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

URACIL LONG TERM STABILITY REPORT: UC4200-029-0121

TABLE OF CONTENTS

1. OVERVIEW:

The purpose of this report is to analyze and conclude on the data obtained from the long-term stability study of Uracil manufactured in 2021 at the Bangor, 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 shelf life for the finished good product.

This real time stability analysis will assess the stability of Uracil lot UC4200-029-0121 that completed forty-eight (48) months of long-term stability in February 2025. This study includes the following analyses, results from all analyses are summarized in Table 2.

TABLE 1: STABILITY SPECIFICATIONS

Analysis	Specification
Appearance and Color	White to Slightly Yellow Powder
Identification (IR)	Passes Test
Reaction	Passes Test
Solubility	Passes Test

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 Uracil. The following product codes are commercially available:

- URAC-4201
- URAC-4301

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 Uracil. Stability samples from this lot were put into P/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 2: PACKAGING DETAILS

Packaging Configuration	Packaging Description
P/P	Samples are packaged into small LLDPE bags and sealed with a zip tie and then are placed into a HDPE pail.

4. STORAGE:

4.1. The USP Packaging and Storage requirements for Uracil are to be in well-closed containers stored at room temperature. For this study, the samples were stored in the Real Time Stability Chamber H03SC01 at the Bangor, PA facility from February 2021 until the last sample time point in February 2025. Storage conditions have been continuously measured and recorded utilizing MadgeTech data loggers with regulated conditions for temperature, relative humidity and Mean Kinetic Temperature. The storage conditions for the time period of this study are detailed in Table 3. Section 5 will include any excursions from these conditions that resulted in an investigation.

TABLE 3: STORAGE CONDITIONS

Condition	Specification	Value
Minimum Temperature	25°C ± 2°C	21.81°C
Maximum Temperature		27.80°C
Average Temperature		25.42°C
Mean Kinetic Temperature	Monitor	25.42°C
Minimum Humidity	60%RH ± 5%RH	31.1%RH
Maximum Humidity		80.5%RH
Average Humidity		61.3%RH

5. INVESTIGATIONS:

5.1. **BDI22-61:** This discrepancy was issued for missing temperature and humidity data points for the long-term stability chamber from 1/28/22-2/9/22. The root cause was determined to be malfunction of the logger or depletion of battery. There was no impact to the material stored in the chamber as the analog chart recorders were on and recording, confirming there were no excursions during the down time of the Madgetech logger.

5.2. **BDI22-138**: This discrepancy was issued for out of range humidity readings for the long-term stability chamber from 0420 on 4/26/22 through 0850 on 4/26/22. The root cause for this discrepancy was determined to be closure of the humidifier valve, thus lowering the humidity in the long-term stability chamber below the required 55% RH. There was no impact to the stability samples in the chamber because the excursion was brief, lasting less than 5 hours.

5.3. **BDI22-143:** This discrepancy was issued for missing temperature and humidity data points for the long-term stability chamber from 11/20/21-12/3/21. The root cause was determined to be depleted batteries in the MadgeTech logger. There was no impact to the material stored in the chamber as the analog chart recorders were on and recording, confirming there were no excursions during the down time of the MadgeTech logger.

5.4. **BDI22-275**: This discrepancy was issued for failure to complete temperature and Humidity assessment forms for the long-term stability chamber for July 2022 within a month of downloading the data. The root cause was determined to be failure to prioritize time sensitive job functions due to poor time management. There is no impact to the stability samples as the temperature and humidity data was not impacted and the assessments were performed.

5.5. **BDI24-13:** This discrepancy was issued for out of range humidity result for long-term stability chamber H03SC01 from 1/15/24-1/17/24. The root cause of this discrepancy was determined to be improper work order completion. The water valve that supplies H03SC01 with water for humidity control was inadvertently closed, therefore causing the humidity to decrease. There was no impact to the product stored within H03SC01.

5.6. **BDI24-126:** Out of specification humidity reading was recorded for H03SC01 on 8/15/24 that was caused by a blown 20-amp fuse. The fuse was replaced the humidity returned to within specification. There was no impact to the material stored in the stability chamber.

6. LOT EVALUATION:

TABLE 4: UC4200-029-0121 P/P

Time Point	Analyses/Specification			
	Appearance and Color	Identification (IR)	Reaction	Solubility
	White to Slightly Yellow Powder	Passes Test	Passes Test	Passes Test
T_0	White Powder	Passes Test	Passes Test	Passes Test
T_3	White Powder	Passes Test	Passes Test	Passes Test
T_6	White Powder	Passes Test	Passes Test	Passes Test
T_9	White Powder	Passes Test	Passes Test	Passes Test
T_{12}	White to Slightly Yellow Powder	Passes Test	Passes Test	Passes Test
T_{18}	White to Slightly Yellow Powder	Passes Test	Passes Test	Passes Test
T_{24}	White to Slightly Yellow Powder	Passes Test	Passes Test	Passes Test
T_{36}	White Powder	Passes Test	Passes Test	Passes Test
T_{48}	White Powder	Passes Test	Passes Test	Passes Test

7. CONCLUSION:

In regards to the Long-Term Stability Study for Uracil 2021 lot UC4200-029-0121, all data met the specifications set forth in the Stability Testing Program for lot stored at the recommended long-term condition. 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 real time conditions. Long-Term Stability Data displayed in this report up to 48 months of testing for this 2021 lot of Uracil manufactured at BioSpectra in the Bangor, PA facility support the current expiration date of 36 months with an extension of up to 60 months upon request for Uracil when stored in P/P packaging for product codes URAC-4201 and URAC-4301.

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 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.