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TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – L-CYSTINE DIHYDROCHLORIDE

PROCESS ROOM N02

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1. PURPOSE:

1.1. The purpose of this document is to provide the user of this product with a Technically Unavoidable Particle Profile (TUPP) for Process Room N02 in BioSpectra's Bangor, PA facility used in the manufacture of cGMP L-Cystine Dihydrochloride Bio Pharma grade.

2. SCOPE:

2.1. This TUPP applies to the manufacturing and packaging process of L-Cystine Dihydrochloride manufactured in BioSpectra's Bangor, PA facility in Process Room N02.

3. REFERENCES:

3.1. IPEC; Technically Unavoidable Particle Profile (TUPP) Guide

4. DEFINITIONS:

4.1. Technically Unavoidable Particle (TUP): A visibly different particle that can be viewed with the naked eye that is inherent to the raw material, manufacturing process or product and doesnot pose risk to patient safety.

4.2. Technically Unavoidable Particle Profiles (TUPPs): A report on all potential known Technically Unavoidable Particles (TUP) for an excipient process that can be shared with a customer or end user.

4.3. Atypical Particles – particles not consistent with the typical particulate profile; not previously encountered or identified.

4.4. Reprocessing: A system of improving an intermediate or finished product that does not conform to established specification by repeating a step or series of steps that are a part of the approved manufacturing process. The reprocessing of a batch of L-Cystine Dihydrochloride was approved as part of the validation of the L-Cystine Dihydrochloride manufacturing process.

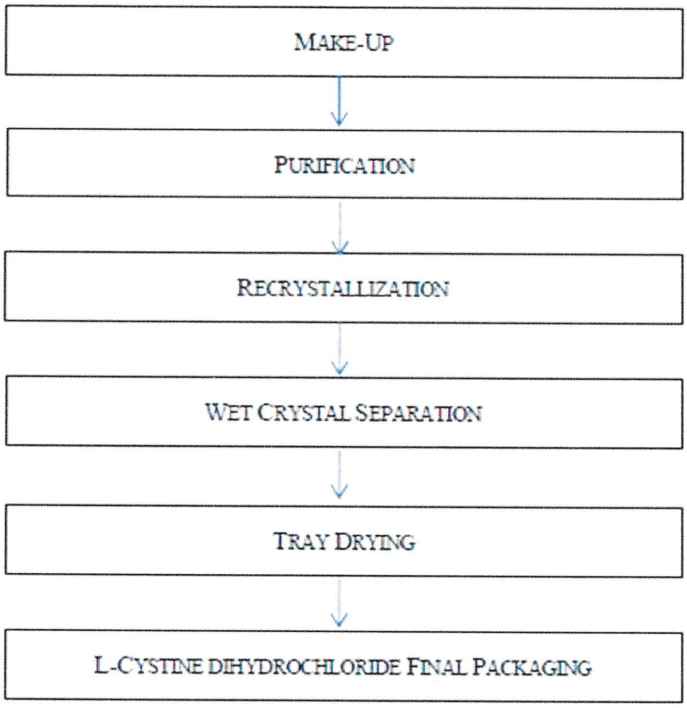
5. TECHNICALLY UNAVOIDABLE PARTICLES (TUP):

5.1. The construction of a technically unavoidable particle profile assumes that GMPs are followed and possible mitigation strategies are taken, the remaining particles, if they pose no risk to safety, are deemed technically unavoidable.

5.2. Technically unavoidable particles could originate from any of the following parts of the manufacturing process: Material of Construction of the manufacturing equipment that is product contacting, consumable process equipment, Material of Construction of the packaging components and any materials that are involved in the manufacturing process that may come into contact with the product that are the lowest risk scenarios. Scenarios that are considered to be the lowest risk are situations in which no mitigation strategies exist or cannot be implemented within reason.

