BIOSPECTRA
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URIDINE 2022
VALIDATION LOTS
REAL TIME STABILITY REPORT:

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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 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 real time analysis will assess the stability of Uridine validation lots URID-0122-00005-PV, URID-0122-00006-PV, and URID-0122-00007-PV that completed six (6) months of real time stability in January 2023 and is scheduled to finish at sixty (60) months in July 2027. This study includes the following analyses: Appearance and Color, Identification (IR), Loss on Drying, Melting Point, pH (5%), Transparency (1%), and UV-Assy. Results from all analyses are summarized in Table 2. 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

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 initially placed on the stability program for real time testing consisted of three lots of Uridine. Stability samples from these lots were put into both P/P and Labline 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**
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 real time study, the samples were stored in the Real Time Stability Chamber 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) and relative humidity (60% ±5). For the time period of July 2022 to December 2022, which covers the start of this study until approximately 3 weeks before the T=6 pulls, the maximum temperature recorded was 25.73°C, the minimum temperature recorded was 25.25°C, the average temperature recorded was 25.49°C, and the average mean kinetic temperature was 25.49°C. The maximum relative humidity was 65.7%, the minimum relative humidity was 56.5%, and the average relative humidity was 61.8%. 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. Finalized temperature and humidity data for January 2023 is not available at the time of this report, and will continue to be monitored. Section 5 will include any excursions from these conditions that resulted in an investigation.

5. INVESTIGATIONS:

5.1. BLI22-31: This discrepancy investigation documents Out of Specification (OOS) and Out of Trend (OOT) data for UV Assay for URID-0122-00006-PV T=3 samples for all conditions and packaging configurations. It was determined that there was a preparation issue, and the retests refuted the original OOS and OOT results. The retests were used as the reported values.

5.2. BDI22-224: Testing for pH (5%) was not complete for the T=0 timepoint for all three lots of Uridine. This test was not required for finished goods (URID-3250) or for the Degradation and Impurity Profile Report: Uridine (Excipient) (BSI-RPT-1005). Testing was not requested for Stability, and it was not done. There is no specification for pH (5%) and the data is only for monitoring purposes.

6. LOT EVALUATION:

TABLE 2A: RESULT OF REAL TIME STABILITY ANALYSES FOR URID-0122-00005-PV P/P

Lot Number	Analysis	Specification	T_0	T_3	T_6	T_9	T_{12}	T_{18}	T_{24}	T_{36}	T_{48}	T_{60}
URID-0122-00005-PV Real Time P/P	Appearance and Color	White to almost white powder	White Powder	White to Almost White Powder	White to Almost White Powder	Scheduled for 04/05/23	Scheduled for 07/05/23	Scheduled for 01/05/24	Scheduled for 07/05/24	Scheduled for 07/05/25	Scheduled for 07/05/26	Scheduled for 07/05/27
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS							
	Loss on Drying	≤ 0.5%	0.1%	0.2%	0.2%							
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.7 – 168.9°C	167.6 – 168.6°C							
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.19	5.10							
	Transparency (1%)	≥ 98.0%	99.6%	99.4%	99.7%							
	UV-Assay	≥ 98.0%	98.4%	99.8%	99.2%							

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2B: RESULT OF REAL TIME STABILITY ANALYSES FOR URID-0122-00005-PV LABLINE

Lot Number	Analysis	Specification	T_0	T_3	T_6	T_9	T_{12}	T_{18}	T_{24}	T_{36}	T_{48}	T_{60}
URID-0122-00005-PV Real Time Labline	Appearance and Color	White to almost white powder	White Powder	White to Almost White Powder	White to Almost White Powder	Scheduled for 04/05/23	Scheduled for 07/05/23	Scheduled for 01/05/24	Scheduled for 07/05/24	Scheduled for 07/05/25	Scheduled for 07/05/26	Scheduled for 07/05/27
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS							
	Loss on Drying	≤ 0.5%	0.1%	0.1%	0.2%							
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.8 – 169.2°C	167.7 – 168.8°C							
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.31	5.13							
	Transparency (1%)	≥ 98.0%	99.6%	99.3%	99.8%							
	UV-Assay	≥ 98.0%	98.4%	100.1%	99.3%							

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2C: RESULT OF REAL TIME STABILITY ANALYSES FOR URID-0122-00006-PV P/P

Lot Number	Analysis	Specification	T_0	T_3	T_6	T_9	T_{12}	T_{18}	T_{24}	T_{36}	T_{48}	T_{60}
URID-0122-00006-PV Real Time P/P	Appearance and Color	White to almost white powder	Almost white powder	White to Almost White Powder	White to Almost White Powder	Scheduled for 04/12/23	Scheduled for 07/12/23	Scheduled for 01/12/24	Scheduled for 07/12/24	Scheduled for 07/12/25	Scheduled for 07/12/26	Scheduled for 07/12/27
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS							
	Loss on Drying	≤ 0.5%	<0.5%	0.2%	0.2%							
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.6 – 168.8°C	167.5 – 168.9°C							
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.22	5.15							
	Transparency (1%)	≥ 98.0%	99.7%	99.7%	99.6%							
	UV-Assay	≥ 98.0%	100.1%	99.2%	99.8%							

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2D: RESULT OF REAL TIME STABILITY ANALYSES FOR URID-0122-00006-PV LABLINE

Lot Number	Analysis	Specification	T_0	T_3	T_6	T_9	T_{12}	T_{18}	T_{24}	T_{36}	T_{48}	T_{60}
URID-0122-00006-PV Real Time Lablline	Appearance and Color	White to almost white powder	Almost white powder	White to Almost White Powder	White to Almost White Powder	Scheduled for 04/12/23	Scheduled for 07/12/23	Scheduled for 01/12/24	Scheduled for 07/12/24	Scheduled for 07/12/25	Scheduled for 07/12/26	Scheduled for 07/12/27
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS							
	Loss on Drying	≤ 0.5%	<0.5%	0.1%	0.2%							
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.7 – 168.6°C	167.5 – 168.8°C							
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.20	5.18							
	Transparency (1%)	≥ 98.0%	99.7%	99.8%	99.5%							
	UV-Assay	≥ 98.0%	100.1%	99.5%	100.4%							

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2E: RESULT OF REAL TIME STABILITY ANALYSES FOR URID-0122-00007-PV P/P

Lot Number	Analysis	Specification	T_0	T_3	T_6	T_9	T_{12}	T_{18}	T_{24}	T_{36}	T_{48}	T_{60}
URID-0122-00007-PV Real Time P/P	Appearance and Color	White to almost white powder	White to Almost White Powder	White to Almost White Powder	White to Almost White Powder	Scheduled for 04/14/23	Scheduled for 07/14/23	Scheduled for 01/14/24	Scheduled for 07/14/24	Scheduled for 07/14/25	Scheduled for 07/14/26	Scheduled for 07/14/27
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS							
	Loss on Drying	≤ 0.5%	0.1%	0.2%	0.2%							
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.3 – 168.6°C	167.5 – 168.8°C							
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.25	5.25							
	Transparency (1%)	≥ 98.0%	99.3%	99.5%	99.0%							
	UV-Assay	≥ 98.0%	99.8%	99.2%	99.5%							

