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FDA U.S. FOOD & DRUG ADMINISTRATION

Drug Device Combination Products and Similarity

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Disclaimer

- The opinions expressed during this session by the respective speakers do not necessarily reflect the official position of the U.S. Food and Drug Administration.

Session Objectives:

Objective:

Understand the regulatory challenges in developing and assessing combination products.

Summary:

1) This session will explore device considerations when comparing generic combination products with the reference listed drug (RLD) and what qualitative and quantitative methods could be used for assessing the comparability of generic drug-device combination products.

2) This session will also explore current thinking with respect to device-related considerations for biosimilars.

Generics vs. Biosimilars

- While the topic covered in this session is generally applicable to both generic and biosimilar combination products – the underlying regulatory authorities for the products have fundamental differences. This will be discussed further during the session.

Faculty

- Karthik Balasubramanium - Teva Pharmaceuticals
- Lisa Bercu, JD - Office of Generic Drug Policy, OGD
- Irene Chan - Division of Medication Errors, OSE
- Dhaval Gaglani - Office of Pharmaceutical Quality
- Sharon Kovacs - Apotex Inc.
- Markham Luke, MD PhD - Office of Research & Standards, OGD
- Sarah Yim, MD - Office of Therapeutic Biologics and Biosimilars

Agenda (live recording)

- 12:00 noon – 12:45 PM
  - Markham Luke – 10 minutes – introduction to the topic
  - Lisa Bercu – 10 -15 minutes – regulatory background – why device constituents for generic drugs do not have to be the same, but should work in a sufficiently similar manner
  - Sarah Yim – 5 minutes – device constituents for BLAs/Biosimilars
  - Karthik Bala – 10 minutes – post-approval changes to RLD and ANDA products and technology advances due to "perceived obsolescence" of some RLD device technology and due to patent restrictions.
  - Sharon Kovaks – 10 minutes – Industry Execution of Comparative Use Human Factors (CUHF) studies - Challenges and Opportunities
- 12:45 PM to 1:30 PM – Panel discussion and Q & A from Audience
  - Industry and FDA Panel, including OTBB and OPQ
  - + Dhaval Gaglani and + Irene Chan from FDA

Complex Drug-Device Combination Products

- Common Examples
  - Autoinjectors (AI)
  - Metered Dose Inhalers (MDIs)
  - Dry Powder Inhalers (DPIs)
  - Soft Mist Inhalers (SMIs)
  - Metered Nasal Sprays
  - Transdermal and Topical Delivery Systems (TDS)

Reasons for Device Differences

- It would be easier for FDA review if device constituents for generic combination products would be the same physically and functionally by design as the RLD, but FDA recognizes that's not always possible.
- Possible reasons for device differences:
  - Differences may not be clinically or functionally significant
  - Patents on the RLD device constituent
  - Sole supplier agreements
  - Inability to locate appropriate contract manufacturer
  - Engineering and manufacturing constraints
    - Unique aspects to how the device is made
    - Inability to manufacture (unavailability of material or machinery)
- There is sometimes a tradeoff between access and absolute similarity

Pre-ANDA Advice on Device Interface

- Pre-ANDA interaction with FDA is a value-added proposition
- Controlled correspondence (CC) and/or Product Development meetings with FDA
  - Use accurate engineering/observations in submission of comparative (threshold) analyses
  - Should be submitted early in development
- The more accurate the description, the better the advice you will get from FDA
- FDA continues to ask for information, such as high resolution photographs or comparative samples, to confirm threshold evaluation

Understanding Difference Risk

- It is not the risk of the product (RLD device constituent risks) that are the main concern for OGD
- Rather, it is the risk of any differences between the RLD and Test products.
- The lack of potential impact for some differences may be obvious (minor differences), however, some “Other design differences" (other than minor) may require additional information and/or data further assessment, (e.g., additional bench comparisons, ergonomic modeling, or Comparative Use Human Factors (CUHF) study).
- **Not every “Other design difference” requires a CUHF study**
  - FDA encourages a PDEV meeting before conducting a CUHF study

Generic Drug Device Assessment Roles

- DTP Combination Product Team (OGD ORS)
  - Research on study designs and methods to identify attributes that need to be the same
  - Pre-ANDA advice via CC on minimizing device differences
  - Pre-ANDA advice via meetings on evidence to support other than minor design differences
- Division of Clinical Review (DCR) in OGD OSCE
  - Assessment of device similarity in ANDA review
  - Consults DMEPA on CUHF studies
- Office of Bioequivalence (OBE) in OGD
  - Evaluation of comparative drug delivery studies (BE) in the ANDA
- Office of Pharmaceutical Quality (OPQ)
  - Assessment of device quality (Collaboration with CDRH)
  - Assessment of device manufacturing (Collaboration with CDRH)

Summary Considerations

- When appropriate, meet with FDA at pre-ANDA meetings
- The generic product device constituent does not have to be an exact copy of the RLD, but all differences should be described in detail with the comparative threshold analyses submission.
- FDA encourages early use of Controlled Correspondences to obtain feedback on potential device design and user interface considerations
- Potential differences may require additional information and/or data
- When differences exist, not every difference requires a CUHF study


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