BIOSPECTRA
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BioSpectra External Validation Report

External Validation Report for the Manufacture of:

MOPS

To be Manufactured as the Following Codes:

MOPS-3200 and Below Compliance Grade

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
ICH Q7 Good Manufacturing Practice Guide

Manufactured to be Suitable for use as:

Bio Excipient for Drug Manufacturing

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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 for MOPS in Process Suite 1 at BioSpectra's Rockdale, PA facility consistently produces material that meets a set of pre-determined specifications and quality attributes as listed in Table 1. This validation study was initiated in accordance with change control SCC23-39 (Cartridge Filter Discontinuation and Replacement), which allowed for the replacement of discontinued cartridge filters with filters of equivalent micron rating, size, and materials of construction.

This MOPS validation study consisted of a concurrent validation with one validation batch to ensure that the MOPS manufacturing process conforms to the pre-established critical process parameters. This concurrent validation study permitted the release of the batch for commercial distribution, relying on the monitoring and analysis of the lot. The lot must conform to finished good specification before release.

2. OBJECTIVE:

The objective of this validation report is to provide a summary of the validation study for the manufacturing process for MOPS in process suite 1 of BioSpectra's Rockdale, PA facility. This validation study will be leveraged as approval for the process suite 2 MOPS manufacturing process as process suite 1 and process suite 2 are equivalent processes. The validation batch of MOPS was manufactured according to the current version of the batch record. Once the manufacturing of the batch was completed, representative samples were submitted to the laboratory and 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 validation report applies to the manufacturing process for MOPS, MOPS-3200 which includes the following process steps: MOPS raw material charged to heated mother liquor, 3 step purification, transfer to final cooling stage, crystal separation through centrifuge, drying through fluid bed dryer, particle manipulation, tray dried to desired moisture and final packaging.

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

4. REFERENCES:

4.1. Reference Documents

4.1.1. BSI-ATM-0008, MOPS Testing Methods

4.1.2. BSI-FRM-0927, MOPS Validation Summary Sheet

4.1.3. BSI-LST-0157, MOPS Stability Data Card

4.1.4. BSI-MPR-0060, MOPS Bio Excipient Grade Batch Record - Centrifuging

4.1.5. BSI-PRL-0196, Degradation and Impurity Profile Protocol: MOPS Bio Excipient Grade

4.1.6. BSI-PRL-0804, MOPS Bio Excipient Grade Validation Protocol – Cartridge Filter Replacement

4.1.7. BSI-RPT-1846, Degradation and Impurity Report: MOPS S01 2024 Filter Validation

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

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

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

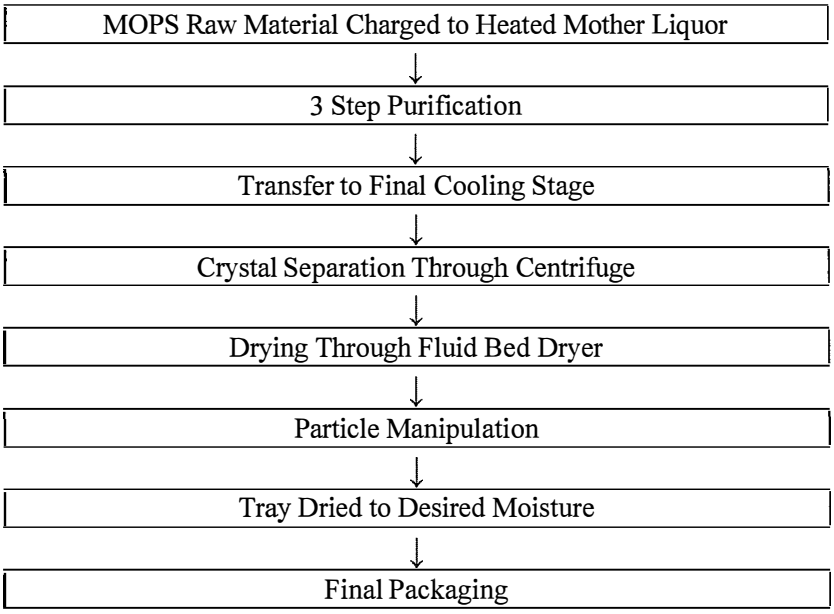
4.1.11. The Joint IPEC-PQG Good Manufacturing Practice Guide

