U.S. FOOD & DRUG ADMINISTRATION

COMPLEX GENERIC DRUG-DEVICE INHALATION PRODUCTS AND USER INTERFACE SAMENESS: SUCCESSFUL OUTCOMES

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Generic Products in the U.S. Marketplace

- Generic drugs offer considerable savings to consumers
- $1.67 trillion saved over last decade
- FDA-approved generics account for 90% of prescriptions dispensed in the U.S.
- More than 1,000 generic products were approved or tentatively approved in 2019
- 10% were first generics, 11% were complex generics

https://www.fda.gov/drugs/generic-drugs/generic-drug-facts
https://www.fda.gov/drugs/buying-using-medicine-safely/generic-drugs
https://www.fda.gov/drugs/generic-drugs/2019-office-generic-drugs-annual-report

How OGD Facilitates OINDP Generic Drug Development

- OGD publishes new and revised Product-Specific Guidances (PSGs), to identify the Agency's current thinking on methodology for developing drugs
- OGD-sponsored research generates evidence needed to support generic approvals
- Pre-ANDA program for complex products [under GDUFA II] allows for substantive scientific interactions and discussions about complex generic drug development to occur throughout development and prior to ANDA submission

https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075207.htm
https://www.fda.gov/drugs/generic-drugs/science-research
https://www.fda.gov/media/101052/download

OINDP= Orally Inhaled and Nasal Drug Products

Generic Drug Product Substitutability

In relation to the 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**

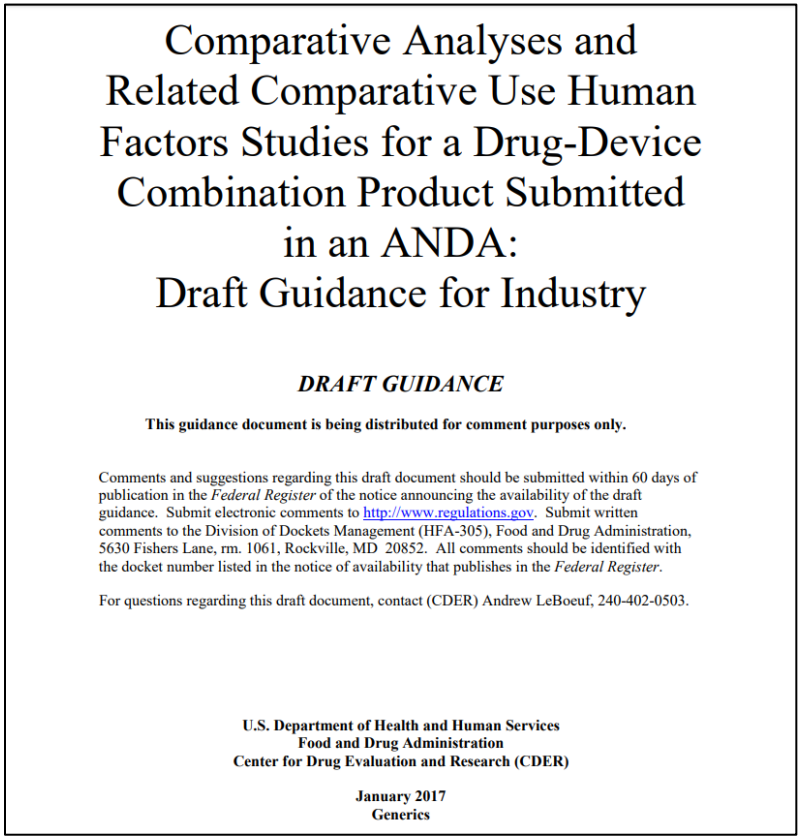
  Approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling

General Principles-Combination Products

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

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.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

January 2017
Generics

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

RECENTLY APPROVED OINDP GENERICS

Example: Dry Powder Inhaler

- Product-Specific Guidance for Fluticasone Propionate/ Salmeterol Xinafoate (FP/SX) posted in September 2013
- Recommendation include studies for bioequivalence, formulation sameness, and device considerations
- First Generic FP/SX DPI approved in January, 2019
- Device and user interface considerations
- Other differences addressed with additional data appropriate for submission in ANDA

