Comparative Analyses for Generic Oral Inhalers

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Disclaimer

This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.

Learning Objectives

- Provide recommendations for conducting comparative (threshold) analyses for generic oral inhalers*

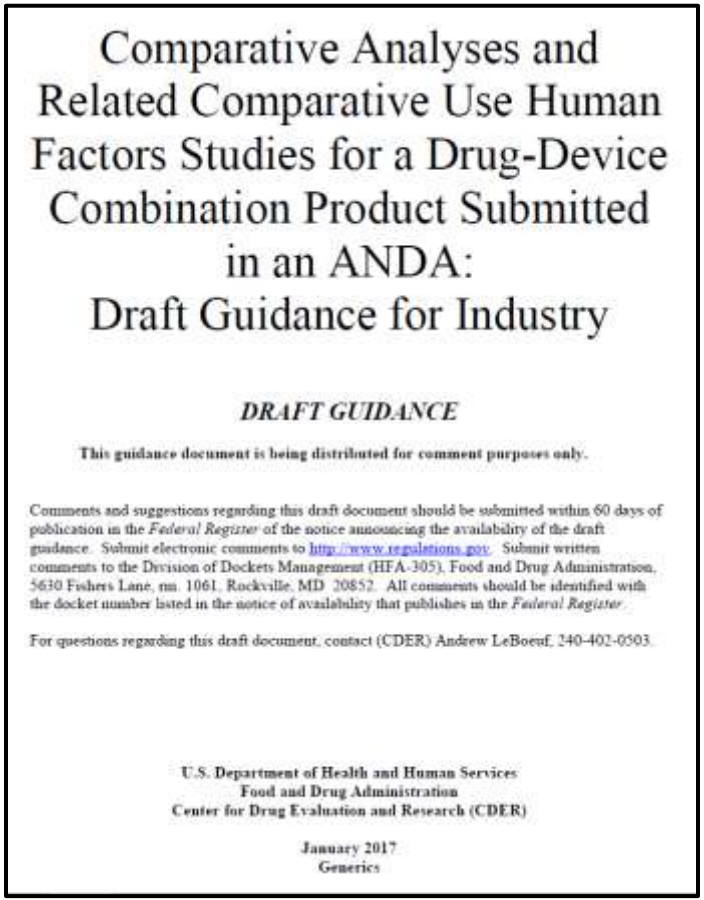
- Discuss considerations and tips during development of generic oral inhalers

*generic drug-device combination orally inhaled drug products including metered dose inhalers and dry powder inhalers

Generic Drug-Device Combination Products

- **Therapeutic equivalence**
  "*. . .* can be expected to 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 reference listed drug (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)

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Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA: Draft Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.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be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance.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

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Comparative (Threshold) 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 proposed generic oral inhaler and its RLD

2. Physical Comparison

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 oral inhaler

3. Comparative Task Analysis

Comparison of the sequential manual and intellectual tasks that end-users need to perform when using the proposed generic oral inhaler and its RLD

Recommendations for Conducting Comparative Analyses for Generic Oral Inhalers

General Recommendations

- Identify and provide adequate justification for **ALL** differences in user interface in comparative analyses
- Design differences are product specific and must be analyzed within the context of **comparison to RLD**

  Example: color change of button or lever of inhaler
- Use the “to-be-marketed” generic oral inhaler in comparative analyses

Recommendations and Suggestions

- Engage early with FDA during product development via controlled correspondence and pre-ANDA meeting processes
- Suggest including summary of all previous communications (example: pre-ANDA communications, etc.) with Agency regarding user interface evaluation or comparative analyses in “Comparative Analyses Study Report” submitted in ANDA
- Suggest including in “Comparative Analyses Study Report” whether any changes have been made to user interface since Agency’s user interface evaluation was completed during pre-ANDA communication

