

BIOSPECTRA

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10N SODIUM HYDROXIDE 2019
REAL-TIME STABILITY REPORT:
NH4100-002-0519-PV, NH4100-003-0519-PV,
NH4100-004-0519-PV, AND
NH4100-005-0619-PV

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1. OVERVIEW:

The purpose of this report is to analyze and conclude on the data obtained from the real-time stability study of 10N Sodium Hydroxide. Testing intervals are designated by T_n , where n designates 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 Real Time Stability analysis will assess the stability of four lots of 10N Sodium Hydroxide that completed three years of real-time stability in June 2022. These lots are NH4100-002-0519-PV, NH4100-003-0519-PV, NH4100-004-0519-PV, and NH4100-005-0619-PV. The study included the following analyses: Appearance and Color, Identification (IR), Normality, and Sodium Carbonate. Results from all analyses are summarized in Tables 2 through 5. 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 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 10N Sodium Hydroxide. The following Product Codes are commercially available.

- NAHY-4122
- NAHY-4150

2. REFERENCES:

- 2.1. BSI-SOP-0136, Stability Testing Program
- 2.2. BSI-SOP-0146, Stability Inventory
- 2.3. Current USP
- 2.4. ICH Q1

3. SAMPLE DESIGNATION:

- 3.1. Samples placed on the stability program consisted of four lots of 10N Sodium Hydroxide. Stability samples from these lots were put into the 500 mL HDPE Bottle packaging configuration. The samples were packaged in accordance with the Stability Inventory SOP. 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
HDPE Bottle	Samples are packaged into HDPE Lab Screw-Top Bottle

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4. STORAGE:

- 4.1. The Packaging and Storage requirements for 10N Sodium Hydroxide are to be stored in a cool, well-ventilated, and dry area in accordance with the SDS. From the time period of May 2019 until March 2022, the samples were stored in the Controlled Climate Room L05. Storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature (15-30°C) and humidity (monitor). The maximum temperature recorded was 29.79°C, the minimum temperature was 17.01°C, the average temperature was 21.4°C, and the Mean Kinetic Temperature was 21.48°C. Refer to section 5 Investigations for any out of specification (OOS) results.
- 4.2. In March 2022, the location for Stability Samples stored under warehouse conditions of temperature (15-30°C) and humidity (monitor) was switched from L05 to the Zone J Warehouse. The samples remained in Zone J Warehouse from March 2022 until May 2022, which was the end of the study (T=36). The maximum temperature recorded was 24.36°C, the minimum temperature was 14.18°C, the average temperature was 21.11°C, and the Mean Kinetic Temperature was 21.13°C. Refer to section 5 Investigations for any out of specification (OOS) results.

5. INVESTIGATIONS:

- 5.1. BDI21-48: This investigation covers lost temperature data for L05 due to a broken data logger. Data for the period of 01/29/21 to 02/22/21 was unable to be recovered for the portion of zone L05 that was being monitored by the broken data logger. A replacement was put in place for the remainder of the time period. It was determined that there was no impact to quality of the material stored in L05 at this time.
- 5.2. BDI21-282: This investigation covers an out of specification result for mean kinetic temperature (MKT) for June 2021. The minimum, maximum, and average MKT for this month was over the specification of $\leq 25^{\circ}\text{C}$, while all other monitoring specifications were met. The root cause was determined to be due to the failure of an air conditioner unit in this area. There were no single temperature excursions outside the specification of 15-30°C for the monitored month, so it was determined that there was no impact to quality of the material stored in L05 at this time.
- 5.3. BDI22-85: This investigation covers out of specification (OOS) low temperature results during February 2022 in the Bangor Zone J Warehouse. The root cause was determined to be the bay door being left open in Zone J leading to the shipping and receiving dock area. Cold drafts affected the temperature data loggers closest to this open bay area, which then led to OOS minimum temperature readings. It was determined that there was no impact to quality of material stored in Zone J due to the short period of time which the temperature readings were OOS.

6. LOT EVALUATION:

TABLE 2: RESULTS OF REAL TIME STABILITY ANALYSES FOR NH4100-002-0519-PV:

Lot Number	Analysis	Specification	T ₀	T ₃	T ₆	T ₉	T ₁₂	T ₁₈	T ₂₄	T ₃₆
NH4100-002-0519-PV	Appearance and Color	¹ Clear/Colorless Liquid	Clear	Clear	Clear	Clear	Clear	Clear	Clear	Clear
	Identification (IR)	² Passes Test for Sodium	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
	Normality	9.9 – 10.1 N	9.99	10.00	10.10	10.04	10.03	10.01	10.01	10.03
	Sodium Carbonate	≤ 0.6%	0.20	0.18	0.17	0.06	0.08	0.09	0.11	0.12

¹Clear/Colorless Liquid will be reported as Clear.²Passes Test for Sodium will be reported as Pass.