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2F: RESULT OF REAL TIME STABILITY ANALYSES FOR URID-0122-00007-PV LABLINE

Lot Number	Analysis	Specification	T_0	T_3	T_6	T_9	T_{12}	T_{18}	T_{24}	T_{36}	T_{48}	T_{60}
URID-0122-00007-PV Real Time Labline	Appearance and Color	White to almost white powder	White to Almost White Powder	White to Almost White Powder	White to Almost White Powder	Scheduled for 04/14/23	Scheduled for 07/14/23	Scheduled for 01/14/24	Scheduled for 07/14/24	Scheduled for 07/14/25	Scheduled for 07/14/26	Scheduled for 07/14/27
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS							
	Loss on Drying	≤ 0.5%	0.1%	0.1%	0.1%							
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.4 – 168.6°C	167.4 – 168.8°C							
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.27	5.20							
	Transparency (1%)	≥ 98.0%	99.3%	99.5%	98.8%							
	UV-Assay	≥ 98.0%	99.8%	100.6%	99.4%							

[1]CSRS = Conforms to Spectrum of Reference Standard

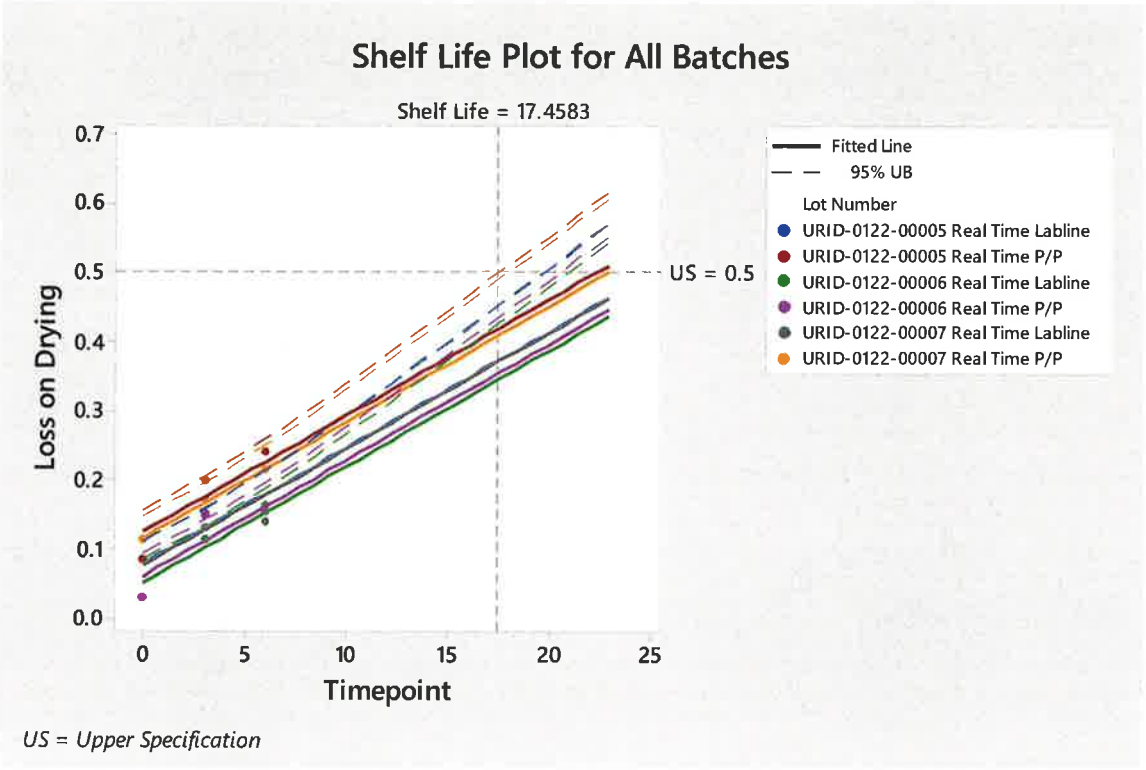
[2]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

GRAPH 1: REAL TIME LOSS ON DRYING



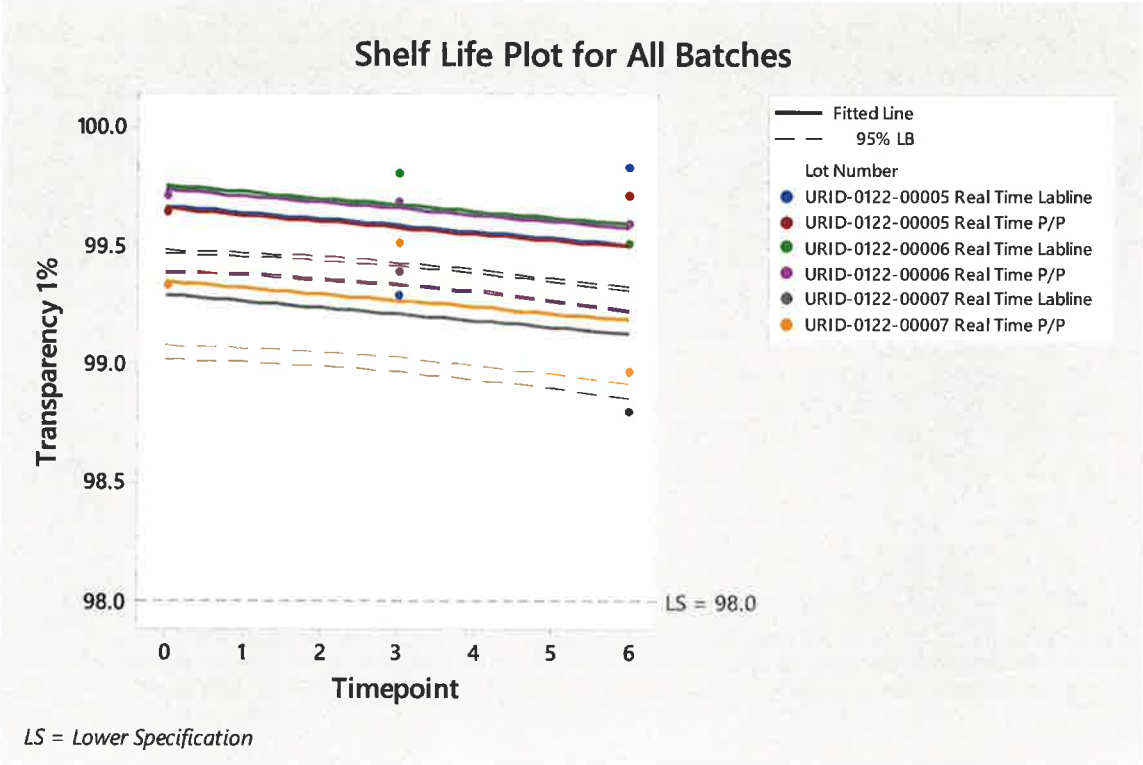
US = Upper Specification

The predicted Shelf-Life for Real Time Loss on Drying was determined to be 17.4583 months at the T=6 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: REAL TIME PH (5%)

A regression graph could not be generated for pH (5%) at this time due to only having two data points. The T=0 was not tested for this product as a finished good, so there is only T=3 and T=6 data available. There is no specification for pH (5%) for this product, but there is a monitored range of 4.0 – 6.0. All data points for all three lots and both packaging configurations did meet this monitored range. Results will continue to be monitored, and a regression graph will be able to be generated at the next time point interval of T=9.

