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

BioSpectra Process Validation External Report

Validation Report for the Manufacture of:

Uridine

To be Manufactured as the Following Codes:

Uridine
URID-3200 and Below Compliance Grades

To be Manufactured at:

BioSpectra, Inc., 100 Majestic Way, Bangor
Pennsylvania, 18013

In Compliance with the Standards of:

The Joint IPEC – PQG Good Manufacturing Practice
Guide ICH Q7
Good Manufacturing Practice Guide

Manufactured to be Suitable for Use as:

An Excipient

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1. INTRODUCTION

The Validation of a manufacturing process used to produce process chemicals is a requirement under IPEC and ICH Q7 guidelines. The objective of this validation study was to assure that the manufacturing process in Process Room N05 at BioSpectra's Bangor, PA facility for product code, URID-3200 and below GMP compliance grades, is a controlled and validated process capable of consistently producing material that meets pre-established specifications and critical quality attributes. This validation study was conducted because the Uridine manufacturing process is a new process. The validation seeks to prove that the researched and developed Uridine manufacturing process is capable of consistently delivering quality product.

This Uridine Validation Study consisted of three prospective validation batches to ensure that the Uridine manufacturing process conforms to the pre-established critical process parameters established in the development studies. This prospective validation study required that the validation of this process is completed before the commercial distribution of the final product.

2. OBJECTIVE

The objective of this Validation Report is to verify and assure that the manufacturing process for Uridine in Process Room N05 at BioSpectra's Bangor, PA facility consistently produces material that meets a set of pre-determined specifications as listed in Table 1 and quality attributes.

The Validation batches of Uridine were manufactured according to the current version of the Batch Record. Once the manufacture of the batches was completed, representative samples were submitted to the QC 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 Uridine, Bio Excipient Grade which includes the following process steps: mother liquor creation/adjustment, Uridine raw material charge, filtration/purification, crystallization, wet crystal collection, drying and testing of the finished goods product.

Specifications and approval requirements for all Raw Materials (RM) and components have been created; therefore, these RM and components are not covered by this Report except that only approved RM and components were used.

4. EXECUTIVE SUMMARY

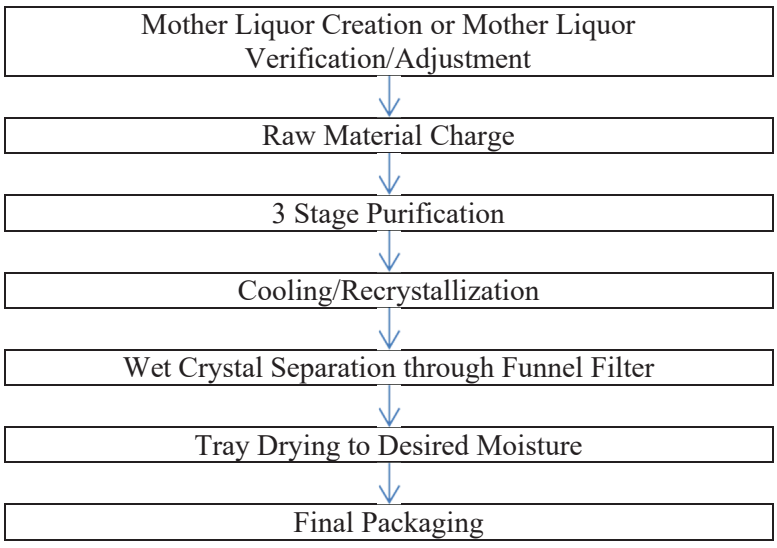
The Uridine manufacturing process is a manufacturing process with Critical Process Parameters as detailed in the Validation Protocol. The CPP's that were developed prior to the validation study were found to be in accordance with BioSpectra's Manufacturing Process Validation Master Plan. The utilities and process used in the manufacture of this product have been qualified in accordance with BioSpectra's Equipment Qualification Master Plan. The parameters for the CPP's were varied for the validation batches to establish proven acceptable ranges for each CPP. The three validation batches manufactured for this Validation were manufactured following the current Uridine Batch Record and CPP parameter values detailed in the Validation Protocol. The manufacturing process for Uridine consistently produces material that meets a set of pre-determined specifications and attributes, passing batch uniformity and Finished Good specification testing.

