



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

TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – MOPS MANUFACTURED IN PROCESS SUITE 1 AND SUITE 2 STROUDSBURG, PA FACILITY

TABLE OF CONTENTS

1.	PURPOSE:.....	3
2.	SCOPE:.....	3
3.	REFERENCES:	3
4.	DEFINITIONS:	3
5.	TECHNICALLY UNAVOIDABLE PARTICLES (TUP):	4
6.	PROCESS FLOW DIAGRAM:.....	5
7.	PROFILE:	5
	TABLE 1: ORIGINATING FROM THE S01 PROCESS SUITE.....	6
	TABLE 2: ORIGINATING FROM THE S02 PROCESS SUITE	9
	TABLE 3: ORIGINATING FROM THE PACKAGING COMPONENTS.....	11
	TABLE 4: ORIGINATING FROM THE PACKAGING COMPONENTS.....	11
	TABLE 5: ORIGINATING FROM PPE/UNIFORMS	12

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 MOPS manufactured in Process Suite 1 and Suite 2 at BioSpectra's Stroudsburg, PA facility.

2. SCOPE:

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

3. REFERENCES:

- 3.1. BSI-DGM-0012, FMEA & CE Matrix Template
- 3.2. BSI-FRM-0501, Contaminant Form
- 3.3. BSI-SOP-0006, Pre-Process Room Inspection SOP
- 3.4. BSI-SOP-0049, Equipment Preventative Maintenance
- 3.5. BSI-SOP-0057, Supplier, Manufacturer, and Service Provider Qualification Master Plan
- 3.6. BSI-SOP-0081, Written and Verbal Complaints
- 3.7. BSI-SOP-0084, Change Control
- 3.8. BSI-SOP-0102, Degradation and Impurity Profiling SOP
- 3.9. BSI-SOP-0137, Discrepancy Investigation Procedure
- 3.10. BSI-SOP-0435, Equipment Qualification Master Plan
- 3.11. IPEC; Technically Unavoidable Particle Profile (TUPP) Guide

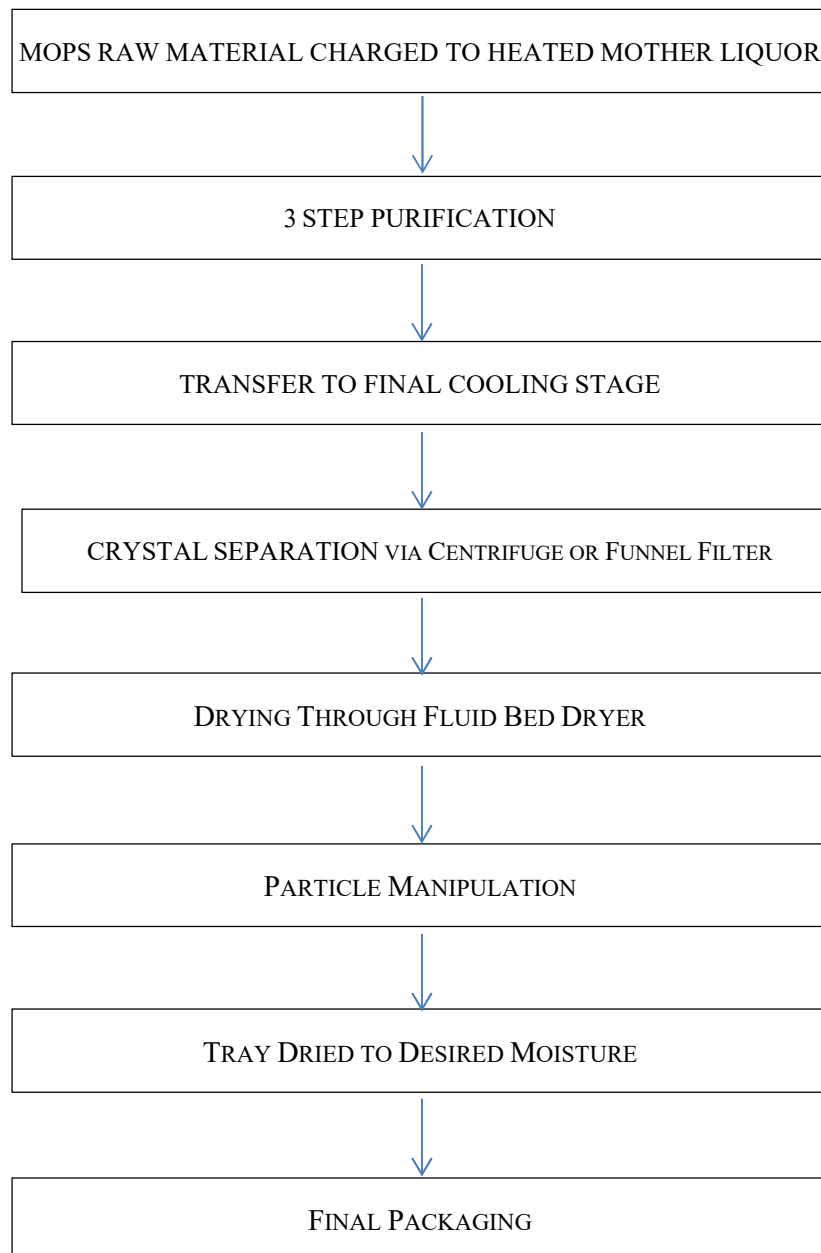
4. DEFINITIONS:

