Device Comparability Autoinjector Bridging

GRx+Biosims™

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Presentation Overview

Autoinjector clinical bridging studies evaluate whether a biosimilar delivered through an autoinjector device can be considered equivalent to a reference product. This session will explore the latest progress and thinking from FDA on autoinjector clinical bridging studies while also providing industry's view on the challenges they face with bringing their autoinjector to patients. While this session is intended to focus on biosimilars, some of the concepts may be applicable to generics.

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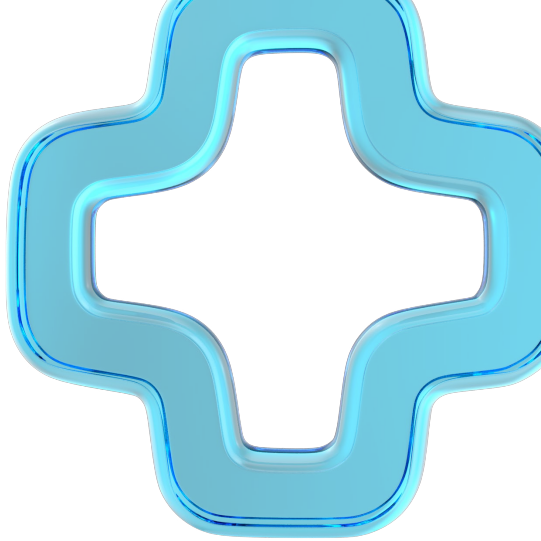

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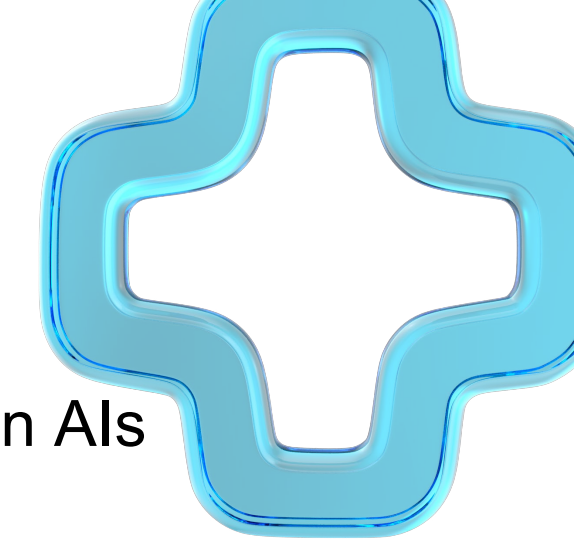
Overview



- Regulatory Framework
- Data Expectations for Biosimilar and Interchangeable Products in AIs
- Bridging Process: Best Practices & Process Example
- Opportunities for FDA Feedback
- Case Study: Reference Product: PFS & AI / Proposed Product: PFS & AI
- Case Study: Reference Product: PFS only/ Proposed Product: PFS & AI
- Industry's View on Challenges
- Q&A

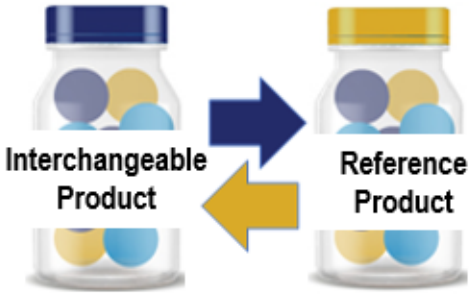
Regulatory Framework – Key definitons

Reference Product

A reference product is the single biological product, already approved by FDA, against which a proposed biosimilar product is compared

