BIOSPECTRA
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# URIDINE 2023
# VALIDATION LOTS
# 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 Uridine. 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 analysis will assess the stability of Uridine validation lots, manufactured in Process Room N02, URID-0123-00005-PV, URID-0123-00006-PV, and URID-0123-00007-PV that completed twenty-four (24) months of long-term stability in June 2025 and is scheduled to finish at sixty (60) months in June 2028. This study includes the analyses listed in the table below.

**TABLE 1: STABILITY SPECIFICATIONS**

| Analysis | Specification |
|---|---|
| Appearance and Color | White to Almost White Powder |
| Identification (IR) | Conforms to Spectrum of Reference Standard |
| Loss on Drying | ≤0.5% |
| Melting Point | Report |
| pH 5% | Report |
| Transparency 1% | ≥ 98.0% |
| UV-Assay | ≥ 98.0% |

Results from all analyses are summarized in Tables 4-9. 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 Uridine. The following Product Codes are commercially available.

- URID-3250, URID-4250

## 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. BSI-RPT-1060, Stability Indicating Report: Uridine
2.5. Current USP
2.6. ICH Q1E

## 3. SAMPLE DESIGNATION:

3.1. Samples initially placed on the stability program for long-term testing consisted of three validation lots of Uridine. Stability samples from these lots were put into both P/P and Labline packaging configurations. The samples were packaged in accordance with the Stability Inventory SOP. Reference Table 2, 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 2: PACKAGING DETAILS**

| Packaging Configuration | Packaging Description |
|---|---|
| Poly/Poly (P/P) | Samples are individually placed into small polyethylene bags and are sealed with a zip tie. All individual bags are then placed into a poly pail and sealed. |
| Labline (HDPE Bottle) | Samples are packaged into a HDPE Lab Screw-Top Bottle |

## 4. STORAGE:

4.1. The packaging and storage requirements for Uridine are to be in a tightly closed container and stored in a dry, well-ventilated area away from incompatible substances. For the long-term study, the samples were stored in the Long-Term Stability Chamber H03SC01 at the Bangor, PA facility. Storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature (25°C ±2), mean kinetic temperature (monitor) and relative humidity (60% ±5). Storage conditions for the time period of June 2023 to June 2025 are detailed in the table below. Maximum and minimum values that are outside the limits for temperature and humidity are due to opening the door of the chamber as explained in the Temperature and Humidity Monitoring Assessments for the chamber. Section 5 will include any excursions from these conditions that resulted in an investigation.

**TABLE 3: STORAGE CONDITIONS**

| Storage Condition | Specification | Value |
|---|---|---|
| Minimum Temperature | 25°C ± 2°C | 21.81°C |
| Maximum Temperature | | 26.20°C |
| Average Temperature | | 25.34°C |
| Mean Kinetic Temperature | Monitor | 25.34°C |
| Minimum Humidity | 60% RH ± 5% RH | 43.6% |
| Maximum Humidity | | 80.5% |
| Average Humidity | | 61.2% |

## 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 range temperature and humidity for H03SC01 were recorded on 8/15/24. During preventative maintenance, it was observed that a main 20-amp fuse had blown. The fuse was replaced and the humidity returned to within the allowable range. There was no impact to the current list of materials stored in the stability chamber, H03SC01.

## 6. LOT EVALUATION:

**TABLE 4: URID-0123-00005-PV P/P**

| Time Point | Analyses/Specifications | | | | | | |
|---|---|---|---|---|---|---|---|
| | Appearance and Color | Identification (IR) | Loss on Drying | [1]Melting Point | [2]pH (5%) | Transparency (1%) | UV-Assay |
| | White to Almost White Powder | Conforms to Spectrum of Reference Standard | ≤ 0.5% | Report 167-170°C | Report 4.0 – 6.0 | ≥ 98.0% | ≥ 98.0% |
| **$T_0$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.0470% | 167.2 – 168.0°C | 5.12 | 99.8174% | 99.19% |
| **$T_3$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1230% | 167.0 – 168.0°C | 5.07 | 99.7386% | 99.12% |
| **$T_6$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1711% | 167.3 – 168.5°C | 5.10 | 99.5674% | 100.0% |
| **$T_9$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.2394% | 167.7 – 168.9°C | 5.08 | 99.6356% | 100.49% |
| **$T_{12}$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1436% | 167.9 – 169.0°C | 5.11 | 99.8494% | 100.45% |
| **$T_{18}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.1402% | 167.9 – 169.6°C | 5.14 | 99.7250% | 100.50% |
| **$T_{24}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.2370% | 168.2 – 169.0°C | 5.12 | 99.5377% | 99.81% |

[1]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

[2]Analysis (pH 5%) is not required for URID-3250. Specification will be Report, and the specification to compare to will be 4.0 – 6.0.

