CDRH PERSPECTIVE: ASSESSING COMBINATION PRODUCT DEVICE CONSTITUENTS

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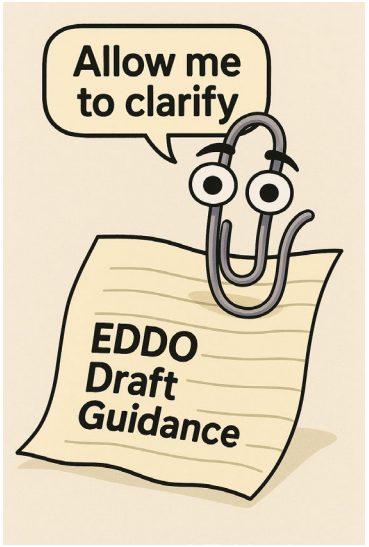
Drug Delivery Devices

- A stand-alone device intended for delivery of a human drug or biological product
- A combination product with a device constituent part intended for delivery of a human drug or biological product constituent part
- Examples: syringe, autoinjector, nasal spray

Combination Product Device Constituent Reviews in CDRH

- **Goal:**
  - Final finished device delivers the intended drug dose to the intended delivery site.
- **How to get there?**
  - Define user needs to achieve adequate initiation, progression, and completion of dose delivery.
  - Identify essential device performance requirements (EPRs) and control strategies necessary to achieve user needs.



EPRs vs. EDDOs – Difference?

Intended to Replace

Essential Performance Requirements

Unofficial Term (currently used)

System-level, key design aspects of a device essential for establishing and assessing drug delivery performance

Examples:
syringe glide force, autoinjector dose accuracy

Essential Drug Delivery Outputs

Unofficial Term (draft guidance)

System-level, key design aspects of a device essential for establishing and assessing drug delivery performance

Examples:
syringe glide force, autoinjector dose accuracy

NDA/BLA/ANDA submissions

CDRH Reviews:

- Verification and Validation of EPRs
  - Final finished combination product
  - Preconditioning to simulate anticipated use conditions
  - Aged devices to support EPRs throughout use life
- Device Labeling
- Risk Management
  - pFMEA, risk categorization, traceability to mitigations
- Control Strategy
  - Purchasing controls, in-coming inspection, in-process controls, lot release criteria, etc.
- Facilities and Quality Systems

Common Review Issues in Generic Combination Product Submissions

- Incomplete device description documentation
- Not considering the full risk profile of the delivery device based on perceived similarity to Reference Listed Drug (RLD) device
- Inadequate EPR V&V for delivery device because focus is on drug product bioequivalence
  - Differences in delivery device design impact testing needed
  - FDA alerts patients, caregivers, and health care providers of cross-compatibility issues with autoinjector devices that are optional for use with glatiramer acetate injection | FDA
- Insufficient stability program
  - Should test 3 lots of final finished combination product

Best Practices for Submissions

- Comprehensive descriptive information on device constituent
- Note to reviewer that traces design controls documentation to the specific module/location (incl. master files)
- Clear justifications for specifications
- Sample sizes should conform to standards; where not prescribed should be risk-based and statistically relevant.
- Reliability documentation and sequential preconditioning for emergency use combination products
- Early selection of all device constituents reduces the need for bridging strategies and saves time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