



TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – BIS-TRIS

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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 E04 at BioSpectra's Bangor, PA facility used in the manufacture of cGMP Bis-Tris Bio Excipient or below compliance grade material.

2. SCOPE:

- 2.1. This TUPP applies to the manufacturing and packaging process of Bis-Tris manufactured at BioSpectra's Bangor, PA facility in Process Room E04.

3. REFERENCES:

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

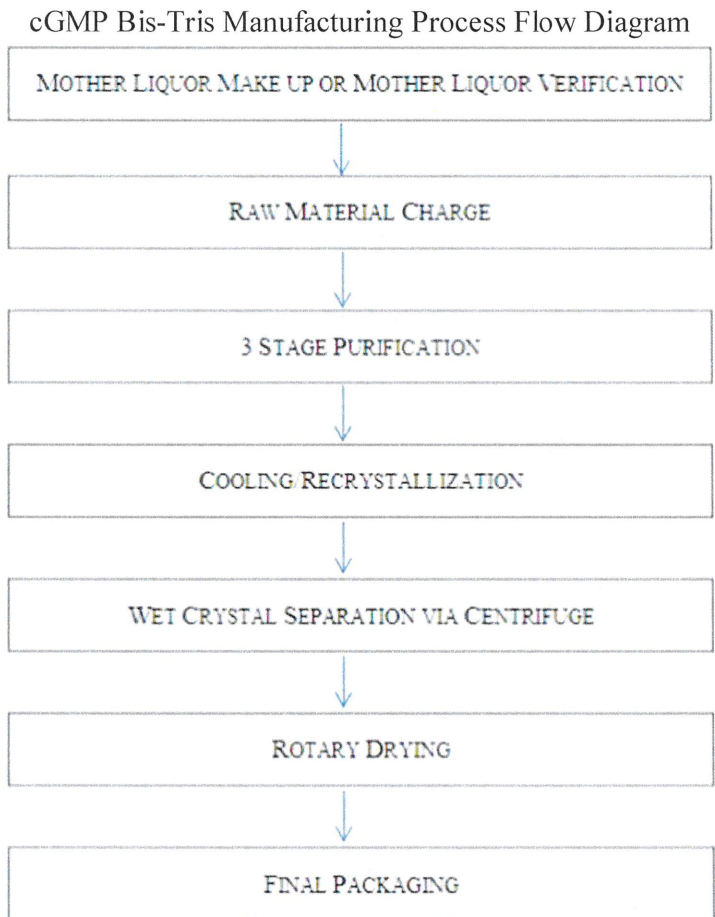
4. DEFINITIONS:

- 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.

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:



7. PROFILE:

7.1. Manufacturing Location:


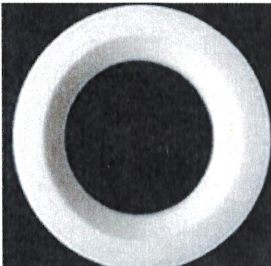



7.1.1. Bangor, PA Facility

7.2. Applicable Product Codes:

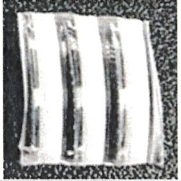
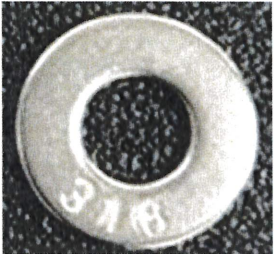
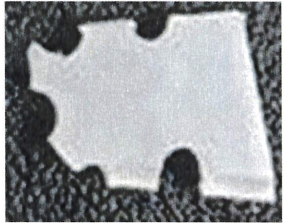
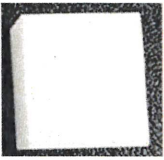

7.2.1. Bis- Tris, BTRI-3200 and below compliance grades

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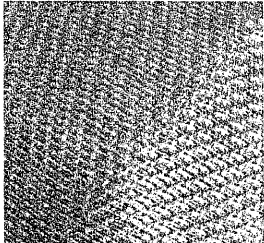
7.3. TUPPs originating from product contacting surfaces in the manufacturing process:

Originating from the Manufacturing Process					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
PVDF	Opaque Plastic	Hot Tank Sensor Cold Tank Sensor	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
PTFE / Teflon	Opaque White Plastic	Hot Tank Gaskets E04AV01 Cold Tank Gaskets E04AV02 Zeta Filter E04CE02 E04RD01	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Red Silicone	Orange Elastomer Fragment	Hot Tank Gaskets Cold Tank Gaskets	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
USP Class VI Silicone	Clear Elastomer	Filter (O-Ring)	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Polyethylene	Opaque White Plastic	Filter Gasket E04ZF01	Filtration Inspection Reprocess Replacement of Filter	Pre-Process Inspection Preventative Maintenance	
		Chemical Hoses	Filtration Inspection Reprocess		
		Scraper	Inspection Reprocess		

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Originating from the Manufacturing Process					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
PVC	White, Clear, or Gray Opaque Plastic	Milk Hoses E04ZF01	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
316 Stainless Steel	Metallic Shavings	E04TH01 and E04TA01 E04AV01 E04CT01 and E04TA02 E04AV02 E04CF01 E04ZF01 E04PF01 Wall Supply and Return E04RD01	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
		Drum Sifting Lid	Inspection Reprocess		
Polypropylene	Opaque Off-White Plastic	Filter Media	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
HDPE	White Plastic	ML Totes	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Cellulose	Fiber	Filter Media	Filtration Reprocessing	Pre-Process Inspection Preventative Maintenance Replacement of Filters	




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Originating from the Manufacturing Process					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Halar	Polymer Lining	E04CE02	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Hastelloy C22	Metallic Shavings	E04CE02	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Viton	Black Elastomer Fragment	E04RD01 Gaskets	Inspection	Pre-Process Inspection	
Polypropylene	Cloth	E04CE02	Inspection	Pre-Process Inspection Preventative Maintenance	

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



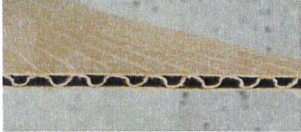

7.4.1. The following TUPPs are dependent on the packaging type.

Originating from the Packaging components					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Hexene LLDPE	Clear Plastic	Liner (Packaging)	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	

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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)	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	
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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