BIOSPECTRA
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DEGRADATION AND IMPURITY PROFILE REPORT: URACIL

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1. PURPOSE AND SCOPE:

1.1. The impurity profiling of Uracil was intended to identify and potentially quantify impurities found in the Uracil product manufactured and purified at BioSpectra, at the BioSpectra Bangor, PA facility.

1.1.1. In the case where a known impurity or degradation product was detected, a limit was set to the maximum allowable without measurable compromise to predetermined critical quality attributes or toxicity. In the case where a limit could not be set, a procedure was written and followed, to identify if the possible impurity was present or not (i.e. an identity test which is qualitative and not quantitative.)

1.1.2. The profiling results and data allowed BioSpectra to monitor the purity and characteristics of Uracil through stages of manufacturing.

1.1.3. The four stages of Uracil that were tested are Raw Material, Mother Liquor, Wet Crystals and the finished product. There was a minimum of one lot, one sample from each stage, used for analysis. A table was generated to include all sample results in the Uracil Degradation and Impurity Profile Report.

1.1.4. The tests that were used to determine the presence of impurities and degradation products are as follows:

1.1.4.1. Appearance and Color

1.1.4.1.1. Raw Material and Finished Goods only.

1.1.4.2. Assay

1.1.4.2.1. Raw Material and Finished Goods only.

1.1.4.3. Identification (IR)

1.1.4.3.1. Raw Material and Finished Goods only.

1.1.4.4. Loss on Drying

1.1.4.4.1. Raw Material and Finished Goods only.

1.1.4.5. pH of 1% Solution or Slurry

1.1.4.5.1. All four stages.

1.1.4.6. Total Alkali

1.1.4.6.1. All four stages.

1.1.4.7. Trace Metals: As, Cu, Fe, Pb, Na,

1.1.4.7.1. All four stages.

1.2. All results were recorded in the proper laboratory documentation. The results are detailed and analyzed in a formal report. This report includes all relevant data required to obtain results. This report discusses any impurities found in the product and includes a specification for any limits on the impurities found if applicable.

2. RESPONSIBILITIES:

2.1. The Quality Control (QC) Manager is responsible for control, implementation, and maintenance of this procedure.

2.2. The QC Analysts are responsible for performing the testing stated in the protocol and recording all results in the proper laboratory documentation.

2.3. The QC Compliance team is responsible for completing the degradation and impurity report.

3. REFERENCES:

3.1. BSI-ATM-0016, Uracil Testing Methods

3.2. BSI-SOP-0255, XL200 pH/mV Conductivity Meter SOP

3.3. BSI-SOP-0303, NexION 350X ICP-MS SOP

4. PROCEDURE:

4.1. APPEARANCE AND COLOR:

4.1.1. Refer to the Degradation and Impurity Profile Protocol: Uracil for testing methods and requirements. The results of the Appearance and Color analysis are detailed in the table below:

TABLE 1: APPEARANCE AND COLOR

Lot Number	Stage	Specification	Result
S/2101002	Raw Material	White to Slightly Yellow Powder	Slightly Yellow Powder
URAC-0121-00021-PV Beginning	Finished Good		White Powder

4.2. ASSAY:

4.2.1. Refer to the Degradation and Impurity Profile Protocol: Uracil for testing methods and requirements. The results of the Assay analysis are detailed in the table below:

TABLE 2: ASSAY

Lot Number	Stage	Specification	Result
S/2101002	Raw Material	97.0-102.0%	98.4%
URAC-0121-00021-PV Beginning	Finished Good		98.2%

4.3. IDENTIFICATION TEST (IR):

Refer to the Degradation and Impurity Profile Protocol: Uracil for testing methods and requirements. The results of the Identification IR analysis are detailed in the table below:

TABLE 3: IDENTIFICATION TEST (IR)

Lot Number	Stage	Specification	Result
S/2101002	Raw Material	Passes Test	Passes Test; 0.98702
URAC-0121-00021-PV Beginning	Finished Good		Passes Test; 0.991259

4.4. **LOSS ON DRYING :**

4.4.1. Refer to the Degradation and Impurity Profile Protocol: Uracil for testing methods and requirements. The results of the Loss on Drying analysis are detailed in the table below:

TABLE 4: LOSS ON DRYING

Lot Number	Stage	Specification	Result
S/2101002	Raw Material	Monitor	0.0657%
URAC-0121-00021-PV Beginning	Finished Good		0.1484%

4.5. **pH @ 25 +/- 2°C :**

4.5.1. Refer to the Degradation and Impurity Profile Protocol: Uracil for testing methods and requirements. The results of the pH analysis are detailed in the table below:

TABLE 5: PH @ 25°C

Lot Number	Stage	Specification	Result
S/2101002	Raw Material	Monitor	4.86 @ 24.1°C
UC4200-030-0121 ML	Mother Liquor		10.03 @ 24.3°C
URAC-0121-00021-PV WC	Wet Crystal		7.76 @ 24.1°C
URAC-0121-00021-PV Beginning	Finished Good		7.79 @ 24.2°C

4.6. **TOTAL ALKALI AS SODIUM HYDROXIDE :**

4.6.1. Refer to the Degradation and Impurity Profile Protocol: Uracil for testing methods and requirements. The results of the Total Alkali as Sodium Hydroxide analysis are detailed in the table below:

TABLE 6: TOTAL ALKALI AS SODIUM HYDROXIDE

Lot Number	Stage	Specification	Result
S/2101002	Raw Material	Monitor	None Detected
UC4200-030-0121 ML	Mother Liquor		2.0292%
URAC-0121-00021-PV WC	Wet Crystal		None Detected
URAC-0121-00021-PV Beginning	Finished Good		None Detected

4.7. **Trace Metals (As, Cu, Fe, Pb, Na):**

4.7.1. Refer to the Degradation and Impurity Profile Protocol: Uracil for testing methods and requirements. The results of the Trace Metal analysis are detailed in the table below: **Refer to BSI-RPT-0103 for Full Elemental Impurity profile.**

TABLE 7: TRACE METALS (AS, CU, FE, PB, NA)

Lot Number	Stage	Specification	Result (ppm)				
			As	Cu	Fe	Pb	Na
S/2101002	Raw Material	Monitor for As, Cu, Fe, Pb, Na	<0.45	<1.5	16	<0.15	<30
UC4200-030-0121 ML	Mother Liquor		<0.45	<1.5	<1.5	<0.15	15000
URAC-0121-00021-PV WC	Wet Crystal		<0.45	<1.5	<1.5	<0.15	940
URAC-0121-00021-PV Beginning	Finished Good		<0.45	<1.5	<1.5	<0.15	3400
URAC-0121-00021-PV Middle[1]			<0.45	<1.5	<1.5	<0.15	2900
URAC-0121-00021-PV End[1]			<0.45	<1.5	<1.5	<0.15	5300

5. CONCLUSION:

5.1. All samples met the specifications for the required analyses as dictated in the Degradation and Impurity Profile Protocol: Uracil.

5.2. Sodium Hydroxide is intentionally introduced into the process during mother liquor creation. The Sodium results in the finished good can be attributed to residual NaOH that was not removed through the wet crystal washing process. Residual sodium has a monitor specification and is not a requirement for any Uracil Bio Pharma Grade product codes.

5.3. It can be concluded that there are no unintentionally introduced impurities present in the manufacturing process of Uracil Bio Excipient material at any stage, as currently validated.

[1] For information purposes only.