- 4.1. Atypical Particles: A visibly different particle that can be viewed with the naked eye, that is not consistent with a Technically Unavoidable Particle Profile (TUPP).
- 4.2. Contaminant: A visibly different particle that is not inherent of the process or is considered to be avoidable.
- 4.3. 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.
- 4.4. Technically Unavoidable Particle Profiles (TUPPs): A report on all potential known Technically Unavoidable Particles (TUP) for an API or below grade process that can be shared with a customer or end user.
- 4.5. Typical Levels: Historical particulate levels seen in (product) produced at BioSpectra's Stroudsburg, PA facility and repackaged at BioSpectra's Bangor, PA facility that has been deemed as acceptable. If historical particulate levels are unavailable, then each particle will be classified utilizing a risk-based approach until a typical level can be established.
- 4.6. Typical Sizes: Historical particle sizes seen in (product) produced at BioSpectra's Stroudsburg, PA facility and repackaged at BioSpectra's Bangor, PA facility. If historical particulate sizes are unavailable, then the lowest insoluble matter specification will be utilized as the maximum allowable particulate size.

5. TECHNICALLY UNAVOIDABLE PARTICLES (TUP):

- 5.1. Technically unavoidable particles that may be present in GMP processes producing API Finished Goods or below are investigated and assessed to ensure there is no risk to the quality of the finished good material. This SOP is not applicable to objectionable particles resulting from contamination or adulteration.
- 5.2. Particles typically described as Technically Unavoidable Particles:
 - 5.2.1. A study should be initiated into the raw material, manufacturing, and packaging processes to identify particles.
 - 5.2.1.1. Charred Particles:
 - 5.2.1.1.1. Discolored due to heat or friction.
 - 5.2.1.2. Materials of Construction (MOC):
 - 5.2.1.2.1. From manufacturing equipment that is product contacting or known to have normal and expected wear.
 - 5.2.1.2.2. From packaging components.
 - 5.2.1.2.3. Documented Risk Assessments for these are available in the associated FMEA and individual product TUPPs.
 - 5.2.1.3. Routinely used gaskets, seals, filters, etc.
 - 5.2.1.3.1. Expected to have normal wear.
 - 5.2.1.4. Lubricants, greases, oils or like materials.
 - 5.2.1.4.1. Discolored due to traces of such materials.
 - 5.2.1.4.2. Should be approved for use as food grade or food contact grade or justified otherwise.
 - 5.2.1.5. Misshapen or morphologically distinct particles.
 - 5.2.1.5.1. Compressions/agglomerations, elongated/tangles, or flakes.
 - 5.2.1.6. Color variation inherent of the product.
 - 5.2.1.7. Intrinsic components carried through from raw materials.
 - 5.2.1.7.1. Mined or sourced from natural products.
 - 5.3. 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.
 - 5.4. 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.

