U.S. FOOD & DRUG ADMINISTRATION

GDUFA Regulatory Science and Research on Generic Drug-Device Combination Products

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What Is A Combination Product?

21 CFR 3.2

1. A product comprised of **two or more regulated components**, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as **a single entity**;
2. Two or more **separate products packaged together** in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;
3. A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is **intended for use only with an approved individually specified** drug, device, or biological product **where both are required** to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or
4. Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is **for use only with another individually specified** investigational drug, device, or biological product **where both are required** to achieve the intended use, indication, or effect.

Generic Drug Products

In relation to its reference listed drug (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

Drug-Device Combination Products

- **There is the same expectation** for generic drug-device combination products
- Generic and RLD do not need to be identical in all respects, as long as differences do not preclude approval under an abbreviated new drug application (ANDA)
- FDA expects that end-users can use the generic combination product when it can be 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

Drug-Device Combination Products

Considerations include, but are not limited to:

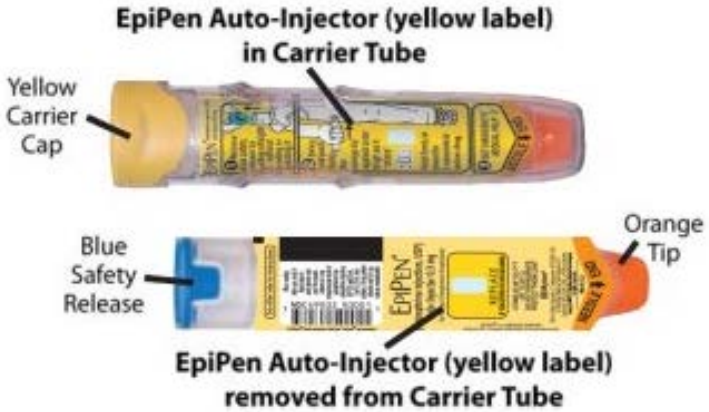
- **Performance Characteristics**
  - FDA takes into consideration the performance of the device constituent and its interaction and impact on the delivery of the drug constituent
- **User Interface**
  - Refers to all components of a product with which a user interacts, including the delivery device constituent part, any associated controls and displays, as well as such as labeling and packaging
  - Draft guidance for industry, *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* (Jan 2017)

Complex Drug-Device Combination Products

Examples include:

- Auto-injectors (AI)
- Metered dose inhalers (MDI)
- Soft mist inhalers
- Metered nasal spray products
- Dry powder inhalers (DPI)
- Transdermal systems

RLD and Generic Epinephrine AI



- A CARRYING TUBE IS NOT PROVIDED AS SEEN WITH OTHER PRODUCTS.
- **Epinephrine Injection, 0.3 mg Auto-Injector (yellow label) with Yellow Cap**

- **Epinephrine Injection, 0.3 mg Auto-Injector (yellow label) with Yellow Cap Removed**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/019430s074lbl.pdf

https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=090589

RLD and Generic FP/SX DPI

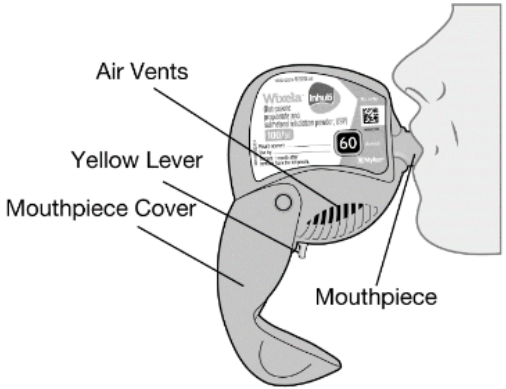
https://www.advair.com/how-to-use-advair.html

