QUALITY PERSPECTIVE: ASSESSING DEVICE DRUG DELIVERY PERFORMANCE OF GENERIC COMBINATION PRODUCTS

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Everyone deserves confidence in their *next* dose of medicine.

Pharmaceutical quality
assures the
availability,
safety,
and efficacy
of *every* dose.

Outline

- Introduction of Draft EDDO Guidance
- CMC Considerations:
  1. Pharmaceutical Development
  2. Performance Testing of Device Constitute Part
  3. Control Strategy
  4. Case Study for QC Control

Guidance: What, How, and Why

1. ***What it covers:***

- Focus on **drug delivery performance** for devices and CDER/CBER-LED combination products
- Complement existing standards and guidance
- Does not cover a full data/information submission for drug delivery devices

2. ***What FDA expects:***

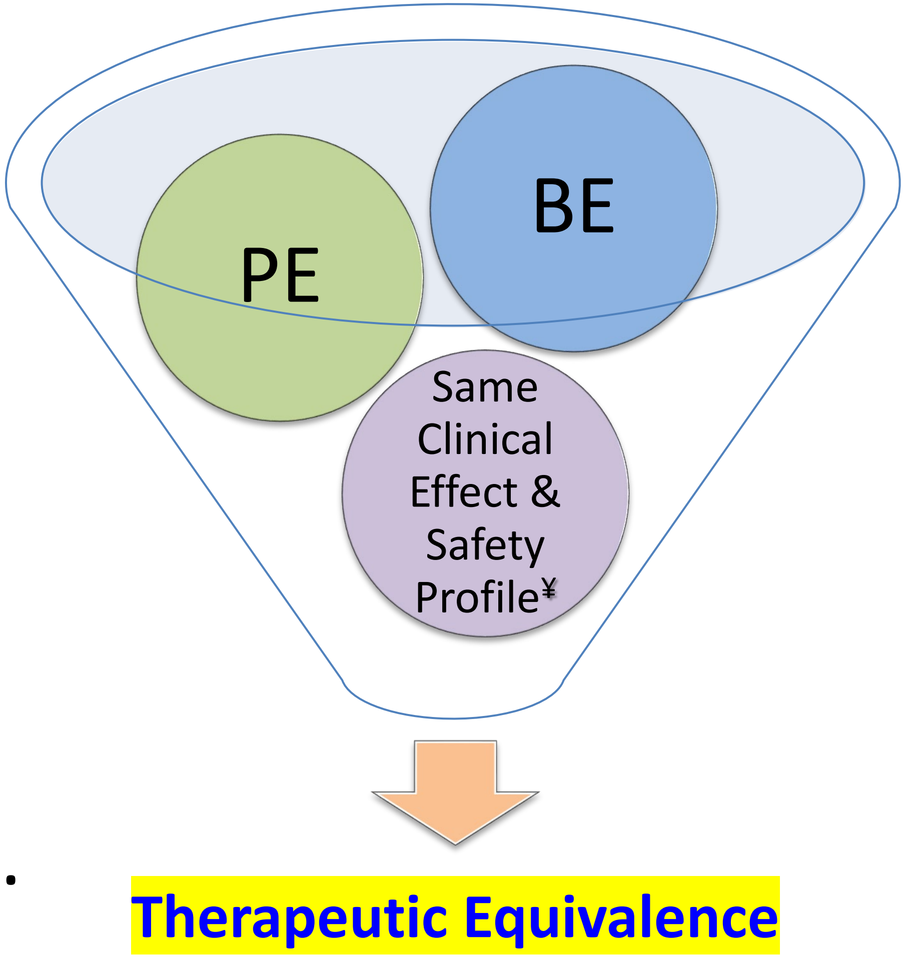
- Provide information essential for establishing and assessing drug delivery performance
- Submit data to demonstrate that the **device drug-delivery function consistently performs as intended**

3. ***Why it matters:***

- Improve consistency of information in regulatory submissions.
- Streamline development and life cycle management.