6. PROCESS FLOW DIAGRAM:










7. PROFILE:





- 7.1. Manufacturing Location:
 - 7.1.1. Stroudsburg, PA Facility
- 7.2. Applicable Product Codes:
 - 7.2.1. All MOPS product codes
- 7.3. TUPPs originating from product contacting surfaces in the manufacturing process:

The information contained herein is the confidential property of BioSpectra. The recipient is responsible for its safe-keeping, and the prevention of unauthorized appropriation, use, disclosure and copying.

Table 1: Originating from the S01 Process Suite

IDENTITY	CHARACTERIZATION	ORIGIN	HOW REMOVED	HOW PREVENTED	PICTURE	TYPICAL SIZES	TYPICAL LEVELS
Carbon	Black particle	Filtration (Filter media) Centrifugal Pump Shaft Seal	3-Step Purification, Reprocessing	Replacement of Filters, Inspection		≤0.05mm	Not Expected - Low Level
UHMW PE	White Plastic	Screw Feeder Tube	Reprocessing	Pre-Process Inspection, Preventative Maintenance	Not Available	≤2mm	Not Expected - Low Level
PTFE	White Plastic	Diaphragm Pump, Filter Gaskets, Sanitary Piping Gaskets, Valve Diaphragms	3-Step Purification, Reprocessing	Replacement of Filters, Pre-Process Inspection, Preventative Maintenance		≤2mm	Not Expected - Low Level
Silicon Carbide	Ceramic Fragment	Centrifugal Pump Stationary Seat	3-Step Purification, Reprocessing	Pre-Process Inspection, Preventative Maintenance		≤0.05mm	Not Expected - Low Level
Viton	Black elastomer fragment	Pumps (O-rings, gaskets), Sanitary Piping Gaskets	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		≤1mm	Not Expected - Low Level
Cellulose	Fiber	Filtration (Filter media)	Polishing Filter	Replacement of Filters, Pre-Process Inspection		≤1mm	Not Expected - Low Level
Silica	White Powder	Filtration (Filter media)	Polishing Filter	Replacement of Filters, Pre-Process Inspection		≤1mm	Not Expected - Low Level
Poly-propylene	Natural colored opaque, opaque off-white, blue, or black plastic	ML Totes, Product shovel, Centrifuge Mesh Cloth Filter Media, Diaphragm Pump, ML Return Tank, process pipe fittings, Filtration, drying trays Media	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		≤2mm	Not Expected - Low Level

The information contained herein is the confidential property of BioSpectra. The recipient is responsible for its safe-keeping, and the prevention of unauthorized appropriation, use, disclosure and copying.

IDENTITY	CHARACTERIZATION	ORIGIN	HOW REMOVED	HOW PREVENTED	PICTURE	TYPICAL SIZES	TYPICAL LEVELS
PVC	White, Clear, Black, Opaque plastic	ML Tote Process hose, Cyclone Exhaust Duct, Dryer Exhaust Duct Portable Sprayer Hose, Process Hose and Piping, Screw Conveyor Hose, Centrifuge Wash Hose	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		$\leq 2\text{mm}$	Not Expected - Low Level
Silicone	Clear, White, and Orange elastomer fragment	Funnel Filter Gaskets, Dryer Bed, Diaphragm Pump Gaskets, Centrifuge Lid Gasket, Process Gaskets	Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		$\leq 1\text{mm}$	Not Expected - Low Level
Polyether-sulfone	White Polymer Fabric	Polishing Filter Media	Inspection of the Product, Reprocessing	Replacement of Filters, Pre-Process Inspection	Not Available	$\leq 2\text{mm}$	Not Expected - Low Level
316 Stainless Steel	Metallic shaving	Process Tank Piping, Tank Shaft, Process Filters, Centrifuge, Centrifugal Pumps, Diaphragm Pump Fittings, Fluid Bed Dryer, Portable Sprayer, Screw Conveyor, Centrifuge Wash Tank, Process Piping, Stokes Grinder, Sifter	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		$\leq 0.05\text{mm}$	Not Expected - Low Level
304 Stainless Steel	Metallic shaving	Process Tanks	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		$\leq 0.05\text{mm}$	Not Expected - Low Level

