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

POTASSIUM BROMIDE REAL-TIME STABILITY REPORT: PB2201-172-0318

TABLE OF CONTENTS

1. OVERVIEW:

The purpose of this report is to analyze and conclude on the data obtained from the real-time stability study of Potassium Bromide (KBr). 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 confirm 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 Real Time Stability analysis will assess the stability of Potassium Bromide lot PB2201-172-0318 that completed three years of real-time stability in March 2021. The study included the following analyses: Absorbance (1M), Assay, Limit of Chlorine and Loss on Drying (LOD). Results from all analyses are summarized in Table 2. The quantitative 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 specifications for the stability indicating analyses are established in accordance with the Stability Indication Protocol BSI-SOP-0289 when a new product is manufactured. 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 of Potassium Bromide (KBr). The following Product Codes are commercially available.

- KBRO-2201
- KBRO-2220
- KBRO-2301
- KBRO-2302

2. REFERENCES:

2.1. BSI-SOP-0136, Stability Testing Program
2.2. BSI-SOP-0146, Stability Inventory
2.3. BSI-SOP-0289, Stability Indication Protocol
2.4. Current USP
2.5. ICH Q1E

3. SAMPLE DESIGNATION:

3.1. Samples initially placed on the stability program consisted of one lot of Potassium Bromide. Stability samples from this batch were put into 2P/P packaging configuration. The samples were packaged in accordance with Stability Inventory DCN: BSI-SOP-0146. Reference Table 1, below, for packaging configuration and description. The type of packaging utilized in this stability study was based on BioSpectra packaging offered to the customer.

TABLE 1: PACKAGING DETAILS

Packaging Configuration	Packaging Description
2P/P	Samples are packaged into small poly bags and sealed with a zip tie. All individual samples are then placed into a larger poly bag, sealed with a zip tie, and then are placed into a poly drum.

4. STORAGE:

4.1. The USP Packaging and Storage requirements for Potassium Bromide are to be in well-closed containers stored at room temperature. For this study, the samples were stored in the Controlled Temperature Room, L05 located in Zone L at the Bangor, PA facility from March 2018 until the last sample time point in March 2021. Storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature (15-30°C) and humidity (monitor). For this period, the maximum temperature recorded was 27.89°C, the minimum temperature was 13.65°C, the average temperature was 22.25°C, and the Average Mean Kinetic Temperature was 22.28°C. Section 5 will include any excursions from these conditions that resulted in an investigation.

5. INVESTIGATIONS:

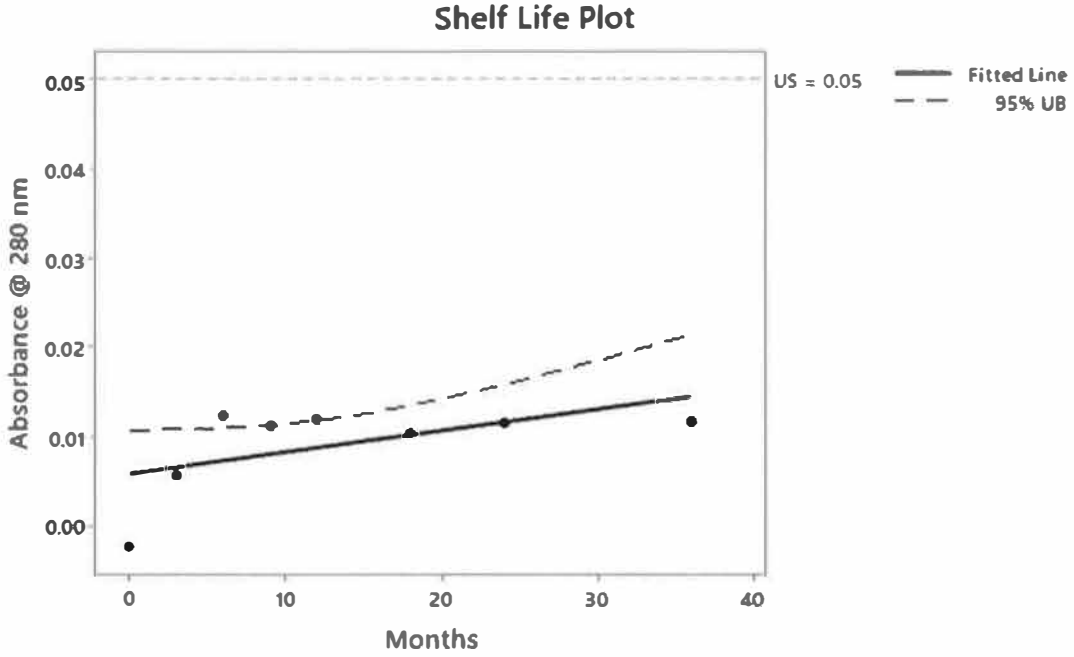
5.1. BDI19-01: Temperature and Humidity Monitoring assessments were not completed on a quarterly basis for multiple locations, including L05. Additionally, upon review of data the minimum temperature was below the specification for readings on 4/4/18. The alarms did not trigger due to how they were established. Alarms were reconfigured to prevent this from happening again.

