



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

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Page 1 of 10

TABLE OF CONTENTS

1. PURPOSE:.....	3
2. SCOPE:.....	3
3. REFERENCES:.....	3
4. DEFINITIONS:.....	3
5. TECHNICALLY UNAVOIDABLE PARTICLES (TUP):.....	3
6. PROCESS FLOW DIAGRAM:	4
7. PROFILE:	4

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. IPEC; Technically Unavoidable Particle Profile (TUPP) Guide

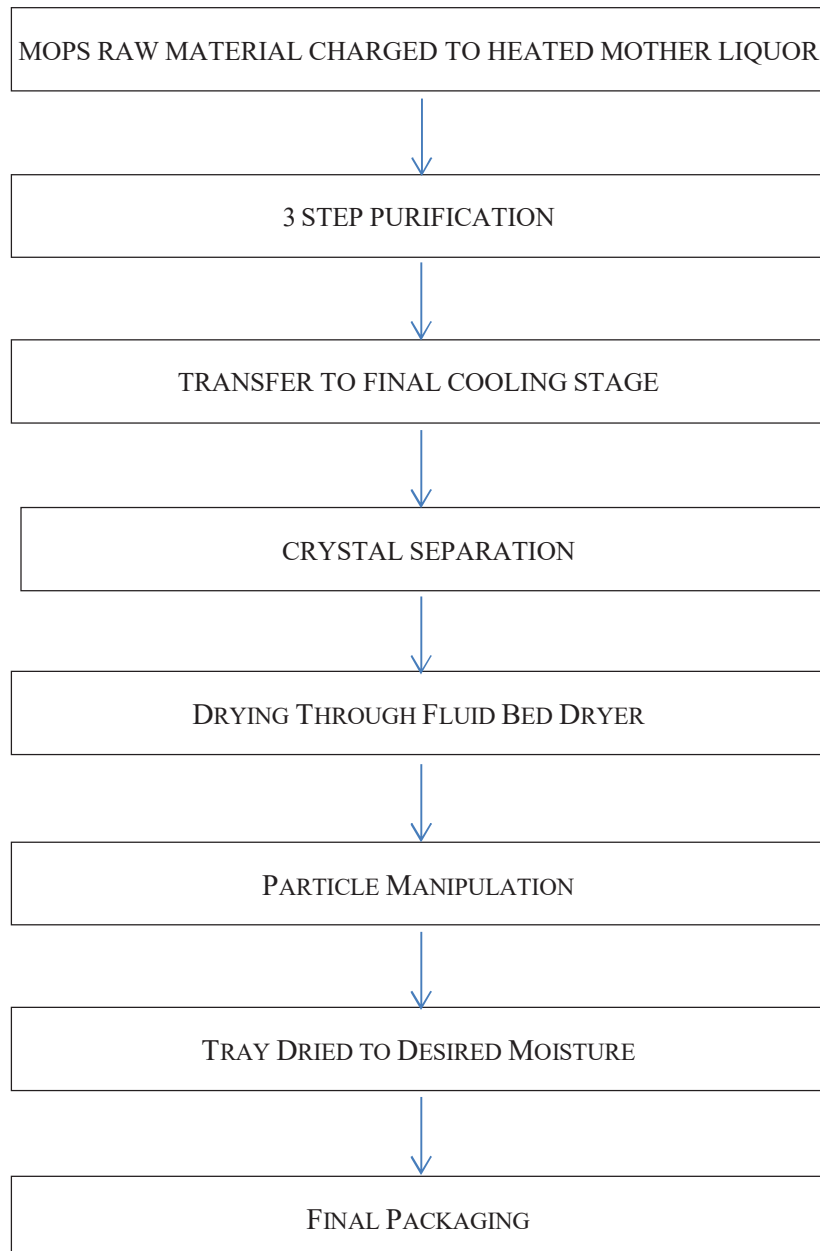
4. DEFINITIONS:

- 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 MOPS was approved as part of the validation of the MOPS 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. 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:





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ORIGINATING FROM THE S01 MANUFACTURING 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

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ORIGINATING FROM THE S01 MANUFACTURING PROCESS SUITE							
IDENTITY	CHARACTERIZATION	ORIGIN	HOW REMOVED	HOW PREVENTED	PICTURE	TYPICAL SIZES	TYPICAL LEVELS
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 MEDIA	3-STEP PURIFICATION, INSPECTION OF THE PRODUCT, REPROCESSING	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤2MM	NOT EXPECTED - LOW LEVEL
PVC	WHITE, CLEAR, 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		≤2MM	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	 	≤1MM	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	≤2MM	NOT EXPECTED - LOW LEVEL

