



TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – GUANIDINE THIOCYANATE PROCESS ROOM E02

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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 E02 at BioSpectra's Bangor, PA facility used in the manufacture of cGMP Guanidine Thiocyanate Bio Excipient or below compliance grade material.

2. SCOPE:

- 2.1. This TUPP applies to the manufacturing and packaging process of Guanidine Thiocyanate manufactured at BioSpectra's Bangor, PA facility in Process Room E02.

3. REFERENCES:

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

4. DEFINITIONS:

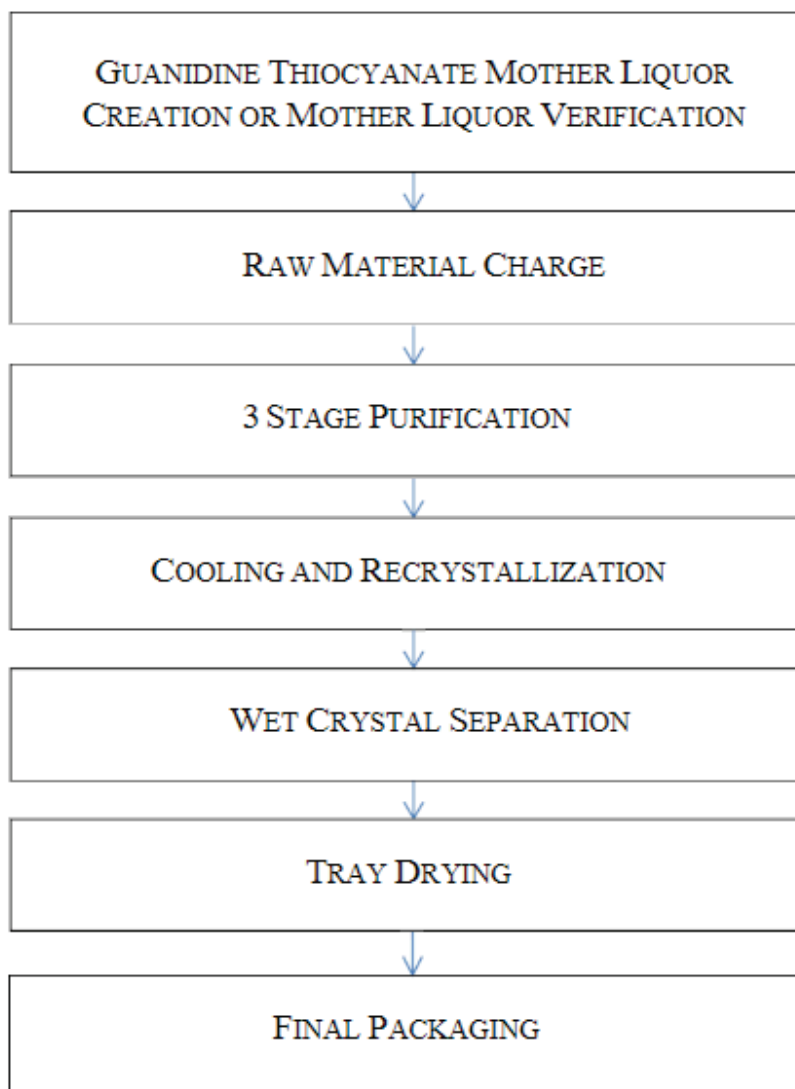
- 4.1. Technically Unavoidable Particle (TUP): A visibly different particle that can be viewed with the naked eye that is inherent to the raw material, manufacturing process or product and does not pose risk to patient safety.
- 4.2. Technically Unavoidable Particle Profiles (TUPPs): A report on all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



7. PROFILE:





7.1. Manufacturing Location:

7.1.1. Bangor, PA Facility

7.2. Applicable Product Codes:

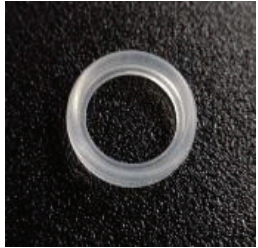



7.2.1. Guanidine Thiocyanate, GTHI-3200 and below compliance grades

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)
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 Hot Tank Air Diaphragm Valve Cold Tank Gaskets Cold Tank Diaphragm Valve Diaphragm Pump Zeta Filter	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	
Carbon	Black or Gray Fragments	Centrifugal Pump (Rotating Carbon Seal)	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	Not Available
Silicon Carbide	Ceramic Fragments	Centrifugal Pump (Stationary Seat)	Inspection Reprocess	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-Ring)	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Polyethylene	Opaque White Plastic	Filter Gasket	Filtration Inspection Reprocess Replacement of Filter	Pre-Process Inspection Preventative Maintenance	
		Chemical Hoses	Filtration Inspection Reprocess		
		Sifting Bin	Inspection Reprocess		
PVC	White, Clear, or Gray Opaque Plastic	Milk Hoses	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
316 Stainless Steel	Metallic Shavings	Hot Tank and Agitator Hot Tank Air Diaphragm Valve Cold Tank and Agitator Cold Tank Air Diaphragm Valve Cartridge Filter Housing Zeta Filter Housing Polishing Filter Housing	Filtration Inspection Reprocess	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)
		Centrifugal Pump Diaphragm Pump Spider Tray Sifter	Inspection Reprocess		
Polypropylene	Opaque Off-White Plastic	Zeta Filter Filter Media	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
		Diaphragm Pump	Inspection Reprocess		
HDPE	White Plastic	Drying Trays	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Cellulose	Fiber	Filter Media	Filtration Reprocessing	Pre-Process Inspection Preventative Maintenance Replacement of Filters	

- 7.4. TUPPs originating from product contacting surfaces of the packaging components:
7.4.1. The following TUPPs are dependent on the packaging type.



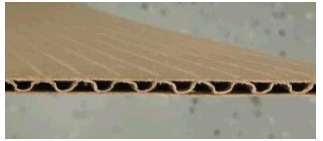

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Originating from the Packaging components					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Hexene LLDPE	Clear Plastic	Liner (Packaging)	Reprocessing	Inspection at time of use	
HDPE	White Plastic	Bottle (Packaging)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