RLD and Generic FP/SX DPI

Figure A

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

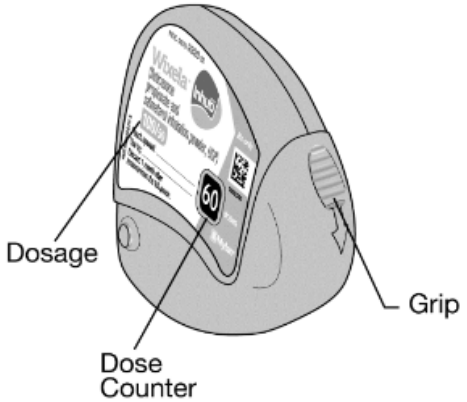
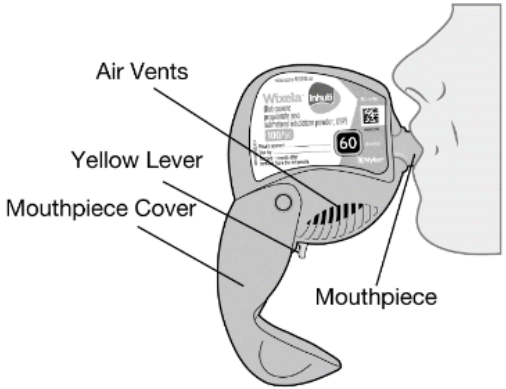


Figure A

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

RLD and Generic FP/SX DPI

Inhale your medicine



Close the device

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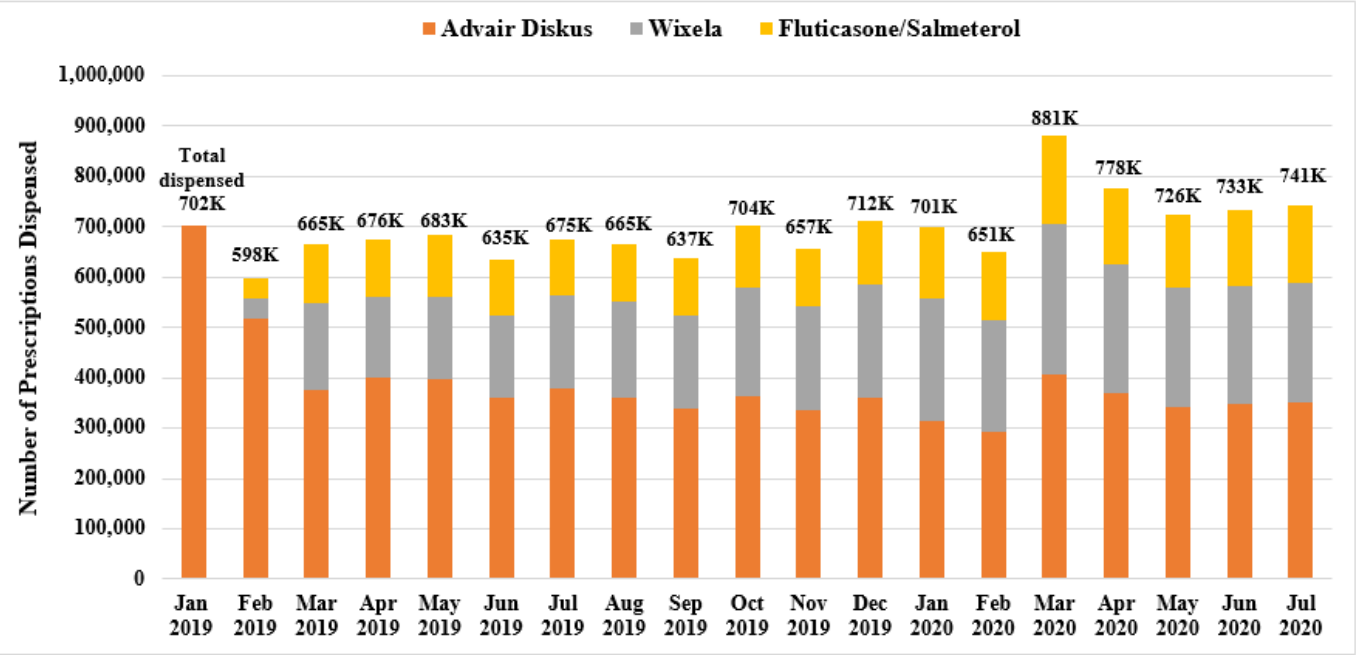
https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208891Orig1s000lbl.pdf