**TABLE 5: URID-0123-00005-PV LABLINE**

| Time Point | Analyses/Specifications | | | | | | |
|---|---|---|---|---|---|---|---|
| | Appearance and Color | Identification (IR) | Loss on Drying | [1]Melting Point | [2]pH (5%) | Transparency (1%) | UV-Assay |
| | White to Almost White Powder | Conforms to Spectrum of Reference Standard | ≤ 0.5% | Report 167-170°C | Report 4.0 – 6.0 | ≥ 98.0% | ≥ 98.0% |
| **$T_0$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.0470% | 167.2 – 168.0°C | 5.12 | 99.8174% | 99.19% |
| **$T_3$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1072% | 167.1 – 168.1°C | 5.06 | 100.0318% | 98.95% |
| **$T_6$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1602% | 167.5 – 168.6°C | 5.02 | 99.8999% | 100.0% |
| **$T_9$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1763% | 167.7 – 168.8°C | 5.15 | 99.8174% | 100.11% |
| **$T_{12}$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1614% | 167.8 – 169.0°C | 5.07 | 99.9439% | 100.22% |
| **$T_{18}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.2182% | 167.9 – 169.7°C | 5.05 | 99.8286% | 100.55% |
| **$T_{24}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.2560% | 168.2 – 169.0°C | 5.12 | 99.7640% | 99.44% |

[1]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

[2]Analysis (pH 5%) is not required for URID-3250. Specification will be Report, and the specification to compare to will be 4.0 – 6.0.

**TABLE 6: URID-0123-00006-PV P/P**

| Time Point | Analyses/Specifications | | | | | | |
|---|---|---|---|---|---|---|---|
| | Appearance and Color | Identification (IR) | Loss on Drying | [1]Melting Point | [2]pH (5%) | Transparency (1%) | UV-Assay |
| | White to Almost White Powder | Conforms to Spectrum of Reference Standard | ≤ 0.5% | Report 167-170°C | Report 4.0 – 6.0 | ≥ 98.0% | ≥ 98.0% |
| **$T_0$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.0596% | 167.6 – 168.1°C | 5.09 | 99.7890% | 99.03% |
| **$T_3$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1438% | 167.0 – 167.8°C | 5.06 | 99.9549% | 98.81% |
| **$T_6$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1901% | 167.5 – 168.6°C | 5.07 | 99.4229% | 99.3% |
| **$T_9$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.2742% | 167.7 – 169.0°C | 5.05 | 99.7454% | 100.17% |
| **$T_{12}$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.2306% | 167.8 – 169.0°C | 5.10 | 99.7136% | 100.38% |
| **$T_{18}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.1354% | 167.8 – 168.8°C | 5.04 | 99.6311% | 101.19% |
| **$T_{24}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.1890% | 168.1 – 169.0°C | 5.14 | 99.6267% | 99.69% |

[1]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

[2]Analysis (pH 5%) is not required for URID-3250. Specification will be Report, and the specification to compare to will be 4.0 – 6.0.

**TABLE 7: URID-0123-00006-PV LABLINE**

| Time Point | Analyses/Specifications | | | | | | |
|---|---|---|---|---|---|---|---|
| | Appearance and Color | Identification (IR) | Loss on Drying | [1]Melting Point | [2]pH (5%) | Transparency (1%) | UV-Assay |
| | White to Almost White Powder | Conforms to Spectrum of Reference Standard | ≤ 0.5% | Report 167-170°C | Report 4.0 – 6.0 | ≥ 98.0% | ≥ 98.0% |
| **$T_0$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.0596% | 167.6 – 168.1°C | 5.09 | 99.7890% | 99.03% |
| **$T_3$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1393% | 167.1 – 168.1°C | 5.07 | 99.7617% | 99.01% |
| **$T_6$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1415% | 167.6 – 168.6°C | 5.07 | 99.7308% | 100.0% |
| **$T_9$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1918% | 167.9 – 169.1°C | 5.16 | 99.9309% | 100.30% |
| **$T_{12}$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1526% | 167.6 – 168.8°C | 5.10 | 99.9972% | 100.47% |
| **$T_{18}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.1680% | 167.8 – 169.6°C | 5.08 | 99.5972% | 98.50% |
| **$T_{24}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.2164% | 168.3 – 169.1°C | 5.12 | 99.7302% | 99.74% |

[1]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

[2]Analysis (pH 5%) is not required for URID-3250. Specification will be Report, and the specification to compare to will be 4.0 – 6.0.

