Considerations for Pre-ANDA Meeting Requests and Case Scenario Setup: Device Constituent of Hypothetical BREATHEATOL Drug Product

AAM 2020: GRx+Biosims Complex Workshop

Session 4: Device Considerations for Complex Drug-Device Combination Products

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Outline

- General considerations for pre-ANDA meeting requests
  - Types of pre-ANDA meetings for complex products
  - Common types of requests
  - General principles
  - User interface considerations (comparative analyses)
- Case scenario setup: Device constituent of hypothetical BREATHEATOL drug product
  - Product-specific guidance (PSG) (device considerations)
  - Reference listed drug (RLD) labeling (including the instructions for use)
- Conclusion & Next Steps

General Considerations for Pre-ANDA Meeting Requests

Types of Pre-ANDA Meetings for Complex Products

- Product Development (PDEV)
  - Provide for discussion of specific scientific issues or questions (e.g., a proposed study design, alternative approach, or additional study expectations), in which FDA will provide targeted advice regarding an ongoing ANDA development program
- Pre-Submission (PSUB)
  - Provide an opportunity for prospective ANDA applicants to discuss and explain the format and content of the ANDA to be submitted (e.g., data to support equivalence claims, types of data that will be contained in the ANDA)

Guidance for Industry: Formal meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA (Oct 2017): https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm578366.pdf

Common Types of Requests Received in PDEV Pre-ANDA Meetings

- There is a Product-Specific Guidance (PSG)
  - Evaluation of proposed alternative approach for bioequivalence
  - Evaluation of proposed study design that deviates from the PSG
  - Multiple questions or complex issues not covered by the PSG
- There is not a PSG
  - Evaluation of proposed approach for bioequivalence

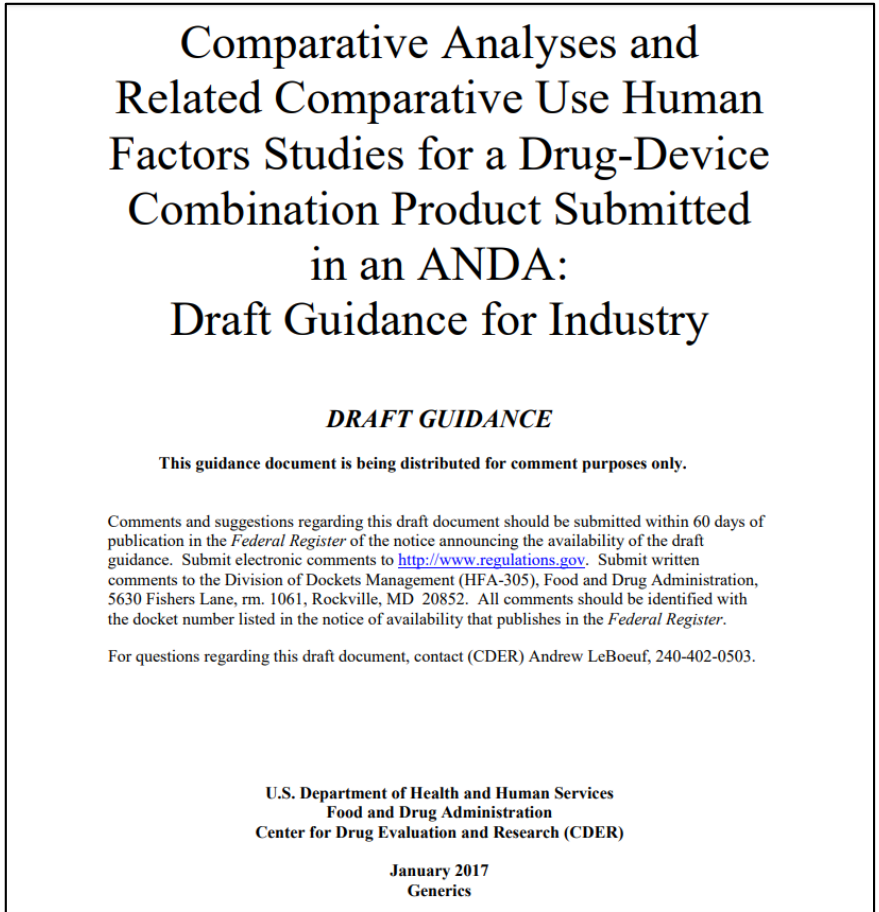
Any type of request can include device-related questions

