BIOSPECTRA
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BioSpectra Process Validation Report

Validation Protocol for the manufacture of:

MOPS, Bio Excipient or below GMP grades

To be manufactured as the following codes:

MOPS-3200 or below GMP grades

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 Process

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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. The objective of this validation study was to assure that the manufacturing process in Process Suite 01 at BioSpectra's Stroudsburg, PA facility for product code, MOPS-3200, 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 MOPS manufacturing process is a new process. The validation seeks to prove that the researched and developed MOPS manufacturing process is capable of consistently delivering quality product.

This MOPS Validation Study consisted of three concurrent validation batches to ensure that the MOPS manufacturing process conforms to the pre-established critical process parameters established in previous validation studies. This concurrent validation study allows for the release of the validation batch for commercial distribution based on approval of the executed batch record and documented evidence that the batch conforms to the finished goods specifications before release.

2. OBJECTIVE

The objective of this Validation Report is to verify and assure that the manufacturing process for MOPS in Stroudsburg's process suite 1 consistently produces material that meets a set of pre-determined specifications as listed in Table 1 and quality attributes.

The Validation batches of MOPS were manufactured according to the current version of the Batch Record. Once the manufacturing 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 MOPS, Bio Excipient Grade which includes the following process steps: charging MOPS raw material (RM) to heated mother liquor, three stage purification, transfer to final cooling stage, crystal separation through centrifuge, drying through a fluid bed dryer, particle manipulation, tray drying to desired moisture content, and final packaging.

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 MOPS 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 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 MOPS Batch Record and CPP parameter values detailed in the Validation Protocol. The manufacturing process for MOPS consistently produces material that meets a set of pre-determined specifications and attributes, passing batch uniformity and Finished Good specification testing.

The manufacturing process requires 2 vessels. Vessel S01HT01 acts as the charging and heating vessel. The charged mixture is filtered into vessel S01CT01, which acts as the crystallization vessel. The filtration is performed using a cartridge filter, zeta filter, and polishing filter along with carbon and Hy-Flo Pumps, filters, and hoses that are dedicated to Process Suite 01 for the MOPS process.

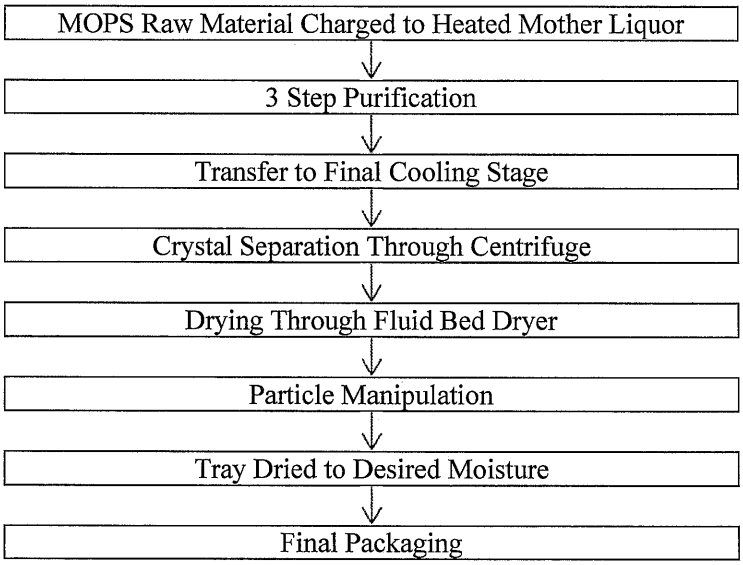
When crystallization is complete, the material is transferred to a centrifuge. The mother liquor (ML) is then extracted and returned to the cold tank for the beginning baskets to thin the current batch. After thinning the batch, the extracted mother liquor is sent to the hot tank for the next batch. The wet crystal (WC) is washed using Purified Water to aid in ML removal from the crystal prior to drying.

The WC is loaded into feed system, S01SC01, for transport to the fluid bed dryers, S01FB01 and S01FB02, for drying. After one pass through the fluid bed dryer's material is then grinded using the Stokes 43-6 Granulator, BioSpectra ID MPSG01 with a #10 U.S. mesh screen. Once the material is ground it is loaded on trays to be dried to a Karl Fischer Water specification of $\leq$0.1% max. During drying, the material is sifted as necessary and reloaded on trays until the moisture specification is achieved. Once the moisture specification is achieved, the material is packaged in the appropriate package configuration as dictated in the current Stroudsburg MOPS Bio Excipient Batch Record – S01.

5. PROCESS FLOW DIAGRAM

MOPS Bio Excipient Manufacturing Process

(Process Room S01)



6. ANALYSIS

The MOPS batches that were manufactured in accordance with the current *MOPS Bio Excipient Grade Batch Record* has met the BioSpectra analytical requirements associated with product code MOPS-3200. 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

CQA	SPECIFICATION	MOPS-0222-00075-PV	MOPS-0222-00076-PV	MOPS-0222-00077-PV
Absorbance (0.1M)	0.020 @ 260nm	0.002	0.002	0.002
	0.020 @ 280nm	0.001	0.002	0.001
Appearance and Color	White / Crystals	White/Crystals	White/Crystals	White/Crystals
Assay, Dried Basis	99.5% Min.	100.3%	100.5%	100.3%
Water (by KF)	0.1% max.[1]	0.06%	0.05%	0.03%
Loss on Drying	1.0% max.[1]	0.05%	0.10%	<0.10%
Solution (10% in Water)	Passes Test	Passes Test	Passes Test	Passes test

[1]Specification is reported to 1 decimal. For this report, results for the Water and Loss on Drying analyses will be reported to two decimals for data assessment.

7. ADDITIONAL INFORMATION

7.1. Degradation and Impurity Profile

7.1.1. A Degradation and Impurity profile was initiated and concurrently being executed for this validation in accordance with DCN: BSI-PRL-0196.

7.2. Stability Study

7.2.1. The Stability Analysis for MOPS consists of an evaluation of the following analyses, and specifications listed in Table 2 below. The Stability Study for MOPS consists of testing at intervals 0, 3, 6, 9, 12, 18, 24, and 36 month intervals. 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.

TABLE 2: Stability Analysis (BSI-LST-0157)

Analysis	Specifications
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
Water (KF)	0.1% maximum
Solutions Test	Passes Test

8. CONCLUSION

BioSpectra has successfully manufactured three batches of validated MOPS, 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 IPEC guidelines and is suitable for use as a GMP manufactured process chemical. The results obtained in this validation report deem MOPS manufactured using this process and analyzed to MOPS-3200 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 MOPS have provided the evidence necessary to state that the approved change, using the Process Suite 01 has not impacted the quality and physical characteristics of MOPS for product code MOPS-3200. All Raw Materials used for the processing of MOPS were approved before use in accordance with RM specifications. The Validation samples of MOPS will be placed into Real Time Stability and will be reported on annually. The Stability Study does not impact the current re-test date or previous stability studies. All FG samples analyzed for batches one through three of this validation study, met Finished Good Specifications for MOPS-3200.