**TABLE 8: URID-0123-00007-PV P/P**

| Time Point | Analyses/Specifications | | | | | | |
|---|---|---|---|---|---|---|---|
| | Appearance and Color | Identification (IR) | Loss on Drying | [1]Melting Point | [2]pH (5%) | Transparency (1%) | UV-Assay |
| | White to Almost White Powder | Conforms to Spectrum of Reference Standard | ≤ 0.5% | Report 167-170°C | Report 4.0 – 6.0 | ≥ 98.0% | ≥ 98.0% |
| **$T_0$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1018% | 167.6 – 168.1°C | 5.02 | 99.8593% | 98.83% |
| **$T_3$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1887% | 167.0 – 168.0°C | 5.08 | 99.9472% | 100.4% |
| **$T_6$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1471% | 167.5 – 168.6°C | 5.09 | 99.6335% | 99.8% |
| **$T_9$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.2127% | 167.8 – 169.1°C | 5.10 | 99.8334% | 100.07% |
| **$T_{12}$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1548% | 167.5 – 169.0°C | 5.10 | 99.8531% | 100.16% |
| **$T_{18}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.1923% | 167.8 – 169.6°C | 5.09 | 99.4374% | 98.85% |
| **$T_{24}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.1607% | 168.4 – 169.1°C | 5.22 | 99.4516% | 99.08% |

[1]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

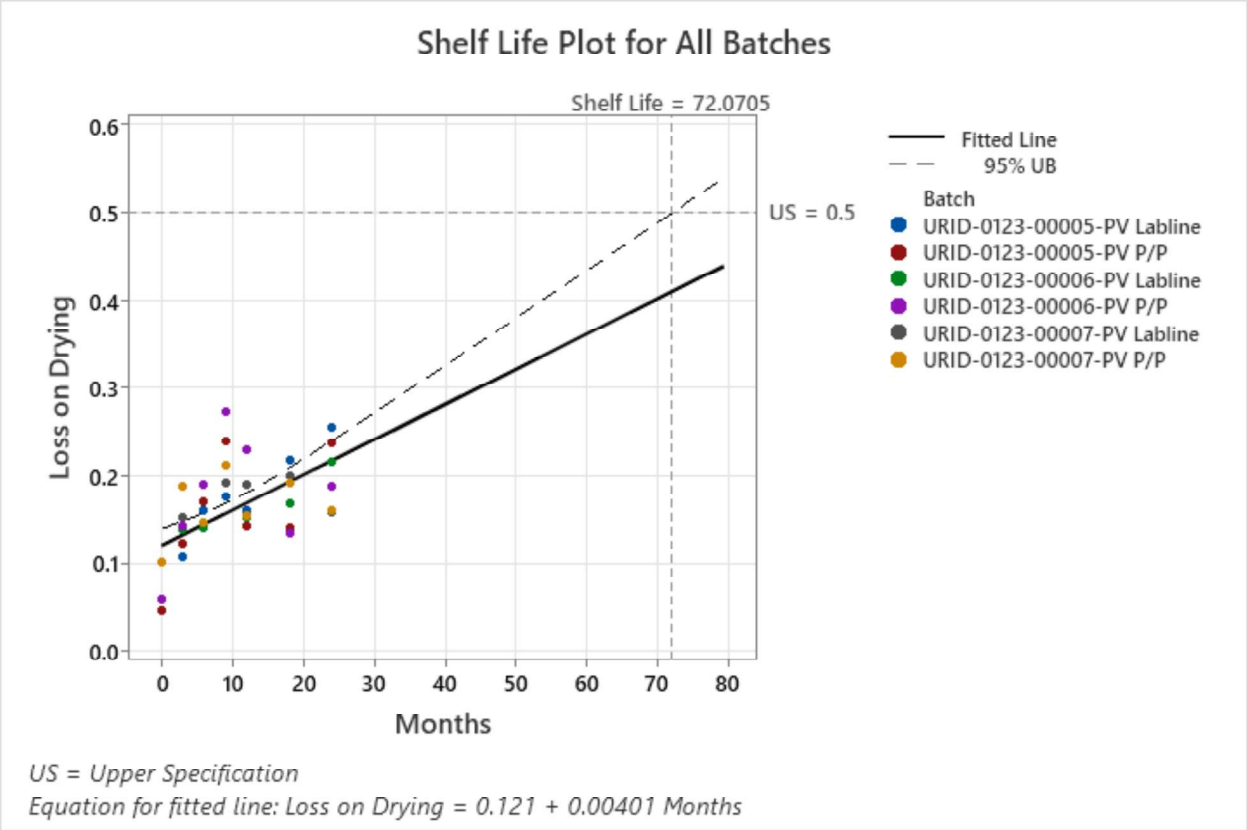
[2]Analysis (pH 5%) is not required for URID-3250. Specification will be Report, and the specification to compare to will be 4.0 – 6.0.

