U.S. FOOD & DRUG ADMINISTRATION

COMPARATIVE ANALYSES: DEVICE AND USER INTERFACE CONSIDERATIONS

Kimberly Witzmann, MD
Acting Deputy Director,
Office of Bioequivalence
Office of Generic Drugs, CDER

September 26, 2019

Generic Drug Product Substitutability

In relation to the RLD, generic products are expected to be:

- **Pharmaceutically Equivalent**

  The same active ingredient, dosage form, strength, route of administration and meet the same compendial standards (strength, quality, purity, and identity)

- **Bioequivalent**

  No significant difference in the rate and extent of absorption of the active ingredient at the site of action

- **Therapeutically Equivalent**

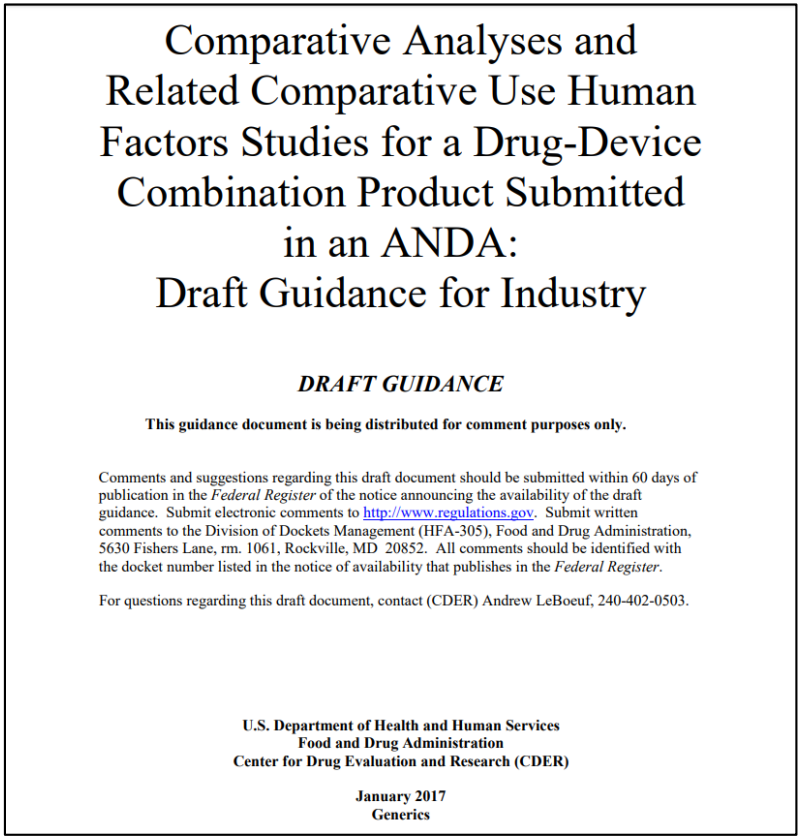
  Approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling

General Principles

Considerations include, but are not limited to:

- Performance characteristics
  - Review of a generic combination product is informed by the general framework for ANDAs, but also takes into consideration the performance of the device constituent and its interaction and impact on the delivery of the drug constituent
- User Interface

Draft Comparative Analyses Guidance



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Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA: Draft Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.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be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance.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.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

January 2017
Generics

Draft Guidance – Key Takeaways

- FDA does not expect that the design of the user interface for a generic drug-device combination product be identical to the design of the user interface for its RLD
- Differences in the design of the user interface should be adequately analyzed, scientifically justified, and not otherwise preclude approval under an ANDA
- FDA intends to assess whether an end-user can use the generic combination product when it is substituted for the RLD without the intervention of the health care provider and/or without additional training prior to use of the generic combination product

Draft Guidance – Key Takeaways

- Certain labeling differences to reflect differences in design of a proposed generic drug-device combination product may be permitted and will be evaluated on a case-by-case basis
- Baseline assessment for any identified differences occurs during comparative analyses and will determine whether additional information and/or data is warranted
  - May include Comparative Use Human Factors Studies

Definitions

User Interface: Refers to all components of a product with which a user interacts, such as labeling and packaging, the delivery device constituent part, and any associated controls and displays

External Critical Design Attributes: Refers to those features that directly affect how users perform a critical task that is necessary in order to use or administer the drug product

Critical Tasks: For example, 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

Comparative Analyses

1. **Labeling Comparison:** Side-by-side, line-by-line comparison of the full prescribing information, instructions for use, and descriptions of the delivery device constituent parts of the generic combination product and its RLD
2. **Comparative Task Analysis:** Comparative task analysis is assessed between the RLD and the proposed generic drug-device combination product
3. **Physical Comparison of Delivery Device Constituent Part:** Visual, auditory, tactile examination of the physical features (size, shape, feedback) of the RLD, compared to those of the delivery device constituent part of the proposed generic combination product

Assessment of Identified Differences

Consider any identified differences between the user interface of a proposed generic combination product and its RLD in the context of the *overall risk profile* of the product

- **No Differences**
- **Minor 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
- **Other 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

Example: Dry Powder Inhaler

- Product Specific Guidance for Fluticasone Propionate/ Salmeterol Xinafoate (FP/SX) posted in September 2013
- Recommendation include studies for bioequivalence, formulation sameness and device considerations
- First Generic FP/SX DPI approved in January, 2019
- Device and user interface considerations
- Other differences addressed with additional data appropriate for submission in ANDA

RLD and Generic FP/SX DPI

Figure A

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021077s061lbl.pdf

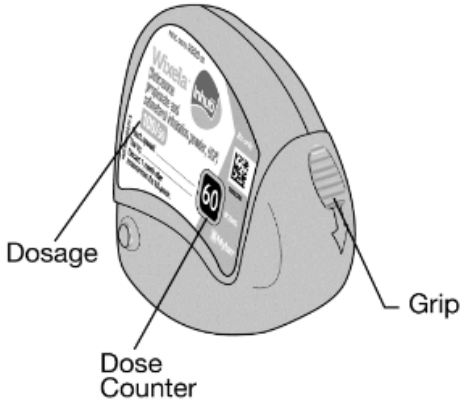
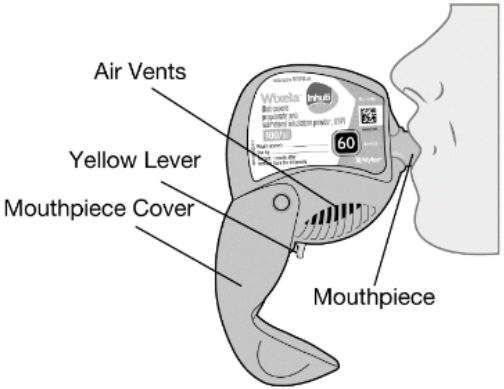


Figure A

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208891Orig1s000lbl.pdf

RLD and Generic FP/SX DPI

Inhale your medicine



Close the device

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021077s061lbl.pdf

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208891Orig1s000lbl.pdf

Recommendations

- Read the draft guidance for industry on *Comparative Analyses*
- Consider user interface and critical tasks of the RLD product and evaluate risks associated with any identified differences in user interface
- Perform comparative analyses throughout development and seek to minimize differences from RLD
- Consider any differences in terms of the risk of impacting an external critical design attribute that involves administration of the product
- Talk early and often with FDA:
  - controlled correspondences
  - pre-ANDA meeting requests for complex products


FDA
U.S. FOOD & DRUG
ADMINISTRATION