BIOSPECTRA
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DEXTRAN SULFATE 8000
2023 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 Dextran Sulfate 8000 manufactured in 2023 at the Majestic, PA facility of BioSpectra. Testing intervals are designated by T_n, where n equals 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 stability report will assess the stability data of Dextran Sulfate 8000 lots DXSE-0123-00004-PV, DXSE-0123-00006-PV and DXSE-0123-00007-PV that completed eighteen (18) months of long-term stability in January 2025. This study includes the following analyses: Appearance, Clarity (20% Solution), Identification (Colorimetric), Loss on Drying (LOD), pH (1% Solution), Endotoxin and Total Bioburden. Results from all analyses are summarized in Table 2 through 4. 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 for Dextran Sulfate 8000. The following product codes are commercially available.

- DXSE-4250
- DXSE-5201

2. REFERENCES:

2.1. BSI-LST-0248, Dextran Sulfate 8000 Stability Data Card
2.2. BSI-PRL-0676, Stability Indicating Protocol: Dextran Sulfate 8000
2.3. BSI-RPT-1348, Stability Indicating Report: Dextran Sulfate 8000
2.4. BSI-SOP-0136, Stability Testing Program
2.5. BSI-SOP-0146, Stability Inventory
2.6. BSI-SOP-0289, Stability Indication Protocol
2.7. Current EP
2.8. Current USP
2.9. ICH Q1E

3. SAMPLE DESIGNATION:

3.1. Samples initially placed on the stability program consisted of three lots of Dextran Sulfate 8000. Stability samples from this lot were put into 2P/P with desiccant 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 with desiccant	Samples are packaged into small poly bags and sealed with a zip tie. All individual samples are then placed into a larger poly bag and sealed with a zip tie. This bag will then get placed into a poly drum with desiccant.

4. STORAGE:

4.1. The packaging and storage requirements for Dextran Sulfate 8000 are to be in well-closed containers stored at room temperature. For this study, Dextran Sulfate 8000 stability samples were stored in the Long-Term Stability Chamber H03SC01 at the Majestic, PA facility for the time period of July 2023 to January 2025. Storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature (25°C ±2), relative humidity (60%RH±5) and mean kinetic temperature (monitored). The maximum temperature recorded was 26.20°C, the minimum temperature was 21.81°C, the average temperature was 25.36°C, and the average Mean Kinetic Temperature was 25.36°C. The maximum relative humidity recorded was 80.5%, the minimum relative humidity was 43.6%, and the average relative humidity was 61.2%. Maximum and minimum values that are outside limits for temperature and humidity are due to opening the door of the chamber as explained in Temperature and Humidity Monitoring Assessments for the chambers. Section 5 will include any excursions from these conditions that resulted in an investigation.

5. INVESTIGATIONS:

5.1. BDI24-13, Out of range humidity for the Long-Term 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 humidity for the Long-Term Stability Chamber H03SC01 caused by a blown main 20-amp fuse. The first out of specification point was on 8/15/24 after which the temperature and humidity dropped until the fuse was fixed on 8/16/24. The temperature and humidity returned to specification and remained in specification the duration of the month. There was no impact to the current list of materials in the stability chamber.

5.3. BLI25-01, during review and completion of LOD testing, it was noted that the results obtained for DXSE-0123-0004-PV and DXSE-0123-00006-PV T=18 2P/P with desiccant had elevated LOD results. Results of 9.3844% and 9.8873% respectively were obtained, which are determined to be out of trend when compared to previous time pulls using a six-pack report. Both lots were retested and confirmed original LOD results. T=extra samples were pulled for both lots and analyzed in an investigation to rule out mishandling of samples due to its hydroscopic nature. The T=extra samples for each lot were analyzed in triplicate by two different analysts. The original out of trend results were refuted and the average of the six retests performed for each lot were reported for the T=18 timepoint.