6. PROCESS FLOW DIAGRAM:

cGMP L-Cystine Dihydrochloride Manufacturing Process Flow Diagram



7. PROFILE:

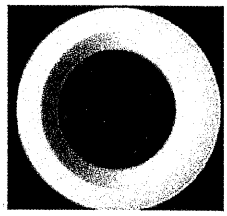
7.1. Manufacturing Location:

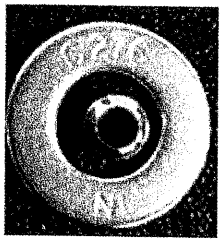
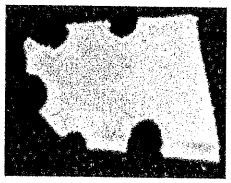
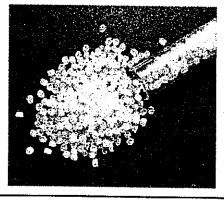
7.1.1. Bangor, PA Facility

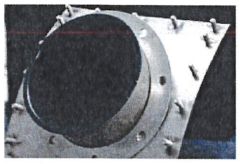
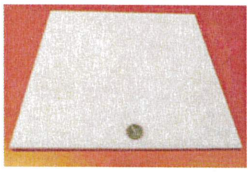
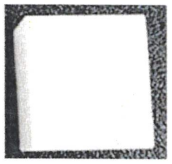
7.2. Applicable Product Codes:

7.2.1. L-CYSTINE dihydrochloride, LCYS-42XX

7.3. TUPPs originating from product contacting surfaces in the manufacturing process:

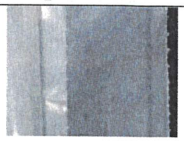
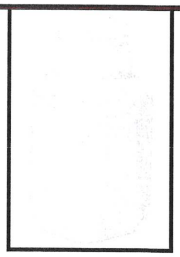
Originating from the Manufacturing Process					
Identity	**Characterization**	**Origin**	**How Removed**	**How Prevented**	**Picture (Example of Source)**
PTFE	Opaque White Plastic	Process Tanks Process Tank Burst Disks Process Tank Pressure Gauges	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
		Centrifugal Pump Centrifuge	Inspection Reprocess		
Tantalum	Metallic Shavings	Process Tanks	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Hastelloy	Metallic Shavings	Process Tanks (Agitator Seals)	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	

Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Hastelloy C276	Metallic Shavings	Cartridge Filter	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Hastelloy C22	Metallic Shavings	Centrifuge	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Polypropylene	Natural Colored Opaque Off-White Plastic	Process Tanks (Fittings) Process Tank Pressure Gauges	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Glass	Glass Fragments	Process Tanks Process Tank Agitators	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	Not Available
PVDF	Opaque Plastic	Centrifugal Pump	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Kalrez	Plastic	Centrifugal Pump	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	

Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Alumina Ceramic	Ceramic Fragments	Centrifugal Pump	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Halar	Polymer Lining	Centrifuge Mother Liquor Trap Tank	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
LLDPE	Opaque Plastic	Sifting Bin	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Extren Fiberglass	White Fiberglass Fragments	Tray Sifter	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
HDPE	White Plastic	Tray Sifter Drying Trays	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	

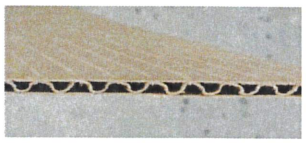
7.4. TUPPs originating from product contacting surfaces of the packaging components:

7.4.1. The following TUPPs are dependent on the packaging type.

Originating from the Packaging components					
Identity	**Characterization**	**Origin**	**How Removed**	**How Prevented**	**Picture (Example of Source)**
Hexene LLDPE	Clear Plastic	Liner (Packaging)	Reprocessing	Inspection at time of use	
HDPE	White Plastic	Bottle (Packaging)	Reprocessing	Inspection at time of use	
Polypropylene	Blue Plastic	Tamper Evident lid (Packaging)	Reprocessing	Inspection at time of use	

7.5. Atypical particles originating from non-product contacting surfaces of the packaging components:

7.5.1. The following Atypical particles are dependent on the packaging type.

Atypical particles: originating from the packaging components					
Identity	**Characterization**	**Origin**	**How Removed**	**How Prevented**	**Picture (Example of Source)**
HMW-HDPE	Blue Plastic	Drum (Packaging)	Reprocessing	Inspection at time of use and Product Care Procedure	
HDPE	Blue or White Plastic	Pail and Lid (Packaging)	Reprocessing	Inspection at time of use and Product Care Procedure	
Fiber	Brown cardboard	Drum (Packaging) Drum (Desiccant Storage)	Reprocessing	Inspection at time of use and Product Care Procedure	
Cardboard	Brown	Pallet Liner	Reprocessing	Inspection at time of use and Product Care Procedure	
Wood	Wood Shaving	Pallet	Reprocessing	Inspection at time of use and Product Care Procedure