Overview of Comparative Analyses

(Clinical Perspective)

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Objectives

- Provide overview of comparative analyses and helpful tips
- Discuss common deficiencies found in drug-device combination products

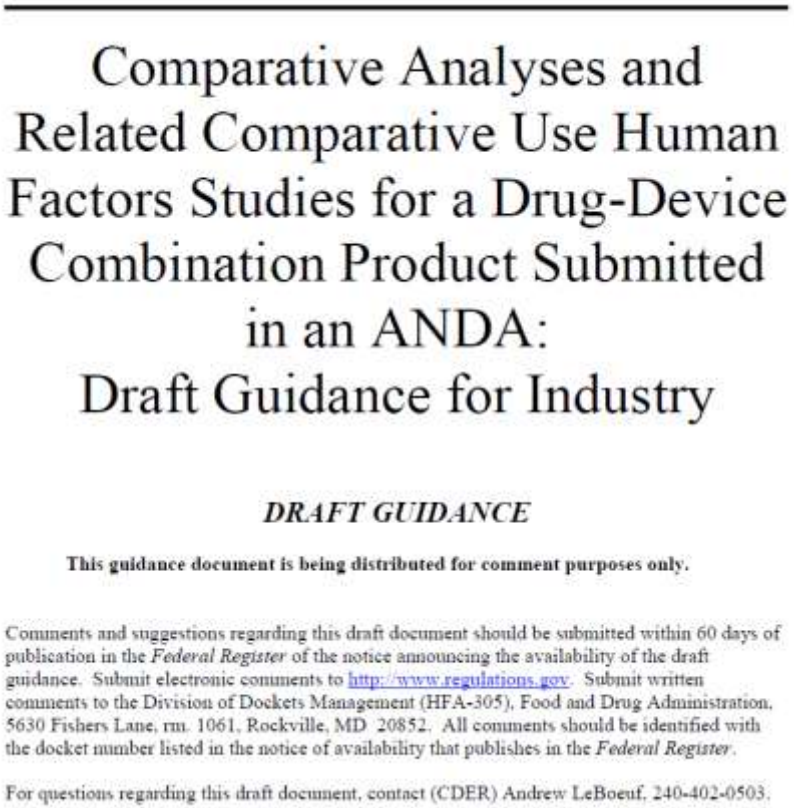
Generic Drug-Device Combination Products

- **Therapeutic equivalence: "…**have the *same clinical effect and safety profile* when administered to patients under the *conditions specified in the labeling*"
- **Same expectations** apply for generic drug-device combination products
  - FDA considers whether end users can use the generic combination product when it is substituted for the RLD without the intervention of the healthcare professional and/or without additional training prior to the use of the generic combination product
- Generic and RLD product do not need to be identical as long as the differences do not preclude approval under an abbreviated new drug application (ANDA)

User Interface

- Refers to all components of a combination product with which a user interacts
  - Instructions for Use (IFU)
  - Packaging
  - Labeling (including container and carton)
  - Device constituent part
  - Associated controls and displays

Draft Guidance – January 2017



Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA:
Draft Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Andrew LeBoeuf, 240-402-0503.

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

Comparative Analyses

1. Labeling comparison
2. Physical comparison of delivery device constituent parts
3. Comparative task analysis

Labeling Comparison

Side-by-side, line-by-line comparison of relevant sections of prescribing information, instructions for use (IFU), and descriptions of the delivery device constituent parts of the generic combination product and its RLD

Physical Comparison of Delivery Device

- Visual and tactile examination of the physical features of the RLD
- Compare them to those of the delivery device constituent part for the proposed generic combination product

Comparative Task Analysis

Systematically analyze and compare the sequential activities required for the end-users to use the device and administer the drug product

Assessment of Identified Differences

- Consider any identified differences in the context of the *overall risk profile* of the product
  - No Differences
  - Minor Differences
    - If the differences in the user interface of the proposed generic combination product, in comparison to the user interface of the RLD do not affect an external critical design attribute
  - Other Difference
    - If any aspect of the comparative analyses suggests that differences in the design of the user interface of a proposed combination product as compared to the RLD *may* impact an *external critical design* attribute that involves administration of the product

Assessment (cont'd)

In instances where ***other differences*** are identified:

- Consider re-designing the user interface to minimize differences from the RLD
- Additional information and/or data to support the user interface design difference must not preclude approval of an ANDA
- The type of information/data will depend on the differences and risks being considered

Assessment (cont'd)

- Labeling differences that stem from differences in design between the user interface for the proposed generic combination product and its RLD may fall within the scope of permissible differences in labeling for a product approved under an ANDA

  [21 CFR 314.94(a)(8)(iv)]

Assessment of Identified Differences: Key Question

Will the generic combination product produce the same clinical effect and safety profile as the RLD under the conditions specified in the labeling?

Assessment of Identified Differences: Considerations

- Complexity of device
- Use environment
  - Home, outpatient facilities, inpatient facilities
- Context of use
  - Emergency vs. non-emergency
  - Single use vs. repeated use
- End-user
  - Patients, caregivers, or healthcare professionals
- Other patient or user related factors
  - Underlying disease that may affect use

Considerations (cont'd)

For identified differences:

- How do they impact the user interface?
- Do they affect external critical design attribute?
  - Difference in size/shape affect ability to properly administer for the end user
  - Absence/presence of tactile feedback that signals delivery of the drug may affect the safety profile and clinical effect of the combination product
- Do they affect a critical task?

Common Deficiencies for Combination Products

Common Deficiencies for Combination Product

- Labeling
  - Illustrations
    - Illustrations do not accurately represent the proposed product
  - Language
    - Proposed labeling contains missing or inconsistent information
    - Proposed labeling is missing information from the RLD labeling
    - Tasks described in the IFU do not represent the steps needed to use the proposed product

Common Deficiencies (cont'd)

- Device
  - Measurement markings
    - Doses recommended in the Prescribing Information are not able to be measured by the device

*Depiction is for illustrative purposes only

Common Deficiencies (cont'd)

- Device
  - Measurement markings
    - Doses recommended in the Prescribing Inform
      able to be measured by the device
    - Change the orientation of the numbers and remove trailing zeroes

*Depiction is for illustrative purposes only

Common Deficiencies (cont'd)

- Device
  - Measurement markings
    - Doses recommended in the Prescribing Inform
      able to be measured by the device
    - Change the orientation of the numbers and
      remove trailing zeroes
    - Remove extraneous measurement markings

*Depiction is for illustrative purposes only

Common Deficiencies (cont'd)

- Device
  - Measurement markings
    - Doses recommended in th… able to be measured by th…
    - Change the orientation of … remove trailing zeroes
    - Extraneous measurement …
  - There should be adequate contrast between the drug product and device

*Depictions are for illustrative purposes only

Useful Guidance Documents

- Safety Considerations for Product Design to Minimize Medication Errors (April 2016)

- Dosage Delivery Devices for Orally Ingested OTC Liquid Drug Products (May 2011)

Summary

- FDA recommends standardized comparative analyses to consistently identify and categorize differences between the user interface of a proposed generic and its RLD
- The goal of comparative analyses is to identify and evaluate if there are differences in user interface
- Focus on potential differences in external critical design attributes and the critical tasks between the RLD and generic combination product.
- Submit controlled correspondence for development questions
- Proposed products may be eligible for FDA advice via pre-ANDA meetings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