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BioBuffer Solutions Validation Summary

Validation summary for the manufacture of:

L-Cystine Dihydrochloride,
Bio Pharma Grade for BioBuffer Solutions Product Line

Manufactured as the following codes:

L-Cystine Dihydrochloride LCYS-42XX or Below Grades

Manufactured By:

Approved Global Supply Chain

In compliance with the standards of:

Approved Supplier's ISO 9001:2015
Certified Management System

Manufactured to be suitable for use as:

Process Chemical

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1. INTRODUCTION:

L-Cystine Dihydrochloride, Bio Pharma Grade for BioBuffer Solutions Product line is manufactured and validated by the Approved Supplier in accordance with their ISO 9001:2015 certified management system. This validation summary is applicable to the validation study conducted by the Approved Supplier to ensure that the process used for manufacturing L-Cystine Dihydrochloride is sufficient to produce material of consistent quality and yield that meets its predetermined specifications.

The L-Cystine Dihydrochloride Validation Study consisted of three concurrent batches to ensure that the L-Cystine Dihydrochloride manufacturing process conforms to the predetermined specifications and quality attributes. The material was manufactured utilizing approved raw materials, as well as qualified and calibrated manufacturing equipment. Calibrated Quality Control instruments were utilized in the analysis of the material. There were no deviations or out of specifications observed during the validation activity.

2. EXECUTIVE SUMMARY:

The L-Cystine Dihydrochloride manufacturing process is a validated manufacturing process with Critical Process Parameters as detailed in the Batch Record. The L-Cystine Dihydrochloride manufacturing process includes treating L-Cystine with a mixture of concentrated Hydrochloride and Purified Water to form the Dihydrochloride of Cysteine in the Reactor, Equipment ID: GLR-202, which is then sent through a Cartridge Filter. The material is crystallized and washed utilizing Isopropyl Alcohol, which then enters the Reaction Mixture, Equipment ID: GLR-207, and is filtered through the Centrifuge, Equipment ID: SCF-201. A Solid Wet Cake is formed and proceeds to the drying stage under vacuum utilizing Equipment ID: RVD-201. The in-process analysis for Dried Material is Loss on Drying with a specification of NMT 1.0%.

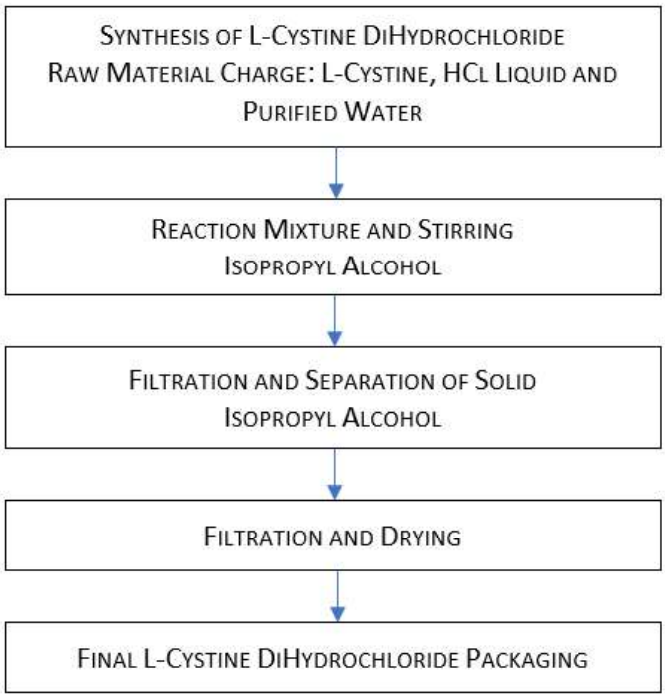

FIGURE 1. PROCESS FLOW DIAGRAM

3. ANALYSIS:

The L-Cystine Dihydrochloride validation batches were manufactured in accordance with the Approved Supplier's current L-Cystine Dihydrochloride Batch Record and have met the analytical requirements associated with the material sold for use as Bio Pharma Grade for BioBuffer Solutions Product line for product codes LCYS-4250. The analytical results for the critical quality attributes (CQA) of the three validation batches can be found in Table 1. All in-process and release analyses were met as required in the validation study and for release.

TABLE 1. RESULTS OF COMPLETE ANALYSIS OF VALIDATION BATCHES

Analysis	Specification	Batch 1 Results	Batch 2 Results	Batch 3 Results
Appearance and Color (Description)	White to slightly yellow Crystalline Powder	Slightly yellow Crystalline Powder	Slightly yellow Crystalline Powder	Slightly yellow Crystalline Powder
Assay (Dried Basis)	98.0%-102.0%	99.48%	99.44%	99.47%
Bioburden	≤100 CFU/g	5 CFU/g	10 CFU/g	5 CFU/g
Chloride	22.2%-23.5%	22.52%	22.51%	22.52%
Endotoxin	<0.02 EU/mg	Complies	Complies	Complies
Heavy Metals	<10ppm	Complies	Complies	Complies
Identification (IR)	Passes test (Conform to Standard)	Complies	Complies	Complies
Loss on Drying (105°C)	≤0.50%	0.09%	0.07%	0.10%
pH (0.1% solution)	Report (Informative)	2.22	2.24	2.21
Residue on Ignition	≤0.1%	0.04%	0.05%	0.06%
Specific Rotation (Free Basis)	-225.0°-215.0°	-219.42°	-218.54°	-218.30°
Solubility	Passes Test	Complies	Complies	Complies

4. CONCLUSION:

The Approved Supplier has successfully manufactured and validated three batches of validated Bio Pharma Grade for BioBuffer Solutions Product line L-Cystine Dihydrochloride to be compliant with key compliance grades up to and including the Bio Pharma Grade for BioBuffer Solutions Product line. This Bio Pharma Grade for BioBuffer Solutions Product line classification requires that a product be manufactured in accordance with the Approved Supplier's ISO 9001:2015 certified management system and is suitable for use as a process chemical. The results obtained in this validation summary deem L-Cystine Dihydrochloride manufactured using this process acceptable. The equipment used in the manufacture of this product have been qualified in accordance with the Approved Supplier's ISO 9001:2015 certified management system. The validation samples of L-Cystine Dihydrochloride were placed onto stability. All finished good samples analyzed for all three batches of this validation study met Finished Good Specifications for product code LCYS-4250 or below compliance grades.