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ORIGINATING FROM THE S01 MANUFACTURING PROCESS SUITE							
IDENTITY	CHARACTERIZATION	ORIGIN	HOW REMOVED	HOW PREVENTED	PICTURE	TYPICAL SIZES	TYPICAL LEVELS
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	3-STEP PURIFICATION, INSPECTION OF THE PRODUCT, REPROCESSING	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤0.05MM	NOT EXPECTED - LOW LEVEL
304 STAINLESS STEEL	METALLIC SHAVING	PROCESS TANKS	3-STEP PURIFICATION, INSPECTION OF THE PRODUCT, REPROCESSING	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤0.05MM	NOT EXPECTED - LOW LEVEL
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	≤2MM	NOT EXPECTED - LOW LEVEL
HDPE	WHITE HDPE	CENTRIFUGE SIGHT GLASS, FUNNEL FILTER, SCREW CONVEYOR, STOKES GRINDER	3-STEP PURIFICATION, INSPECTION OF THE PRODUCT, REPROCESSING	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤2MM	NOT EXPECTED - LOW LEVEL
CPVC	GRAY PLASTIC	ML RETURN TANK PIPING	3-STEP PURIFICATION, INSPECTION OF THE PRODUCT, REPROCESSING	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤2MM	NOT EXPECTED - LOW LEVEL

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ORIGINATING FROM THE S02 MANUFACTURING PROCESS

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	3 STEP PURIFICATION, INSPECTION OF THE PRODUCT	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤0.05mm	NOT EXPECTED - LOW LEVEL
304 STAINLESS STEEL	METALLIC SHAVING	PROCESS TANKS	3 STEP PURIFICATION, INSPECTION OF THE PRODUCT	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤0.05mm	NOT EXPECTED - LOW LEVEL
PTFE	OPAQUE WHITE PLASTIC	DIAPHRAGM PUMPS, SANITARY PIPING GASKETS, SCREW CONVEYER SEALS	3 STEP PURIFICATION, INSPECTION OF THE PRODUCT	REPLACEMENT OF FILTERS, PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤2mm	NOT EXPECTED - LOW LEVEL
CARBON	BLACK OR GRAY FRAGMENTS	CENTRIFUGAL PUMP SEALS	INSPECTION OF THE PRODUCT	REPLACEMENT OF FILTERS, INSPECTION		≤0.05mm	NOT EXPECTED - LOW LEVEL
HDPE	PLASTIC	FUNNEL FILTER (INTERNAL SUPPORTS) HOT TANK	INSPECTION OF THE PRODUCT	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤2mm	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		≤2mm	NOT EXPECTED - LOW LEVEL

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ORIGINATING FROM THE S02 MANUFACTURING PROCESS

IDENTITY	CHARACTERIZATION	ORIGIN	HOW REMOVED	HOW PREVENTED	PICTURE	TYPICAL SIZES	TYPICAL LEVELS
PVC	WHITE, CLEAR, OPAQUE PLASTIC	PROCESS HOSES AND PIPE FITTINGS	3 STEP PURIFICATION, INSPECTION OF THE PRODUCT	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤2MM	NOT EXPECTED - LOW LEVEL
VITON	BLACK ELASTOMER	SANITARY PIPING GASKETS	3 STEP PURIFICATION, INSPECTION OF THE PRODUCT	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE		≤1MM	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		≤1MM	NOT EXPECTED - LOW LEVEL
POLYCARBONATE	CLEAR PLASTIC	FLUID BED DRYER SIGHT GLASSES,	INSPECTION OF THE PRODUCT	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE	NOT AVAILABLE	≤2MM	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	≤2MM	NOT EXPECTED - LOW LEVEL
CELLULOSE	FIBER	FILTRATION (FILTERMEDIA)	POLISHING FILTER	REPLACEMENT OF FILTERS, PRE-PROCESS INSPECTION		≤1MM	NOT EXPECTED - LOW LEVEL
SILICA	WHITE POWDER	FILTRATION (FILTERMEDIA)	POLISHING FILTER	REPLACEMENT OF FILTERS, PRE-PROCESS INSPECTION		≤1MM	NOT EXPECTED - LOW LEVEL
UHMW PE	WHITE PLASTIC	SCREW FEEDER TUBE	REPROCESSING	PRE-PROCESS INSPECTION, PREVENTATIVE MAINTENANCE	NOT AVAILABLE	≤2MM	NOT EXPECTED - LOW LEVEL

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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	LINER (PACKAGING)	INSPECTION AT TIME OF USE	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)	INSPECTION AT TIME OF USE	INSPECTION AT TIME OF USE	
CARDBOARD	BROWN	PALLET LINER	INSPECTION AT TIME OF USE	INSPECTION AT TIME OF USE	
WOOD	WOOD SHAVING	PALLET	INSPECTION AT TIME OF USE	INSPECTION AT TIME OF USE	
BSI PLASTIC	BLUE, GREEN, OR GRAY PLASTIC	PALLET	INSPECTION AT TIME OF USE	INSPECTION AT TIME OF USE	

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