Pharmaceutical Development

- Define QTPP:
  - Include device specific functional property requirements of device constituent part*
- Identify CQAs & conduct risk assessment
  - Evaluate device drug-delivery function/ performance early
- Suitability Studies
  - Demonstrate functioning properly for performance features€
- Comparative device performance data vs. RLD
  - FDA CMC Guidance & PSG



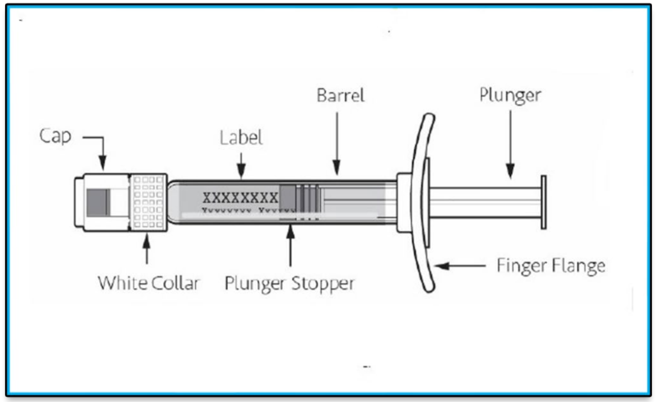
[*Transdermal and Topical Delivery Systems - Product Development and Quality Considerations (Draft, 11/19)]
[€CCS for Packaging Human Drugs and Biologics (07/99)]
[¥Evaluation of Therapeutic Equivalence (07/22)]

Demonstrate Performance/Functionality

- Performance of the CCS = ability to function as designed [CCS Guidance].
- Demonstrate the ability of the device to deliver the product in an **accurate** and **reproducible** way (e.g., dose) [Q8(R2)].
- Test conditions should closely simulate the use of the DP [Q8(R2)] (per labeling).
- **Ensure delivery of the intended drug dose to the intended delivery site** [EDDO Guidance].

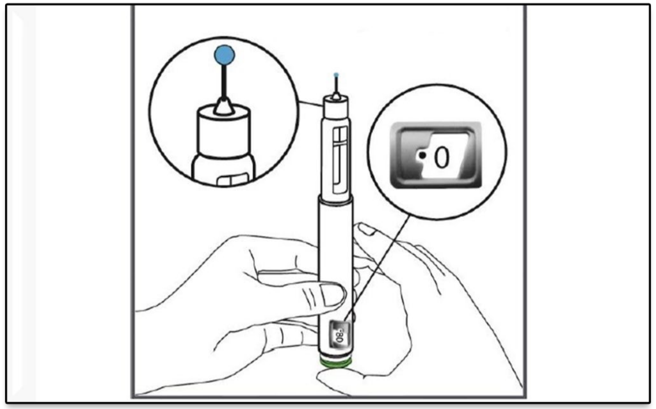
Examples of Drug Delivery Performance Highlighted in FDA Guidance

Pre-filled Syringes



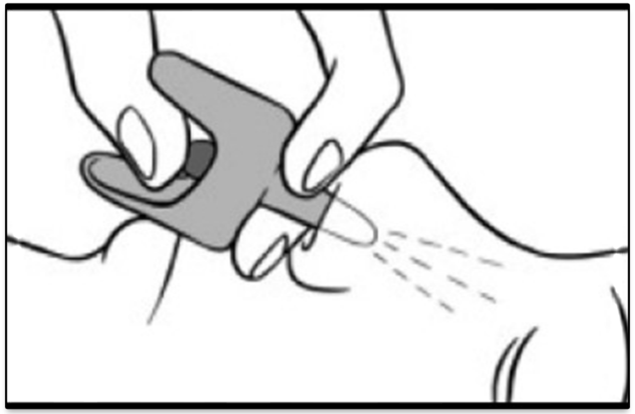
- Delivered volume (dose accuracy)
- Breakloose force
- Glide force

Pen Injectors



- Dose accuracy
- Injection force
- Cap removal force
- Feedback: Audible/visual/tactile (dose completion)

Nasal Sprays*



- Pump Delivery (Spray weight)
- Spray content uniformity
- Spray pattern
- Plume geometry (one-time)
- Droplet size distribution
- Particle size distribution (suspensions)
- Activation Force

Ref: Uzedy PI (Drugs@FDA) - for illustration purposes only.
Ref: Tymlos PI (Drugs@FDA) - for illustration purposes only.
*Nasal Spray and Inhalation Solution, Suspension, and Spray DPs--CMC Documentation (07/02)

