BIOSPECTRA
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BioSpectra External Validation Report

Validation Protocol for the manufacture of:

Urea Continuous

To be manufactured as the following codes:

Urea-3200

To be manufactured at:

BioSpectra, Inc., 1474 Rockdale Lane
Stroudsburg, Pennsylvania 18360

In compliance with the standards of:

The Joint IPEC – PQG Good Manufacturing Practices
Guide for Bio Excipients
ICH Q7 Guidance

Manufactured to be suitable for use as:

Bio Excipient for Drug Manufacturing

TABLE OF CONTENTS

1. INTRODUCTION:

The validation of a manufacturing process used to produce process chemicals is a requirement under IPEC-PQG Joint Good Manufacturing Practice Guide and ICH Q7 guidelines. The objective of this validation study was to assure that the manufacturing process in Manufacturing Suite 4 at BioSpectra's Stroudsburg, PA facility for Urea Bio Excipient, product code UREA-3200, is a controlled and validated process capable of consistently producing material that meets pre-established specifications and critical quality attributes. This validation was initiated by change control SCC23-53, Cartridge Filter Discontinuation and Replacement. The current approved manufacturer of cartridge filters is discontinuing the manufacture of these cartridge filters. A replacement was sourced, evaluated and approved for use in manufacturing. The replacement cartridge filters are of equivalent micron rating, size, and materials of construction. The validation was performed to prove the cartridge filter manufacturer change is capable of consistently delivering quality product and remains in a validated state.

This Urea Continuous Bio Excipient Grade validation study consisted of one concurrent validation batch to ensure that the Urea Continuous Bio Excipient Grade manufacturing process conforms to the pre-established critical process parameters established using tools such as process mapping, failure modes effect analysis (FMEA) and cause & effect matrix, the development study, and historical manufacturing data. A concurrent validation is a validation study in which the batch can be released for commercial distribution based on the monitoring and analysis of the lot. The lot must conform to finished goods specifications before release.

2. OBJECTIVE:

The objective of this validation report is to verify and assure that the manufacturing process for Urea Continuous Bio Excipient Grade in Manufacturing Suite 4 of BioSpectra's Stroudsburg, PA facility consistently produces material that meets a set of pre-determined specifications as listed in Table 1 for quality attributes.

The validation batch of Urea Continuous Bio Excipient Grade was manufactured according to the current version of the Bio Excipient batch record. Once the manufacturing of the validation batch was completed, representative samples were submitted to the Laboratory and were tested against finished good specifications. This was conducted to verify that the process is capable of consistently producing material that meets finished good specifications.

3. SCOPE:

This report applies to the manufacturing process for Urea Continuous Bio Excipient Grade, which includes the following process steps: charging the raw materials, mixing and heating, purification, cooling to crystallize, separation of the crystallized product, drying of the wet material and final packaging of the final product. Specifications and approval requirements for all raw materials (RM) and components have been created; therefore, the RM and components utilized are not covered by this report except that only approved RM and components were used.

4. REFERENCES:

4.1. Reference Documents

4.1.1. BSI-LST-0155, Urea Stability Data Card

4.1.2. BSI-MPR-0013, Urea Continuous Batch Record – S04

4.1.3. BSI-PRL-0136, Degradation and Impurity Protocol: Urea

4.1.4. BSI-PRL-0778, Urea Continuous Validation Protocol-Cartridge Filter Replacement

4.1.5. BSI-SOP-0292, Manufacturing Process Validation Master Plan

4.1.6. BSI-SOP-0435, Equipment Qualification Master Plan

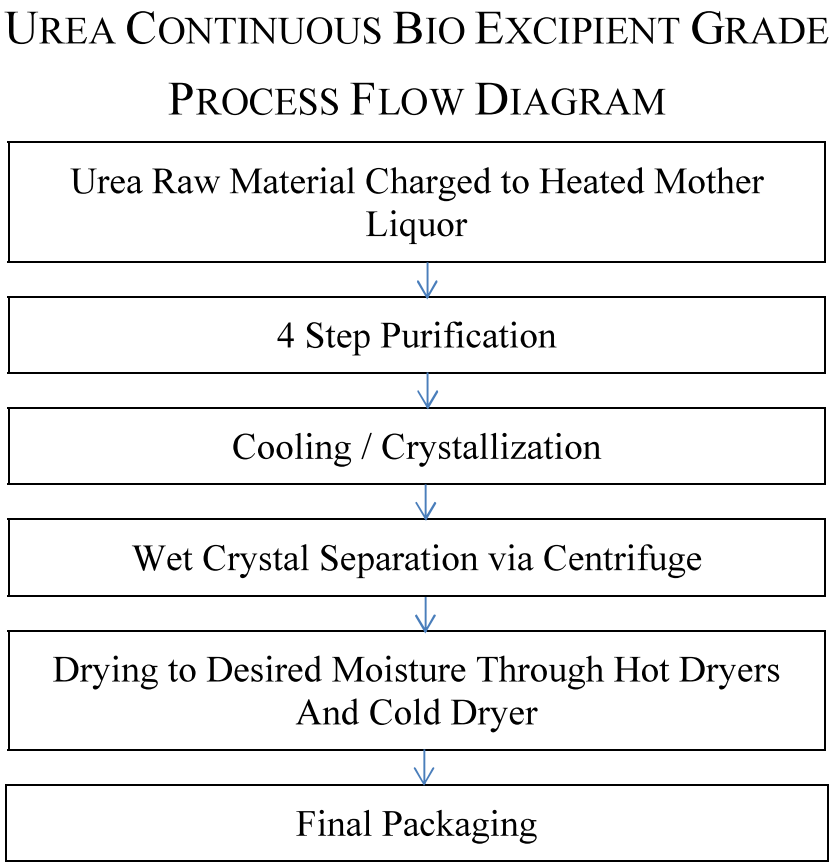
4.1.7. ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients

