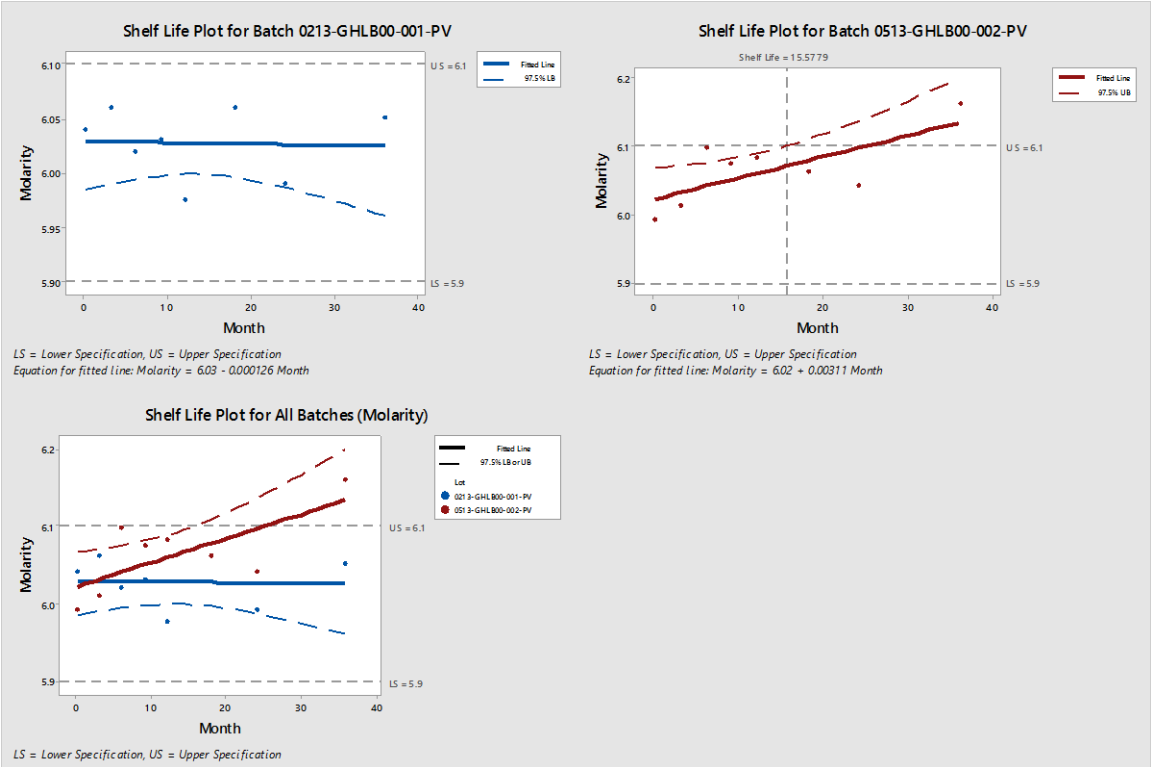
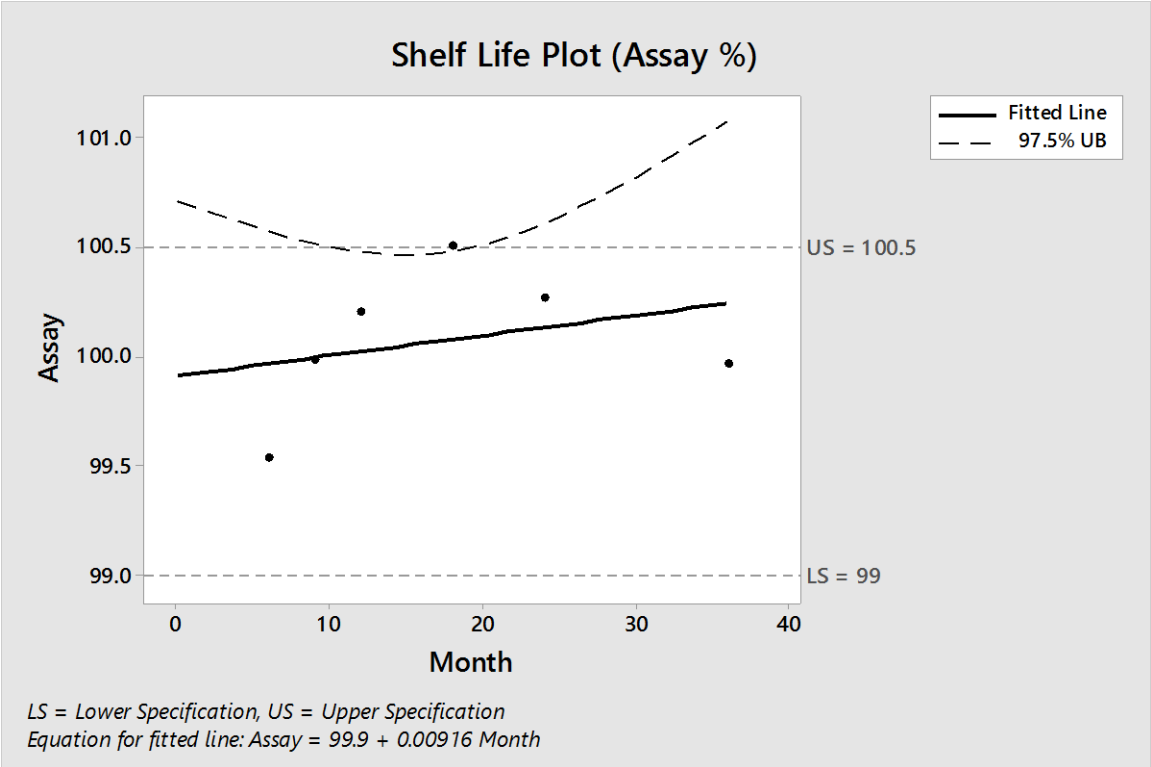
Graph 3. Molarity for 2013