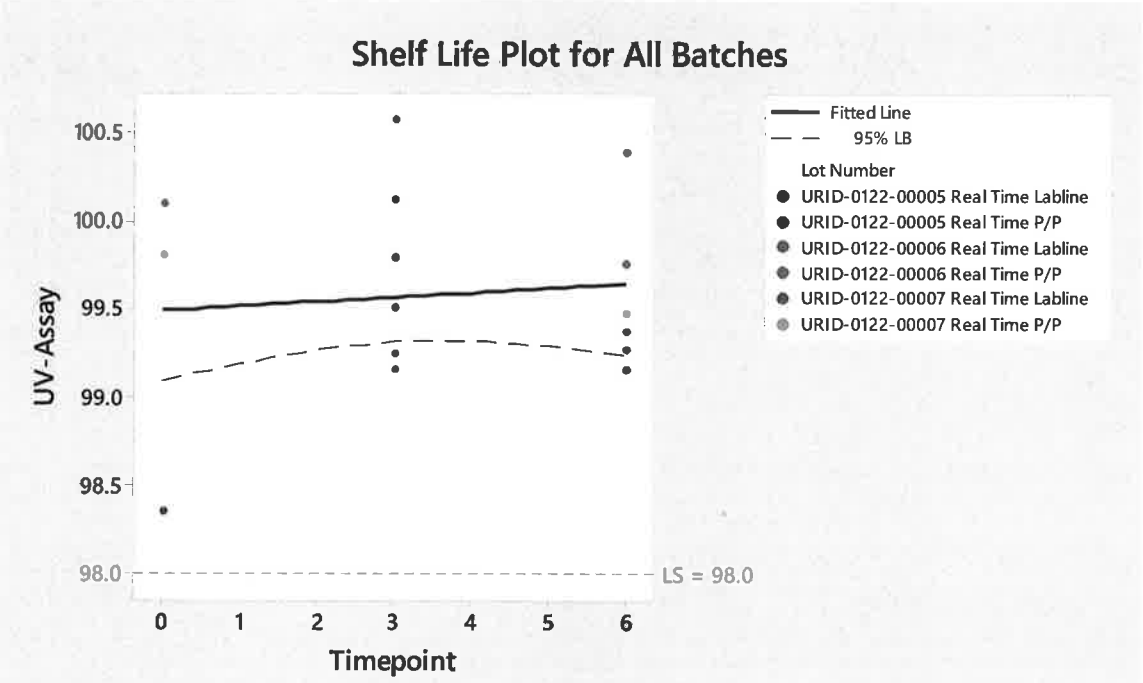
GRAPH 3: REAL TIME TRANSPARENCY (1%)



LS = Lower Specification

No Shelf-Life was able to be determined for Real Time Transparency (1%), as the mean response slope is not significantly different from zero using 95% confidence at the T=6 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: REAL TIME UV-ASSAY



LS = Lower Specification
Equation for fitted line: UV-Assay = 99.5 + 0.0253 Timepoint

No Shelf-Life was able to be determined for UV-Assay, as the mean response slope is not significantly different from zero using 95% confidence at the T=6 month time interval. Results will continue to be monitored. There is no impact to the product or currently assigned retest period of this material.

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 real time stability data, but should be no more than 12 months beyond for real time conditions. Real-Time Stability Data displayed in this report up to 6 months for Uridine manufactured at BioSpectra in the Bangor, PA facility, along with the predicted shelf-life plots, would support a retest date of 12 months and will continued to be monitored. Samples have met specifications as of T=6 (6 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.

8.2. 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 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.

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URIDINE 2022 VALIDATION LOTS COLD STORAGE AND ACCELERATED STABILITY REPORT:

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1. OVERVIEW:

The purpose of this report is to analyze and conclude on the data obtained from the cold storage and Accelerated stability study of Uridine. Testing intervals are designated by T_n, where n = the number of months on stability. Testing is performed every month for six months 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 Cold Storage and Accelerated analysis will assess the stability of Uridine validation lots URID-0122-00005-PV and URID-0122-00006-PV that completed six (6) months of cold storage and accelerated stability in January 2023. This study includes the following analyses: Appearance and Color, Identification (IR), Loss on Drying, Melting Point, pH (5%), Transparency (1%), and UV-Assy. Results from all analyses are summarized in Table 2. 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

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 initially placed on the stability program for Cold Storage and Accelerated testing consisted of two lots of Uridine. Stability samples from these lots were put into both P/P and Labline 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**
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 Cold Storage portion of the study, the samples were stored in refrigerated storage unit A01RC04 at the Bangor, PA facility. Storage conditions have been continuously measured and recorded utilizing Tempmate data loggers with regulated conditions for temperature (2-8°C). For the time period of July 2022 to December 2022, which covers the start of this study until the T=6 time interval, the maximum temperature recorded was 29.8°C, the minimum temperature was 2.7°C, the average temperature was 6.0°C, and the Mean Kinetic Temperature was 6.1°C. The T=6 samples remained in this storage area until they were pulled for testing in January 2023. Temperature data for A01RC04 for January 2023 is not available at this time, but will continue to be monitored. Section 5 will include any excursions from these conditions that resulted in an investigation.

4.2. 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 Accelerated Storage portion of the study, the samples were stored in the Accelerated Stability Chamber at the Bangor, PA facility. Storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature (40°C ±2) and relative humidity (75% ±5). For the time period of July 2022 to December 2022, which covers the start of this study until the T=6 time interval, the maximum temperature recorded was 40.09°C, the minimum temperature recorded was 38.35°C, the average temperature recorded was 39.89°C, and the average mean kinetic temperature was 39.89°C. The maximum relative humidity was 81.9%, the minimum relative humidity was 53.8%, and the average relative humidity was 78.0%. 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. The T=6 samples remained in this storage area until they were pulled for testing in January 2023. Temperature and humidity data for the Accelerated Stability Chamber for January 2023 is not available at this time, but will continue to be monitored. Section 5 will include any excursions from these conditions that resulted in an investigation.