Biosimilar Product

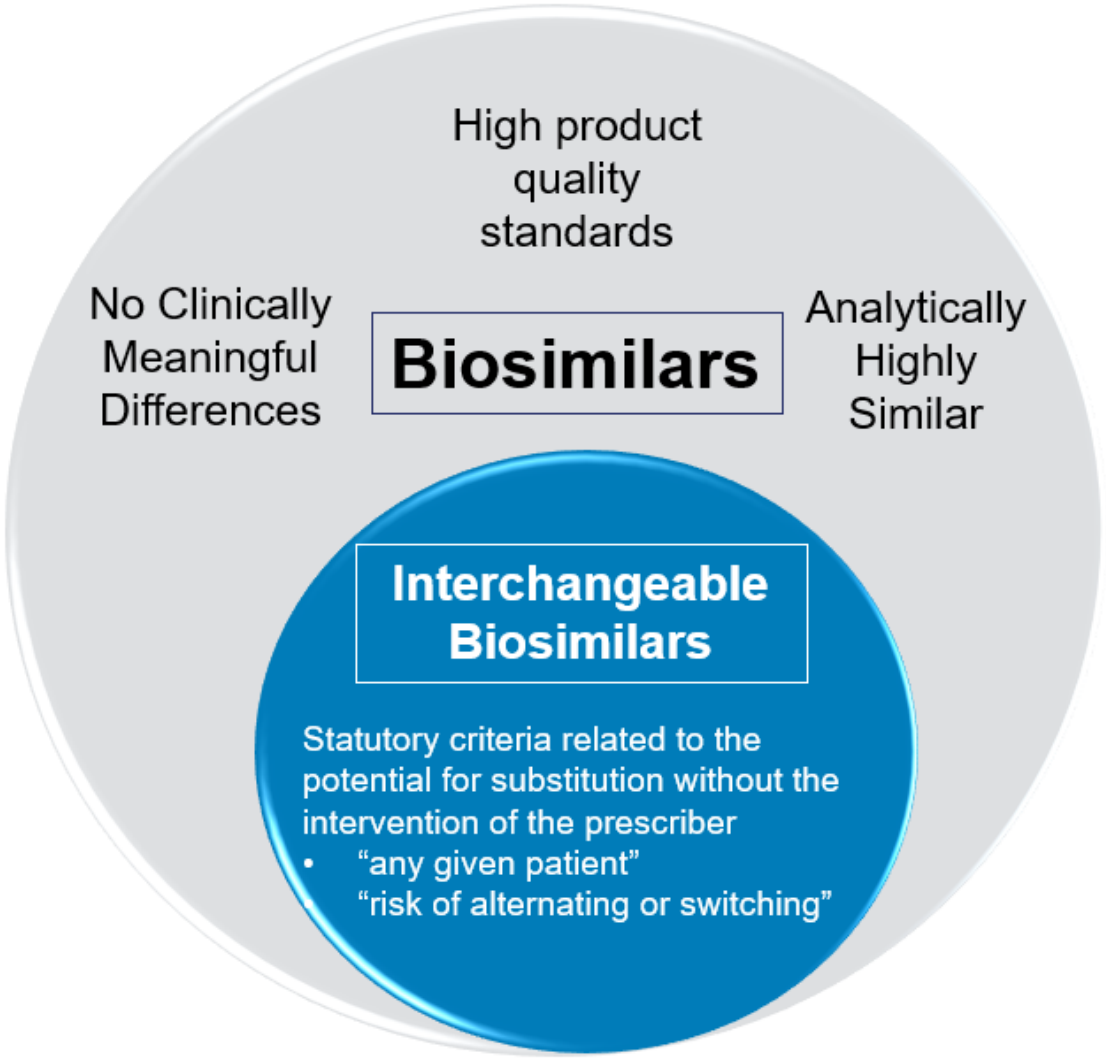
A biosimilar is a biological product that is **highly similar to and has no clinically meaningful differences from** an existing FDA-approved reference product



Interchangeable Product

- Is a biosimilar
- Expected to produce the same clinical result as the reference product (RP) in any given patient
- Switching between the proposed product and the RP does not ↑safety risks or ↓effectiveness compared to using the RP without switching