**TABLE 9: URID-0123-00007-PV LABLINE**

| Time Point | Analyses/Specifications | | | | | | |
|---|---|---|---|---|---|---|---|
| | Appearance and Color | Identification (IR) | Loss on Drying | [1]Melting Point | [2]pH (5%) | Transparency (1%) | UV-Assay |
| | White to Almost White Powder | Conforms to Spectrum of Reference Standard | ≤ 0.5% | Report 167-170°C | Report 4.0 – 6.0 | ≥ 98.0% | ≥ 98.0% |
| **$T_0$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1018% | 167.6 – 168.1°C | 5.02 | 99.8593% | 98.83% |
| **$T_3$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1530% | 167.2 – 168.1°C | 5.08 | 99.9895% | 100.0% |
| **$T_6$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1468% | 167.5 – 168.6°C | 5.07 | 99.3662% | 100.2% |
| **$T_9$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1932% | 167.8 – 168.9°C | 5.05 | 99.9679% | 99.83% |
| **$T_{12}$** | White To Almost White Powder | Conforms to Spectrum of Reference Standard | 0.1914% | 167.6 – 169.0°C | 5.11 | 99.9430% | 100.17% |
| **$T_{18}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.2011% | 167.8 – 169.6°C | 5.08 | 99.6001% | 99.17% |
| **$T_{24}$** | White Powder | Conforms to Spectrum of Reference Standard | 0.1583% | 168.1 – 169.1°C | 5.16 | 99.3171% | 99.08% |

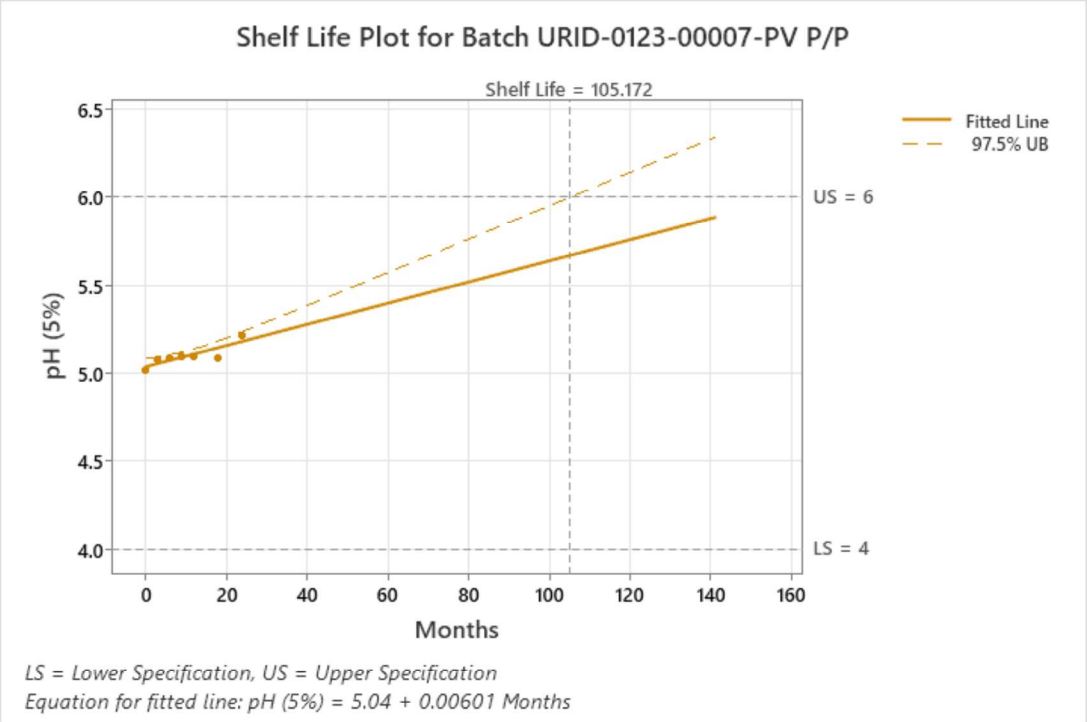
[1]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