5.2. BDI21-48: There was temperature and humidity monitoring data from 1/29/21-3/1/21 for one data logger position that was unable to be retrieved due to the logger being dislodged from the holder. There were no out of specification readings from the two loggers which were not impacted by the discrepancy, therefore there was no impact to the stability study.

6. LOT EVALUATION:

TABLE 2: PB2201-172-0318 2P/P

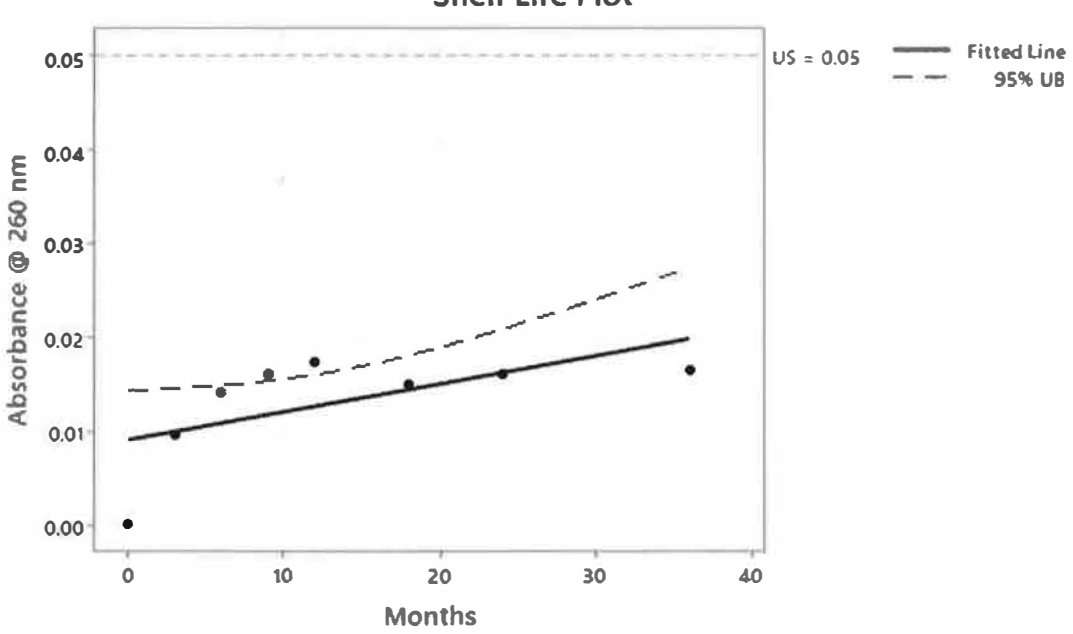
Analysis	Specification	T_0	T_3	T_6	T_9	T_{12}	T_{18}	T_{24}	T_{36}
Absorbance (1M) @ 280 nm	Monitor	<0.003 a.u.	0.0057 a.u.	0.0123 a.u.	0.0113 a.u.	0.0119 a.u.	0.0104 a.u.	0.0116 a.u.	0.0117 a.u.
Absorbance (1M) @ 260 nm	Monitor	0.0003 a.u.	0.0098 a.u.	0.0143 a.u.	0.0162 a.u.	0.0174 a.u.	0.0151 a.u.	0.0162 a.u.	0.0166 a.u.
Assay	98.0 – 100.5%	98.71%	100.07%	99.93%	98.62%	98.52%	100.33%	98.53%	99.00%
Limit of Chlorine	0.6% maximum	<0.01%	0.01%	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%	0.01%
Loss on Drying	1.0% maximum	0.0622%	0.0660%	0.1393%	0.0456%	<0.0075%	0.0235%	0.0385%	0.0234%



US = Upper Specification
Equation for fitted line: Absorbance @ 280 nm = 0.00583 + 0.000240 Months

