COMPARATIVE ANALYSES: FOCUS ON INJECTABLE DRUG-DEVICE COMBINATION PRODUCTS

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Objectives

- Understand comparative analyses (CA) approach to injectable combination products
- Identify common CA deficiencies for injectable combination products
- Provide product development tips

Injectable Combination Products

- Prefilled Syringes
- Injection Kits
- Pen Injectors
- Autoinjectors

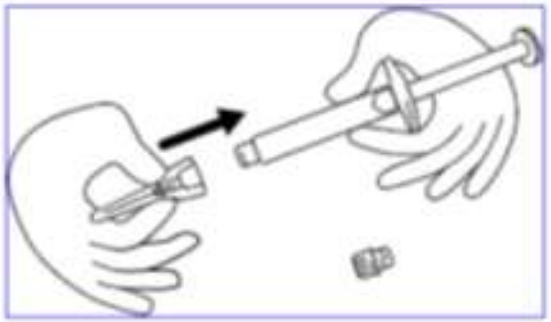
Comparative Analyses Approach

- Three comparative analyses
  - Labeling, Task Analysis, Physical Comparison
- Focus on Product and Device Characteristics:
  - Context of use: emergency vs. non-emergency
  - End-user: patient vs. health-care professional
  - Complexity of device
  - Use environment: home, outpatient or inpatient facilities
  - Other patient factors: underlying disease

Key Definitions

- External critical design attributes
  - Features that directly affect how users perform a critical task that is necessary in order to use or administer the drug product
- Critical tasks may be considered as:
  - A user task that, if performed incorrectly or not performed at all, would or could cause harm to the patient or user, where harm is defined to include compromised care

Prefilled Syringes



- Healthcare or patient administered
- Multiple routes of administration
  - SQ, IV, IM, Other
- Preassembled with needle or user must attach needle
- RLD is also prefilled syringe or ampule vial for injection
- Usually least complicated injectable combination product

Prefilled Syringe Case Study

- Prefilled syringe for emergency use
- After connecting needle, self-injected by patient
- Applicant proposes needle safety guard not present in RLD
- ***Other design difference***: may potentially affect an external critical design attribute that involves administration (clinical use and performance) when substituted for the RLD.

RLD

Generic (hypothetical)

https://www.bd.com/en-us/offerings/capabilities/syringes-and-needles/safety-syringes-and-needles/safety-needles/bd-eclipse-needle

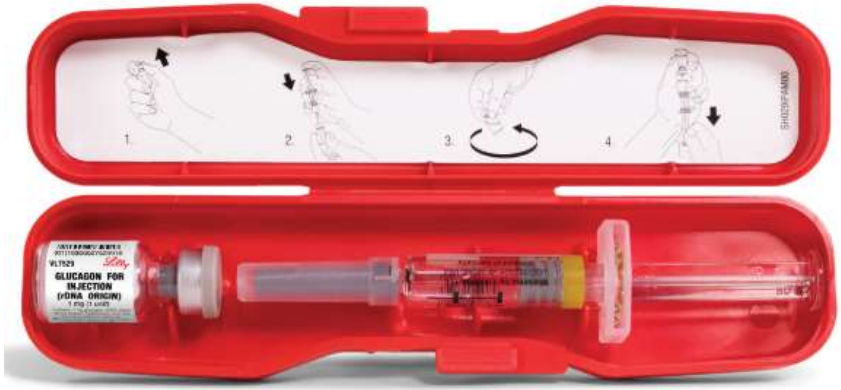
Injection Kits

- Usually healthcare professional administered
- Assembly and reconstitution often required by healthcare professional
- Emergency or non-emergency use

Injection Kit Case Study

- Emergency use product, administered by patient or caregiver
- Critical Tasks:
  - Remove needle cover
  - Insert needle into vial
  - Remove needle, reconstitute solution
  - Insert same syringe to withdraw liquid

RLD Injection Kit



- ***Other Design Difference:*** Difference in external critical design attributes impacting a critical task (e.g. significantly shorter plunger length may make it be more difficult to grasp flange to withdraw drug prior to injection)

https://www.lillyglucagon.com/taking-glucagon/glucagon-kits-for-emergencies

Pen Injector

- Patient administered
- Multi-dose prefilled delivery device
- Variety of indications and patient populations

Pen Injector Case Study

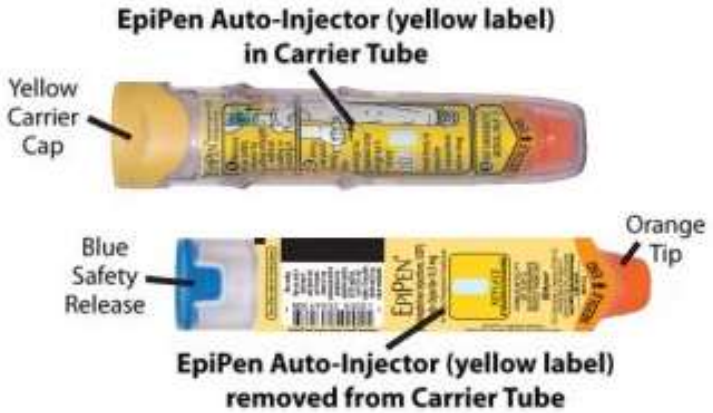
- Chronic use product, injected daily by patient.
- RLD device contains ergonomics and tactile features.
- Consider all RLD device features when designing generic pen injector.

RLD Pen Injector

Autoinjector

- Patient administered
- Single-use, typically emergency use
- Equivalent delivery of drug to site of action is dependent upon device constituent functioning the same as the RLD

Autoinjector Case Study: EpiPen (Epinephrine injection)



https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/019430s074lbl.pdf

https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=090589

RLD and Generic Epinephrine

Prepare Injection

Pull off blue safety release

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/019430s074lbl.pdf

https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=090589

Acceptable Minor Design Differences (all Injectable)

- Physical color components
  - Unless color associated with external critical design attribute
- Device material

Other Common Deficiencies (all Injectable)

- Instructions for use (labeling) does not accurately represent proposed test product
- Images in labeling do not accurately represent proposed test product
- Dose/measurement markings don’t correspond to dose recommended in prescribing information.

Injectable Devices Development Tips

- Understand clearly if RLD is patient administered or administered by health care professional, and incorporate into risk assessment of CAs
- Recognize if product is for emergency/acute use or non-emergency/chronic use
- Ensure labeling accurately describes all tasks necessary for proposed product
- Design the user interface to minimize differences from the RLD (e.g., no new critical tasks or design features not present in the RLD)
- Request assessment in controlled correspondence or via pre-ANDA meeting with specific product development questions

Conclusions

- Injectable Drug-Device Combination Products come in a variety of delivery systems.
- Generic development of these products should include comparative analyses to assess potential differences, with focus on minimizing those differences.
- When developing the test product, generic development should focus on RLD device features and the setting of use:
  - Complexity of device (injector pen vs. pre-filled syringe)
  - Patient vs. healthcare professional administered
  - Emergency vs. chronic use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