5. INVESTIGATIONS:

5.1. BLI22-31: This discrepancy investigation documents Out of Specification (OOS) and Out of Trend (OOT) data for UV Assay for URID-0122-00006-PV T=3 samples for all conditions and packaging configurations. It was determined that there was a preparation issue, and the retests refuted the original OOS and OOT results. The retests were used as the reported values.

5.2. BDI23-09: This discrepancy covers one of the temperature data loggers being missing for the time period of 06/23/22 to 09/14/22, and not being able to retrieve data for that area of Cold Storage Container A01RC04. There were also out of specification (OOS) results obtained that could not be explained by container entrances. The root cause was determined to be the style of temperature data logger being used is easily knocked down and could possibly be removed on pallets stored in the unit. The OOS results were determined to be from entry into the unit that was not recorded in the log book. It was determined that there was no impact on samples stored in the unit.

5.3. BDI22-224: Testing for pH (5%) was not complete for the T=0 timepoint for all three lots of Uridine. This test was not required for finished goods (URID-3250) or for the Degradation and Impurity Profile Report: Uridine (Excipient) (BSI-RPT-1005). Testing was not requested for Stability, and it was not done. There is no specification for pH (5%) and the data is only for monitoring purposes.

5.4. BDI23-18: This discrepancy covers out of specification (OOS) results for the period of 09/14/22 to 12/21/22 for A01RC04 that are not explained by container entrances. The root cause was determined to be entry into this storage unit that was not logged into the book. It was determined that there was no impact on samples stored in this unit.

6. LOT EVALUATION:

TABLE 2A: RESULT OF COLD STORAGE STABILITY ANALYSES FOR URID-0122-00005-PV P/P

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00005-PV Cold Storage P/P	Appearance and Color	White to almost white powder	White powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	0.1%	0.2%	0.3%	0.3%	0.2%	0.2%	0.2%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.5 – 168.8°C	167.6 – 168.8°C	167.8 – 168.8°C	167.6 – 168.5°C	167.5 – 168.6°C	167.6 – 168.4°C
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.17	5.18	5.18	5.08	5.18	5.14
	Transparency (1%)	≥ 98.0%	99.6%	99.8%	99.8%	99.1%	99.7%	99.7%	99.7%
	UV-Assay	≥ 98.0%	98.4%	99.1%	99.2%	99.7%	101.8%	100.2%	99.0%

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2B: RESULT OF COLD STORAGE STABILITY ANALYSES FOR URID-0122-00005-PV LABLINE

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00005-PV Cold Storage Labline	Appearance and Color	White to almost white powder	White powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	0.1%	0.1%	0.2%	0.1%	0.1%	0.1%	0.2%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.5 – 168.8°C	167.6 – 169.5°C	167.7 – 169.1°C	167.4 – 168.3°C	167.6 – 168.6°C	167.5 – 168.8°C
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.14	5.17	5.17	5.07	5.14	5.14
	Transparency (1%)	≥ 98.0%	99.6%	99.8%	99.8%	99.1%	99.6%	99.8%	99.7%
	UV-Assay	≥ 98.0%	98.4%	99.3%	98.9%	99.3%	99.7%	99.4%	99.9%

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2C: RESULT OF COLD STORAGE STABILITY ANALYSES FOR URID-0122-00006-PV P/P

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00006-PV Cold Storage P/P	Appearance and Color	White to almost white powder	Almost white powder	White to almost white powder	White powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	≤ 0.5%	0.1%	0.1%	0.2%	0.2%	0.2%	0.3%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.3 – 168.8°C	167.8 – 169.0°C	167.6 – 168.8°C	166.8 – 168.3°C	167.6 – 168.8%	167.5 – 168.8%
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.26	5.22	5.21	5.19	5.30	5.16
	Transparency (1%)	≥ 98.0%	99.7%	99.9%	99.7%	99.8%	99.7%	99.8%	99.6%
	UV-Assay	≥ 98.0%	100.1%	99.7%	99.6%	99.1%	100.1%	99.0%	98.9%

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2D: RESULT OF COLD STORAGE STABILITY ANALYSES FOR URID-0122-00006-PV LABLINE

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00006-PV Cold Storage Labline	Appearance and Color	White to almost white powder	Almost white powder	White to almost white powder	White powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	≤ 0.5%	0.1%	0.1%	0.1%	0.1%	0.2%	0.1%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.3 – 168.8°C	167.6 – 169.0°C	167.5 – 168.8°C	167.6 – 169.1°C	167.7 – 168.8°C	167.5 – 168.8°C
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.27	5.21	5.22	5.19	5.20	5.15
	Transparency (1%)	≥ 98.0%	99.7%	99.8%	99.6%	99.8%	99.7%	99.9%	99.4%
	UV-Assay	≥ 98.0%	100.1%	99.4%	100.2%	98.9%	99.2%	99.5%	99.4%

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2E: RESULT OF ACCELERATED STABILITY ANALYSES FOR URID-0122-00005-PV P/P

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00005-PV Accelerated P/P	Appearance and Color	White to almost white powder	White powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	0.1%	0.2%	0.2%	0.3%	0.2%	0.2%	0.3%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.5 – 168.8°C	167.7 – 169.1°C	167.8 – 169.1°C	167.5 – 168.0°C	167.6 – 168.3°C	167.5 – 168.8°C
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.14	5.15	5.13	5.08	5.10	5.11
	Transparency (1%)	≥ 98.0%	99.6%	99.8%	99.7%	99.3%	99.6%	99.6%	99.4%
	UV-Assay	≥ 98.0%	98.4%	100.2%	99.3%	99.2%	100.5%	99.5%	99.2%

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2F: RESULT OF ACCELERATED STABILITY ANALYSES FOR URID-0122-00005-PV LABLINE

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00005-PV Accelerated Labline	Appearance and Color	White to almost white powder	White powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	0.1%	0.2%	0.2%	0.2%	0.2%	0.2%	0.3%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.5 – 168.8°C	167.8 – 168.9°C	167.8 – 169.0°C	167.6 – 168.5°C	167.5 – 168.2°C	167.3 – 168.3°C
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.15	5.15	5.15	5.10	5.09	5.10
	Transparency (1%)	≥ 98.0%	99.6%	99.9%	99.7%	99.5%	99.7%	99.8%	99.8%
	UV-Assay	≥ 98.0%	98.4%	99.5%	99.1%	98.9%	98.4%	99.4%	99.1%

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2G: RESULT OF ACCELERATED STABILITY ANALYSES FOR URID-0122-00006-PV P/P

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00006-PV Accelerated P/P	Appearance and Color	White to almost white powder	Almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	≤ 0.5%	0.2%	0.3%	0.2%	0.2%	0.2%	0.3%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.3 – 168.8°C	167.8 – 169.0°C	167.5 – 168.8°C	166.1 – 168.1°C	167.7 – 168.8°C	167.7 – 168.9°C
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.24	5.18	5.18	5.18	5.15	5.12
	Transparency (1%)	≥ 98.0%	99.7%	99.9%	99.7%	99.8%	99.7%	99.7%	99.4%
	UV-Assay	≥ 98.0%	100.1%	99.7%	99.6%	99.1%	100.1%	99.7%	99.2%