4.1.8. The Joint IPEC-PQG Good Manufacturing Practice Guide

5. EXECUTIVE SUMMARY:

The Urea Continuous Bio Excipient Grade manufacturing process is a manufacturing process with critical process parameters as detailed in the validation protocol. The CPP's that were developed prior to the validation study were found to be in accordance with BioSpectra's Manufacturing Process Validation Master Plan. The utilities and processes used in the manufacturing of this product have been qualified in accordance with BioSpectra's Equipment Qualification Master Plan. The validation batch manufactured for this validation study was manufactured following the current Urea Continuous Bio Excipient Grade Batch Record and CPP parameter values detailed in the validation protocol. The manufacturing process for Urea Continuous Bio Excipient Grade consistently produces material that meets a set of pre-determined specifications and attributes, passing batch uniformity and finished good specification testing.

6. PROCESS FLOW DIAGRAM:



7. ANALYSIS:

The Urea Continuous Bio Excipient Grade validation batch that was manufactured in accordance with the current Urea Continuous Bio Excipient Grade Batch Record and has met the BioSpectra analytical requirements associated with product code UREA-3200 and below compliance grade. The analytical results for the critical quality attributes (CQA) of the validation batch can be found in Table 1. All in-process and finished goods analyses met specifications as required in the validation study allowing the finished good material to be suitable for release.

TABLE 1: CRITICAL QUALITY ATTRIBUTES RESULTS FROM THE 2024 VALIDATION

Composite			
CQA Analysis		**Specification**	**Lot Number**
			UREA-0224-00001-PV
Appearance		White / Crystals	White / Crystals
Alcohol Insoluble Matter		≤ 0.04%	< 0.04%
Assay (USP)		98.0 – 102.0%	99.0%
Absorbance (5M)		≤ 0.03 a.u. at 280 nm	< 0.03 a.u. at 280 nm
		≤ 0.05 a.u. at 260 nm	< 0.05 a.u. at 260 nm
Biuret-UV		≤ 0.01 a.u. @ 540 nm	< 0.01 a.u. @ 540 nm
Conductivity		≤ 30 µS/cm	16 µS/cm @ 24.5°C
Melting Range		132 – 135°C	134-135°C
Organic Impurities	Urea Related Compound A	≤ 0.1%	0.05%
	Any Individual Unspecified Impurity	≤ 0.1%	<0.05%
	Total Impurities	≤ 2.0%	0.05%

8. ADDITIONAL INFORMATION:

8.1. Degradation and Impurity Profile

8.1.1. A degradation and impurity profile was performed for this validation in accordance with the Degradation and Impurity Profile Protocol: Urea, DCN: BSI-PRL-0136. The degradation and impurity profile will be reported on in a degradation and impurity profile report.

8.2. Stability Study

8.2.1. The stability analysis for Urea Bio Excipient Grade consists of an evaluation of the following analyses and associated specifications detailed in Table 2. These analyses were selected based on a combination of incoming raw material specifications, finished goods requirements and known process information and the specifications were set based on this same information. Each batch placed on the real time stability program will undergo stability analysis at intervals 0, 3, 6, 9, 12, 18, 24, 36, 48 and 60-month intervals.

TABLE 2: STABILITY ANALYSIS

ANALYSES	SPECIFICATION
Assay	98.0 – 102.0%
Conductivity	30 µS/cm maximum
Moisture (Moisture Balance)	0.5% maximum
Melting Range	132° - 135°C
Impurities – Organic	NMT 0.1%
Impurities – Total	NMT 2.0%
Impurities - Unspecified	NMT 0.1%

9. CONCLUSION:

BioSpectra has successfully manufactured a batch of Urea Continuous Bio Excipient Grade material to be compliant with key compliance grades up to and including the Bio Excipient Grade. This Bio Excipient Grade classification requires that a product be manufactured in accordance with IPEC and ICH Q7 guidelines and is suitable for use as an excipient. The results obtained in this validation report deem Urea Continuous Bio Excipient Grade manufactured using this process acceptable. The utilities and process used in the manufacture of this product have been qualified in accordance with BioSpectra's Equipment Qualification Master Plan. The results reported from the validation study for Urea Bio Excipient Grade have provided the evidence necessary to state that the approved cartridge filter manufacturer change has not impacted the quality and physical characteristics of Urea Continuous Bio Excipient Grade material for product code UREA-3200 and below compliance grades. All raw materials used for the processing of Urea Continuous Bio Excipient Grade were approved before use in accordance with raw material specifications. The validation samples of Urea Continuous Bio Excipient Grade will be placed onto real time stability and will be reported on annually. The stability study does not impact the current retest date or previous stability studies. All finished good samples analyzed for this validation study met finished good specifications for product code UREA-3200 or below compliance grades.