6. LOT EVALUATION:

TABLE 2: DXSE-0123-00004-PV 2P/P WITH DESICCANT

Time Point	Analysis						
	Appearance (Off White to Light Yellow Powder)	**Clarity (20% Solution)** (Absorbance @ 360 nm ≤ 0.9 OD unit)	**Endotoxin** (≤ 0.012 EU/mg)	**Loss on Drying** (≤10.0%)	**Identification (Colorimetric)** (Passes Test)	**pH (1%)** (5.0 – 7.5)	**Total Bioburden** (≤100 CFU/g)
T_0	Off White to Light Yellow Powder	0.1043 OD unit	<0.0050 EU/mg	7.0928%	Passes Test	6.94	<10 CFU/g
T_3	Off White to Light Yellow Powder	0.0950 OD unit	<0.0050 EU/mg	6.9291%	Passes Test	7.04	<10 CFU/g
T_6	Off White to Light Yellow Powder	0.0874 OD unit	<0.0050 EU/mg	7.5443%	Passes Test	7.16	<10 CFU/g
T_9	Off White to Light Yellow Powder	0.0924 OD unit	<0.0050 EU/mg	7.6049%	Passes Test	7.23	<10 CFU/g
T_{10}	Off White to Light Yellow Powder	0.0866 OD unit	<0.0050 EU/mg	7.0558%	Passes Test	7.22	<10 CFU/g
T_{12}	Off White Powder	0.0936 OD unit	<0.0050 EU/mg	6.5471%	Passes Test	7.19	<10 CFU/g
T_{15}	Off White to Light Yellow Powder	0.0963 OD unit	<0.0050 EU/mg	6.1282%	Passes Test	7.24	<10 CFU/g
T_{18}	Off White to Light Yellow Powder	0.0728 OD unit	<0.0050 EU/mg	6.8325%	Passes Test	7.18	<10 CFU/g

- **REMAINING TESTING INTERVAL PULL DATES**
  - T = 24; Scheduled for July 6, 2025
  - T = 36; Scheduled for July 6, 2026
  - T = 48; Scheduled for July 6, 2027
  - T = 60; Scheduled for July 6, 2028

TABLE 3: DXSE-0123-00006-PV 2P/P WITH DESICCANT

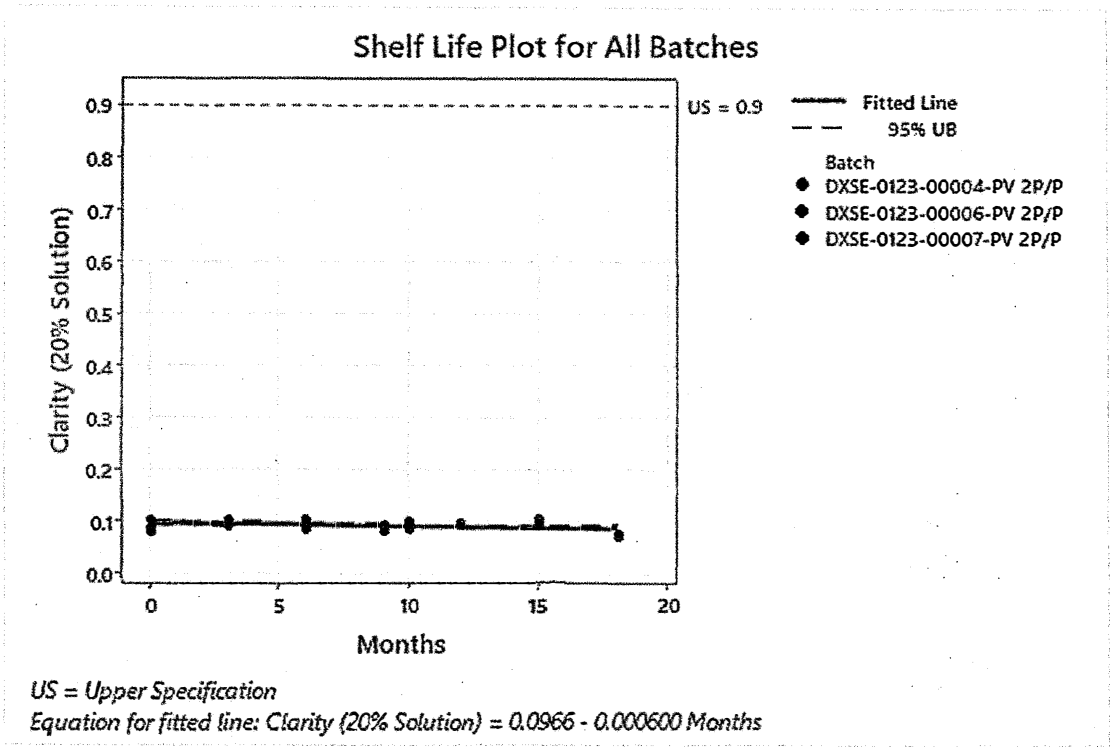
Time Point	Analysis						
	Appearance (Off White to Light Yellow Powder)	**Clarity (20% Solution)** (Absorbance @ 360 nm ≤ 0.9 OD unit)	**Endotoxin** (≤ 0.012 EU/mg)	**Loss on Drying** (≤10.0%)	**Identification (Colorimetric)** (Passes Test)	**pH (1%)** (5.0 – 7.5)	**Total Bioburden** (≤100 CFU/g)
T_0	Off White to Light Yellow Powder	0.0905 OD unit	<0.0050 EU/mg	7.5457%	Passes Test	6.85	<10 CFU/g
T_3	Off White to Light Yellow Powder	0.1036 OD unit	<0.0050 EU/mg	7.3964%	Passes Test	6.80	<10 CFU/g
T_6	Off White to Light Yellow Powder	0.1040 OD unit	<0.0050 EU/mg	8.0251%	Passes Test	6.85	<10 CFU/g
T_9	Off White to Light Yellow Powder	0.0923 OD unit	<0.0050 EU/mg	7.9194%	Passes Test	6.88	<10 CFU/g
T_{10}	Off White to Light Yellow Powder	0.1001 OD unit	<0.0050 EU/mg	7.2904%	Passes Test	6.89	<10 CFU/g
T_{12}	Off White Powder	0.0964 OD unit	<0.0050 EU/mg	7.5089%	Passes Test	6.90	<10 CFU/g
T_{15}	Off White to Light Yellow Powder	0.1051 OD unit	<0.0050 EU/mg	6.6207%	Passes Test	6.93	<10 CFU/g
T_{18}	Off White to Light Yellow Powder	0.0687 OD unit	<0.0050 EU/mg	7.8596%	Passes Test	6.92	<10 CFU/g