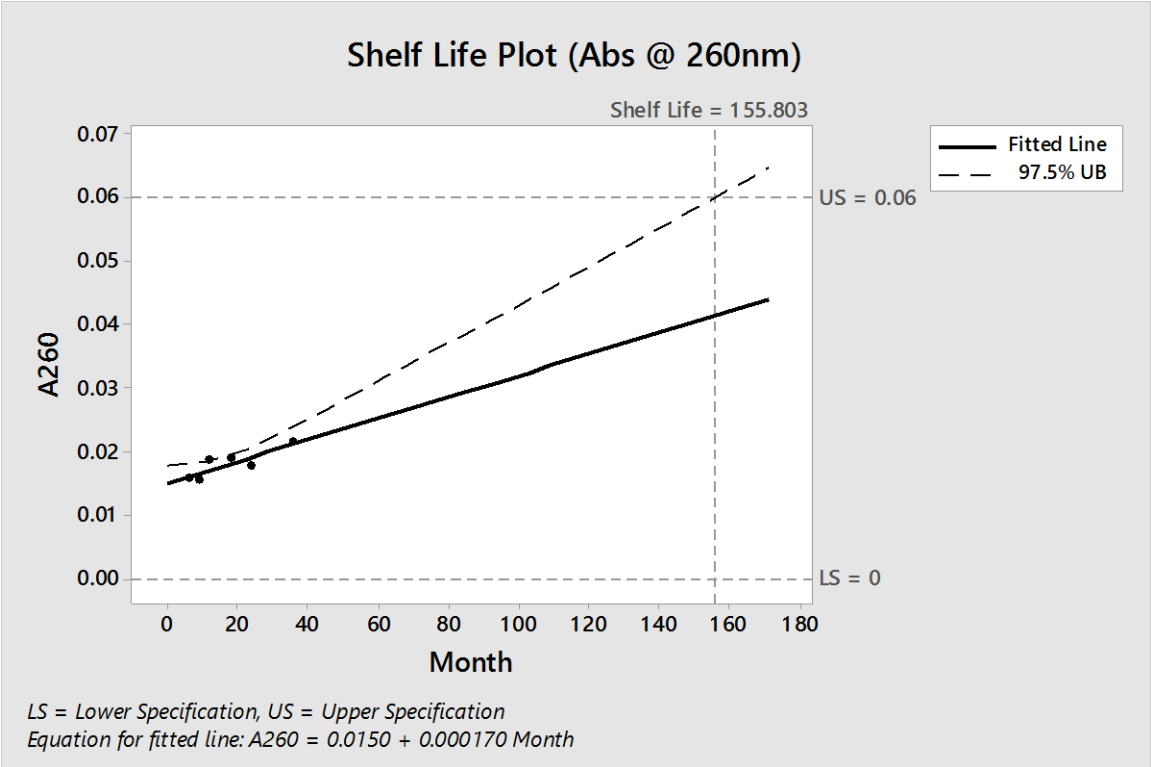
A Shelf life of 15.5779 months was predicted based on data for molarity for 0513-GHLB00-002-PV. The predicted shelf life does not exceed the current 24 month retest date as well as the 36 month maximum expiration date assigned to this material. However this is most likely due to an OOS results obtained from the T=36 time point for this lot. An investigation was initiated for this result and it was concluded that it was an isolated incident. No further action was taken due the OOS occuring at T=36 since the assigned retest date was 24 months. The shelf life graph for the pooled data of both 2013 lots shows no predictable shelf life as the mean response slope is not significantly different from zero. This is observed as there is negligible degradation of the product shown from these analyses in the 36 month analysis time frame.