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
  - It refers to all components of the combination product with which a user interacts – the delivery device constituent and any associated controls and displays, as well as product labeling and packaging

Draft Guidance: Comparative Analyses



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

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**
  - Do not affect an external critical design attribute
- **Other Differences**
  - *May* impact an external critical design attribute that involves administration of the product
  - Prospective applicants should consider re-design to minimize differences from the RLD
  - Potential need for additional information and/or data beyond the comparative analyses (e.g., in vivo or in vitro data, or comparative use human factors studies) to support the ANDA submission

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
- Communicate early and often with FDA:
  - controlled correspondences (CC)
  - pre-ANDA meeting requests for complex products

Proposed Test Device (User Interface)

- FDA assessment
  - Comparative (threshold) analyses as per the FDA guidance, *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* (Jan 2017)
    - Labeling comparison
    - Comparative task analysis
    - Physical comparison of the delivery device constituent part
- Information to submit
  - Samples of Test and RLD devices
  - Comparative (threshold) analyses per guidance above
  - Specific question(s) based on the outcomes of comparative analyses

Note: *Device (user interface) questions may be submitted as standard CC (60-day clock), but it may be converted to complex CC (120-day clock).*

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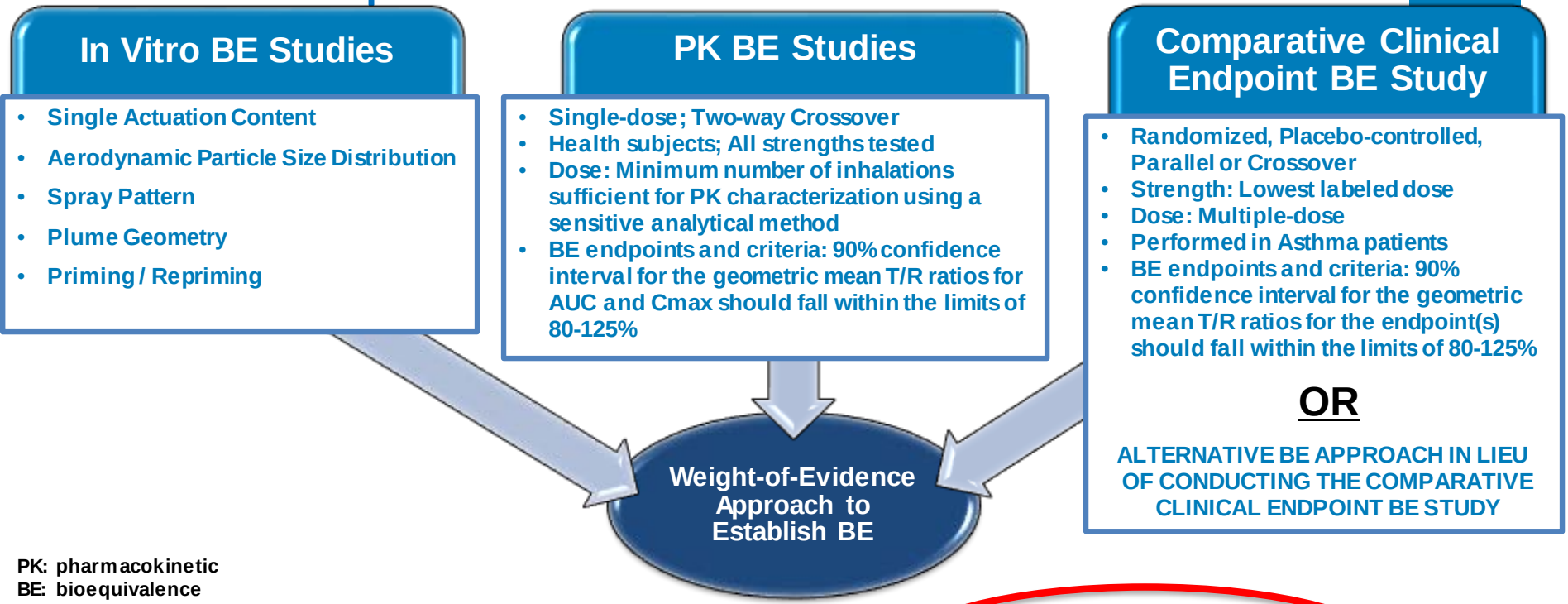
Case Scenario Setup: Device Constituent of Hypothetical BREATHEATOL Drug Product