The information contained herein is the confidential property of BioSpectra. The recipient is responsible for its safe-keeping, and the prevention of unauthorized appropriation, use, disclosure and copying.











IDENTITY	CHARACTERIZATION	ORIGIN	HOW REMOVED	HOW PREVENTED	PICTURE	TYPICAL SIZES	TYPICAL LEVELS
Poly-carbonate	Clear Plastic	Centrifuge Sight Glass, Dryer Sight Glass, Cyclone	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance	Not Available	$\leq 2\text{mm}$	Not Expected - Low Level
HDPE	White HDPE	Centrifuge Sight Glass, Funnel Filter, Screw Conveyor	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		$\leq 2\text{mm}$	Not Expected - Low Level
CPVC	Gray Plastic	ML Return Tank Piping	3-Step Purification, Inspection of the Product, Reprocessing	Pre-Process Inspection, Preventative Maintenance		$\leq 2\text{mm}$	Not Expected - Low Level
Vinyl plastic	Blue	Sanitary fitting cover	Inspection at time of use	Inspection at time of use		$\leq 2\text{mm}$	Not Expected - Low Level

Table 2: Originating from the S02 Process Suite

Identity	Characterization	Origin	How Removed	How Prevented	Picture	Typical Sizes	Typical Levels
316 Stainless Steel	Metallic Shaving	Screw Conveyor, Portable Sprayer, Process Filter Housings, Process Piping, Tank Agitators, Centrifugal Pumps, Tray Sifter, Fluid Bed Dryers, Funnel Filter fasteners and Fittings, Sifter	3 Step Purification, Inspection of the product	Pre-Process Inspection, Preventative Maintenance		$\leq 0.05\text{mm}$	Not Expected - Low Level
304 Stainless Steel	Metallic Shaving	Process Tanks	3 Step Purification, Inspection of the product	Pre-Process Inspection, Preventative Maintenance		$\leq 0.05\text{mm}$	Not Expected - Low Level
PTFE	Opaque White Plastic	Diaphragm Pumps, Sanitary Piping Gaskets, Screw Conveyor Seals	3 Step Purification, Inspection of the product	Replacement of Filters, Pre-Process Inspection, Preventative Maintenance		$\leq 2\text{mm}$	Not Expected - Low Level
Carbon	Black or Gray Fragments	Centrifugal Pump seals	Inspection of the product	Replacement of Filters, Inspection		$\leq 0.05\text{mm}$	Not Expected - Low Level
HDPE	Plastic	Funnel Filter (Internal Supports), Hot Tank	Inspection of the product	Pre-Process Inspection, Preventative Maintenance		$\leq 2\text{mm}$	Not Expected - Low Level
Poly-propylene	Natural Colored Opaque Off-White, Blue Plastic	Funnel Filter Cloth, Diaphragm Pump, Filtration Media	Inspection of the product	Pre-Process Inspection, Preventative Maintenance		$\leq 2\text{mm}$	Not Expected - Low Level
Vinyl plastic	Blue	Sanitary fitting cover	Inspection at time of use	Inspection at time of use		$\leq 2\text{mm}$	Not Expected - Low Level

The information contained herein is the confidential property of BioSpectra. The recipient is responsible for its safe-keeping, and the prevention of unauthorized appropriation, use, disclosure and copying.