TABLE 3: RESULTS OF REAL TIME STABILITY ANALYSES FOR NH4100-003-0519-PV:

Lot Number	Analysis	Specification	T ₀	T ₃	T ₆	T ₉	T ₁₂	T ₁₈	T ₂₄	T ₃₆
NH4100-003-0519-PV	Appearance and Color	¹ Clear/Colorless Liquid	Clear	Clear	Clear	Clear	Clear	Clear	Clear	Clear
	Identification (IR)	² Passes Test for Sodium	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
	Normality	9.9 – 10.1 N	10.07	10.06	10.10	10.02	10.03	10.05	10.03	10.00
	Sodium Carbonate	≤ 0.6%	0.06	0.17	0.14	0.06	0.07	0.09	0.12	0.07

¹Clear/Colorless Liquid will be reported as Clear.²Passes Test for Sodium will be reported as Pass.

TABLE 4: RESULTS OF REAL TIME STABILITY ANALYSES FOR NH4100-004-0519-PV:

Lot Number	Analysis	Specification	T ₀	T ₃	T ₆	T ₉	T ₁₂	T ₁₈	T ₂₄	T ₃₆
NH4100-004-0519-PV	Appearance and Color	¹ Clear/Colorless Liquid	Clear	Clear	Clear	Clear	Clear	Clear	Clear	Clear
	Identification (IR)	² Passes Test for Sodium	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
	Normality	9.9 – 10.1 N	10.01	10.05	10.00	10.01	10.03	10.00	10.01	10.02
	Sodium Carbonate	≤ 0.6%	0.03	0.16	0.20	0.07	0.06	0.07	0.10	0.06

¹Clear/Colorless Liquid will be reported as Clear.²Passes Test for Sodium will be reported as Pass.

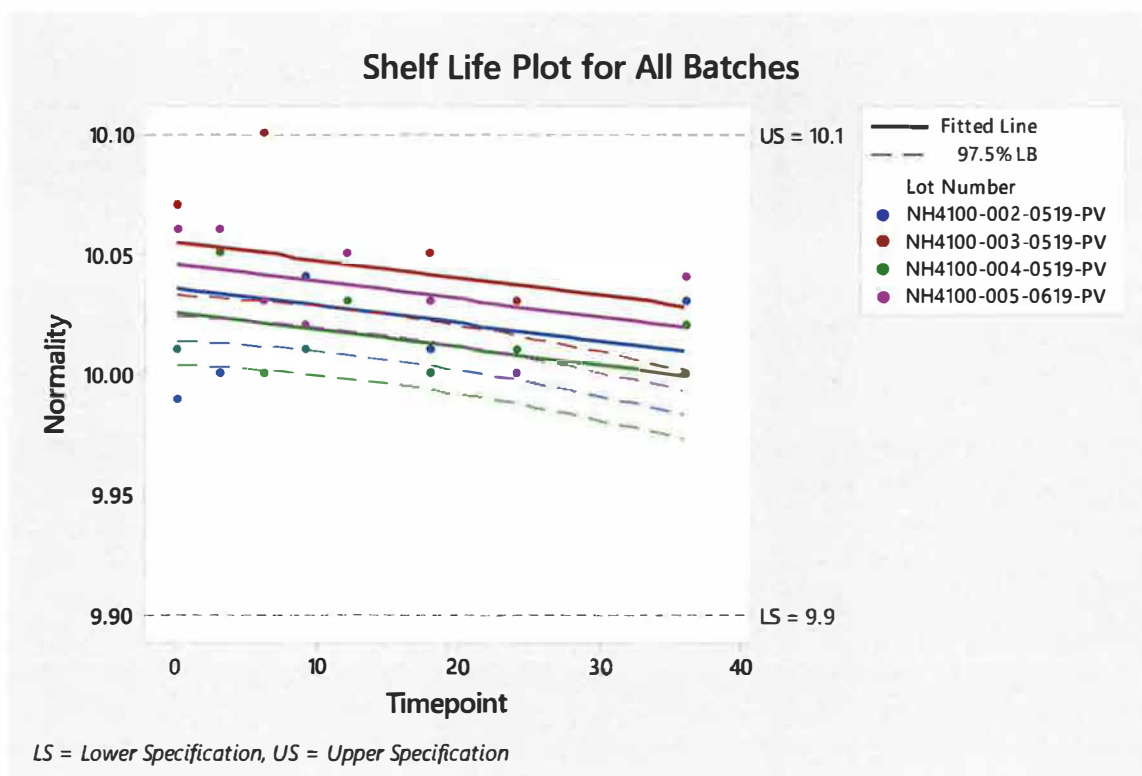
TABLE 5: RESULTS OF REAL TIME STABILITY ANALYSES FOR NH4100-005-0619-PV:

Lot Number	Analysis	Specification	T ₀	T ₃	T ₆	T ₉	T ₁₂	T ₁₈	T ₂₄	T ₃₆
NH4100-005-0619-PV	Appearance and Color	¹ Clear/Colorless Liquid	Clear	Clear	Clear	Clear	Clear	Clear	Clear	Clear
	Identification (IR)	² Passes Test for Sodium	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
	Normality	9.9 – 10.1 N	10.06	10.06	10.03	10.02	10.05	10.03	10.00	10.04
	Sodium Carbonate	≤ 0.6%	0.20	0.04	0.14	0.06	0.05	0.08	0.10	0.09

¹Clear/Colorless Liquid will be reported as Clear.

