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TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – TRIS MANUFACTURED IN PROCESS SUITE 1 AND SUITE 4 STROUDSBURG, PA FACILITY

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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 Tris manufactured in Process Suite 1 and Process Suite 4 at BioSpectra's Stroudsburg, PA facility.

2. SCOPE:

- 2.1. This TUPP applies to the manufacturing and packaging process of Tris, Excipient, at BioSpectra's Stroudsburg, PA facility.

3. REFERENCES:

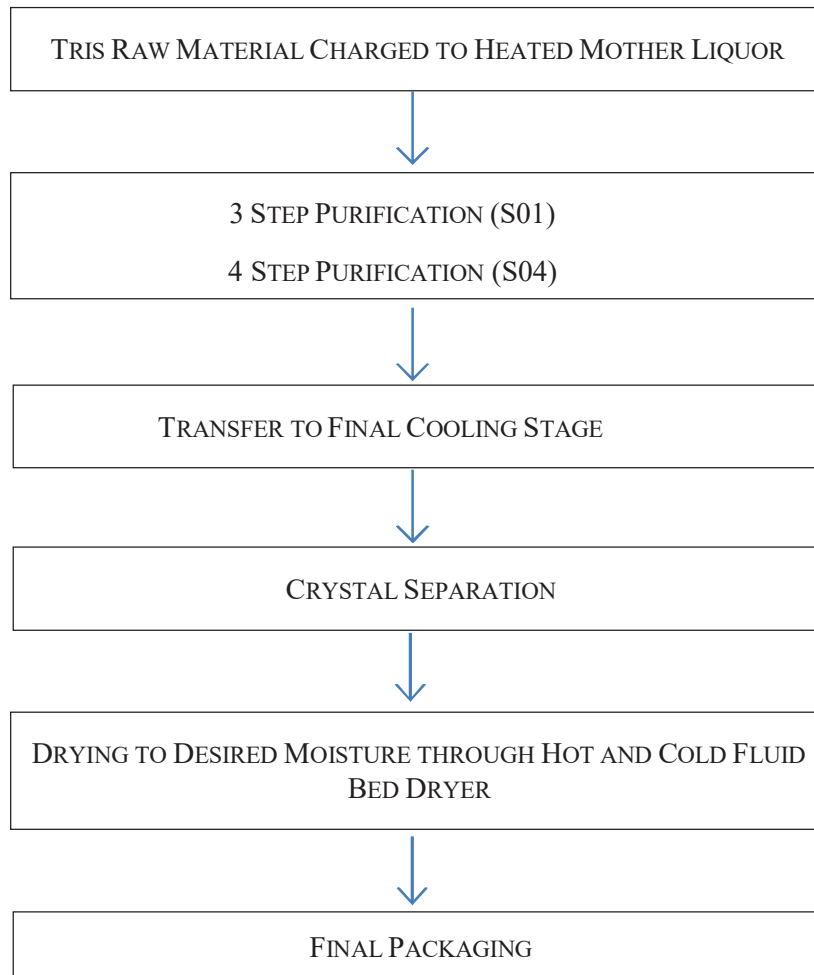
- 3.1. IPEC; Technically Unavoidable Particle Profile (TUPP) Guide

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 Tris was approved as part of the validation of the Tris 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. Process Suite 1 and Process Suite 4 in BioSpectra's Stroudsburg, Pa Facility




7.2. Applicable Product Codes:

7.2.1. TRIS-32XX and lower compliance grades




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

Originating from the S01 Manufacturing Process Suite					
Identity	Characterization	S01 Origin	How Removed	How Prevented	Picture
Cellulose	Fiber	Filtration (Filter media)	3-Step Purification, Reprocessing	Replacement of Filters, Inspection	
Silica	White Powder	Filtration (Filter media)	3-Step Purification, Reprocessing	Replacement of Filters, Inspection	