Graph 4. Assay (%) for 0214-GHLB00-001



Results for assay showed no predictable shelf life as the mean response slope is not significantly different from zero. This is observed as there is negligible degradation of the product shown from these analyses in the 36 month analysis time frame.

Graph 5. Abs @ 260nm For 0214-GHLB00-001



A Shelf life of 155.803 months was predicted based on data for absorbance @ 260nm. The predicted shelf life exceeds the current 24 month retest date as well as the 36 month maximum expiration date assigned to this material.

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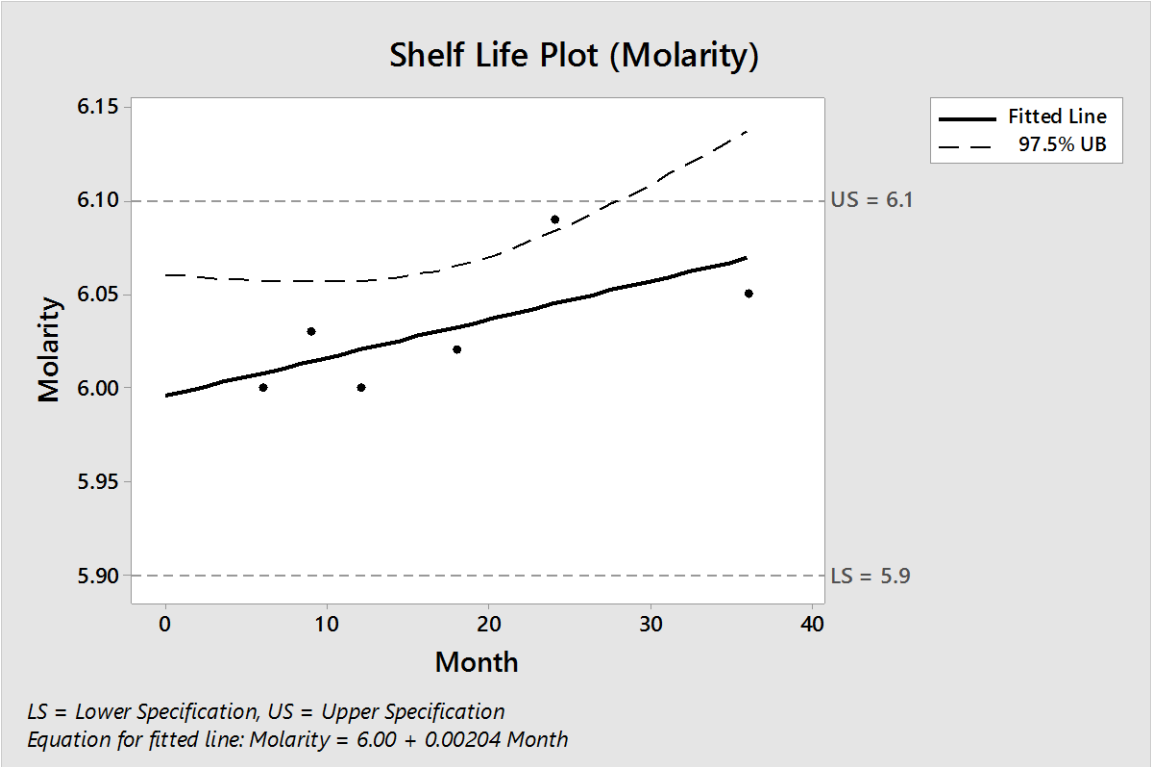
Graph 6. Molarity for 0214-GHLB00-001



Results for molarity showed no predictable shelf life as the mean response slope is not significantly different from zero. This is observed as there is negligible degradation of the product shown from these analyses in the 36 month analysis time frame.

6. CONCLUSION:

Long Term Stability Data obtained for lots manufactured in 2013 and 2014 indicate that the material packaged in totes is stable for a minimum of 36 months. The OOS molarity result for 0513-GHLB00-002-PV T=36 is considered acceptable as it was concluded to be an isolated incident. A 2 year retest date remains for this material packaged in totes since all lots that have reached the 24 month data point have met specifications. Additional time after the two years may be given based on historical and current data up to one year after a retest has been conducted.

7. STATEMENT OF COMMITMENT:

- BioSpectra is responsible for the following regarding Stability Data in this report:

- In the event that any 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.
    - 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.
- If a stability analysis is found to be out of specification, the batch will be withdrawn from the market through communication with the Applicant and any additional customer. Additionally, an investigation will be conducted to determine the possible withdrawal of the batches produced before and after the batch in question.
- In the event that any out of specification results are confirmed, all authorized users of the material will be notified.