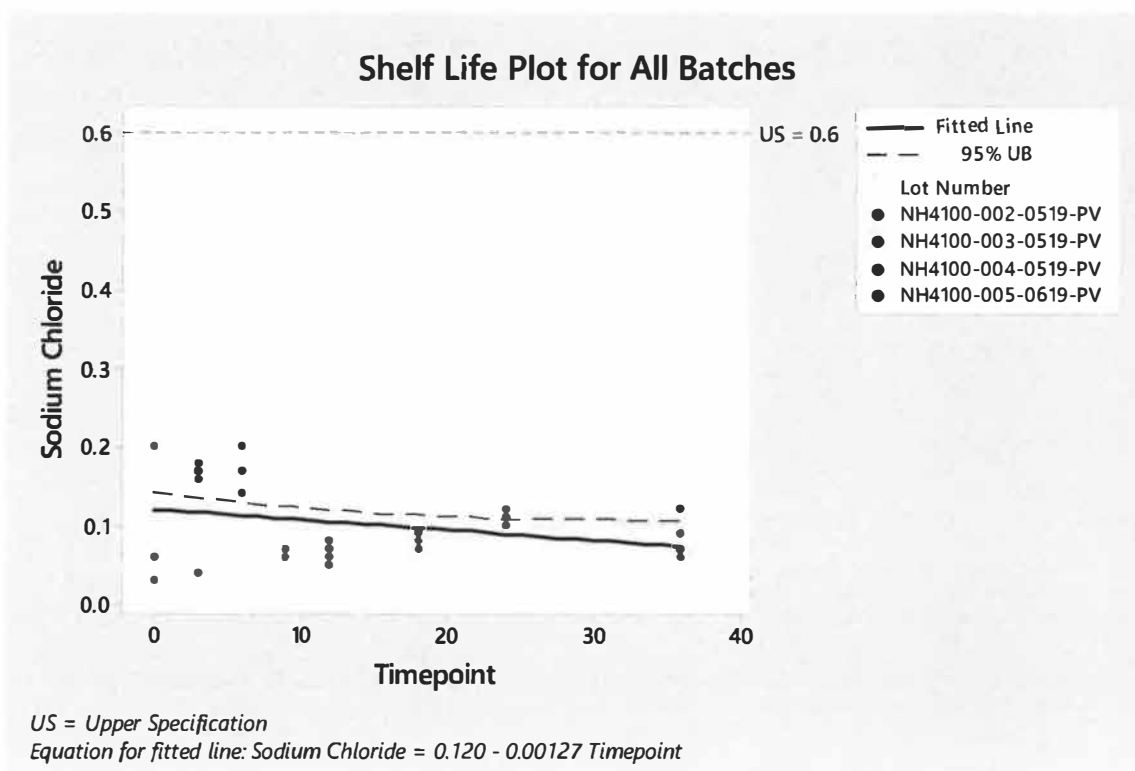
²Passes Test for Sodium will be reported as Pass.

GRAPH 1: NORMALITY



No Shelf Life was able to be determined for Normality using the statistical analysis for Shelf Life Plot, as the mean response slope is not significantly different from zero using 95% confidence. There is no impact to the product or currently assigned expiration of this material as represented by this data up to 36 months.

GRAPH 2: SODIUM CARBONATE



No Shelf Life was able to be determined for Sodium Carbonate using the statistical analysis for Shelf Life Plot, as the mean response slope is not significantly different from zero using 95% confidence. There is no impact to the product or currently assigned expiration of this material as represented by this data up to 36 months.

7. CONCLUSION:

7.1. All data met the specifications set forth in the Stability Testing Program. In accordance with ICH Q1E 2.4.2.1, 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. Real-Time Stability Data displayed in this report, along with the predicted shelf-life plots, supports the current expiration date of 24 months for 10N Sodium Hydroxide manufactured at BioSpectra in the Bangor, PA facility. Due to the completion of 10N Sodium Hydroxide 36 month stability study, a 24 month retest date will be assigned and a 36 month expiration date may be assigned upon request.

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.
 - 8.1.1.1. 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.
 - 8.1.2. If a stability analysis is found to be out of specification, the batch will be withdrawn from the market through communication with the customer. Additionally, an investigation will be conducted to determine the possible withdrawal of the batches produced before and after the batch in question.
 - 8.1.3. In the event that any out of specification results are confirmed, all authorized users of the material will be notified.