Identity	Characterization	Origin	How Removed	How Prevented	Picture	Typical Sizes	Typical Levels
PVC	White, Clear, Black, Opaque Plastic	Process Hoses and Pipe Fittings	3 Step Purification, Inspection of the product	Pre-Process Inspection, Preventative Maintenance		$\leq 2\text{mm}$	Not Expected - Low Level
Viton	Black Elastomer	Sanitary Piping Gaskets	3 Step Purification, Inspection of the product	Pre-Process Inspection, Preventative Maintenance		$\leq 1\text{mm}$	Not Expected - Low Level
Silicone	Clear, White, or Orange Elastomer	Sanitary Piping Gaskets, Process Gaskets	3 Step Purification, Inspection of the product	Pre-Process Inspection, Preventative Maintenance		$\leq 1\text{mm}$	Not Expected - Low Level
Polycarbonate	Clear Plastic	Fluid Bed Dryer Sight glasses,	Inspection of the product	Pre-Process Inspection, Preventative Maintenance	Not Available	$\leq 2\text{mm}$	Not Expected - Low Level
Polyether-sulfone	White Polymer Fabric	Polishing Filter Media	Inspection of the Product, Reprocessing	Replacement of Filters, Pre-Process Inspection	Not Available	$\leq 2\text{mm}$	Not Expected - Low Level
Cellulose	Fiber	Filtration (Filter media)	Polishing Filter	Replacement of Filters, Pre-Process Inspection		$\leq 1\text{mm}$	Not Expected - Low Level
Silica	White Powder	Filtration (Filter media)	Polishing Filter	Replacement of Filters, Pre-Process Inspection		$\leq 1\text{mm}$	Not Expected - Low Level
UHMW PE	White Plastic	Screw Feeder Tube	Reprocessing	Pre-Process Inspection, Preventative Maintenance	Not Available	$\leq 2\text{mm}$	Not Expected - Low Level

The information contained herein is the confidential property of BioSpectra. The recipient is responsible for its safe-keeping, and the prevention of unauthorized appropriation, use, disclosure and copying.

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

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


Table 3: Originating from the Packaging Components


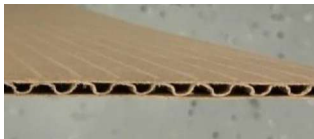

Identity	Characterization	Origin	How Removed	How Prevented	Picture
Hexene LLDPE	Clear Plastic	Liner (Packaging)	Inspection at time of use	Inspection at time of use	
HDPE	White Plastic	Bottle (Packaging)	Reprocessing	Inspection at time of use	
Polypropylene	Blue Plastic	Tamper Evident lid (Packaging)	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.



Table 4: Originating from the Packaging Components

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


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	
Cardboard	Brown	Pallet Liner	Reprocessing	Inspection at time of use	
Wood	Wood Shaving	Pallet	Reprocessing	Inspection at time of use	

7.6. Atypical particles originating from personal protective equipment (PPE) or manufacturing uniforms:

Table 5: Originating from PPE/Uniforms

Identity	Characterization	Origin	How Removed	How Prevented	Picture	Typical Sizes	Typical Levels
Nitrile	Blue	Gloves	Inspection at time of use	Inspection at time of use		$\leq 2\text{mm}$	Not Expected – Low Level
Tyvek	White	Disposable Lab Jackets, Coveralls, PAPRs and Sleeves	Inspection at time of use	Inspection at time of use		$\leq 2\text{mm}$	Not Expected – Low Level

The information contained herein is the confidential property of BioSpectra. The recipient is responsible for its safe-keeping, and the prevention of unauthorized appropriation, use, disclosure and copying.

Identity	Characterization	Origin	How Removed	How Prevented	Picture	Typical Sizes	Typical Levels
Polyester	Blue and Black Fibers	Manufacturing Uniform and PAPRs	Inspection at time of use	Inspection at time of use		≤2mm	Not Expected – Low Level