https://www.wixela.com/

FP/SX= Fluticasone Propionate and Salmeterol Xinafoate

RLD and Generic FP/SX DPI

Inhale your medicine



Close the device

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

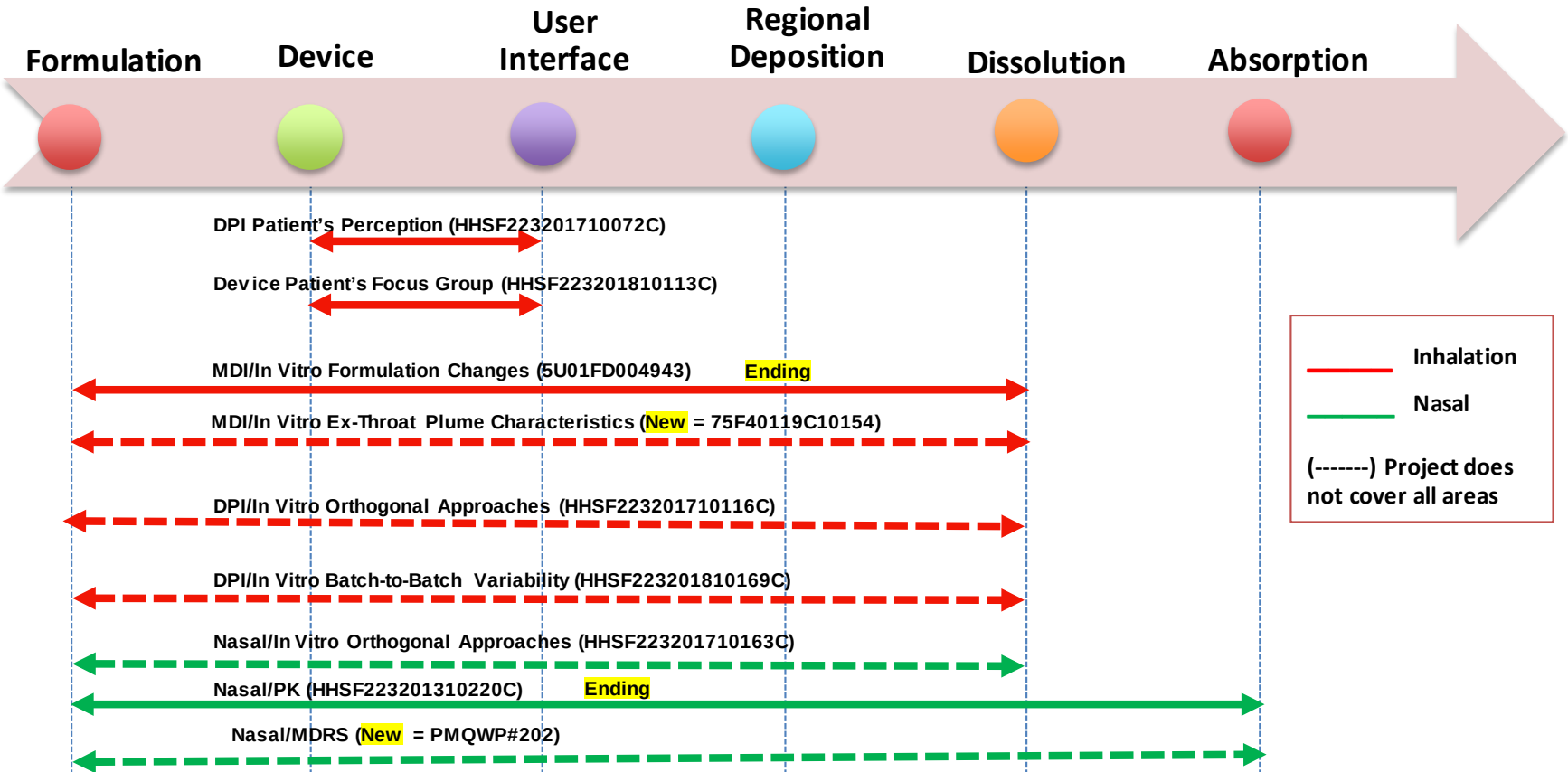
https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208891Orig1s000lbl.pdf

RLD and Generic Albuterol MDI

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021457s036lbl.pdf
www.proair.com

https://www.youtube.com/watch?v=wfQvv9TO4GE

Current External GDUFA Regulatory Science Projects for Orally Inhaled and Nasal Drug Products



https://www.fda.gov/drugs/generic-drugs/science-research

GDUFA= Generic Drug User Fee Amendments

Session II: Breakout 2

- Complex generic drug-device combination products lag behind other product categories for approved generics
- OGD is actively facilitating complex generic drug-device combination product development through our scientific research and communication programs
- Ultimate goal of making safe, effective, and affordable generic drug-device combination products available to the American public

Expert Discussants

- Markham Luke, MD PhD – FDA, Division of Therapeutic Performance (DTP)
- Molly Story, PhD – Sanofi, Medical Device Development Unit
- Ravi Harapanhalli, PhD - Amneal
- Roisin Wallace, PhD - Mylan
- Christoph Zauner, PhD - Fresenius-Kabi
- Elizabeth Bielski, PhD – FDA, Inhaled Products Team, DTP
- Priyanka Ghosh, PhD – FDA, Topical Products Team, DTP
- Bin Qin, PhD – FDA, Complex Injectables & API Team, DTP
- Kimberly Witzmann, MD – FDA, Office of Bioequivalence
- Bing Cai, PhD – FDA, Office of Pharmaceutical Quality (OPQ), Office of Lifecycle Drug Products
- Changning Guo, PhD – FDA, OPQ, Testing and Research
- Dhaval Gaglani – FDA, OPQ, Office of Lifecycle Drug Products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