Labeling Comparison

- Ensure that labeling, including Instructions for Use and images accurately describe the:
  - generic oral inhaler
  - all tasks necessary to use the generic oral inhaler
- Generic drug product labeling generally must be the same as the RLD
  - Certain limited exceptions* – evaluated on case by case basis
  - Note: “think alternative way is better” is unlikely to be adequate justification for change in labeling

*As per 21 CFR 314.94(a)(8)(iv)

Physical Comparison

- Include visual, auditory, tactile examination of the external physical features of proposed generic inhaler and compared them to the RLD

  Example: size, shape, color, texture, resistance, weight, thickness, sound

- Include all components necessary to deliver drug

  Example: capsules, packaging, and device

- **Do not** include components or physical features with which end-users **do not** interact

  Example: internal spring design mechanism

Physical Comparison: Dose Counter Considerations

- Inhaler specific considerations include comparison of appearance of dose counter
  - Beginning of use (prior to priming, after initial priming, etc.)
  - End of use
- Identify and provide justification for **ALL** differences in dose counter appearance including changes in color(s), interval for counting doses, location of dose counter, etc.
- Recommend to include clear and detailed color photographs of proposed generic oral inhaler and RLD
  - If dose counter is present, suggest to provide close and detailed photographs throughout entire use
    - Beginning of use (prior to priming, after initial priming, etc.)
    - End of use

Comparative Task Analysis

- Systematically analyze and compare the sequential activities required for the end-users to use the generic oral inhaler and administer the drug product
- Include all steps with which end-users need to perform to use the inhaler

  Example: opening the packaging to disposing of the product

- Critical tasks may be considered as:
  - For example, 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 Task Analysis

- Recommend to carefully compare steps needed to perform the following tasks (if applicable) between the RLD and the proposed generic oral inhaler:
  - Initial preparation
  - Priming/Re-priming instructions (if indicated)
  - Use/Actuating instructions
  - Cleaning instructions

Considerations and Tips During Development of Generic Oral Inhalers

Tips for Generic Oral Inhaler Development

- Where able, design the generic product to minimize differences in user interface as compared to the RLD
- Suggest avoid adding new critical tasks or design features not present in the RLD oral inhaler
- Consider context of use: rescue vs. maintenance (controller) inhaler

Tips for Generic Oral Inhaler Development

- Incorporate recommendations in Draft Comparative Analyses Guidance throughout combination product development
- Perform comparative analyses throughout development program, especially if changes are made
- Early and frequent communication with FDA is highly encouraged through:
  - Controlled correspondence
  - Pre-ANDA meeting request

Tips for Combination Product Development

- Submit comparative analyses, samples of inhalers, and specific questions in pre-ANDA communications request
- If an “other design difference” is present, recommend discussing early with FDA
  - Include your justification and/or proposal of additional information or data to assess the acceptability of differences identified in the user interface
  - Submit specific questions with your proposal

Challenge Question #1

A Comparative Analyses should contain all of the following EXCEPT:

A. Physical Comparison
B. Comparative Task Analysis
C. Comparison of internal parts that end-users do not interact with
D. Labeling Comparison

Challenge Question #2

Which of the following statements is NOT true?

A. Applicants should identify and provide adequate justification for all differences in user interface in comparative analyses.

B. Controlled correspondence and pre-ANDA meeting are two methods that Applicants can use to obtain feedback regarding user interface and comparative analyses from FDA during product development.

C. Physical features such as size and shape or resistance should not be included in the physical comparison of a comparative analyses.

D. Generic and RLD products do not need to be identical as long as the differences do not preclude approval under an abbreviated new drug application (ANDA).

Summary

- Refer to the Draft Comparative Analyses Guidance for recommendations
- All design differences should be identified, adequately analyzed, and scientifically justified
- Recommend to carefully design and evaluate any differences in the appearance of the dose counter and instructions for actuating, cleaning, or priming the inhaler
- Engage early with FDA during generic oral inhaler development