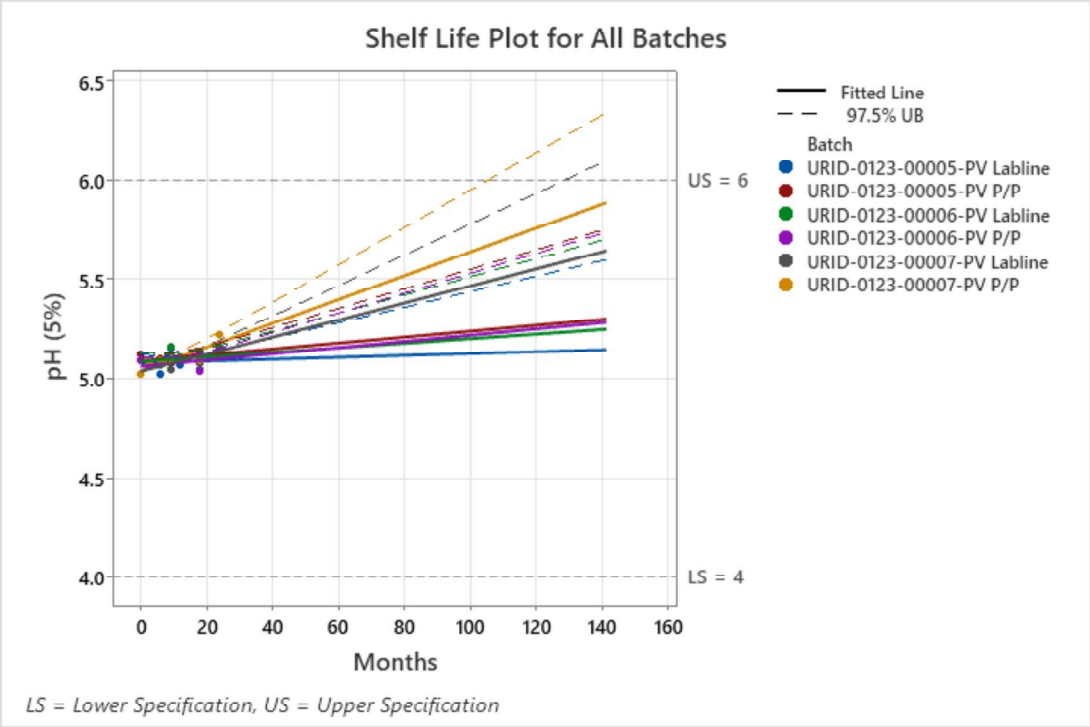
[2]Analysis (pH 5%) is not required for URID-3250. Specification will be Report, and the specification to compare to will be 4.0 – 6.0.




