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# TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP): CYSTEAMINE HCL (2-MEA)

## 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 at BioSpectra's Bangor, PA facility used in the manufacture of cGMP Cysteamine HCl (2-MEA) BioExcipient grade.

**2. SCOPE:**

- 2.1. This TUPP applies to the manufacturing and packaging process of Cysteamine HCl (2-MEA) manufactured at BioSpectra's Bangor, PA facility in Process Room N02.

**3. REFERENCES:**

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

**4. DEFINITIONS:**

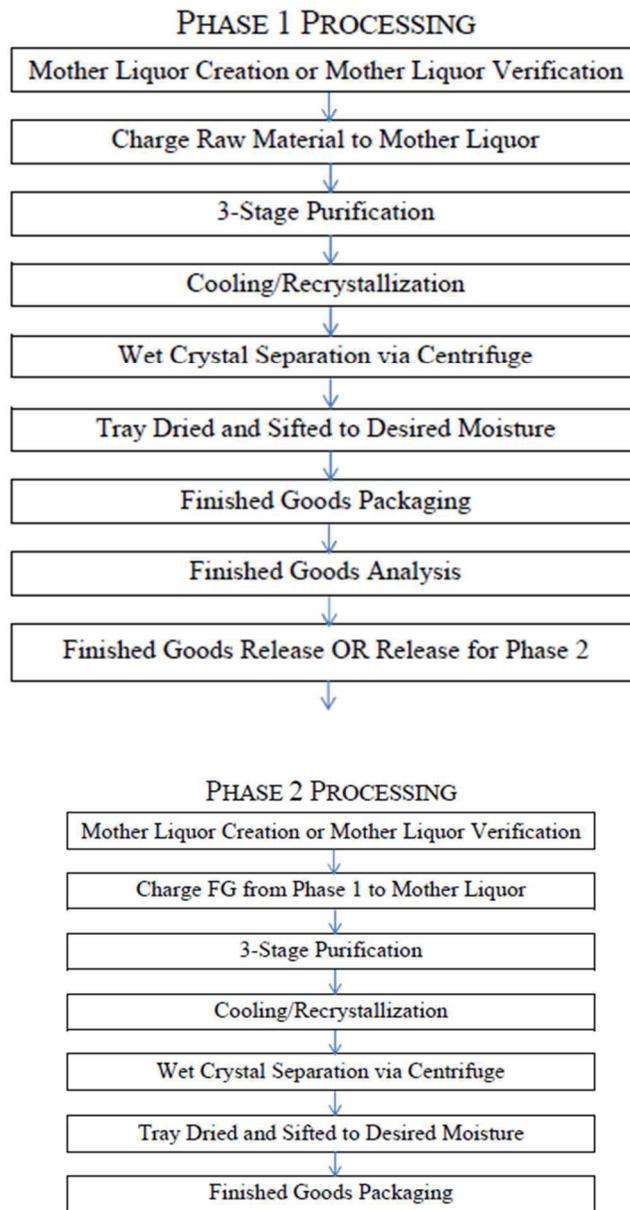
- 4.1. Technically Unavoidable Particle (TUP): A visibly different particle that can be viewed with the naked eye that is inherent to the raw material, manufacturing process or product and does not pose risk to patient safety.
- 4.2. Technically Unavoidable Particle Profiles (TUPPs): A report on all 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 Cysteamine HCl (2-MEA) may be approved as part of the validation via execution of a Phase II Process validation.

**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 Cysteamine HCl (2-MEA) Manufacturing Process Flow Diagram



## 7. PROFILE:

7.1. Manufacturing Location:

7.1.1. Bangor, PA Facility

7.2. Applicable Product Codes:

7.2.1. CSMH-3250

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

Originating from the Manufacturing Process					
Identity	Characterization	Origin	How it is Removed	How it is Prevented	Picture (Example of Source)
Polytetrafluoroethylene (PTFE)/ Teflon	Opaque White Plastic	Process Tanks	Purification Inspection	Pre-Process Inspection Preventative Maintenance	
		Centrifugal Pump Diaphragm Pump Centrifuge	Inspection		
Glass	Glass Fragment	Process Tanks	Purification Inspection	Pre-Process Inspection Preventative Maintenance	Not Applicable
Tantalum	Metallic Shavings	Process Tanks	Purification Inspection	Pre-Process Inspection Preventative Maintenance	
Halar	Polymer Lining	Centrifuge Mother Liquor Trap Tank	Inspection	Pre-Process Inspection Preventative Maintenance	
Hastelloy	Metallic Shaving	Process Tanks	Purification Inspection	Pre-Process Inspection Preventative Maintenance	
Hastelloy C22	Metallic Shaving	Centrifuge	Inspection	Pre-Process Inspection Preventative Maintenance	

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Hastelloy C-276	Metallic Shaving	Centrifugal Pump	Inspection	Pre-Process Inspection  Preventative Maintenance	
		Cartridge Filter Zeta Filter	Purification Inspection		
Polypropylene	Natural Colored Opaque Off-White Blue Plastic	Process Tank	Purification Inspection	Pre-Process Inspection  Preventative Maintenance	
Polypropylene Conductive	Natural Colored Opaque Off-White Blue Plastic	Diaphragm Pump	Inspection	Pre-Process Inspection  Preventative Maintenance	
HDPE	White Plastic	Mother Liquor Holding Tank  Tray Sifter	Inspection	Pre-Process Inspection  Preventative Maintenance	
PVDF	Opaque Plastic	Centrifugal Pump	Inspection	Pre-Process Inspection  Preventative Maintenance	
Kalrez	Plastic	Centrifugal Pump	Inspection	Pre-Process Inspection  Preventative Maintenance	

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Alumina Ceramic	Ceramic Fragment	Centrifugal Pump	Inspection	Pre-Process Inspection Preventative Maintenance	
LLDPE	Opaque Plastic	Sifting Bin	Inspection	Pre-Process Inspection Preventative Maintenance	
316 Stainless Steel	Metallic Shaving	Diaphragm Pump	Inspection	Pre-Process Inspection Preventative Maintenance Inspection at Time of Use	
Extren Fiberglass	White Fiberglass Fragment	Tray Sifter	Inspection	Pre-Process Inspection Preventative Maintenance Inspection at Time of Use	
Polyethylene	Opaque White Plastic	Chemical Hoses	Inspection	Pre-Process Inspection Preventative maintenance	Not Available
PVC	White, Clear, or Gray Opaque Plastic	Milk Hoses	Inspection	Pre-Process Inspection Preventative Maintenance	

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

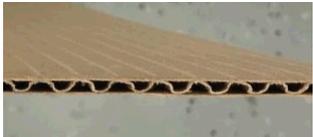
7.4.1. The following TUPPs are dependent on the packaging type.

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

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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)	Inspection	Inspection at time of use and Product Care Procedure	
HDPE	Blue or White Plastic	Pail and Lid (Packaging)	Inspection	Inspection at time of use and Product Care Procedure	
Fiber	Brown cardboard	Drum (Packaging) Drum (Desiccant Storage)	Inspection	Inspection at time of use and Product Care Procedure	
Cardboard	Brown	Pallet Liner	Inspection	Inspection at time of use and Product Care Procedure	
Wood	Wood Shaving	Pallet	Inspection	Inspection at time of use and Product Care Procedure	

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