Medical Device Sterilization:
From Possibilities to Practice
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Sterilization Conversions

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Sterilization Modality Conversion Overview

- Over the years, companies have pursued conversion of EtO products to radiation sterilization for their overall risk profile relative to the use of chemicals (Prop 65, ISO 10993-7, pediatric product use)
- Material compatibility and device functionality (electronics) has sometimes been a limitation to convert from EtO to radiation sterilization
- Projections of Cobalt 60 supply limitations in the future, along with improved cycle time/supply chain efficiencies of E-Beam and X-Ray have prompted companies to convert from Gamma sterilization

EtO to Gamma Conversion

- Some IV Administration sets and blood collection sets were historically EtO sterilized in house.
- Upon the Abbott HPD spin of Hospira in 2004, EtO sterilization of these products was transferred to contract sterilization in the EU
- Over the course of 2004 to 2016, the EtO sterilized products had material changes to allow for sterilization conversion from EtO to Gamma
- The last Ethylene Oxide sterilization cycles for these products were performed in 2016
- This established the device portfolio as all Gamma sterilized products

Gamma to E-Beam Conversion

Development in 2009

- Method 2A dose setting study performed for E-Beam sterilization of IV Administration sets.
- E-Beam sterilized product was put on 3 year stability for feasibility
- E-Beam conversion was targeted to reduce turn time and reduce shipping cost to LATAM market. Product manufactured in Costa Rica could be E-Beam sterilized in Costa Rica instead of Gamma in USA
- Product and package stability completed in 2012
- Previous Gamma stability studies leveraged for materials that were deemed worst case with Gamma compared to E-Beam

Gamma to E-Beam Conversion

Implementation

- 2015 decision to convert Gamma to E-Beam for LATAM
- 2017 divestiture of Hospira Device business from Pfizer changed scope to entire global product portfolio
- Design transfer for E-Beam conversion leveraged past Gamma stability studies and conducted verification testing for high risk materials for E-Beam treatment
- One density family grouping (0.02 g/cc – 0.21 g/cc) for Gamma PQ correlated to 132 density family groupings (product density, packaging, and product orientation) for E-Beam PQ; E-Beam PQs and design transfers were prioritized by product volumes
- 80-90% of Gamma product converted to E-Beam by 2018
- Prior approval and audit of substantial change required by notified body for CE marked product

Gamma to E-Beam Conversion

Key Sterilization Considerations

- Dose Audits using E-Beam dose setting needed prior to and after implementation
- E-Beam penetration may not be effective for product densities above 0.25 g/cc, whereas Gamma can be used up to 0.4 g/cc
  - Hospira Device Product portfolio ranged from 0.02 – 0.21 g/cc density
- Packaging and product orientation consistency required for validation/dose mapping and routine production control
- More product family groupings are needed for E-Beam PQ than for Gamma PQ (AAMI TIR 29 section 6.3)
- Dose Uniformity Ratios for product mix was around 1.6 max/min for Gamma and 2.0 max/min for E-Beam
- Treatment time is a matter of hours for Gamma and a matter of minutes for E-Beam, resulting in more efficient throughput and improved supply chain
- Product heat build up and product oxidation potential are lower for E-Beam with the lower treatment times, reducing potential for product performance degradation

Gamma to E-Beam Conversion

Key Materials Considerations

- High risk materials for E-Beam compatibility needed to be evaluated for design verification. Some examples include:

Material Family	Potential Impact of E-Beam
Polypropylene	Degradation
Polytetrafluoroethylene (PTFE)	Degradation
Silicone rubber	Crosslinking
Polyisoprene	Crosslinking

- High risk materials for degradation should have verification testing with product treated above the maximum sterilization dose
- Materials that require strengthening should have verification testing with product treated below the minimum sterilization dose
- A “blue tint” may be used in materials to mask discoloration for clear components or opaque colorants when clarity is not required (discoloration is a common effect for plastics)
- Package integrity verification at expiry needed to support Maintenance of Sterility

EtO to E-Beam Conversion

- In November 2014, Hospira began to contract manufacture Sapphire Infusion sets for Q-Core in Costa Rica sterilized with EtO under an International Distribution Agreement for Sapphire Infusion System
- As a part of the Hospira re-design to manufacture under their own label, product were designed with radiation compatible materials
- Redesigned radiation compatible Sapphire products were adopted into the IV Administration Sets product family
- Around 2018, the contract manufactured EtO sterilized product was phased out of Hospira contract manufacturing, and the Hospira branded E-Beam sterilized products were launched.
- 510(k) Regulatory submissions made for US and Canada markets to launch products

Sterilization Conversion – Key Takeaways

- Product conversions to radiation compatible materials if feasible for product function may pave the way to convert from EtO to Radiation sterilization modalities
- Product conversions to radiation or across radiation modalities can be facilitated more quickly if products can be adopted into existing product families – dose audit program specific to a new modality to be performed for the new radiation sterilization modality
- Material compatibility assessment plays a big role in feasibility of transfer from one radiation sterilization modality to another radiation sterilization modality, and leveraging existing worst case radiation modalities for stability studies can facilitate conversion projects
- Regulatory submission strategies for markets where products are sold are key deliverables for sterilization conversion projects

Questions?

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