



100 Majestic Way, Bangor, PA 18013 / www.biospectra.us

TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – MES, MONOHYDRATE & MES HYDRATE

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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 Excipient Cell 1 Room E02, Excipient Cell 2 Room E03 and API Suite 1 Room E05 at BioSpectra's Bangor, PA facility. These rooms are utilized in the manufacturing of cGMP MES, Monohydrate and MES, Hydrate Bio Excipient and Bio Pharma grades.

2. SCOPE:

- 2.1. This TUPP applies to the manufacturing and packaging process of MES, Monohydrate and MES Hydrate manufactured at BioSpectra's Bangor, PA facility in Excipient Cell 1 Room E02, Excipient Cell 2 Room E03 or API Suite 1 Room E05.

3. REFERENCES:

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

4. DEFINITIONS:

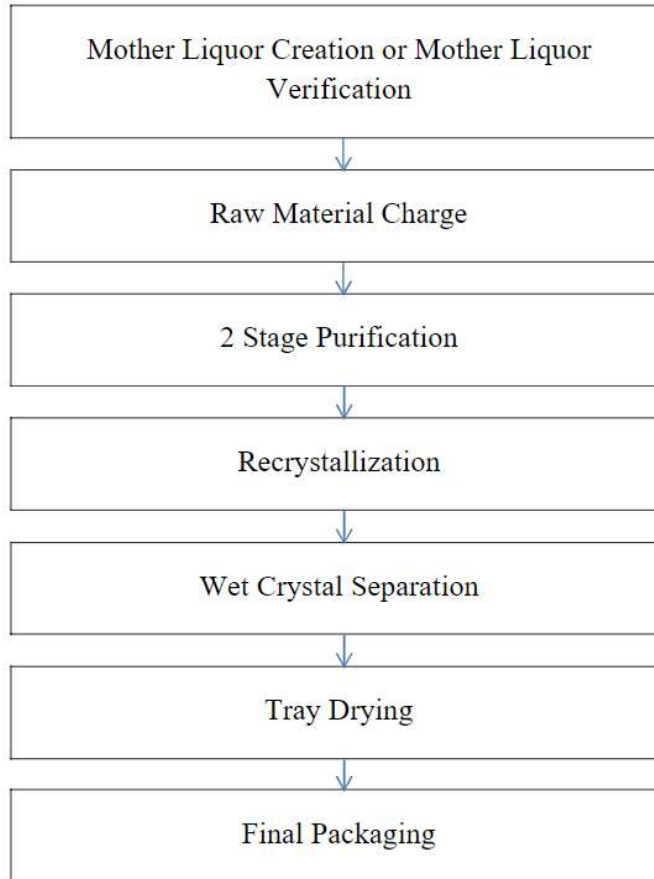
- 4.1. Technically Unavoidable Particle (TUP): A visibly different particle that can be viewed with the naked eye that is inherent to the raw material, manufacturing process or product and does not pose risk to patient safety.
- 4.2. Technically Unavoidable Particle Profiles (TUPPs): A report on all 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 MES, Monohydrate and MES, Hydrate was approved as part of the validation of the MES, Monohydrate 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 MES, Monohydrate & MES, Hydrate Manufacturing Process Flow Diagram



7. PROFILE:

7.1. Manufacturing Location:





7.1.1. Bangor, PA Facility

7.2. Applicable Product Codes:







7.2.1. MESM-32XX and below compliance grades



7.2.2. MESH-32XX and below compliance grades

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)
316 Stainless Steel	Metallic Shaving	Process Tanks, Agitator, Shaft/Blades, Pilot Agitators, Diaphragm Valves, Process Piping, Filter Housings	Purification, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
		Centrifugal Pump Head and Impeller Diaphragm Pump Fittings Tray Sifter	Reprocessing		
PTFE	Opaque White Plastic	Process Tank Gaskets Process Tank Diaphragm Valves Sanitary Piping Gaskets Process Piping Valve Diaphragms Diaphragm Pump Diaphragm Diaphragm Pump Check Valve Balls Filter O-ring	Purification, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Red FDA Silicone	Orange elastomer Fragment	Process Tank Gaskets Diaphragm Pump Gaskets Filter O-Ring	Purification, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Polypropylene	Natural Colored Opaque Off-White, Blue Plastic	Diaphragm Pump Fittings Diaphragm Pump Fluid Covers Diaphragm Pump Manifolds Diaphragm Pump Check Valve Seats Product Scoops Zeta Filter Nut	Reprocessing	Pre-Process Inspection, Preventative Maintenance	

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Originating from the Manufacturing process					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
USP Class VI Silicone	Clear Elastomer	Filter O-rings Sanitary Piping Gaskets	Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Silicon Carbide	Ceramic Fragment	Centrifugal Pump Stationary seat	Reprocessing	Pre-Process Inspection, Preventative Maintenance	
HDPE	White HDPE	Funnel Filter Support structure Drying Trays	Reprocessing	Pre-Process Inspection, Preventative Maintenance	
CPVC	Gray Plastic	Funnel Filter Fittings	Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Hexene LLDPE	Clear plastic	Liners	Reprocessing	Inspection at the time of use	
Carbon	Black or Gray Fragments	Centrifugal Pump Rotating Carbon Seal, Filtration	Reprocessing	Pre-Process Inspection, Preventative Maintenance	

Originating from the Manufacturing process- Mobile Equipment					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
316 Stainless Steel	Metallic Shaving	Funnel Filter Fittings	Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Polypropylene	Natural Colored Opaque Off- White, Blue Plastic	Funnel Filter Shell Funnel Filter Perforated plate Filter Cloth	Reprocessing	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.


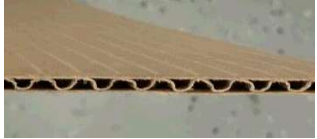

Originating from the Packaging components					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Hexene LLDPE	Clear Plastic	Liner (Packaging)	Reprocessing	Inspection at time of use	
HDPE	White Plastic	Bottle (Packaging)	Reprocessing	Inspection at time of use	
Polypropylene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

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Atypical particles: originating from the packaging components					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
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	

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