BIOSPECTRA
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DATA EQUIVALENCY STUDY

Date: June 23, 2022

Product Number	Product Name	Grade
MOPS-3201 MOPS-3220	MOPS	Bio Excipient

Change Control Number: SCC22-06, SCC22-11, and SCC22-12

Process of Record Qualified Practice (PQR):

Process Suite 2 at the Stroudsburg, PA facility manufactures MOPS Bio Excipient Grade using a batch to batch process. The MOPS process charges approved MOPS raw material into the hot tank for heating. Once solubilized, the batch undergoes the purification process using approved filter media. Next, the heated saturated solution is transferred through a 3-step purification to the cold tank. In the cold tank, the batch is cooled for crystallization, and the crystallized material is then sent to the funnel filter for wet crystal separation. The mother liquor is pulled through the filter cloth through vacuum generated via a pump and is returned to the hot tank for the next batch. Upon completion of the wet crystal separation, the material is dried utilizing the process room fluid bed drying system. After [redacted] passes through the fluid bed drying system, the dried material is loaded into bins and is ground using a granulator with an approved screen. Finally, the ground crystals are loaded into trays and dried until they reach the product moisture specification. This batch process yields approximately [redacted] per batch.

New Practice to Be Qualified (NEW):

Process Suite 1 at the Stroudsburg, PA facility manufactures MOPS Bio Excipient Grade using a batch to batch process. The MOPS process charges approved MOPS raw material into the hot tank for heating. Once solubilized, the batch undergoes the purification process using approved filter media. Next, the heated saturated solution is transferred through a 3-step purification to the cold tank. In the cold tank, the batch is cooled for crystallization, and the crystallized material is then sent to the centrifuge for separation via a pump. The centrifuge supernatant is pumped back to the hot tank for the next batch. Upon completion of the wet crystal separation, the material is dried utilizing the process room fluid bed drying system. After a single pass through the fluid bed dryer system, the dried material is loaded into bins and is ground using a granulator with an approved screen. Finally, the ground crystals are loaded into trays and dried until they reach the product moisture specification. This batch process yields approximately [redacted] per batch.

Objective: The purpose of this equivalency study is to demonstrate the MOPS material manufactured in Process Suite 2 and a lower batch charge of [redacted] kg (PQR) is equivalent to the MOPS material manufactured in Process Suite 1 and a higher batch charge of [redacted] kg (New).

Methodology:

Process	Packaging/Re-Packaging Plant	Specifications	Test Methods
PQR	Stroudsburg, PA facility	MOPS-3201 MOPS-3220	MOPS Testing Methods, DCN: BSI-ATM-0008
New	Stroudsburg, PA facility	MOPS-3201 MOPS-3220	MOPS Testing Methods, DCN: BSI-ATM-0008

Success Criteria:

- The PQR MOPS, Bio Excipient Grade, is manufactured in Process Suite 2 in accordance with Batch Record, DCN: BSI-MPR-0014. The NEW material MOPS, Bio Excipient Grade, is manufactured in Process Suite 1 in accordance with Batch Record, DCN: BSI-MPR-0060. Material manufactured in Process Suite 2 with a lower batch charge (PQR) or Process Suite 1 with a higher batch charge (NEW) must meet the product code specifications.
- The t-test is performed to assess the differences between the quality attributes of the PQR material when compared to the NEW material. A P-Value > 0.05 demonstrates processes are not significantly different within the 95% confidence interval.

Results:

Refer to the Data Summary and T-tests on pages 6 and 7 for a complete overview of the PQR material in comparison to the NEW material.

Conclusion:

All 2021 manufactured MOPS Finished Good batches manufactured in Process Suite 2 at the BioSpectra, Stroudsburg, PA facility were compared to the NEW MOPS validation batches, which were manufactured in Process Suite 1 and utilized a higher initial batch charge. This comparison utilized a t-test with un-pooled variances to demonstrate that the processes are not significantly different. Any p-value lower than 0.05 were considered showing significant difference and were assessed in this report. Based on the statistical analyses performed, only the Absorbance 1M @ 260nm and Assay (Dried Basis) CQA's are considered statistically different between the PQR and the NEW process at the 95% CI. All results met specification and demonstrated equivalency except the Absorbance 1M @ 260nm and Assay (Dried Basis) which had a p-values < 0.05 when compared to the PQR data. The Absorbance 1M @ 260nm results for the new process is significantly lower than PQR results. This data does not impact the conclusion of equivalency and even suggests better product quality because less impurities are present in the crystal structure of the product, leading to the lower absorbance of the 1M solution @ 260nm. Additionally, the standard deviation for the NEW Absorbance 1M @ 260nm is lower compared to PQR data, indicating improved process consistency. The t-test results for the Assay (Dried Basis) CQA also determined there to be a statistically significant difference between the NEW process and the PQR. However, it can be confirmed that the processes are equivalent because the results of the Assay for the NEW process are within product code specifications, and the standard deviation is lower than the PQR. It can be confirmed that the processes are equivalent when comparing the results from the MOPS manufactured in Process Suite 1 with a higher batch charge and centrifuge crystal recovery method is equivalent to the MOPS manufactured in Process Suite 2 with a lower batch charge and funnel filter crystal recovery method. The data shown herein is considered acceptable and the process is considered equivalent.