**GRAPH 1: LONG TERM LOSS ON DRYING**

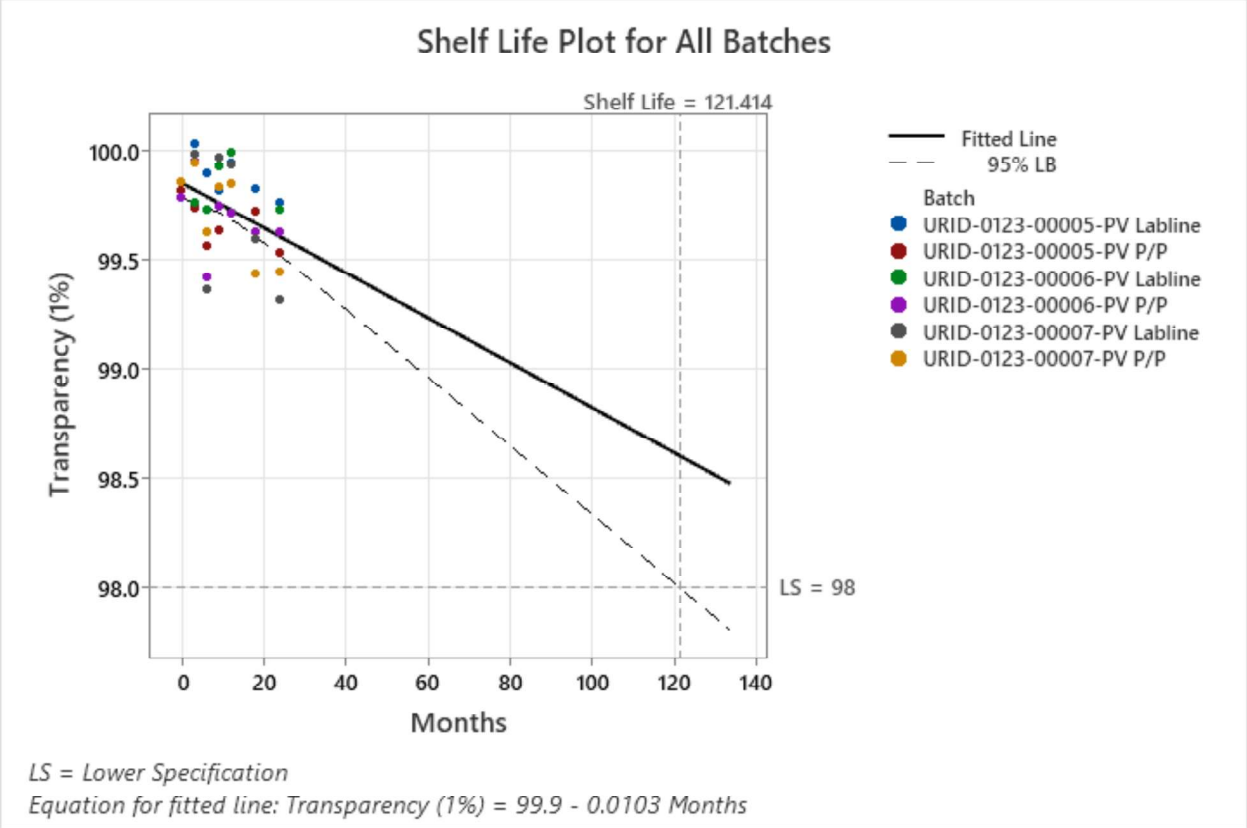
The predicted Shelf-Life for the Long-Term Loss on Drying was determined to be 72.0705 months at the T=24-month time interval. Results will continue to be monitored. There is no impact to the product or currently assigned retest period of this material.




**GRAPH 2: LONG TERM PH (5%)**

The predicted Shelf-Life for the Long-Term pH (5%) was determined to be 105.172 months at the T=24-month time interval. There is no impact to the product or currently assigned retest period of this material. There is no specification for pH (5%) for this product code, but there is a monitored range of 4.0 – 6.0. As per BDI22-224, the data "will not be used to calculate a shelf-life trending plot" a shelf life plot was generated for informational purposes.