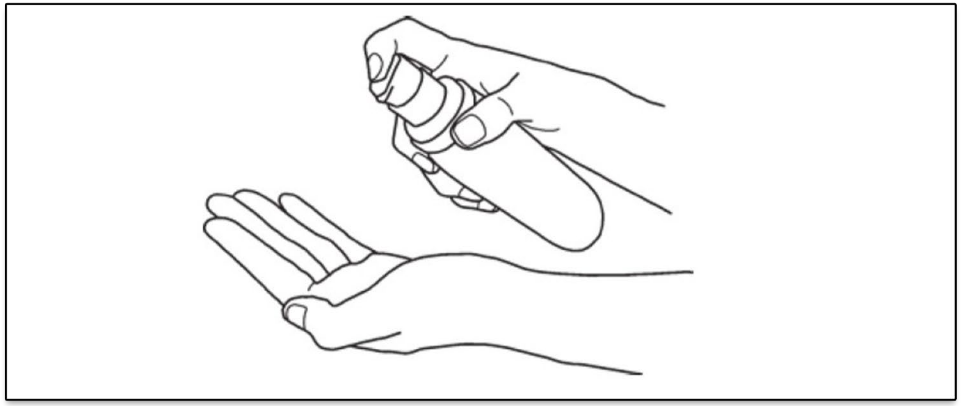
Additional Examples of Drug Delivery Performance

Topical Ophthalmic Solution in Eye Dropper Bottles

One-time drop size study*

- Drop weight/volume
- # of drops per container
- Holding angle during dosing

Topical Liquid/Semi-solid in Metered-dose airless pump



- Mean Dose Weight
- Total # of doses per container
- Delivered Dose Uniformity
- Actuation Force
- Pumps to Prime (USP <3>)
- Total amount dispensed (USP <3>)

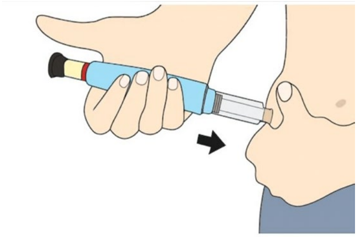
Ref: Image fron Amcon Blog for illustration purposes only
Ref: Pennsaid PI (Drugs@FDA) - for illustration purposes only.
*Quality Considerations for Topical Ophthalmic DPs (Draft 12/23)

Designing a Risk-Based Control Strategy

- Design a control strategy to ensure that the device drug-delivery function consistently performs as intended
- Number and types of controls, and control strategy information should match **product risk** (e.g., complexity of design and manufacturing) [EDDO Guidance]
- Align performance tests and acceptance criteria with dosage form, route of administration, and device design features [CCS Guidance]
- Apply compendial and recognized standards (e.g., USP, ISO)

QC Control Case Study: Pen Injector

Injectable Solution, 1560 mcg / 1.56 mL (1000 mcg/mL)
Pre-assembled disposable pen
30-day supply (40 mcg once daily, 40 µL/dose)



QC Specifications (Fully Assembled Pen)	Alignment with EDDO Guidance (with USP/ICH considerations)
Dose accuracy*: e.g., 30–50 µL/injection	Ensure intended dose to site delivery
Injection force* within specified range	Demonstrate consistent performance as intended
Total # of doses: NLT 30 doses per Pen	Verify pen delivers all labeled doses under stability testing through expiry
Container content: ≥ 1.5 mL	Confirm sufficient excess volume (per USP <697>) to support all labeled doses

*Depending on pen injector design, additional performance tests may be required.

References: Draft FDA EDDO Guidance (2024); USP <697>; ICH Q1A(R2), Stability Testing

Summary

- **EDDO guidance:** Framework to demonstrate drug delivery devices perform as intended
- **Performance**: Consistent, reproducible, and aligned with labeling
- **Controls**: QC verifies performance at release and throughout shelf life
- **Integration**: Early evaluation of device drug delivery performance streamlines development, support regulatory submissions, and accelerates patient access

FDA CMC Guidance

- Container Closure Systems for Packaging Human Drugs and Biologics, 1999
- Parenteral
  - Glass Syringes for Delivering Drug and Biological Products: Technical Information to Supplement International Organization for Standardization (ISO) Standard 11040-4 (Draft), 2013
  - Technical Considerations for Pen, Jet, and Related Injectors Intended for Use with Drugs and Biological Products, 2013
- Inhalation/Nasal
  - Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products — Chemistry, Manufacturing, and Controls Documentation, 2002
  - Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Products - Quality Considerations (Rev.1), 2018
- Transdermal/Topical Delivery Systems
  - Transdermal and Topical Delivery Systems - Product Development and Quality Considerations (Draft), 2019
- Ophthalmic:
  - Certain Ophthalmic Products: Policy Regarding Compliance With 21 CFR Part 4, Mar 2022
  - Quality Considerations for Topical Ophthalmic Drug Products (Draft), Dec 2023

Acknowledgements

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