- **REMAINING TESTING INTERVAL PULL DATES**
  - T = 24; Scheduled for July 6, 2025
  - T = 36; Scheduled for July 6, 2026
  - T = 48; Scheduled for July 6, 2027
  - T = 60; Scheduled for July 6, 2028

TABLE 4: DXSE-0123-00007-PV 2P/P WITH DESICCANT

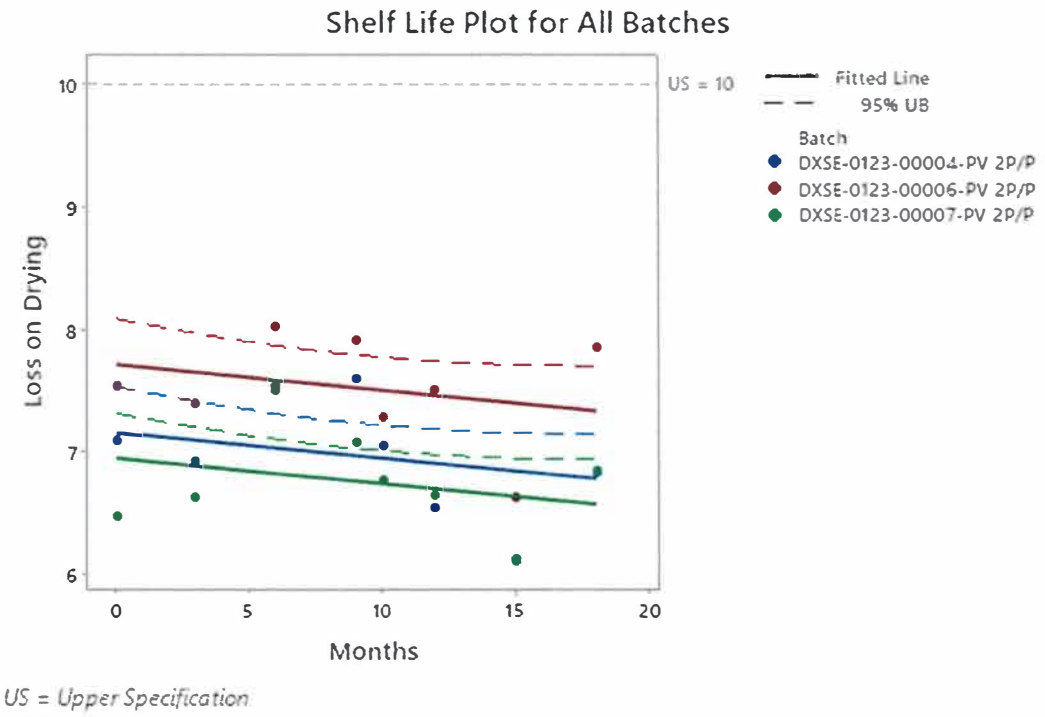
Time Point	Analysis						
	Appearance (Off White to Light Yellow Powder)	**Clarity (20% Solution)** (Absorbance @ 360 nm ≤ 0.9 OD unit)	**Endotoxin** (≤ 0.012 EU/mg)	**Loss on Drying** (≤10.0%)	**Identification (Colorimetric)** (Passes Test)	**pH (1%)** (5.0 – 7.5)	**Total Bioburden** (≤100 CFU/g)
T_0	Off White to Light Yellow Powder	0.0801 OD unit	<0.0050 EU/mg	6.4679%	Passes Test	6.94	<10 CFU/g
T_3	Off White to Light Yellow Powder	0.0936 OD unit	<0.0050 EU/mg	6.6306%	Passes Test	6.82	<10 CFU/g
