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TECHNICALLY UNAVOIDABLE PARTICLE PROFILE (TUPP) – POTASSIUM BROMIDE

API SUITE 1, PROCESS ROOM E05

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
 FIGURE 1: CGMP POTASSIUM BROMIDE MANUFACTURING PROCESS FLOW DIAGRAM.....4
7. PROFILE:4
 TABLE 1: ORIGINATING FROM THE MANUFACTURING PROCESS5
 TABLE 2: ORIGINATING FROM THE PACKAGING COMPONENTS7
 TABLE 3: ATYPICAL PARTICLES: ORIGINATING FROM THE PACKAGING COMPONENTS.....8

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 API Suite 1, Process Room E05 at BioSpectra's Majestic, PA facility used in the manufacture of cGMP Potassium Bromide Bio Active grade.

2. SCOPE:

- 2.1. This TUPP applies to the manufacturing and packaging process of Potassium Bromide manufactured at BioSpectra's Majestic, PA facility in API Suite 1, Process Room 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 Potassium Bromide was approved as part of the validation of the Potassium Bromide 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:

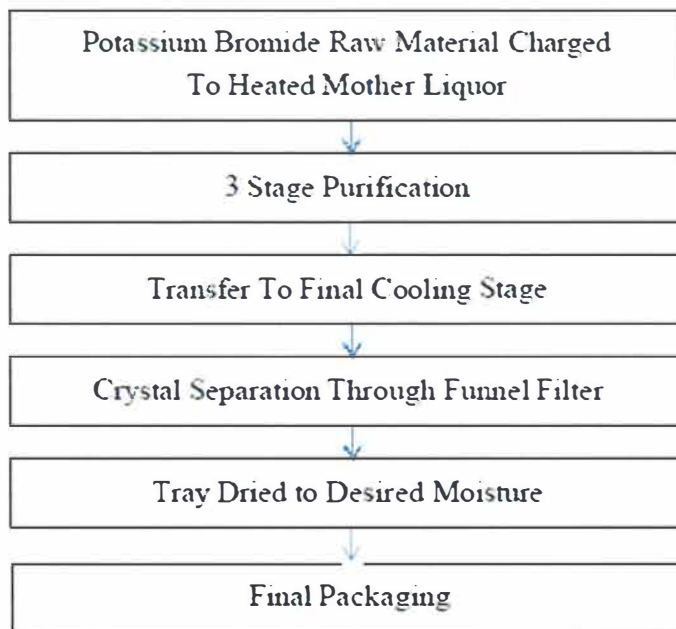


Figure 1: cGMP Potassium Bromide Manufacturing Process Flow Diagram

7. PROFILE:

7.1. Manufacturing Location:

7.1.1. Majestic, PA Facility

7.1.2. API Suite 1, Process Room E05

7.2. Applicable Product Codes:

7.2.1. Potassium Bromide, KBRO-2XXX

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

Table 1: Originating from the Manufacturing Process

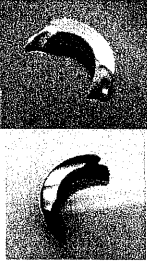
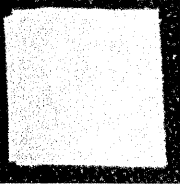
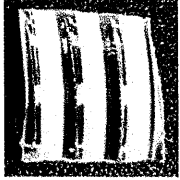
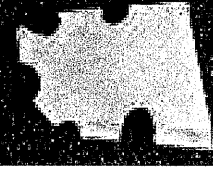

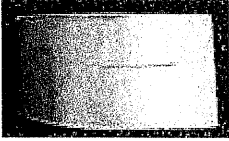





Identity	Characterization	Origin	How Removed	How Prevented	Picture (Example of Source)
Carbon	Black or Gray Fragments	Centrifugal Pump (Rotating Carbon Seal)	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	Not Available
Silicon Carbide	Ceramic Fragment	Centrifugal Pump (Stationary Seat)	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Silicone	Clear or White Elastomer	Filtration	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
PVC	White, Clear, or Gray Opaque Plastic	Filtration Milk Hoses	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Polypropylene	Natural Colored Opaque Off-White Plastic	Filter Funnel (Shell and Perforated Plate) Sifting Bin	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
HDPE	White Plastic	Filter Funnel (Support Structure) Drying Trays	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
CPVC	Gray Plastic	Filter Funnel (Fittings)	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	

Table 1: 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 Hot Tank Agitator Cold Tank and Standpipe Cold Tank Agitator Filtration Spider Filter Funnel (Fittings) Tray Sifter Wall Supply Wall Return Centrifugal Pump (Pump Head and Impeller)	Filtration Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	
Polyethylene	Opaque White Plastic	Chemical Hoses	Inspection Reprocess	Pre-Process Inspection Preventative Maintenance	





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 2: 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.

Table 3: 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 Shaving	Pallet	Reprocessing	Inspection at time of use and Product Care Procedure	