[1]CSRS = Conforms to Spectrum of Reference Standard

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

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

TABLE 2H: RESULT OF ACCELERATED STABILITY ANALYSES FOR URID-0122-00006-PV LABLINE

Lot Number	Analysis	Specification	T_0	T_1	T_2	T_3	T_4	T_5	T_6
URID-0122-00006-PV Accelerated Labline	Appearance and Color	White to almost white powder	Almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder	White to almost white powder
	[1]Identification (IR)	Conforms to Spectrum of Reference Standard	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS	CSRS
	Loss on Drying	≤ 0.5%	≤ 0.5%	0.1%	0.2%	0.2%	0.2%	0.2%	0.2%
	[2]Melting Point	Report 167 - 170°C	167.1 – 168.5°C	167.3 – 168.8°C	167.8 – 169.0°C	167.5 – 168.8°C	167.7 – 169.1°C	167.6 – 168.8°C	167.4 – 168.8°C
	[3]pH (5%)	Report 4.0 – 6.0	[4,5]N/A	5.23	5.18	5.18	5.18	5.15	5.15
	Transparency (1%)	≥ 98.0%	99.7%	99.8%	99.8%	99.8%	99.7%	99.9%	99.5%
	UV-Assay	≥ 98.0%	100.1%	98.6%	100.5%	99.8%	100.2%	100.0%	99.3%

[1]CSRS = Conforms to Spectrum of Reference Standard

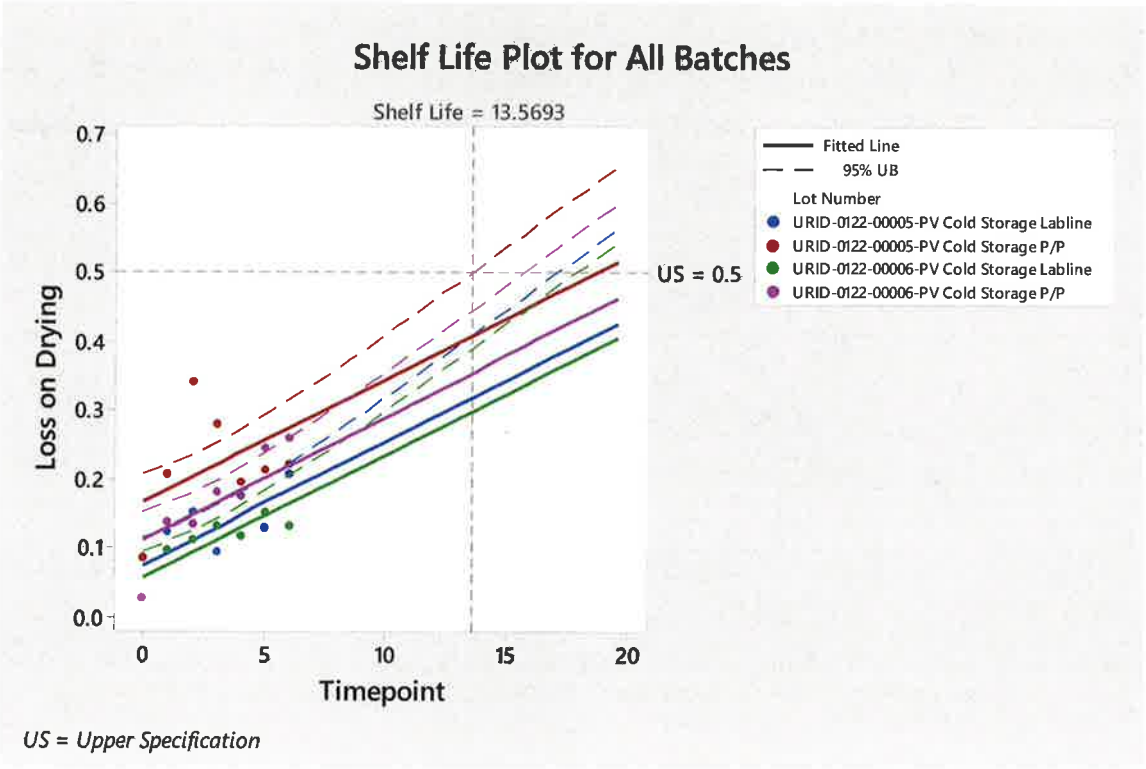
[2]Analysis (Melting Point) is not required for URID-3250. Specification will be Report, and specification to compare to will be 167 – 170°C.