T_6	Off White to Light Yellow Powder	0.0854 OD unit	<0.0050 EU/mg	7.5069%	Passes Test	6.93	<10 CFU/g
T_9	Off White to Light Yellow Powder	0.0818 OD unit	<0.0050 EU/mg	7.0808%	Passes Test	6.95	<10 CFU/g
T_{10}	Off White to Light Yellow Powder	0.0901 OD unit	<0.0050 EU/mg	6.7624%	Passes Test	6.97	<10 CFU/g
T_{12}	Off White Powder	0.0914 OD unit	<0.0050 EU/mg	6.6455%	Passes Test	7.05	<10 CFU/g
T_{15}	Off White to Light Yellow Powder	0.1003 OD unit	<0.0050 EU/mg	6.1148%	Passes Test	6.95	<10 CFU/g
T_{18}	Off White to Light Yellow Powder	0.0746 OD unit	<0.0050 EU/mg	6.8456%	Passes Test	6.97	<10 CFU/g

- **REMAINING TESTING INTERVAL PULL DATES**
  - T = 24; Scheduled for July 6, 2025
  - T = 36; Scheduled for July 6, 2026
  - T = 48; Scheduled for July 6, 2027
  - T = 60; Scheduled for July 6, 2028



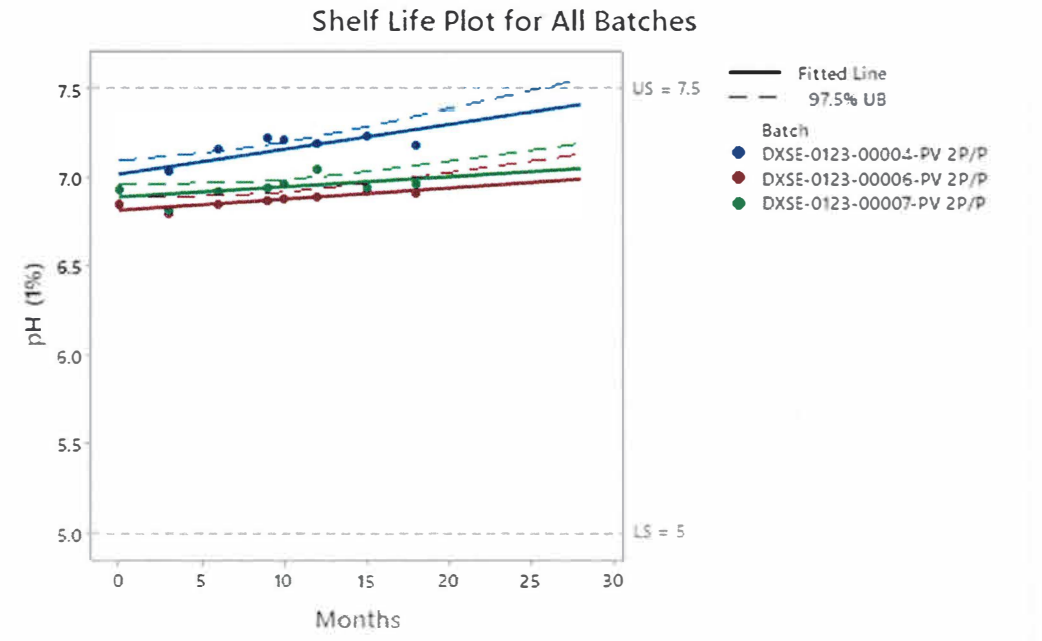
GRAPH 1: CLARITY (20% SOLUTION)

