Workshop 2
Beyond the Molecule: Navigating Comparability Across Drug Delivery Presentations

What does comparability mean to you?

comparability (noun)

käm-p(ə-)rə-ˈbi-lə-tē

the quality or state of being comparable

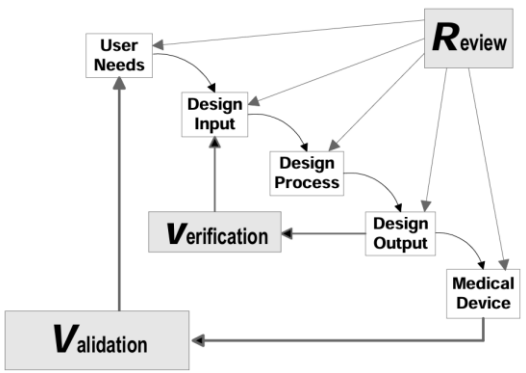
Workshop Objectives

- Provide foundational overview on comparability
- Identify key requirements when transitioning between vials, prefilled syringes, and autoinjectors
- Case study and group discussion
  - Presentation transition for vaccines and therapeutic biologics
  - Development and post-approval changes

Comparability Regulations and Guidance

- ICH Q5E Comparability of Biotechnological/Biological Products Subject To Changes In Their Manufacturing Process
- FDA Guidance- Demonstration of Comparability of Human Biological Products, Including Therapeutic Biotechnology-derived Products
- FDA Guidance- Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA

Changes to a Combination Product Device Constituent



- 21 CFR Part 4 provides a streamlined (cGMP) approach for combination products
- Design controls (21 CFR 820.30)
  - Ensures devices are designed, tested, verified and validated to meet user needs, intended use and safety and performance requirements
  - Covers requirements for device-related changes

- For a combination product, changes to a drug/biologic need to be assessed to determine if they impact and require a change to the device

Device: Design Change	**Drug: Change Management**
Review, validate/verify and approve change before implementation, ensuring the device meets its requirements	Formulation, process and analytical comparability ensure consistent identity, strength, quality and purity

Reference: Design Controls Guidance

Combination Product Impact Considerations

Considerations for a **DRUG** Change

- **Example: New DS manufacturing site:**
  - Impact on molecule structure characteristics
  - Impact on safety related impurities
  - Impact on stability
- **Example: Formulation change:**
  - Impact on Stability
  - Impact on forming particulate matter

Considerations for a **DEVICE** Change

- **Example: New device component supplier:**
  - Impact on functionality tests of the device
  - Impact on meeting the user requirements of the device that are no routinely included in the device release spec.

COMBINATION PRODUCT Considerations

- Consider impact on each constituent ***and*** interaction between constituent parts

- **Example**: Drug formulation change → increased viscosity → increase autoinjector injection force

Regulatory Reporting (US)

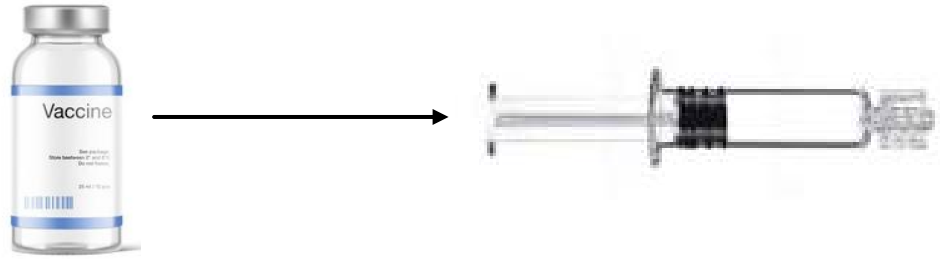
Module 3.2.P.2 Pharmaceutical Development

- Narrative of product development journey, including rationales for choices and changes
- Comparative data support choices and changes during product development

Reporting based on potential to adversely affect safety and effectiveness

- **Minimal** – Annual Report
- **Moderate** – Supplement – Changes Being Affected (CBE, CBE30)
- **Significant** – Prior Approval Supplement (PAS)

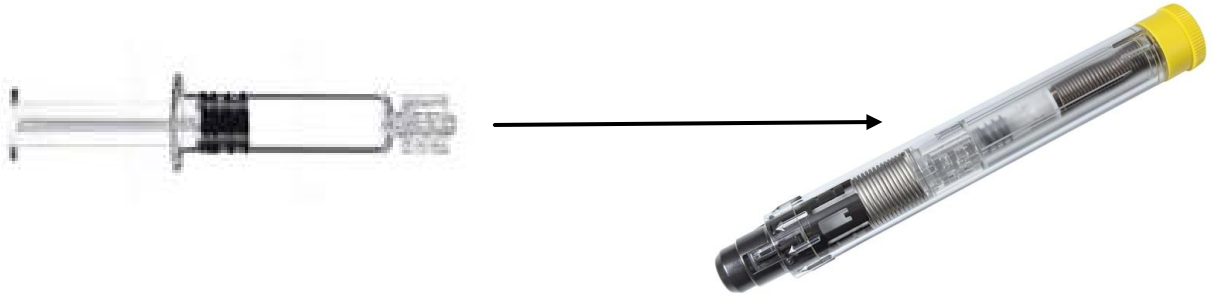
Case Study 1: Vaccine – **Vial** to **PFS**



- **Changes**:
  - Container closure
  - Suppliers
  - Materials
  - Fill volume
  - New filling line at manufacturing site
  - Secondary Packaging
  - Labeling
- **Timing**: Prior to Phase 3 registration trials

- **Unchanged**:
  - US Market
  - Formulation
  - Dose
  - Users (HCPs)
  - Use environment (clinic)
  - Population (Adults)

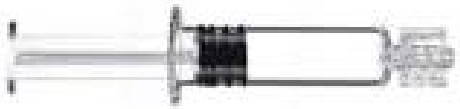
Case Study 2: mAb – **PFS** to **Autoinjector**



- **Changes**:
  - Suppliers
  - Materials
  - New assembly and packaging manufacturing sites
  - Secondary Packaging
  - Labeling
- **Timing**: Post-market

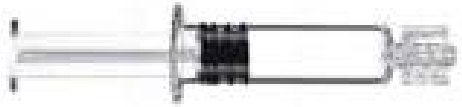
- **Unchanged**:
  - US Market
  - Formulation
  - Dose
  - Primary container closure materials Users (HCPs)
  - Use environment (clinic)
  - Population (Adults)

Case Study 1: Vaccine – **Vial** to **PFS**



- **Changes**:
  - Container closure
  - Suppliers
  - Materials
  - Fill volume
  - New filling line at manufacturing site
  - Secondary Packaging
  - Labeling
  - **Dose**
  - **Population (Adults + Children ≥2 years)**
- **Unchanged**:
  - US Market
  - Formulation
  - Users (HCPs)
  - Use environment (clinic)
- **Timing**: Prior to Phase 3 registration trials

Case Study 2: mAb – **PFS** to **Autoinjector**



- **Changes**:
  - Suppliers
  - Materials
  - New assembly and packaging manufacturing sites
  - Secondary Packaging
  - Labeling
  - **Users (patient)**
  - **Use environment (home use)**
- **Timing**: Post-market
- **Unchanged**:
  - US Market
  - Formulation
  - Dose
  - Primary container closure materials
  - Population (Adults)