LIFE TESTING FOR DEVICE COMBINATION PRODUCTS

APPROACHES AND CHALLENGES FOR INTEGRATING DEVICES INTO A COMPREHENSIVE STABILITY PROGRAM

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INTRODUCTION

• What is shelf life for a device?
• Mapping shelf life and leveraging design controls
• How is shelf life established and tested?
• Shelf life for combination products
• Example challenges and approaches
WHAT IS SHELF LIFE FOR A DEVICE?

- **Shelf life is the term or period during which a commodity remains suitable for the intended use.**
  
  - FDA Guidance “Shelf Life of Medical Devices” (April 1991)

- **The duration and conditions over which required performance is achieved.**
REQUIRED PERFORMANCE

• What is required to be suitable for the intended use(s)?
  – What is potentially affected by shelf life?
  – What is the relationship with the drug product?
• Capture explicitly as design input
• Examples: sterility, delivered volume, reliability, cycle life
  – “The device shall be X% reliable over a Y shelf life.”

Focus on safety and effectiveness, risk, and critical quality attributes.
DURATION

- Period(s) with a defined start, duration, and end.
  - Examples: date of manufacture, assembly, sterilization, first use
  - End Examples: use by, package by, expiration date
- Capture in **design inputs and design outputs** where appropriate.
CONDITIONS

• Factors that potentially affect performance over time.
  – Examples: storage conditions, interactions, processing, cycling, maintenance, sterilization, shipping / transit

• Capture in design inputs and design outputs where appropriate.
Device shelf life is comprised of multiple stages, each with unique durations and conditions.

- i.e. room temp. vs cold storage, partial vs. full assembly, bulk vs individual packaging, pre vs. post sterilization, etc.
- Consider what design requirements and controls are appropriate for each stage

**MAPPING DEVICE SHELF LIFE**

- Raw Materials
- Components
- Device Constituents
- Combination Product
- Final Use
LEVERAGING DESIGN & PURCHASING CONTROLS

- 820.30(b) Design & Development Planning
- 820.30(c) Design Input
- 820.30(d) Design Output
- 820.30(e) Design Review
- 820.30(f) Design Verification
- 820.30(g) Design Validation (Risk Analysis)
- 820.30(h) Design Transfer
- 820.30(i) Design Changes
- 820.50 Purchasing Controls

Consider shelf life throughout the process!
HOW ESTABLISH AND TEST SHELF LIFE

• Identify target shelf life
  – Consider user needs, drug product expiration, supply chain
• Establish design inputs for key stages
• Develop design outputs and identify critical components
• Create verification plan
• Apply preconditions and aging (i.e. sterilization, transit, current drain)
• Verify requirements after accelerated and real time aging
• Control the process
SHELF LIFE FOR COMBINATION PRODUCTS

- Applicable 800 series requirements
- 211.137 Expiration dating
- 211.166 Stability testing
- CGMP Requirements for Combination Products January 2017
  - Clarifies expiration assignment for combination product
  - Device and drug product constituents may have different expiration
- Expiration for kits or integral products set to earliest of constituent parts.
CHALLENGES AND APPROACHES

- Changing storage and assembly conditions
- Drug product and material sensitivities
- Use of surrogates and bracketing
- Date formats
- Nominal vs. limit testing
- Lab vs. actual storage

Approach these challenges based on product risk and intended use!
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