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

[4]N/A = Not Applicable

[5]Refer to BDI22-224 for missing data for pH (5%) at T=0

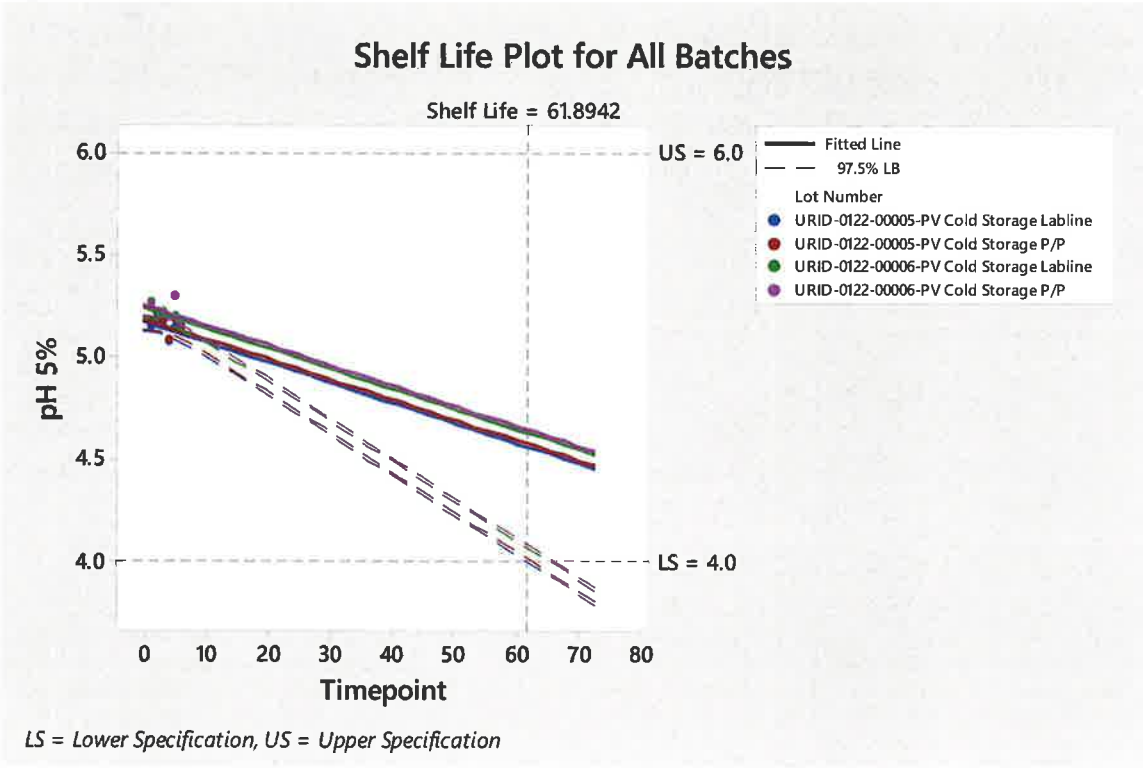
GRAPH 1: COLD STORAGE LOSS ON DRYING



US = Upper Specification

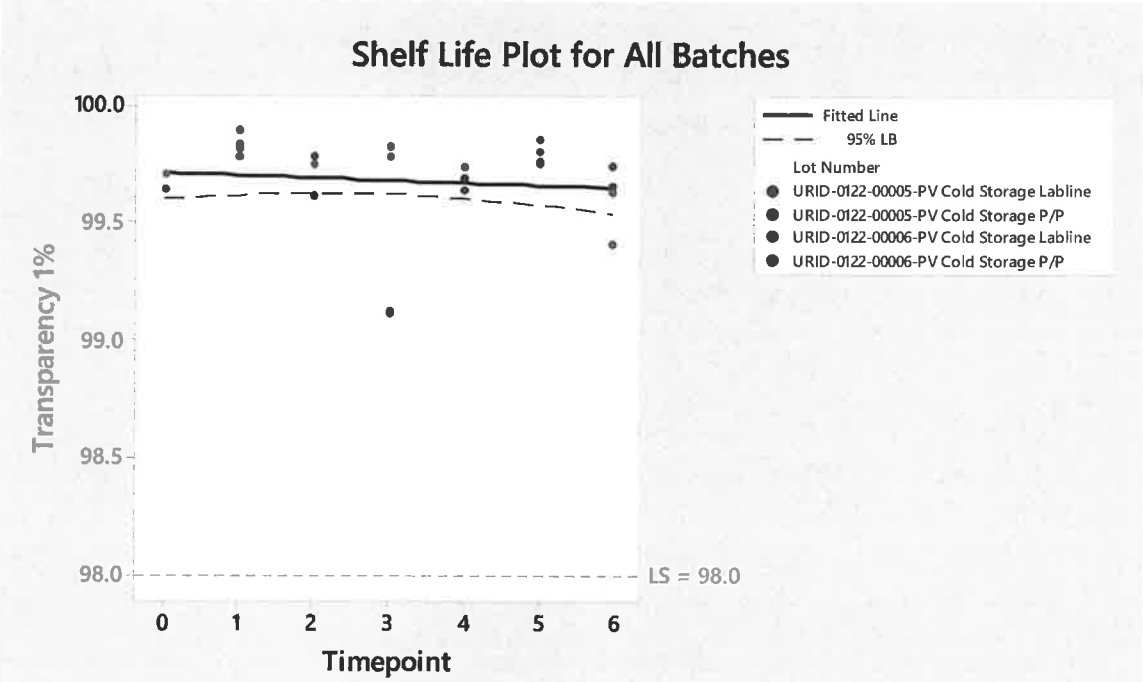
The predicted Shelf-Life for Cold Storage Loss on Drying was determined to be 13.5693 months at the final T=6 month time interval.

GRAPH 2: COLD STORAGE PH (5%)



The predicted Shelf-Life for Cold Storage pH (5%) was determined to be 61.8942 months at the final T=6 month time interval.

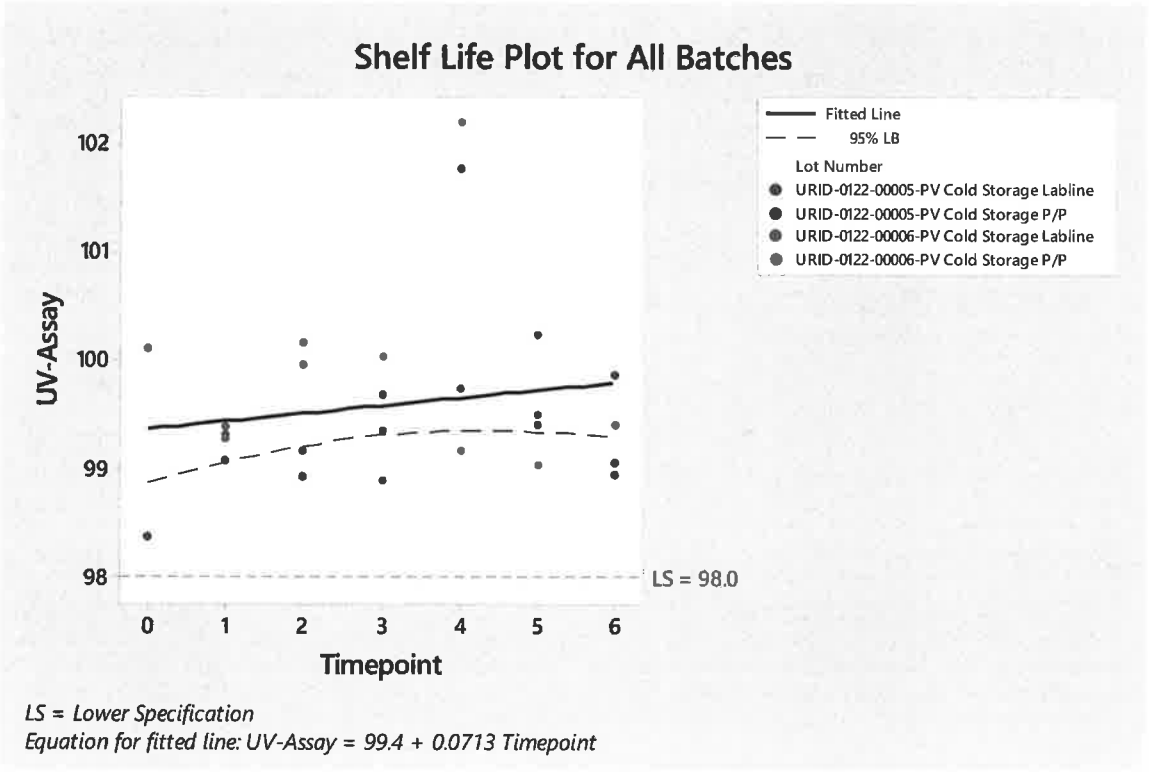
GRAPH 3: COLD STORAGE TRANSPARENCY (1%)



LS = Lower Specification
Equation for fitted line: Transparency 1% = 99.7 - 0.0106 Timepoint

