



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

TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – URACIL

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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 Rooms E02, E03, E04/E06 and E05 at BioSpectra's Bangor, PA facility used in the manufacture of cGMP Uracil Bio Pharma grade.

2. SCOPE:

- 2.1. This TUPP applies to the manufacturing and packaging process of Uracil manufactured at BioSpectra's Bangor, PA facility in Process Rooms E02, E03, E04/E06 and E05.

3. REFERENCES:

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

4. DEFINITIONS:

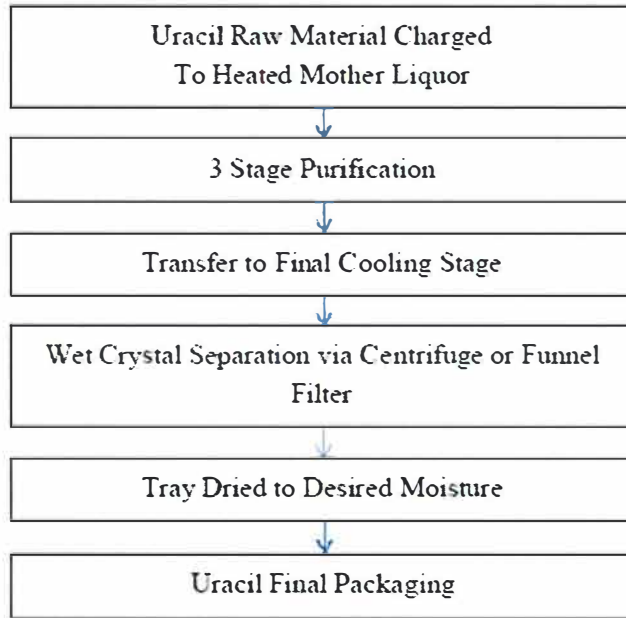
- 4.1. Technically Unavoidable Particle (TUP): A visibly different particle that can be viewed with the naked eye that is inherent to the raw material, manufacturing process or product and does not pose risk to patient safety.
- 4.2. Technically Unavoidable Particle Profiles (TUPPs): A report on all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

5. TECHNICALLY UNAVOIDABLE PARTICLES (TUP):

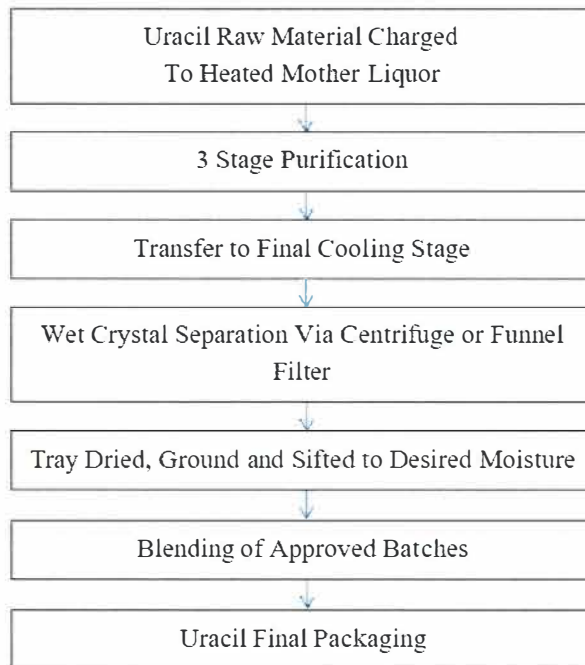
- 5.1. The construction of a technically unavoidable particle profile assumes that GMPs are followed and possible mitigation strategies are taken, the remaining particles, if they pose no risk to safety, are deemed technically unavoidable.
- 5.2. Technically unavoidable particles could originate from 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 Uracil Manufacturing Process Flow Diagram



cGMP Uracil Manufacturing and Blending Process Flow Diagram



7. PROFILE:

7.1. Manufacturing Location:

7.1.1. Bangor, PA Facility

7.2. Applicable Product Codes:

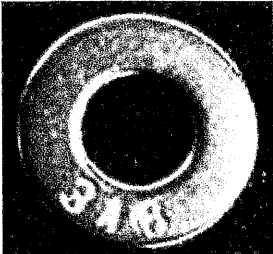
7.2.1. URAC-4201

7.2.2. URAC-4202


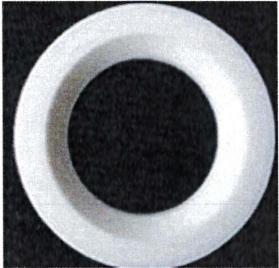



7.2.3. URAC-4250

7.2.4. URAC-4301

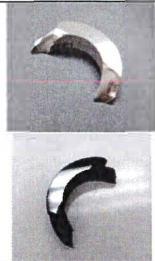
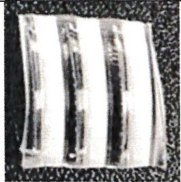


7.3. TUPPs originating from product contacting surfaces in the manufacturing process:

Originating from the Manufacturing Process					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
316 Stainless Steel	Metallic Shavings	Hot Tank and Standpipe	Filtration Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
		Hot Tank Agitator			
		Hot Tank Air Diaphragm Valve (Piping)			
		Cold Tank and Standpipe			
		Cold Tank Agitator			
		Cold Tank Air Diaphragm Valve (Piping)			
		Cartridge Filter			
		Zeta Filter			
		Polishing Filter			
		Centrifugal Pump			
		Diaphragm Pump	Reprocess		
		Spider	Inspection		
		Funnel Filter (fittings)			

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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 Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
PTFE / Telfon	Opaque White Plastic	Hot Tank (Gaskets) Hot Tank Air Diaphragm Valve Cold Tank (Gaskets) Cold Tank Air Diaphragm Valve Zeta Filter	Filtration Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
		Diaphragm Pump (Valve Balls)	Reprocess Inspection		
Red Silicone	Orange Elastomer Fragment	Hot Tank (Gaskets) Cold Tank (Gaskets)	Filtration Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
USP Class VI Silicone	Clear Elastomer	Zeta Filter (Gasket O-Ring) Polishing Filter (Gasket O-Ring)	Filtration Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
Polypropylene	Natural Colored Opaque Off-White Plastic	Zeta Filter Diaphragm Pump Separation Cloth	Reprocess Inspection	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)
Carbon	Black or Gray Fragments	Centrifugal Pump (Rotating Carbon Seal)	Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	Not Available
Silicon Carbide	Ceramic Fragment	Centrifugal Pump (Stationary Seat)	Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
PVC	White, Clear, or Gray Opaque Plastic	Milk Hoses	Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
Polyethylene	Opaque White Plastic	Chemical Hoses	Filtration Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
HDPE	White Plastic	Drying Trays	Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
Porcelain	Natural/White Fragment	Drying Equipment	Reprocess Inspection	Pre-Process Inspection	Not Available

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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.


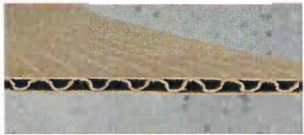

Originating from the Packaging components					
Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Hexene LLDPE	Clear Plastic	Liner (Packaging)	Reprocessing	Inspection at time of use	
HDPE	White Plastic	Bottle (Packaging)	Reprocessing	Inspection at time of use	
Polypropylene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