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Originating from the S01 Manufacturing Process Suite					
Identity	Characterization	S01 Origin	How Removed	How Prevented	Picture
Carbon	Black particle	Filtration (Filter media) Centrifugal Pump Shaft Seal	3-Step Purification, Reprocessing	Replacement of Filters, Inspection	Not Available
UHMW PE	White Plastic	Screw Feeder Tube	Reprocessing	Pre-Process Inspection, Preventative Maintenance	Not Available
PTFE	White Plastic	Diaphragm Pump, Filter Gaskets, Sanitary Piping Gaskets	3-Step Purification, Reprocessing	Replacement of Filters, Pre-Process Inspection, Preventative Maintenance	
Silicon Carbide	Ceramic Fragment	Centrifugal Pump Stationary Seat	3-Step Purification, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Viton	Black elastomer fragment	Pumps (O-rings, gaskets) Process piping	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	








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Originating from the S01 Manufacturing Process Suite					
Identity	Characterization	S01 Origin	How Removed	How Prevented	Picture
Polypropylene	Natural colored opaque, opaque off-white, blue plastic	ML Totes Funnel Filter Pumps Product shovel Centrifuge Mesh cloth Filter Media Diaphragm Pump Piping/ Fluid Covers/ Manifolds/ Check Valve Seats ML Return Tank	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
PVC	White, Clear, Opaque plastic	ML Tote Process hose (Fittings) Centrifuge ML Return Cyclone Exhaust Duct Dryer Exhaust Duct Portable Sprayer Piping Screw Conveyor Hose Centrifuge Wash Tank Piping	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Silicone	Clear plastic, Orange elastomer fragment	Funnel Filter Gaskets Dryer Bed	Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	

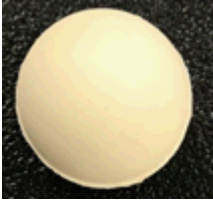


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Originating from the S01 Manufacturing Process Suite					
Identity	Characterization	S01 Origin	How Removed	How Prevented	Picture
Stainless Steel 316	Metallic shaving	Process Tank Piping Agitator Blade/ Shaft Filter Housing Filter Basket Filter Piping Centrifuge BasketCentrifuge ML Return Centrifugal Pump Head/ Impeller/ Back Plate Diaphragm PumpPiping Dryer Body/Bed Portable SprayerScrew ConveyorFlytes/ Cover/ Hopper/ Grate/ Hardware Centrifuge Wash Tank/ Piping	3-Step Purification, Inspection ofthe Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Stainless Steel 304	Metallic shaving	Process Tank/ Lid	3-Step Purification, Inspection ofthe Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Polycarbonate	Clear Plastic	Centrifuge SightGlass Cyclone	3-Step Purification, Inspection ofthe Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	Not Available
HDPE	White HDPE	Centrifuge SightGlass, Funnel Filter, Screw Conveyor	3-Step Purification, Inspection ofthe Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
CPVC	Gray Plastic	ML Return TankPiping	3-Step Purification, Inspection ofthe Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	


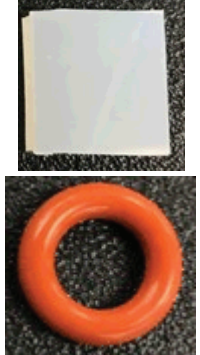
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Originating from the S04 Manufacturing Process Suite					
Identity	Characterization	S04 Origin	How Removed	How Prevented	Picture
Cellulose	Fiber	Filtration (Filtermedia)	4-Step Purification, Reprocessing	Replacement of Filters, Inspection	
Silica	White Powder	Filtration (Filtermedia)	4-Step Purification, Reprocessing	Replacement of Filters, Inspection	
Carbon	Black particle	Filtration (Filter media) Centrifugal Pump Shaft Seal, Tank agitator seals	4-Step Purification, Reprocessing	Replacement of Filters, Inspection	
UHMW PE	White Plastic	Screw Feeder Tube	Reprocessing	Pre-Process Inspection, Preventative Maintenance	
PTFE	White Plastic	Filter Gaskets, Sanitary Piping Gaskets, Centrifuge Gaskets	4-Step Purification, Reprocessing	Replacement of Filters, Pre-Process Inspection, Preventative Maintenance	
Silicon Carbide	Ceramic Fragment	Centrifugal Pump Stationary Seat	4-Step Purification, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Viton	Black elastomer fragment	Pumps (O-rings, gaskets) Process piping gaskets	4-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	