Background for Your Pre-ANDA Meeting Request: PSG for BREATHEATOL



PK: pharmacokinetic
BE: bioequivalence

Formulation Sameness + Device Similarity

https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm

Background for Your Pre-ANDA Meeting Request: PSG for BREATHEATOL

- Device
  - Applicants should refer to FDA's Guidance for Industry, *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* (January 2017), which, when finalized, will provide the Agency's current thinking on the identification and assessment of any differences in the design of the user interface for a proposed generic drug-device combination product when compared to its RLD.
  - FDA recommends that applicants consider the following characteristics of the RLD product when designing the Test product:
    - Size and shape
    - Number of doses
    - External operating principles and external critical design attributes
    - Dose indicator/counter

Background for Your Pre-ANDA Meeting Request: Labeling for BREATHEATOL

- The approved labeling for an RLD provides important information that prospective applicants should consider early in their generic drug development program
- Suppose your company is in the early stages of developing a generic version of BREATHEATOL and your team was tasked to work on the proposed test device constituent (user interface)
  - What is some of the key information from BREATHEATOL labeling that may be helpful for your device development program?

Hypothetical BREATHEATOL Labeling

Step 1: Read the labeling and get familiar with the RLD product

Step 2: Collect information about the RLD product and device

- Indication (disease type, severity, emergency situations)
- User population (patients, caregivers, health care professionals)
- Dosage, administration, frequency of use
- Device features (mechanism of function, priming, dose counter)
- How supplied (single entity, co-packaged, cross-labeled)
- Instructions for use (steps, critical tasks)

Hypothetical BREATHEATOL Labeling

Step 3: Identify key information about the RLD product and device

- What is the drug class and indication?
  - A corticosteroid indicated for maintenance treatment of asthma.
- What is the user population?
  - Patients 5 years and older.
- What is the administration route and dosage?
  - Oral inhalation.
  - 1 or > actuations (depending on the strength and patient's age) twice daily (~ 12 h apart).

Hypothetical BREATHEATOL Labeling

Step 3: Identify key information about the RLD product and device

- What are the key device features?
  - Pressurized, metered-dose inhaler (MDI) aerosol with a dose counter.
  - Conventional press-and-breathe MDI.
  - It should be primed prior to taking the first dose from a new canister (3 actuations) or when the inhaler has not been used for more than 7 days.
  - Single-entity drug-device combination product (supplied in a box with one canister, a plastic actuator with a dose counter, and dust cap).

Hypothetical BREATHEATOL Labeling

Step 3: Identify key information about the RLD product and device

- What are the key device features?
  - Dose counter is attached to the back of actuator:
    - A black solid line appears in the viewing window until the inhaler as been primed (3 actuations into the air).
    - After priming, the total number of actuations (120) is displayed.
    - Dose counter counts each time an actuation is released; viewing window displays the number of actuations left in the inhaler in units of one (e.g., 120, 119, 118, etc.).
    - When it reaches 20, the color of numbers change to orange to remind the patient to obtain a new refill soon.
    - When it reaches 0, the background will change to solid red to indicate the inhaler should be discarded.

Hypothetical BREATHEATOL Labeling

Step 3: Identify key information about the RLD product and device

- What are the key instructions for use (IFU) steps?
  - Remove the cap.
  - Prime the inhaler before the first use after purchase and when the inhaler has not been used for > 7 days by releasing 3 sprays into the air.
  - Breathe out.
  - Hold the inhaler in vertical position, lips closed around the mouthpiece and tongue below it.
  - Breathe in deeply and slowly and, at the same time, press down the canister with pointer finger; hold breath for about 10 seconds.
  - Take pointer finger off the canister and remove inhaler from mouth.
  - Rinse mouth with water.
  - Replace cap over the mouthpiece after use.
  - Clean inhaler's mouthpiece weekly with a clean, dry tissue or cloth; do not wash the inhaler.

Conclusion

- Device-related questions focused on user interface are appropriate for PDEV pre-ANDA meeting requests or controlled correspondences and should be informed, at minimum, by the following sources of information:
  - Draft guidance on Comparative Analyses
  - PSG
  - RLD labeling
  - RLD instructions for use (IFU)

Next Steps

- In preparation for your mock virtual PDEV pre-ANDA meeting with FDA, you will
  - Evaluate potential candidates for your proposed Test device and identify design differences (minor vs. other)
  - Select your proposed Test device
  - Elaborate your Test device questions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