



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

TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – URIDINE

PROCESS ROOM N02

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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 N02 at BioSpectra's Bangor, PA facility used in the manufacturing of cGMP Uridine Bio Excipient grade material.

2. SCOPE:

- 2.1. This TUPP applies to the manufacturing and packaging process of Uridine manufactured at BioSpectra's Bangor, PA facility in Process Room N02.

3. REFERENCES:

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

4. DEFINITIONS:

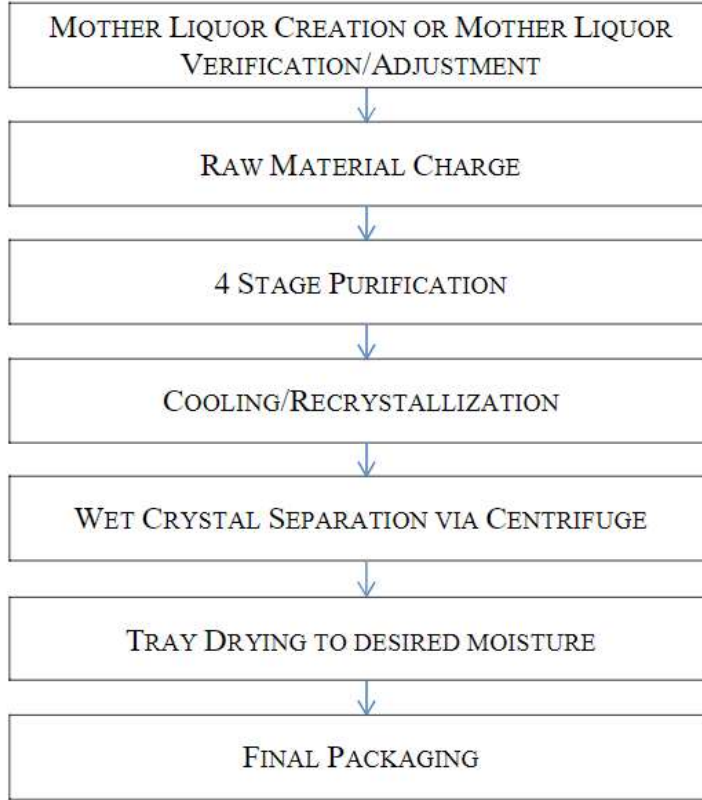
- 4.1. Technically Unavoidable Particle (TUP): A visibly different particle that can be viewed with the naked eye that is inherent to the raw material, manufacturing process or product and does not pose risk to patient safety.
- 4.2. Technically Unavoidable Particle Profiles (TUPPs): A report on all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



7. PROFILE:





7.1. Manufacturing Location:

7.1.1. Bangor, PA Facility





7.2. Applicable Product Codes:

7.2.1. Uridine, URID-3200 and below compliance grades

Table 1: 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)
PTFE	Opaque White Plastic	Process Tanks (N02PT01),(N02PT02) Centrifugal Pump (N02CP01) Centrifuge (N02CE01) Diaphragm Pump (N02DP03) Zeta Filter Process Gaskets	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	
Tantalum	Metallic Shavings	Process Tanks (N02PT01, N02PT02)	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	
Hastelloy	Metallic Shavings	Process Tanks (N02PT01, N02PT02) Process Tank Agitators (N02TA01, N02TA02) Centrifuge (N02CE01)	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	
Hastelloy C-276	Metallic Shavings	Cartridge Filter (N02CF01) Zeta Filter (N02ZF01)	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	
Glass	Glass Fragments	Process Tanks (N02PT01, N02PT02) Process Tank Agitators (N02TA01, N02TA02)	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	Not Available




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Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Polypropylene	Natural Colored Opaque Off White Plastic	Process Tanks (N02PT01, N02PT02) 5 Micron Cartridge Filter Zeta Filter Filter Capsule Centrifuge Cloth Product Scoop Mobile Basket Filter	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance Replacement of Filters	
PVDF	Opaque Plastic	Centrifugal Pump (N02CP01) Portable Sprayer Nozzle (NPS01)	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance	
Kalrez	Black Plastic	Centrifugal Pump (N02CP01)	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance	
Alumina Ceramic	Ceramic Fragments	Centrifugal Pump (N02CP01)	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance	
USP Silicon	Clear Elastomer	Filter Gaskets/O-Rings (N02ZF01, N02CF01) Process Gaskets	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance	
Viton	Black Elastomer Fragment	Process O-Rings and Gaskets Process Piping	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance	

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Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
PVC	White, Clear, or Gray Opaque Plastic	Milk Hoses Portable Sprayer (N02PS01)	Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
Polyethylene	Opaque White Plastic	Chemical Hoses Sifting Bin (N02SB01) Filter Gaskets	Filtration Reprocess Inspection	Pre-Process Inspection Preventative Maintenance	
Active Carbon	Black or Gray Fragments	Zeta Filter	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance Replacement of Filters	Not available
Cellulose	Fiber	Zeta Filter	Filtration Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance Replacement of Filters	
Polyether Sulfone	Opaque White Plastic	Filter Capsule	Inspection of product post- filtration	Pre-Process Inspection Preventative Maintenance Replacement of Filters	Not Available


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Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
316 Stainless Steel	Metallic Shavings	Process Tanks (N02PT01, N02PT02) Process Tank Agitators (N02TA01, N02TA02) Tray Sifter (N02TS01) Sifting Bin Wheels (N02SB01) Portable Sprayer (NPS01) Sanitary Clamps Diaphragm Pump (N02DP03) Centrifugal Pump (N02CP01) Filter Housings (N02ZF01, N02CF01) Process Tank Stand Pipes (N02PT01, N02PT02)	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	
HDPE	White Plastic	ML Holding Tank (N02ML01) Drying Trays (N02DR01) Product Scraper	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	
CPVC	Gray Plastic	Filter Fittings Portable Sprayer Hose (N02PS01)	Filtration Inspection of product post-filtration	Pre-Process Inspection Preventative Maintenance	
Halar	White or Black Fragments	Centrifuge (N02CE01) Liquid Seal Tank (N02MT01)	Filtration	Filtration Inspection of product post-filtration	Not Available

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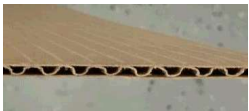

7.3. The following TUPPs are dependent on the packaging type.

Table 2: TUPPs originating from product contacting surfaces of the packaging components:

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	

7.4. Atypical particles originating from non-product contacting surfaces of the packaging components:

Table 3: 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	
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 Shavings	Pallet	Reprocessing	Inspection at Time of Use and Product Care Procedure	

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