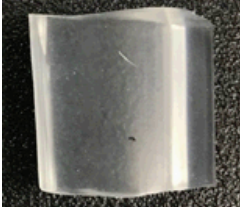

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Originating from the S04 Manufacturing Process Suite					
Identity	Characterization	S04 Origin	How Removed	How Prevented	Picture
Neoprene	White Elastomer	Siever (Gaskets)	Not Applicable	Pre-Process Inspection, Preventative Maintenance	
FEP	White Plastic	Process Hose Lining	4-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	N/A
Polypropylene	Natural colored opaque, opaque off-white plastic	ML Return Tank, Process Piping, Screw Conveyor Hopper	4-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Kynar	Translucent Natural Plastic	Hot Tank Temperature Probe	Not Applicable	Pre-Process Inspection, Preventative Maintenance	

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Originating from the S04 Manufacturing Process Suite					
Identity	Characterization	S04 Origin	How Removed	How Prevented	Picture
PVC	White, Clear, Opaque plastic	ML Tote Process hose (Fittings), Centrifuge ML Return Hose, Dryer Exhaust Duct, Process Piping, Screw Conveyor Hose Centrifuge Wash Tank Piping	4-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Silicone	Clear plastic, Orange elastomer fragment	Piping Gaskets, Dryer Bed Gaskets	Inspection of the Product, Reprocessing, 4-step Purification	Pre-Process Inspection, Preventative Maintenance	


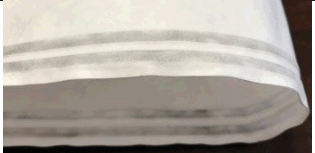


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Originating from the S04 Manufacturing Process Suite					
Identity	Characterization	S04 Origin	How Removed	How Prevented	Picture
Stainless Steel 316	Metallic shaving	Screw Conveyor, Hopper, Agitator (Body of Unit) Portable Sprayer (Vessel) Filter Housing Piping Tank Agitators (Body of Unit) UREA Wash Tank (Vessel) Centrifugal Pump (Housing) Centrifuge (Body of Unit) Fluid Bed Dryer (Body of Unit) Hot/Cold Tanks (Vessel)	4-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Stainless Steel 304	Metallic shaving	Siever	Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
Tygon	Clear Elastomer	ML Pump Tubing	4 Step Purification,	Pre-Process Inspection, Preventative Maintenance	
Polycarbonate	Clear Plastic	Screw Conveyor Sight Glass, Dryer Sight Glass, Cyclone	4-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	Not Available
HDPE	White HDPE	Centrifuge Sight Glass, Funnel Filter, Screw Conveyor	4-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	
CPVC	Gray Plastic	Filter Housing Piping	4 Step Purification	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.



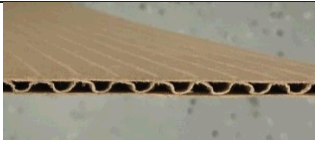

Originating from the Packaging materials					
Identity	Characterization	Origin	How Removed	How Prevented	Picture
Hexene LLDPE	Clear plastic	Poly Liner	Reprocessing	Inspection at time of use	
Tyvek	White Plastic	Tyvek Liner	Reprocessing	Inspection at time of use	
HDPE	White Plastic	Bottle (Packaging)	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.

Originating from the Packaging materials					
Identity	Characterization	Origin	How Removed	How Prevented	Picture
HMW-HDPE	Blue Plastic	Drum (Packaging)	Reprocessing	Inspection at time of use	

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Originating from the Packaging materials					
Identity	Characterization	Origin	How Removed	How Prevented	Picture
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	
Cardboard	Brown	Pallet Liner	Reprocessing	Inspection at time of use	
Wood	Wood Shaving	Pallet	Reprocessing	Inspection at time of use	

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