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US Manufactured Premium Pharmaceutical Ingredients

BioSpectra Liner Assessment Anti-Block/Anti-Static Statements

Discussion Points

- Primary Packaging
  - Liners
  - Stability Assessment
    - Tris
    - Tris HCl
- Anti-Slip Declaration
- Anti-Block Declaration
- Regulatory Statements

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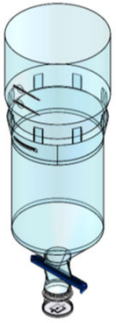
Primary Packaging

Currently Used for BioSpectra Products

- Linear low density polyethylene liners used for BioSpectra Tris and Tris HCl Crystalline Powder
- Sierra Packaging (multiple sizes based on secondary outer package and qty of material)

ILC Dover Option

- Polyethylene Permanent anti-stat provides better than 1 x 10^{11} Ohms per square surface resistivity



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Stability Assessment Tris

- Multiple studies performed since the initial Validated Batch
  - Validation Batches, one lot per year
  - 36 month stability study using the following intervals- 0, 3, 6, 9, 12, 18, 24, and 36
  - Real Time Conditions
    - 15-30°C and monitored humidity
    - Stability Indicating Analysis includes:
    - In all packaging configurations using LLDPE liners
    - No Significant change observed

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Stability Assessment Tris Hydrochloride

- Multiple studies performed since the initial Validated Batch
  - Validation Batches, one lot per year
  - 36 month stability study using the following intervals- 0, 3, 6, 9, 12, 18, 24, and 36
  - Real Time Conditions
    - 15-30°C and monitored humidity
    - Stability Indicating Analysis includes:
    - In all packaging configurations using LLDPE liners
    - No Significant change observed

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Anti-Slip/Anti-Static Declaration

- Sierra Packaging
  - No slip or antistatic additives
  - Comment:
    - LLDPE Resin Details

Chemical

ExxonMobil™ LLDPE LL 3201 Series
Linear Low Density Polyethylene Resin

Product Description			
LL 3201 resins are LLDPE hexene copolymer film resins. Film made from LL 3201 resins have outstanding tensile, stiffness and toughness properties. These superior properties, along with good drawdown capability, permit usage in many demanding packaging applications.			
General			
Availability [1]	• Latin America	• North America	• South America
Additive	• LL 3201.36: Antiblock: 5000 ppm; Processing Aid: Yes; Slip: No; Thermal Stabilizer: Yes • LL 3201.69: Antiblock: No; Processing Aid: Yes; Slip: No; Thermal Stabilizer: Yes		
Applications	• Freezer Film • Grocery Sacks	• Heavy Duty Bags • Merchandise Bags	
Revision Date	• 10/2008		

- ILC Dover
  - Permanent static dissipative properties (antistat), no slip agents
  - Comment:
    - Antistatic vs static dissipative
    - Permanent antistat replaces migrating additives

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Anti-Block Declaration

- Sierra Packaging
  - Anti-block additives talc (magnesium silicate hydrate) and diatomaceous earth (flux calcinated silica)
    - Additives are less than 5000ppm
    - Alternative sources state 1-2%

- ILC Dover
  - Information not provided
  - No Slip Agents
  - Static Dissipative

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Regulatory Statements

- Sierra Packaging
  - 21CFR 177.1520 c(2.1), c(3.2a) Olefin Polymers
  - 21CFR 178.3860 Erucamide
  - 21CFR 184.1191 Calcium Carbonate
  - European Directives 90/128.EEC
  - EU No 10/2011 and Amendments
- **Comments:**
  - Per 21 CFR 177.1520 (c)2.1, Polyethylene for use in articles that contact food except for articles used for packing or holding food during cooking have the following specifications:
    - Density 0.85-1.00
    - Maximum extractable fraction (expressed as percent by weight of the polymer) in N-hexane at specified temperatures: 5.5% at 50°C
    - Maximum soluble fraction (expressed as percent by weight of polymer) in xylene at specified temperatures: 11.3% at 25°C
  - Per 21 CFR 178 Indirect Food Additives: Adjuvants, Production Aids, and Sanitizers, Subpart D Certain Adjuvants and Production Aids, Section 178.3860 Release agents, Erucamide (erucylamide) may be safely used as a release agent in polymeric resins that contact food. The quantity used shall not exceed the amount reasonably required to accomplish the intended technical effect. There are no limitations prescribed for Erucamide (erucylamide).
  - Per 21 CFR part 184 Direct Food Substances Affirmed as Generally Recognized as Safe, Subpart B, Section 184.1191 Calcium carbonate (c) the ingredient is used in food with no limitation other than current good manufacturing practice.

- ILC Dover
  - FDA 21 CFR compliant
  - Fully compliant to EU Regulation 10/2011 and amendments
  - EP 3.1.3 test parameters
  - Passes USP <661>, USP <88>, USP <87>
  - Food Contact
- DMF filed with FDA
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  - 21CFR 184.1191 Calcium Carbonate
  - European Directives 90/128.EEC
  - EU No 10/2011 and Amendments

Comments:

- Per Regulation EU No 10/2011 on plastic materials and articles intended to come into contact with food. This regulation details requirements for starting materials, migration limits, applicable testing methods, and information regarding the following applicable additives:
  - Talc (615) is permitted for use as an additive or polymer production aid, with no restrictions
  - Diatomaceous earth (707) and Diatomaceous earth, soda ash flux-calcined (734) are permitted for use as an additive or polymer production aid, with no restrictions
  - Erucamide (271) is permitted for use as an additive or polymer production aid, with no restrictions

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Final Discussion Points

- Compliance statements to support no migrating additives,
- Anti-static does not mean anti-block.
- Anti-block criteria established
  - 1-2% vs <5%
- Percent anti-block statement is the quantity found in the resin used to prepare the liner.

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