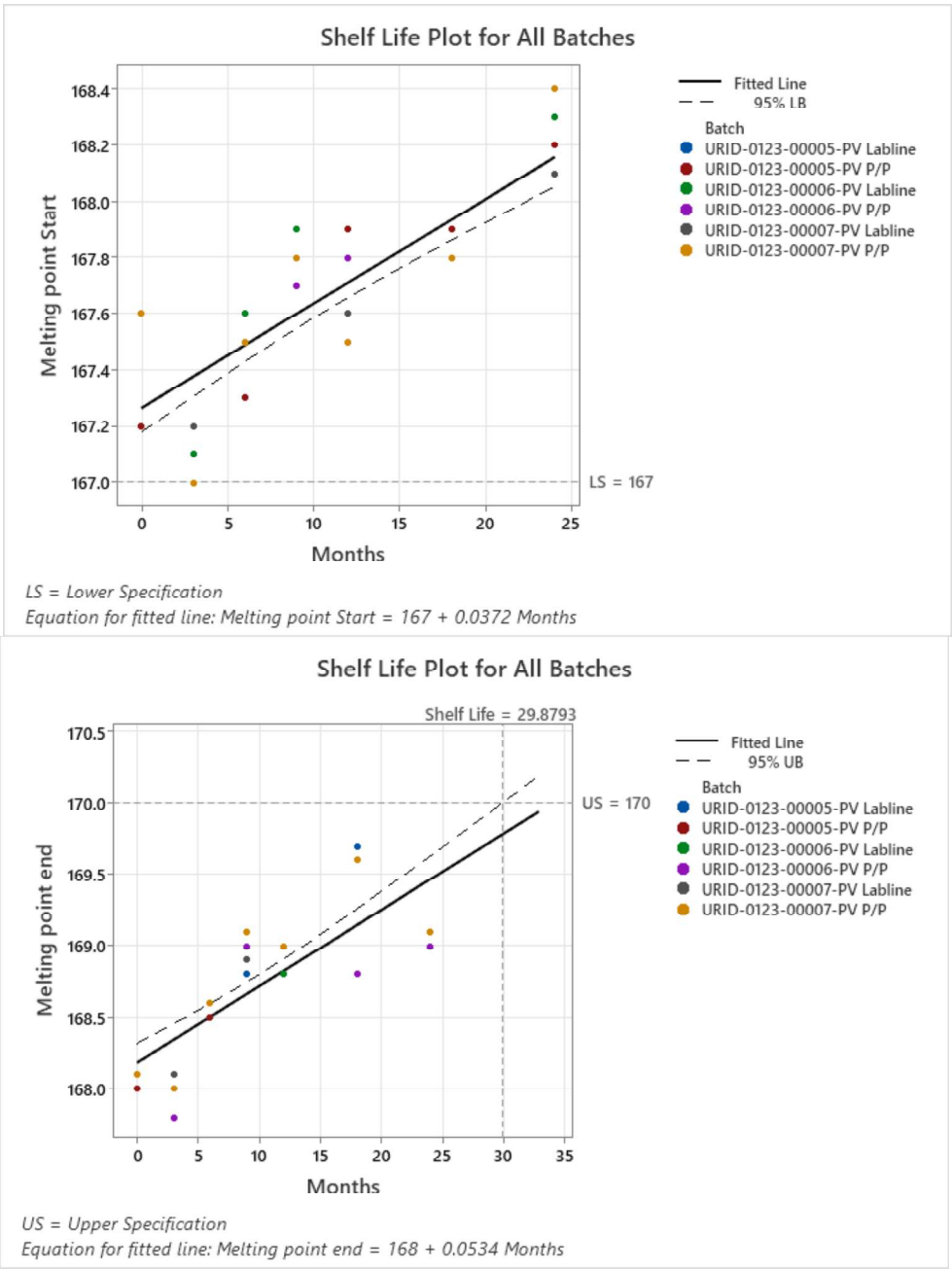



**GRAPH 3: LONG TERM TRANSPARENCY (1%)**

The predicted Shelf-Life for the Long-Term Transparency (1%) was determined to be 121.414 months at the T=24-month time interval. Results will continue to be monitored. There is no impact to the product or currently assigned retest period of this material.


**GRAPH 4: LONG TERM UV-ASSAY**

No Shelf-Life was able to be determined for the Long-Term UV-Assay, as the mean response slope is not significantly different from zero using 95% confidence at the T=24-month time interval. Results will continue to be monitored. There is no impact to the product or currently assigned retest period of this material.




**GRAPH 5: LONG TERM MELTING POINT**

No Shelf-Life was able to be determined for Melting Point Start, as the mean response slope is not significantly different from zero using 95% confidence at the T=24-month time interval. Results will continue to be monitored. The predicted Shelf-Life for Long-Term Melting Point End was determined to be 29.87893 months at the T=24-month time interval. Results will continue to be monitored. There is no impact to the product or currently assigned retest period of this material as there is no specification for melting point for this product code, but there is a monitored range of 167-170°C.

## 7. CONCLUSION:

7.1. All data met the specifications set forth in the Stability Testing Program. 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 long-term conditions. Long-term Stability Data displayed in this report up to 24 months for Uridine manufactured at BioSpectra in the Bangor, PA facility, along with the predicted shelf-life plots, support a 24 month retest date, an extension to an expiration date of 36 months upon request is acceptable and will continue to be monitored. Samples have met specifications as of T=24 (24 months) and will continue to be monitored.

## 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.

8.1.2. 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, 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.

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