5. EXECUTIVE SUMMARY:

The MOPS manufacturing process has critical process parameters (CPP's) as detailed in the MOPS Bio Excipient Grade Validation Protocol – Cartridge Filter Replacement, DCN: BSI-PRL-0804 v.1.0. 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 parameters for the CPP's were set for the validation batch to establish proven acceptable ranges for each CPP. The validation batch manufactured for this validation was manufactured following the current MOPS batch record and CPP parameter values detailed in the validation protocol. Through developmental studies utilizing a worst-case scenario approach, it was determined that a one batch validation would be sufficient in ensuring that the manufacturing process for MOPS in Process Suite 1 consistently produced material that meets a set of pre-determined specifications and attributes, passing batch uniformity and finished good specification testing.

6. PROCESS FLOW DIAGRAM:

MOPS PROCESS FLOW DIAGRAM



7. ANALYSIS:

The MOPS validation batch that was manufactured in accordance with the current MOPS batch record met the BioSpectra analytical requirements associated with the Bio Excipient grade specifications. The analytical results for the critical quality attributes (CQA) of the validation batch can be found in Table 1. All in-process and finished good analyses were met as required in the validation study and for finished good release.

TABLE 1: CRITICAL QUALITY ATTRIBUTES RESULTS

Composite			
CQA Analysis		**Specification**	**Lot Number**
			MOPS-0224-00130-PV
Absorbance (0.1M)	260 nm	≤ 0.020	0.002 a.u.
	280 nm	≤ 0.020	0.002 a.u.
Appearance and Color		White/Crystals	White/Crystals
Assay, Dried Basis		≥ 99.0%	100.2%
Water (by KF)		≤ 0.1%	0.1%
Loss on Drying		≤ 1.0%	0.1%
Solution (10% in water)		Passes Test	Passes Test

8. ADDITIONAL INFORMATION:

8.1. Degradation and Impurity Profile

8.1.1. A degradation and impurity profile was initiated and concurrently executed for this validation in accordance with DCN: BSI-PRL-0196. The results for the degradation and impurity profile are detailed in the Degradation and Impurity Profile Report, DCN: BSI-RPT-1846.

8.2. Stability Study

8.2.1. The stability analysis for MOPS consists of an evaluation of the following analyses and specifications listed in Table 2 below. These analyses were selected based on a combination of the stability indication study, incoming raw material specifications, finished goods requirements and known process information and the specifications were set based on this same information. The stability study for MOPS consists of testing at intervals 0, 3, 6, 9, 12, 18, 24, 36, 48 and 60-month intervals.

TABLE 2: MOPS STABILITY ANALYSIS (BSI-LST-0157)

ANALYSES	SPECIFICATION
Absorbance (0.1M) @ 260 nm	0.02 a.u. maximum
Appearance and Color	White/Crystals
Assay (Dried)	99.0% minimum
Loss on Drying	1.0% maximum
Solutions Test	Passes Test
Identification (IR)	Passes Test
Water (KF)	0.1% maximum

9. CONCLUSION:

BioSpectra has successfully manufactured one validation batch of MOPS, Bio Excipient grade, to be compliant with key compliance grades up to and including the Bio Excipient grade during the validation study. This Bio Excipient grade classification requires that a product be manufactured in accordance with ICH Q7 and IPEC guidelines and is suitable for use as a Bio Excipient for drug manufacturing. This validation study has proven that MOPS manufactured utilizing the above-mentioned manufacturing process and analyzed to the Bio Excipient grade is acceptable and approved for release. The utilities and equipment used in the manufacturing process for MOPS have been qualified in accordance with BioSpectra's Equipment Qualification Master Plan. The results reported from the validation study of MOPS have provided the evidence necessary to state that the manufacturing process for MOPS is in a state of control and validation. All raw materials used for the manufacturing of MOPS were approved before use in accordance with RM specifications.

The stability samples of MOPS obtained during the execution of this validation study were placed on the stability program for real time stability studies and will be reported annually. The stability study data will be utilized to determine the shelf life of MOPS manufactured by BioSpectra. All finished goods samples analyzed for this validation study met finished good specifications.