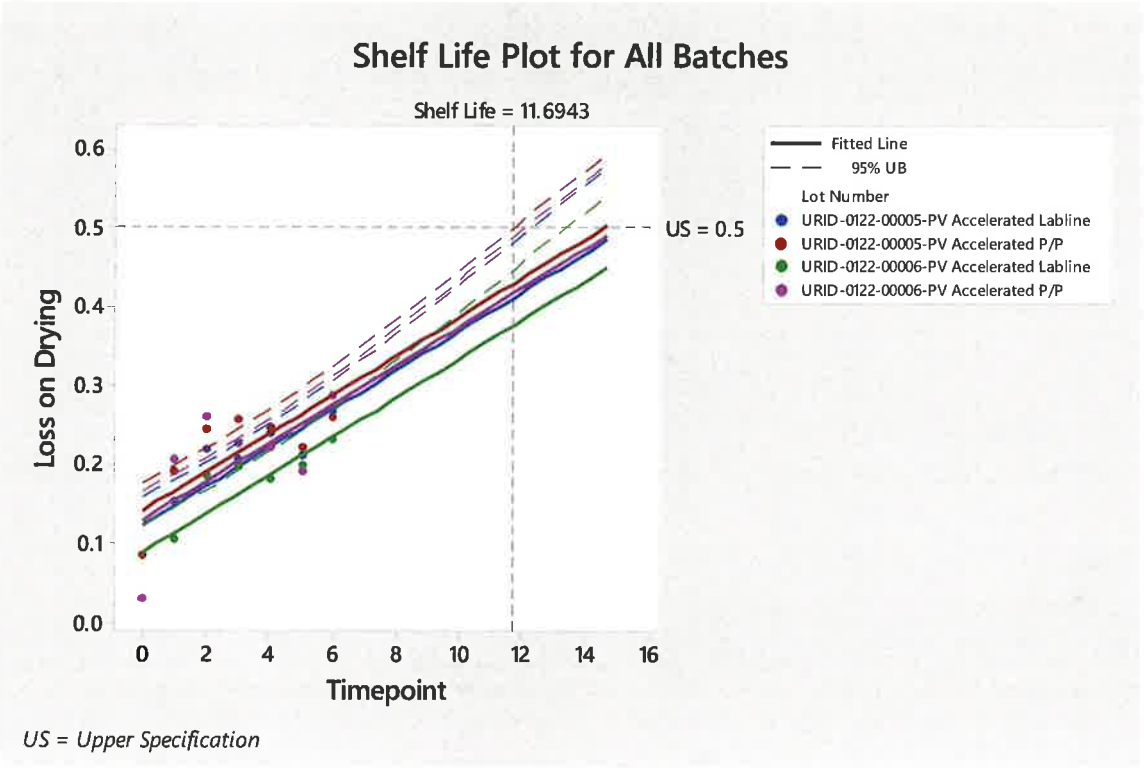
No Shelf-Life was able to be determined for Cold Storage Transparency (1%), as the mean response slope is not significantly different from zero using 95% confidence at the final T=6 month time interval.

GRAPH 4: COLD STORAGE UV-ASSAY



No Shelf-Life was able to be determined for Cold Storage UV-Assay, as the mean response slope is not significantly different from zero using 95% confidence at the final T=6 month time interval.