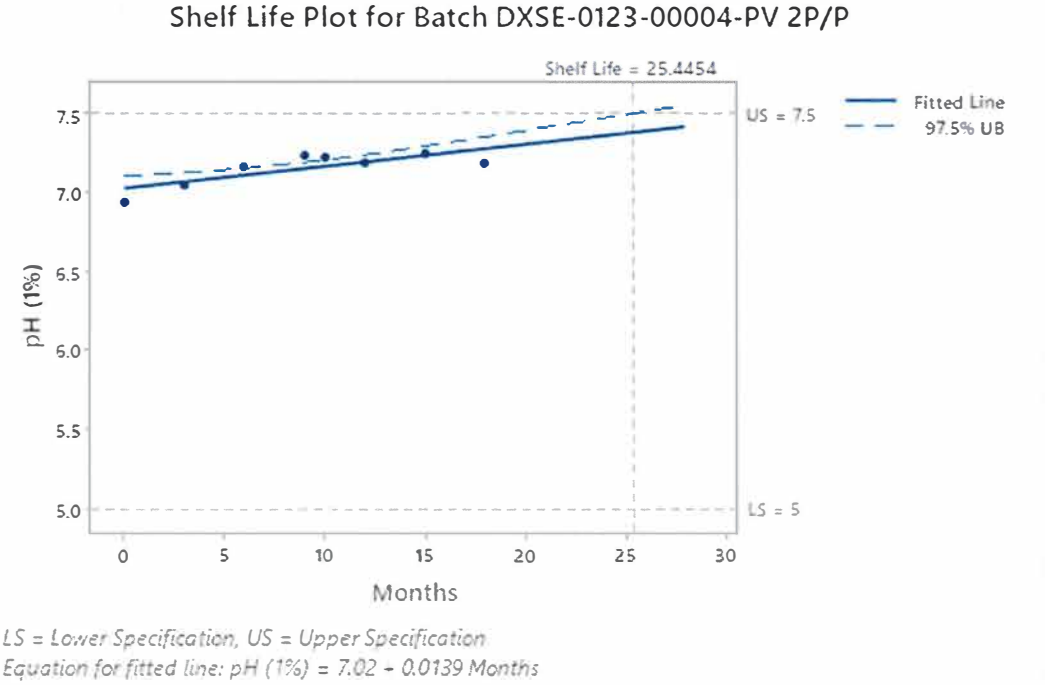
No Shelf-Life was able to be determined for Clarity as of the 18-month time interval, as the mean response slope is not significantly different from zero using 95% confidence. There is no impact to the product or currently assigned retest period of this material.



GRAPH 2: LOSS ON DRYING

No Shelf-Life was able to be determined for Loss on Drying as of the 18-month time interval, 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 period of this material.





GRAPH 3: PH (1% SOLUTION)

The predicted Shelf-Life for pH (1% Solution) was determined to be 25.4454 months as of the 18-month time interval for the DXSE-0123-00004-PV data. There is no impact to the product or currently assigned retest period of this material.

7. CONCLUSION:

In regards to the Long-Term Stability Study for Dextran Sulfate 8000 2023 lots, all data met the specifications set forth in the Stability Testing Program for the lots stored at the recommended long-term storage conditions. 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 of up to 18 months of testing for the 2023 lots of Dextran Sulfate 8000 manufactured at BioSpectra in the Majestic, PA facility, along with the predicted shelf-life plots, support a retest date of 25 months based on the Minitab plot of pH (1%) for lot of Dextran Sulfate 8000 manufactured at BioSpectra in the Majestic, PA facility. The shelf life for the product code DXSE-5201, material packaged from approved supplier, is set at 36-months based on historical data provided by the approved Raw Material Supplier.

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 real time/ long term 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 and the product has an established shelf life, the batch will be withdrawn from the market through communication with any 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.