GRAPH 1: 1M ABSORBANCE @ 280 NM

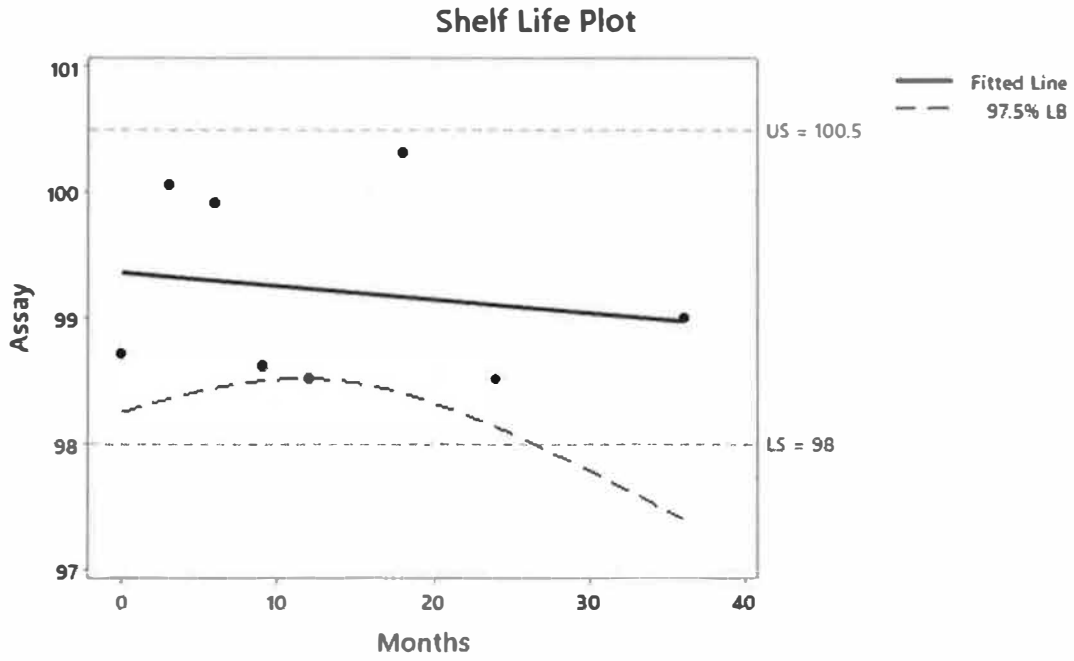
No Shelf-Life was able to be determined for Absorbance @ 280 nm, as the mean response slope is not significantly different from zero using 95% confidence. There is no impact to the product or currently assigned retest or expiration of this material.



US = Upper Specification
Equation for fitted line: Absorbance @ 260 nm = 0.00924 + 0.000296 Months

GRAPH 2: 1M ABSORBANCE @ 260 NM

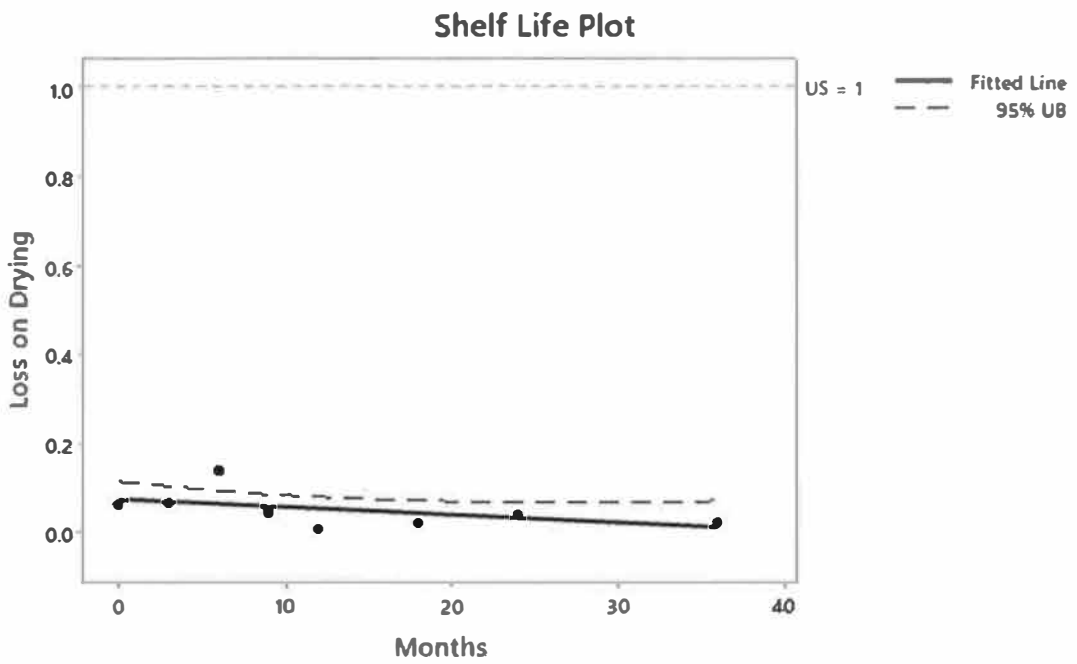
No Shelf-Life was able to be determined for Absorbance @ 260 nm, as the mean response slope is not significantly different from zero using 95% confidence. There is no impact to the product or currently assigned retest or expiration of this material.



LS = Lower Specification, US = Upper Specification
Equation for fitted line: Assay = 99.4 - 0.0107 Months

GRAPH 3: ASSAY

No Shelf-Life was able to be determined for Assay, 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 or expiration of this material.



US = Upper Specification
Equation for fitted line: Loss on Drying = 0.0743 - 0.00174 Months

GRAPH 4: LOSS ON DRYING

No Shelf-Life was able to be determined for Loss on Drying, 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 or expiration of this material.

7. CONCLUSION:

All data met the specification set forth in the Stability Testing Program for this lot PB2201-172-0318 when package in 2P/P packaging. 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. The data obtained during this stability study indicates that Potassium Bromide material packaged in 2P/P packaging is stable for 36 months. This supports the currently assigned 24-month retest date and 36-month expiration date.

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 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.

8.2. 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.

8.2.1. 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.

8.3. In the event that any out of specification results are confirmed, all authorized users of the material will be notified.