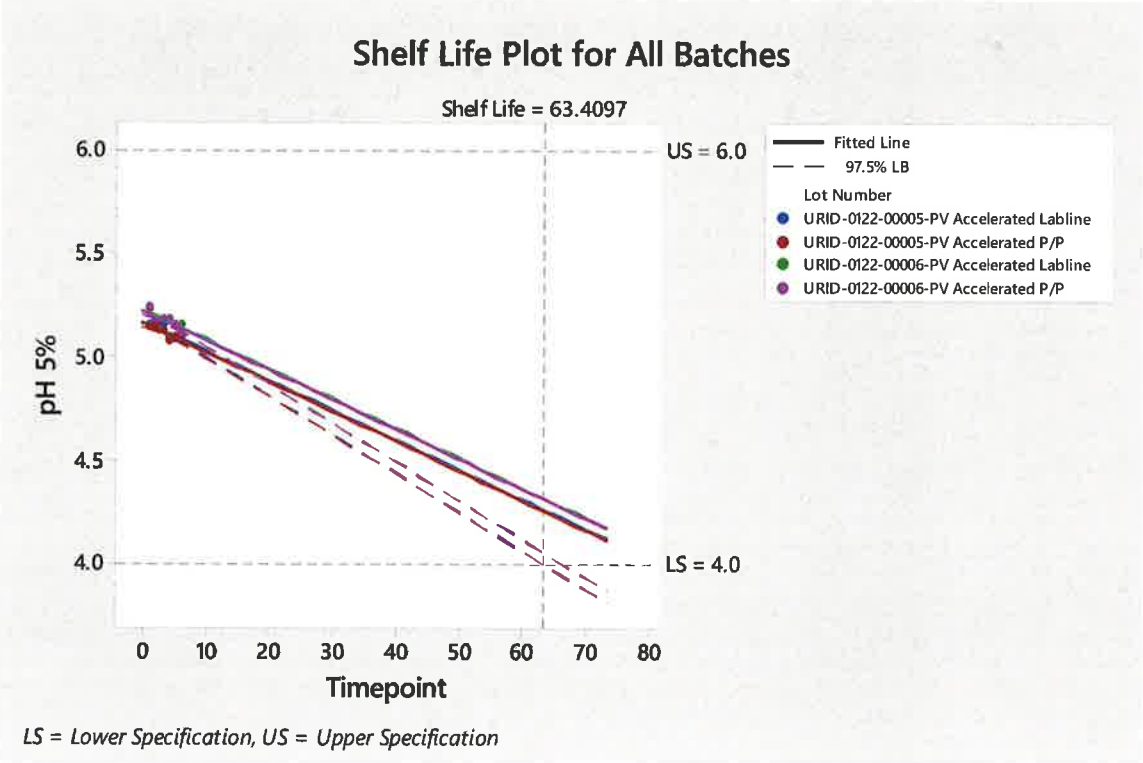
GRAPH 5: ACCELERATED LOSS ON DRYING



US = Upper Specification

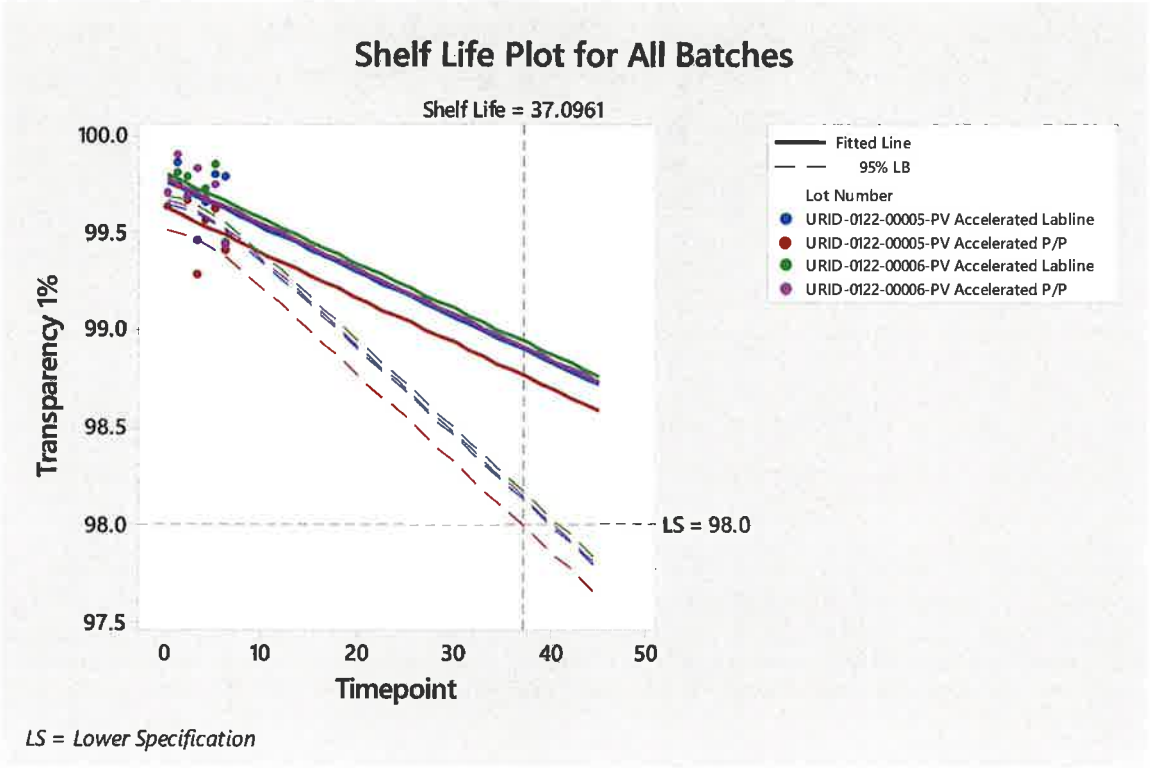
The predicted Shelf-Life for Accelerated Loss on Drying was determined to be 11.6943 months at the final T=6 month time interval.

GRAPH 6: ACCELERATED PH (5%)



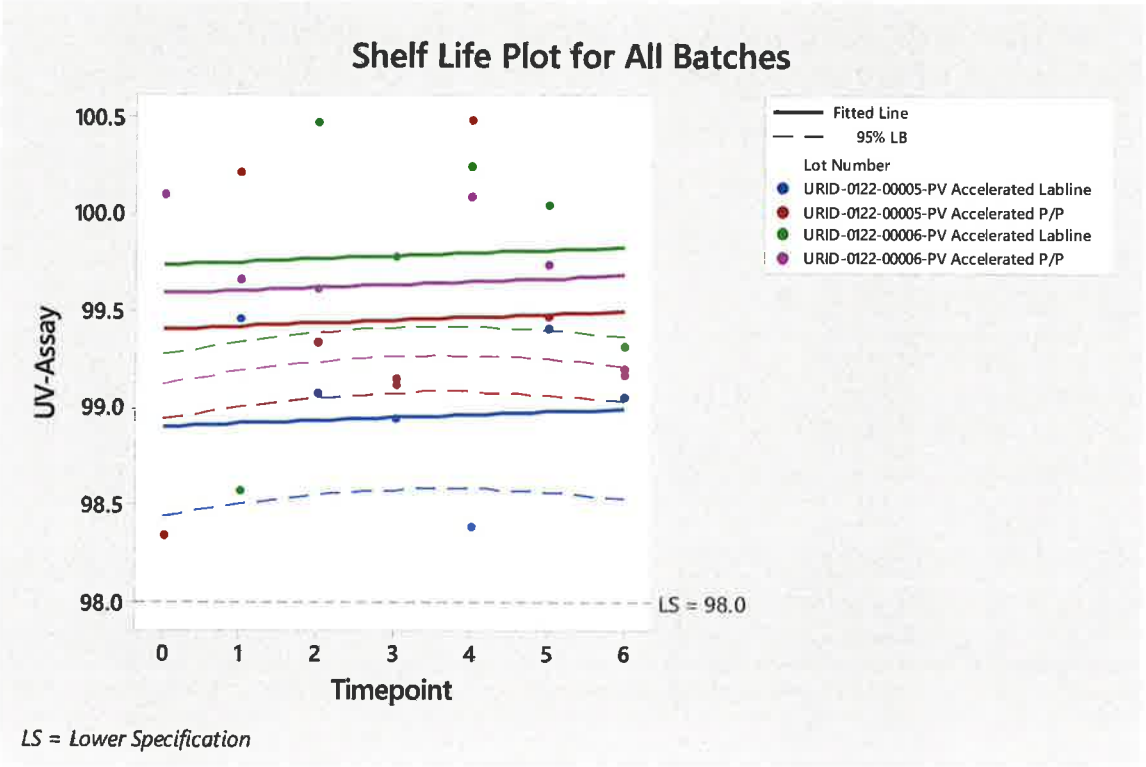
The predicted Shelf-Life for Accelerated pH (5%) was determined to be 63.4097 months at the final T=6 month time interval.

GRAPH 7: ACCELERATED TRANSPARENCY (1%)



The predicted Shelf-Life for Accelerated Transparency (1%) was determined to be 37.0961 months at the final T=6 month time interval.

GRAPH 8: ACCELERATED UV-ASSAY



No Shelf-Life was able to be determined for Accelerated UV-Assay, as the mean response slope is not significantly different from zero using 95% confidence at the final T=6 month time interval.

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 1.5x, where x is the period covered by cold storage (refrigerated) and accelerated stability data, but should be no more than 6 months beyond for both refrigerated and accelerated conditions.

7.2. The Cold Storage Stability Data displayed in this report along with the predicted shelf-life plots would support a retest date of 13.5693 months, with Loss on Drying being the limiting factor for predicted shelf life plots. However, with 6 months of stability data acquired, which completes this study, the stability report supports a retest date of 9 months (based on ICH guidelines where retest date can be calculated as 1.5 x 6 = 9) for Uridine manufactured at BioSpectra in the Bangor, PA facility that is held at Cold Storage conditions.

7.3. The Accelerated Stability Data displayed in this report along with the predicted shelf-life plots would support a retest date of 11.6943 months, with Loss on Drying being the limiting factor for predicted shelf life plots. However, with 6 months of stability data acquired, which completes this study, the stability report supports a retest date of 9 months (based on ICH guidelines where retest date can be calculated as 1.5 x 6 = 9) for Uridine manufactured at BioSpectra in the Bangor, PA facility that is held at Accelerated Storage conditions.

7.4. This study concludes that Uridine manufactured at BioSpectra in the Bangor, PA facility will remain stable under the extreme conditions monitored in this study (Cold Storage and Accelerated Storage conditions) for up to 9 months. This data can be used together with Real Time Stability data (Refer to BSI-RPT-1231) to establish the overall stability of Uridine.

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 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.