



Post-filling steam/radiation sterilization (for diluent or small molecule)

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INTRODUCTION

SiO₂ Materials Science, Inc. (SiO₂) manufactures primary containers (vials, syringes and cartridges) in ready to use (RTU) format. In 2015, SiO₂ completed the process validation of the 6 mL vial. Shelf life stability studies were conducted with 6 mL vials manufactured from the validated process. The shelf life stability studies included both empty container and filled container shelf life. The data from the shelf life studies show that the SiO₂ barrier system coated 6 mL vials are stable throughout the shelf life.

SHELF LIFE STUDY OVERVIEW

The 6 mL vials were manufactured in April-May of 2015 using a validated molding and barrier system coating process. The study was composed of two sections: Dry Study (empty container storage) and Wet Study (filled container storage). The barrier system coated 6 mL vials used in this study were divided into two populations: (1) one set of vials were e-beam sterilized at 35 kGy and (2) one set of vials were sterilized with ethylene oxide.

DRY STUDY

- Accelerated Aging at 55°C, data pulls at 0 and 91 days
- Real-time Warehouse Storage at (16-35°C), data pulls at 0 and 24 months

WET STUDY

- Accelerated Aging at 40°C, data pulls at 0, 65, 90, 129, 258 days
- Real-time Warehouse Storage at (16-35°C), data pulls at 0, 6, 8.5, 12, 24 months
- Challenge solutions: WFI and phosphate buffered saline (pH 7.4)
- E-beam sterilized vials were filled with the challenge solutions, then stoppered and steam sterilized at 121°C for 20 min.
- Ethylene oxide (ETO) sterilized vials were filled with the challenge solutions, then stoppered and steam sterilized at 121°C for 20 min.

TEST CONDUCTED

The vials in the dry and wet studies were subjected to the following tests: (1) dimensions, (2) visual (clarity and light transmission), (3) mechanical strength, (4) particles and (5) coating integrity using an in-house method referred as CI-9.

1. Dimensions are critical quality characteristics (CTQs) for:
 - Compatibility with standard components (stoppers, crimp seal)
 - Compatibility with standard material handling equipment and drug-filling machines
 - Container closure integrity (CCI)
2. Clarity and Light Transmission
 - An assessment for color change due to aging and sterilization effect. Use Lightness, Chroma and Hue (LCH) color space.
3. Mechanical Strength
 - An assessment of physical stability of the vial and tri-layer coating
 - Apply 100 lbs top & side loading of the vial – conduct visual assessment of vial for cracks
4. Particles
 - Used to assess potential delamination of the tri-layer coating system
 - Particle specifications:
 - >10 micron is < 600 / vial (6000 per USP 788) using Light Obscuration
 - >25 micron is < 60 / vial (600 per USP 788) using Light Obscuration
5. Coating Integrity (CI-9)
 - Vials are filled with a pH 9 challenge solution, stoppered and stored at 50°C for 72 hours.
 - The challenge solution is removed from the vial and tested using an ICP/OES instrument for elemental silicon.
 - The barrier system coating is silicon-based. The amount of silicon in solution is measure of coating integrity. The specification for Si is < 6.55µg in CI9 Testing.

TESTS AND RESULTS

<u>Sample Type</u>	<u>Study</u>	<u>Clarity and Light Transmission</u>	<u>Dimensions</u>	<u>Mechanical Strength</u>	<u>Particles</u>	<u>Coating Integrity</u>
e-beam real time	Empty	Pending	Pending	Pending	Pending	Pending
ETO real time	Empty	Pending	Pending	Pending	Pending	Pending
e-beam accelerated	Empty	Passed	Passed	Passed	Passed	Passed
ETO accelerated	Empty	Passed	Passed	Passed	Passed	Passed
e-beam WFI real time	Filled	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months
ETO WFI real time	Filled	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months
e-beam PBS real time	Filled	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months
ETO PBS real time	Filled	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months	Passed through 12 months
e-beam WFI accelerated	Filled	Passed	Passed	Passed	Passed	Passed
ETO WFI accelerated	Filled	Passed	Passed	Passed	Passed	Passed
e-beam PBS accelerated	Filled	Passed	Passed	Passed	Passed	Passed
ETO PBS accelerated	Filled	Passed	Passed	Passed	Passed	Passed

24-month data will be available in August 2017.

CONCLUSION

The data show that the SiO₂ barrier system coated vials are stable in both empty and filled configurations.

The data show that the coating integrity is maintained with filled vials that have been irradiated with e-beam at 35 kGy and then steam sterilized at 121°C for 20 minutes.

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