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

AAM 2020: GRx+Biosims Complex Workshop

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Outline

- General overview of combination products
- Regulatory considerations for drug-device combination products submitted in abbreviated new drug applications (ANDAs)
- Content of Session 4: Device Considerations for Complex Drug-Device Combination Products
  - Part 1: Brief Scientific and Regulatory Presentations
  - Part 2: Mock Product Development Pre-ANDA Meeting

What is a Combination Product?

- A “combination product” is:
  - A product comprised of two or more different types of medical products (e.g., drug and device, drug and biological product, device and biological product, or all three together).

Types of Combination Products

	"Single-entity"	"Co-packaged"
Description	Chemically or physically combined constituent parts	Constituent parts packaged together
Examples	• Drug-eluting stent • Prefilled syringe • Transdermal patch • Bone void fillers with drugs	• First-aid or surgical kit • Syringe packaged with vial of drug • Drug + prefilled diluent, reconstitution/ transfer device, fillable cartridge and wearable patch
Reference	21 CFR 3.2(e)(1)	21 CFR 3.2(e)(2)

- There is another type of combination product, which includes constituent parts that are packaged separately, but specifically labeled for use with one another to achieve the intended therapeutic effect.

Primary Mode of Action

- Combination products have multiple "modes of action" (see 21 CFR 3.2(k))
- There are three potential modes of action for a combination product:
  - Drug
  - Device
  - Biological product
- Combination products are assigned to a "Lead Center" having primary responsibility for their review
  - Will consult with non-Lead Center via Inter-Center Consult process, where appropriate
- Lead Center is based on:
  - The "primary mode of action" (PMOA): Constituent part that provides the greatest contribution to the product's intended therapeutic effects.

Drug-Device Combination Products














General Framework for ANDAs

- Approval of generic drug starts with a listed drug – generally an innovator product approved under 505(c).
- ANDA relies on FDA's finding of safety and effectiveness for listed drug.
- Requires demonstration of "sameness" of a number of characteristics + additional information to permit reliance on the reference listed drug (RLD).
- In the context of drug-device combination products, applicants should generally seek approval of a presentation approved for the RLD (e.g., autoinjector).

Generic Drug Product Substitutability

In relation to the RLD, generic drug 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 drug-device 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**
  - Generic and RLD do not need to be identical, as long as differences do not preclude approval under an ANDA.
  - FDA expects that end-users 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.

Complex Drug-Device Combination Products

- As defined in the GDUFA II Commitment Letter, complex products are:
  - Products with complex active ingredients, complex formulations, complex routes of administration, or complex dosage forms;
  - **Complex drug-device combination products**; and
  - Other products where complexity or uncertainty concerning the approval pathway or possible alternative approach would benefit from early scientific engagement.
- Examples of a **complex drug-device combination product:**
  - Prefilled auto-injectors
  - Metered-dose inhalers, dry powder inhalers
  - Transdermal and topical delivery systems
- Examples of a **non-complex drug-device combination product:**
  - Dosing cups and syringes for oral liquid formulations

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

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

Part 1: Brief Scientific and Regulatory Presentations

Title	Speaker
The Impact of Actuator Device Design on Metered Dose Inhaler (MDI) In Vitro Performance	Dr. Elizabeth Bielski, PhD
Computational Fluid Dynamics (CFD) Modeling for Optimization of Device Design and Understanding of Product Performance	Dr. Ross Walenga, PhD
Quality Considerations for Injectable Drug-Device Combination Products in Abbreviated New Drug Applications (ANDAs)	Dr. Richard Chang, PhD
Device Considerations from a User Interface Perspective: Comparative Analyses	Dr. Betsy Ballard, MD

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

Part 2: Mock Product Development Pre-ANDA Meeting

- General Considerations for Pre-ANDA Meeting Requests
- Case Scenario Setup: Device Constituent of a Hypothetical BREATHEATOL Drug Product
  - Product-specific guidance (PSG)
  - Relevant sections of product labeling including the instructions for use (IFU)
- Mock Virtual Pre-ANDA Meeting – Preparation
  - Evaluate potential candidates for the proposed Test device
  - Identify device design differences from the RLD
  - Elaborate questions for the proposed Test device
- Mock Virtual Pre-ANDA Meeting with FDA
  - Present your questions for your proposed Test device
  - Discuss with FDA representatives

Sneak Peek

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BREATHEATOL safely and effectively. See full prescribing information for BREATHEATOL Inhalation Aerosol.

BREATHEATOL (API HFA), inhalation aerosol, for oral inhalation use

INDICATIONS AND USAGE

BREATHEATOL is a corticosteroid indicated for:

- Maintenance treatment of asthma as prophylactic therapy in patients 5 years of age and older. **(1)**

Important Limitations:

- Not indicated for the relief of acute bronchospasm. **(1)**

DOSAGE AND ADMINISTRATION

For oral inhalation only. **(2.1)**

- Starting dosage is based on prior asthma therapy and disease severity. **(2.2)**
- Treatment of asthma in patients 12 years and older: 50 mcg, 100 mcg, 200 mcg, or 400 mcg twice daily. **(2.2)**
- Treatment of asthma in patients 5 to 11 years of age: 50 or 100 mcg twice daily. **(2.2)**
- Discard BREATHEATOL inhaler when the dose counter displays 0 or after the expiration date on the product, whichever comes first. **(2.1)**

DOSAGE FORMS AND STRENGTHS

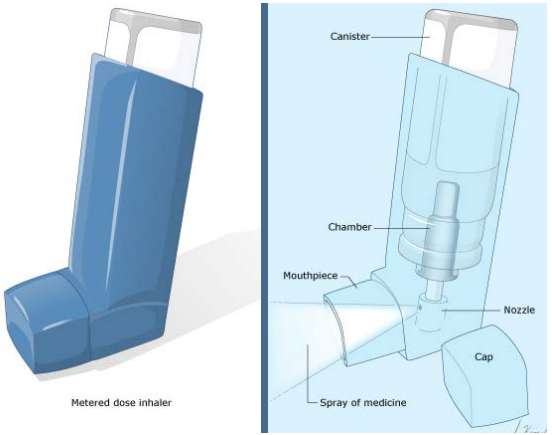
Inhalation aerosol: 50 or 100 mcg per actuation **(3)**

CONTRAINDICATIONS

- Primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required. **(4)**
- Hypersensitivity to any of the ingredients of BREATHEATOL. **(4)**

WARNINGS AND PRECAUTIONS

- Localized infections: *Candida albicans* infection of the mouth and throat may occur. Monitor patients periodically for signs of adverse effects on the oral cavity. Advise patients to rinse the mouth with water without swallowing after inhalation. **(5.1)**



https://www.uptodate.com/contents/asthma-inhaler-techniques-in-children-beyond-the-basics/print

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Thank you!

See you soon at Session 4 “Device Considerations for Complex Drug-Device Combination Products”


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