RLD and Generic FP/SX DPI

Estimated Number of Prescriptions Dispensed for Advair Diskus, Wixela, and Fluticasone/Salmeterol from U.S. Outpatient Retail, Mail-Order, and Long-term Care Pharmacies from January 2019 through YTD 2020, annually.



Source: IQVIA NPA™ database. Data years: Jan 2019 through July 2020. Data extracted: September 2020. File: NPA Advair Diskus, Wixela, and Fluticasone-Salmeterol Products.xlsx.

**This slide contains proprietary drug use data obtained by FDA under contract, provided through the FDA/CDER Office of Surveillance and Epidemiology

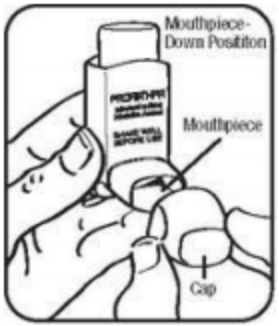
Example: Albuterol Metered Dose Inhaler

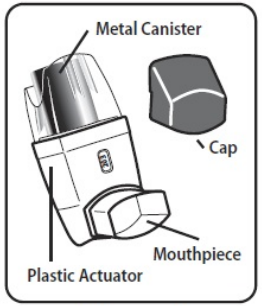
- Product-Specific Guidance for Albuterol Sulfate (aerosol metered inhalation) posted in April 2013
- Revised June 2013, Dec 2016, March 2020
- Recommendation include studies for bioequivalence, formulation sameness and device considerations
- First Generic Albuterol MDI approved in February, 2020
- Second generic Albuterol MDI approved in April, 2020
- Third generic Albuterol MDI approved in August 2020
- Device and user interface considerations

RLDs and Generic Albuterol MDIs

ProAir HFA

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





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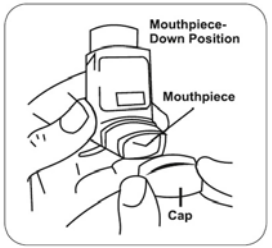


https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=973b8686-c6ce-4280-85c4-c1e7ceab3c09

Proventil HFA

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020503s054lbl.pdf

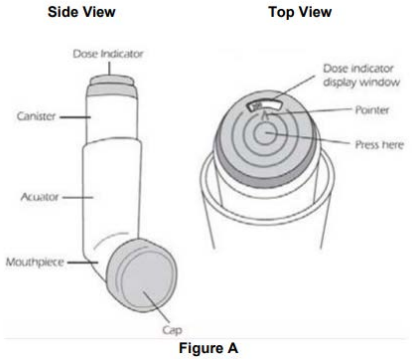
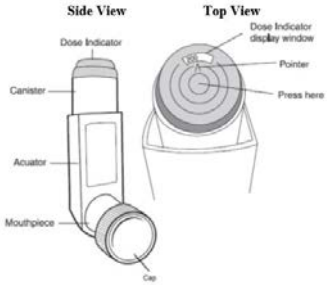


Figure A



https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=c4d6d76a-14b8-411a-8019-e2c923c2c532

Conclusions

- FDA-approved generics account for the majority of prescriptions dispensed in the U.S., and convey considerable cost savings
- Due to their complexity, OINDPs lag behind other product categories for approved generics
- OGD is actively facilitating complex generic OINDP development through our scientific research and communication programs
- OGD has recently approved some complex generic combination OINDP products
- Ultimate goal of bringing safe, effective, and affordable generic drug products available to the American public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