User Interface Considerations for Drug-Device Combination Products Submitted in an ANDA

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Division of Medication Error Prevention and Analysis (DMEPA)

• Created in 1999
• Scientists and healthcare professionals with varied backgrounds
• 43 FTE’s
• Aligned by therapeutic areas
• Leads CDER review pertaining to medication error prevention and analysis and human factors for drug and therapeutic biologics
DMEPA Mission

To increase the **safe use** of drug products by minimizing use error that is related to the **naming, labeling, packaging, or design** of drug products
Combination Products

• Formal Definition in 21 CFR 3.2:
  – Therapeutic and diagnostic products
  – Combine >1: drugs, devices, biological products

• They can be:
  – Physically or chemically combined (21 CFR 3.2(e)(1))
  – Co-packaged in a kit (21 CFR 3.2(e)(2))
  – Separate, cross-labeled products (21 CFR 3.2(e)(3) or (4))
CDER-Led Combination Product Examples

- Prefilled Syringes
- Pen Injectors, Autoinjectors
- Pharmaceutical Aerosol Delivery Devices/Inhalation Products
- Transdermal Delivery Systems
- Kits containing drug and administration devices
Definition of User Interface (UI)*

Refers to all components of a product with which a user interacts.

E.g.,
- Labels
- Packaging
- Delivery device constituent part, and any associated controls and displays

*Draft Guidance for Industry: Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA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

Ergonomics (or human factors) is the scientific discipline concerned with the understanding of interactions among humans and other elements of a system, and the profession that applies theory, principles, data and methods to design in order to optimize human well-being and overall system performance.

International Ergonomics Association (IEA)
Removal of Use Errors through HF

- **Optimized design**
- **Original UI design**
- **Reduce risk through Human Factors**

Low risk product

High risk product

Risk Level

Low

High
Traditional HF Validation Studies

Demonstrate interface supports safe and effective use with representative users in expected use environment(s)
Draft Guidance

- Focuses on the analysis of the proposed user interface for the generic drug-device combination product (generic combination product) when compared to the user interface for the reference listed drug (RLD)
  - Issued January 2017
  - To ensure that FDA considers your comments on this draft guidance before we begin work on the final version, submit comments by March 20, 2017.
Answering A Different Question

• Traditional HF Validation Studies
  – Question 1: Does the proposed user interface support the safe and effective use of the product by intended users for intended uses and environments of use?

• Comparative HF Studies
  – Question 2: Do user interface design difference(s) between a generic and the RLD impact the clinical effect or safety profile of the proposed generic product
Comparative Use HF Studies

Are not considered to be clinical investigations intended to demonstrate the safety or effectiveness of the proposed generic combination product
Scope of Draft Guidance

• Focus on analysis of the proposed user interface, but not intended to address all information necessary to support approval of a generic combination product

• Provide clarity on FDA’s expectations for the user interface of a generic drug-device combination product when compared to its RLD

• Provide clarity as to when additional information and/or data, such as data from comparative use human factors studies, may be warranted to support differences in design between a proposed generic drug-device combination product and its RLD
Abbreviated New Drug Application (ANDA)

• Under section 505(j), an ANDA applicant can rely on FDA’s previous finding that the reference listed drug (RLD) is safe and effective
  – Applicant demonstrates that the proposed drug product and the RLD are the same with respect to active ingredient(s), dosage form, route of administration, strength, and with certain exceptions, labeling

• ANDA must also include sufficient information to demonstrate that the proposed product is bioequivalent to the RLD, and that the ANDA meets the approval requirements relating to chemistry, manufacturing, and controls (CMC)
Abbreviated New Drug Application (ANDA)

• Drug products that are approved in ANDAs are generally considered by FDA to be therapeutically equivalent (TE) to their RLD.
  – A generic combination product classified as therapeutically equivalent to the RLD can be expected to produce the same clinical effect and safety profile as the RLD under conditions specified in labeling
    • Proposed generic combination product and its RLD do NOT need to be IDENTICAL in all respects
      – Sponsors should generally seek approval of a presentation approved for the RLD
Substitution of ANDA for RLD

• In general, the FDA expects that the end-users* of generic combination products can use the generic combination product when it is substituted for the RLD
  – Without intervention of the health care provider and/or
  – Without additional training prior to the use of the generic combination product

*Including but not limited to lay-persons, such as patients, and/or caregivers
Threshold Analyses

- **Labeling Comparison**
  - Side-by-side, line-by-line comparison of the full prescribing information, instructions for use, and descriptions of the delivery device constituent part(s) of the generic drug-device combination product and its RLD.

- **Comparative Task Analysis**
  - Comparative task analysis between the proposed generic drug-device combination product and its RLD.
  - Critical tasks are user tasks 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 medical care.

- **Physical Comparison of Delivery Device Constituent Part**
  - Examine (e.g., visual and tactile examination) the physical features of the delivery device constituent part for the proposed generic drug-device combination product and compare them to those of the RLD.
Assessment of Identified Differences

• Minor Design Differences
  – Guidance describes a design difference as minor 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. External critical design attributes are those features that directly affect how users perform a critical task that is necessary in order to use or administer the drug product.

• Other Design Differences
  – FDA may not view a design difference as minor if any aspect of the threshold analyses suggests that differences in the design of the user interface of a proposed generic combination product as compared to the RLD may impact an external critical design attribute that involves administration of the product.
Assessment of Identified Differences

- In instances when differences other than minor differences are identified:
  - Strongly consider re-design of the user interface to minimize differences from the RLD
  - FDA may request for additional information and/or data to support the ANDA submission
    - Draft guidance recommends that potential applicants contact FDA through a pre-ANDA submission/controlled correspondence before conducting comparative use human factors studies
Comparative Use HF Studies

• Objective
  – To demonstrate that the use error rate, associated with a change in an external critical design attribute for the proposed user interface, does not preclude approval of the proposed product in an ANDA
    • Designed to provide sufficient data to confirm that the use error rate for the critical task(s) is not worse than the corresponding use error rate for the RLD when used by patients and caregivers in representative use scenarios and use environments consistent with the labeled conditions of use.
Comparative Use HF Studies

• Non-Inferiority (NI) Study Design
  – NI tests comparing use error rates with the user interface of a proposed generic combination product to those of the RLD are similar to usual statistical tests for a difference, but translated to account for allowable differences in error rates between the proposed generic drug-device combination product and its RLD
  – Comparison of rates of errors observed when using the proposed generic combination product when compared to the error rates when using the RLD with respect to a critical task impacted by a change in critical external design attribute
Summary of Key Messages in Draft Guidance

• Emphasizes that FDA does not expect that the design of a generic drug-device combination product be identical to the design of its RLD
• Focuses on the early development phases of the proposed generic drug-device combination product and encourages early collaboration with FDA
• Recommends that potential applicants minimize design differences between a proposed generic drug-device combination product and its RLD
• Allows for flexibility in the types of information and/or data that may be necessary to support differences in design between the user interface of the proposed generic drug-device combination product and its RLD
• Clarifies that the draft guidance is not intended to cover all information (e.g., CMC) that may be necessary to support the user interface of the proposed generic drug-device combination product
Key Takeaway Point

Collaborate with FDA in the early development of any proposed generic combination product!
Partnership

Better Outcomes for Patients
Questions

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