Process Comparison

Process Step	PQR	New
Manufacturing Process	Process Suite 2 at the Stroudsburg, PA facility manufactures MOPS Bio Excipient Grade using a batch to batch process. The MOPS process charges approved MOPS raw material into the hot tank for heating. Once solubilized, [redacted] added to the charged MOPS solution in the hot tank and is pumped to the cold tank through a 3-step purification process for crystallization. Upon crystallization, the slurry is transferred to the funnel filter for wet crystal separation and then transferred to the fluid bed drying system. After [redacted] passes, the dried crystal is ground in a stokes granulator and tray died to moisture specification before final packaging.	Process Suite 1 at the Stroudsburg, PA facility manufactures MOPS Bio Excipient Grade using a batch to batch process. The MOPS process charges approved MOPS raw material into the hot tank for heating. Once solubilized, [redacted] is added to the charged MOPS solution in the hot tank and is pumped to the cold tank through a 3-step purification process for crystallization. Upon crystallization, the slurry is transferred to the centrifuge for wet crystal separation and then transferred to the fluid bed drying system. After passes, the dried crystal is ground in a stokes granulator and tray died to moisture specification before final packaging.
Testing Methods	MOPS Testing Methods, DCN: BSI-ATM-0008	MOPS Testing Methods, DCN: BSI-ATM-0008
Test Location	Stroudsburg, PA facility Bangor, PA facility	Stroudsburg, PA facility Bangor, PA facility
Specifications	MOPS-3201 MOPS-3220	MOPS-3201 MOPS-3220

Risk Assessment

Criteria		Impact
1	Complexity of change	No quality impact to MOPS Finished Good material as the manufacturing processes in Process Suite 1 and Process Suite 2 are deemed equivalent.
2	Historical norms	No quality impact based on the historical data of MOPS Finished Good material as demonstrated though T-tests.
3	Impact on chemical properties	No quality impact on chemical properties.
4	Impact on physical properties	No quality impact on the physical properties.
5	Impact on microbiological properties	No quality impact on microbiological properties.
6	Impact on composition profile	No quality impact on composition profile.
7	Impact on origin, type or site of raw materials	No quality impact to Finished Good material.
8	Impact on distribution of product	No quality impact on distribution of product.
9	Impact on origin and/or type of packaging and/or labeling	No quality impact on packaging or labeling.
10	Impact on product stability	No quality impact on product stability.
11	Impact on regulatory status	No regulatory status impact. The material is of the same compliance requirements.
12	Impact on compliance to a compendia or other regulation	No quality impact on compliance to a compendia or other regulation.
13	Potential to change intended performance of the product	No quality impact to the performance of the product.

Evaluation Batches

PQR	New
[redacted] Batches Manufactured in 2021 MP3200-333-0121 through MP3200-344-0221, MOPS-0221-0012 through MOPS-0221-0147, and MOPS-0221-00023 through MOPS –0221-00092	MOPS-0222-00075-PV
	MOPS-0222-00076-PV
	MOPS-0222-00077-PV

Results of Evaluation

Parameter	Significant Change?	Justification
Absorbance (1M) @ 260nm	Yes	The completed T-tests were found to demonstrate a statistically significant change based on the value of the 95% CI specification. Although the T-tests performed were found to demonstrate a statistically significant change, data from the validation batches indicate that MOPS product meets the Bio Excipient Grade product code specifications and can be manufactured reproducibly. There is no impact to the quality of material, and the processes are considered equivalent.
Assay (Dried-Basis)	Yes	The completed T-tests were found to demonstrate a statistically significant change based on the value of the 95% CI specification. Although the T-tests performed were found to demonstrate a statistically significant change, data from the validation batches indicate that MOPS product meets the Bio Excipient Grade product code specifications and can be manufactured reproducibly. There is no impact to the quality of material, and the processes are considered equivalent.
Loss on Drying	No	There is no statistically significant difference between PQR and NEW Material based on the t-test results.
Moisture (KF)	No	There is no statistically significant difference between PQR and NEW Material based on the t-test results.

DATA Summary

PQR product data was generated from MOPS Finished Good material manufactured in 2021 using a total of [redacted] manufactured batches.

New product data was generated from MOPS Finished Good lots: MOPS-0222-00075-PV, MOPS-0222-00076-PV and MOPS-0222-00077-PV.

Parameter		Specification	PQR		New		
			AVG	3 Sigma	MOPS-0222-00075-PV	MOPS-0222-00076-PV	MOPS-0222-00077-PV
Absorbance (1M)	260nm	0.02 a.u. max.	0.0039	0.0707	0.0018	0.002	0.0016
Assay	Dried-Basis	99.0% min.	100.13	1.17	100.29	100.46	100.26
Moisture (Karl Fischer)		0.1% max.	0.04	0.05	0.06	0.05	0.03
Loss on Drying		1.0% max.	0.0459	0.1218	0.0530	0.0998	0.0066

T-Tests

Parameter	PQR			New			P Value	Significant Difference (Yes/No)
	Mean	SD	95% Cl	Mean	SD	95% Cl		
Absorbance @ 260nm	0.003918	0.002358	(0.003292, 0.004543)	0.001800	0.000200	(0.001303, 0.002297)	0.000	Yes
Assay (Dried-Basis)	100.13	0.39	(100.03, 100.23)	100.34	0.11	(100.07, 100.60)	0.049	Yes
Moisture (Karl Fischer)	0.045891	0.040598	(0.035119, 0.056663)	0.046667	0.015275	(0.008721, 0.084612)	0.945	No
Loss on Drying	0.042807	0.016448	(0.038443, 0.047171)	0.053133	0.046600	(-0.062628, 0.168895)	0.739	No

P-Value >0.05 demonstrates processes are not significantly different within the 95% confidence interval.