The manufacturing process consists of charging and heating of mother liquor for raw material charge, purification of mother liquor. Crystallization, then separation of the product and washing with IPA raw material via funnel filter. Product is then loaded onto product dedicated HDPE drying trays for drying at a designated temperature until the desired moisture is reached.

5. PROCESS FLOW DIAGRAM

Uridine Bio Excipient Manufacturing Process

(Process Room N05)



6. ANALYSIS

The Uridine batches that were manufactured in accordance with the current Uridine Bio Excipient Grade Batch Record have met the BioSpectra analytical requirements associated with product code URID-3250. The analytical results for the critical quality attributes (CQA) of the three validation batches can be found in Table 1. All in-process and Finished Goods analyses were met as required in the Validation study and for finished good release

TABLE 1: Critical Quality Attributes Results from the Current 2022 Validation

Uridine 2022 Validation Composite					
Analysis		**Specification**	**URID-0122-00005-PV**	**URID-0122-00006-PV**	**URID-0122-00007-PV**
Appearance and Color		White to Almost White Powder	White Powder	Almost White Powder	White to Almost White Powder
Bioburden	TAMC	≤100 CFU/g	< 100 CFU/g	< 100 CFU/g	< 100 CFU/g
	TYMC	≤100 CFU/g	< 100 CFU/g	< 100 CFU/g	< 100 CFU/g
Endotoxin		≤0.5 EU/mg	< 0.5 EU/mg	< 0.5 EU/mg	< 0.5 EU/mg
Heavy Metals		≤10 ppm	< 10 ppm	< 10 ppm	< 10 ppm
HPLC Purity		95.0 – 105.0%	99.9%	99.9%	99.9%
Identification (IR)		Conforms to Spectrum of Reference Standard	Conforms to Spectrum of Reference Standard	Conforms to Spectrum of Reference Standard	Conforms to Spectrum of Reference Standard
Loss on Drying		≤0.5%	0.1%	< 0.5%	0.1%
Residue on Ignition		≤0.1%	< 0.1%	< 0.1%	< 0.1%
Transparency (1%)		≥ 98.0%	99.6%	99.7%	99.3%
UV Assay		≥ 98.0%	98.4%	100.1%	99.8%

7. ADDITIONAL INFORMATION

7.1. Degradation and Impurity Profile

7.1.1. A Degradation and Impurity profile was initiated and was concurrently executed for this validation in accordance with DCN: BSI-PRL-0557.

7.2. Stability Study

7.2.1. The Stability Analysis for Uridine consists of an evaluation of the following analyses, and specifications listed in Table 2 below. The Stability Study for Uridine consists of testing at 0, 3, 6, 9, 12, 18, 24, 36, 48, and 60 month intervals. These analyses were selected based on the execution of the Stability Indicating Protocol, BSI-PRL-0541 and concluded on in the Stability Indicating Report, BSI-RPT-1060.The specifications were set based on the current finished good specifications.

TABLE 2: Stability Analysis

Analysis	Specifications
Appearance and Color	White to almost white powder
Identification (IR)	Conforms to Spectrum of Reference Standard
Loss on Drying	≤ 0.5%
Melting Point	Report
pH 5%	Report
Transparency 1%	≥ 98.0%
UV-Assay	≥ 98.0%

8. CONCLUSION

BioSpectra has successfully manufactured three batches of Uridine, Bio Excipient Grade, 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 ICH Q7 Good Manufacturing guidelines and is suitable for use as an excipient. The results reported in this validation report deem Uridine manufactured using this process and analyzed to URID-3250 acceptable. The utilities and process used in the manufacture of this product have been qualified in accordance with BioSpectra's Equipment Qualification Master Plan. All Raw Materials used for the processing of Uridine were approved before use in accordance with RM specifications. The Validation samples of Uridine have been placed into Real Time Stability and will be reported on annually. The Stability Study will be utilized to establish a retest date. All Finished Goods samples analyzed for the three batches of this validation study, met Finished Good Specifications for URID-3250.