New Vial Technologies for Pharmaceutical Products

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Agenda

- Background
- Filling Line Trials
- Learnings/Considerations
- Lyophilization Comparability
- Control Strategy
- Lessons Learned/Conclusions

Background

Introduction of new vial technology, Valor™ Vial:

1. Establish global cross functional team
2. Create standard approach to assess impact of vial
3. Develop network wide strategy for implementation
   - Multiple products
   - Multiple sites
   - Multiple images

Filling Line Trials

- Objective of the filling line trials was to assess:
  - Machinability performance
  - Particulate generation
  - Interventions
  - Glass breakage
  - Visual inspection performance

- Multiple line trials on the same line demonstrated ability to run at higher effective line speed with less interventions and lower particulates
- Line trials on different filling lines resulted in similar observations
- Line trials ranged in size from:
  - 50 K to 1+ MM
  - 2 hours to 1 week

Machinability Outcomes – Speed, Interventions, Particulates

- Effective Line Speed: → ~25% improvement in effective line speed
- Interventions: → ~61% reduction in interventions
- Particulates: → ~92% reduction in non-viable particles at in-feed location

Eliminated application of lubricant typically used to improve glass flow during line trial

Learnings/Considerations: Reduced Friction

- Coating on Valor™ vial significantly reduces frictive nature of glass
  - Flow of Valor glass is different than borosilicate glass
- Filling lines designed to transfer glass with the following mechanisms may require timing adjustments to accommodate new flow pattern
  - "en masse" with accumulation points
  - glass moved via backpressure

EXAMPLE:

washer → depyrogenation tunnel → filler

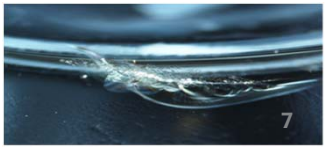
Learnings/Considerations: Crack Prevention Mechanism

- Improper set-up more readily detected by Valor™ vial

  EXAMPLES

  – Transition not aligned causing impact to heel and results in breakage
  – Capper set up causes disk/rail to damage neck causing breakage
  – Needle strike at top of vial causes breakage

Examples above lead to breakage with Valor™ vial, but will not result in significant checks or CRACKS



Approach for Assessing Lyophilization Comparability

1. Establish equivalence for critical dimensions between Valor vial and current vial
2. Perform lab scale run to assess freezing kinetics
   a. Head to head with borosilicate using gravimetric analysis
   b. Sublimation rate data used to determine relative heat transfer coefficients via mathematical modeling
3. Perform commercial scale run
   a. Freezing Profile
   b. Moisture Mapping
   c. Chamber Pressure
   d. Lyo Cake Appearance

Results of Lyophilization Comparability Assessment

Lab Scale Results:

- Valor vial had a slightly lower heat transfer coefficient, but **no** anticipated impact to lyo product cycle with current primary drying time

Commercial Scale Results:

- Freezing profile and chamber pressure were comparable
- Moisture results were within specification and process capability limits
- No change in lyo cake appearance
- Demonstrated no need for change in lyo cycle parameters

Lyophilization Performance Deemed Equivalent

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Control Strategy Considerations

1. What different types of responses during operations could be observed?
   a. Degradation of coating from extended times at high temperatures, e.g. line stoppages in depyrogenation tunnel
      - Monitor duration at high temperatures
      - Control measures to reduce temperature during extended stoppages
   b. Damage will result in breakage
      - Precision of set-up
      - Sensitivity to dimensional variation
      - Breakage should be an early indicator of a problem

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Control Strategy Considerations (Cont'd)

2. What are the differences between the Valor™ vial and current vial?
   a. Dimensions
      - Evaluate critical dimensions to confirm machinability
      - Evaluate critical dimensions for lyophilization equivalency
   b. Increased Strength of vial
      - Ensure equipment has appropriate overtorque settings to prevent damage
      - Ensure materials of construction are compatible with vial strength
   c. Heat Transfer Coefficient (Lyo only)
      - Evaluate difference in heat transfer coefficient
      - Based on difference assess potential impact to lyophilization process

Lessons Learned

- Cross-functional team with appropriate subject matter expertise
  - Glass manufacturing and handling
  - Product impact/stability
  - Manufacturing process
  - Quality risk management
  - Regulatory
- Significant line trials to develop experience with vial
- Sponsorship to support resources, line time and expenses for implementation
- Regulatory strategy to support implementation including early engagement with regulatory authorities to ensure success

Conclusions

- Overall Improvements
  1. Higher effective speed
  2. Reduced interventions
  3. Lower particulates
  4. No cracks
- Control Strategy for Unique Characteristics
  1. Reduced friction
  2. Crack prevention mechanism
  3. Increased strength
  4. Degradation of coating
  5. Heat transfer characteristics (lyo)

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QUESTIONS