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Agenda

• Combination Product development overview
• What are Essential Performance Requirements and Essential Design Outputs?
• How do we determine them?
• What do we do with them?
Combination Product Development

Quality by Design

QTTP & CQA → Control Strategy & Specs → Demo Batch → Clinical Trial → Tech Transfer & PPQ

Discovery & Feasibility

GxP Product Development

Life Cycle Mgmt.

Design Controls

Inputs → Outputs → Verification → Validation → Design Transfer

EPRs → EDOs
EPRs and EDOs - Where do I start?

- Are you developing your Combination Product under Design Controls?
- Are you performing Risk Management on your Combination Product?
- You’re 95% of the way there
Essential Performance Requirements (IEC 60601-1:2005)

- Performance of a clinical function, other than that related to basic safety, where loss or degradation beyond the limits specified by the manufacturer results in an unacceptable risk.
- “Note that it is possible to have a medical device with no Essential Performance Requirements. What that means is that the device risks are controlled in such a way that the loss or degradation of any of its clinical functions do not result in unacceptable risk.”  
  

- What about Efficacy?
  - Life Saving Treatment – Delivered Volume IS an EPR
  - Non-Life Saving Treatment – Delivered Volume is NOT an EPR
Essential Performance Requirements (FDA)

• “We are focused on device clinical performance at the time of use” - CAPT Alan M. Stevens
• What about Safety?
  • Life Saving Treatment – Cap Removal Force IS an EPR
  • Non-Life Saving Treatment – Cap Removal Force is NOT an EPR
• Other FDA examples for an Autoinjector
  • Activation Force
  • Needle insertion depth
  • Delivered Volume
  • Injection Time
Essential Performance Requirements (Proposed)

- EPRs are the subset of Design Inputs that impact safety or clinical performance at the time of use by the patient or user.
- We don’t submit our Design History File and Risk Management File to CDER and CBER so we need an executive summary in our submission!
What about Essential Design Outputs?

- Essential Design Output (FDA) – Design Outputs that are essential for the proper functioning of the device.
- Are there Design Outputs that aren’t essential?
- Essential Design Output (proposed) – Design Output that traces to at least one EPR in the Trace Matrix is an EDO
Inspectional Objectives

• “5. Verify that the design outputs that are essential for the proper functioning of the device were identified.”
CQAs and EPRs/EDOs in CP Development

Summary

- EPRs and EDOs come from your Design Control and Risk Management Process
- EPRs and their controls should be clearly specified in your submission
  - NDA, ANDA, and BLA submission formats are not intuitively set up for Combination Product submissions.
  - Pick a section for EPRs and their controls and draw attention to it
  - FDA will be looking for analogous Drug Product information in 3.2.P.2 Pharmaceutical Development Report
- EDOs and their controls should be available during inspections
  - Have your Trace Matrix ready with your EDOs and their controls highlighted