Regulatory Framework



- Applicants can request licensure as a biosimilar or interchangeable biosimilar
- The analytical similarity and product quality standards are **the same** for biosimilars and interchangeable biosimilars
- Statutory criteria related to the potential for substitution without the intervention of the prescriber
- HCPs prescribe reference products or biosimilars **by name**
- A pharmacist can substitute an interchangeable product for the reference product without consulting the prescribing HCP (subject to state laws)

Data Expectations[1] for Biosimilar and Interchangeable Products in Autoinjectors

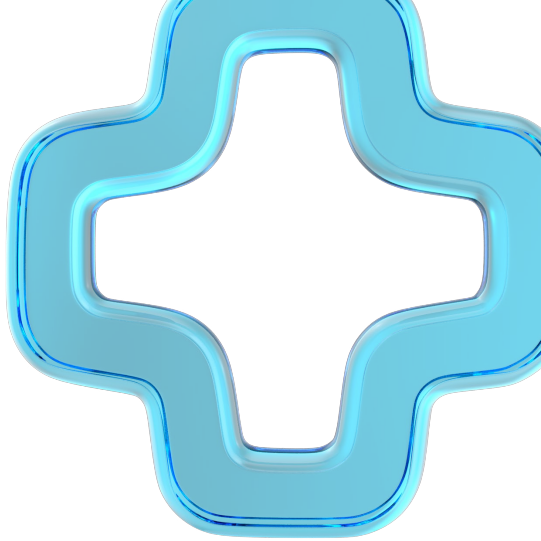
1. Adequate product quality information including performance and compatibility data

2. Comparable exposure between the proposed product and the reference product
   - PK study comparison or justification per the Bridging for Drug-Device and Biologic-Device Combination Products Guidance https://www.fda.gov/media/133676/download

3. Comparison of the user interface[2]
   - Results from human factor (HF) study(ies) or other information if "*other (than minor) differences"* exist

[1] Related to the autoinjector component of the combination product
[2] Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA Guidance https://www.fda.gov/media/102349/download

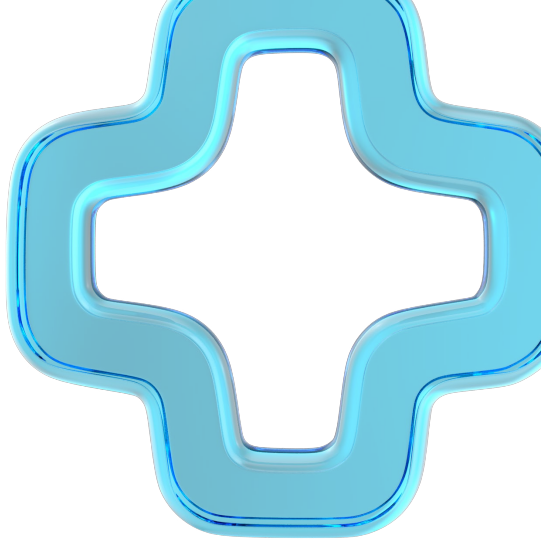
Bridging Process: Best Practices



- Follow Draft Guidance “Bridging for Drug-Device and Biologic Device Combination Products” (December 2019)[1]
- Identify all differences that can impact quality, safety, efficacy, purity and potency
- Identify all existing data to support proposed combination product
- Bridge existing data to proposed combination product
- Confirm if any gaps exist
- Supplement with additional data to address any gaps
- Solicit FDA Feedback along the way

[1] https://www.fda.gov/media/133676/download

Process Example: Identifying All Differences and Mapping



1

- Identify
  - Changes to DP Constituent Part: e.g., concentration, viscosity, formulation/composition
  - Changes to Device Constituent Part: e.g., new primary container/closure, needle size, AI differences
  - Changes to the Combination Product (CP) (as a whole) : e.g., injection rate, depth, dose accuracy, tissue plane, rate of infusion, spray patterns, tissue deposition
  - Changes to Process (DP, Device, CP): assembly process, additional time out of refrigeration/light exposure for assembly, etc.

Don't forget secondary impact i.e., changes to extractable/leachable profiles due to formulation or primary container changes

2

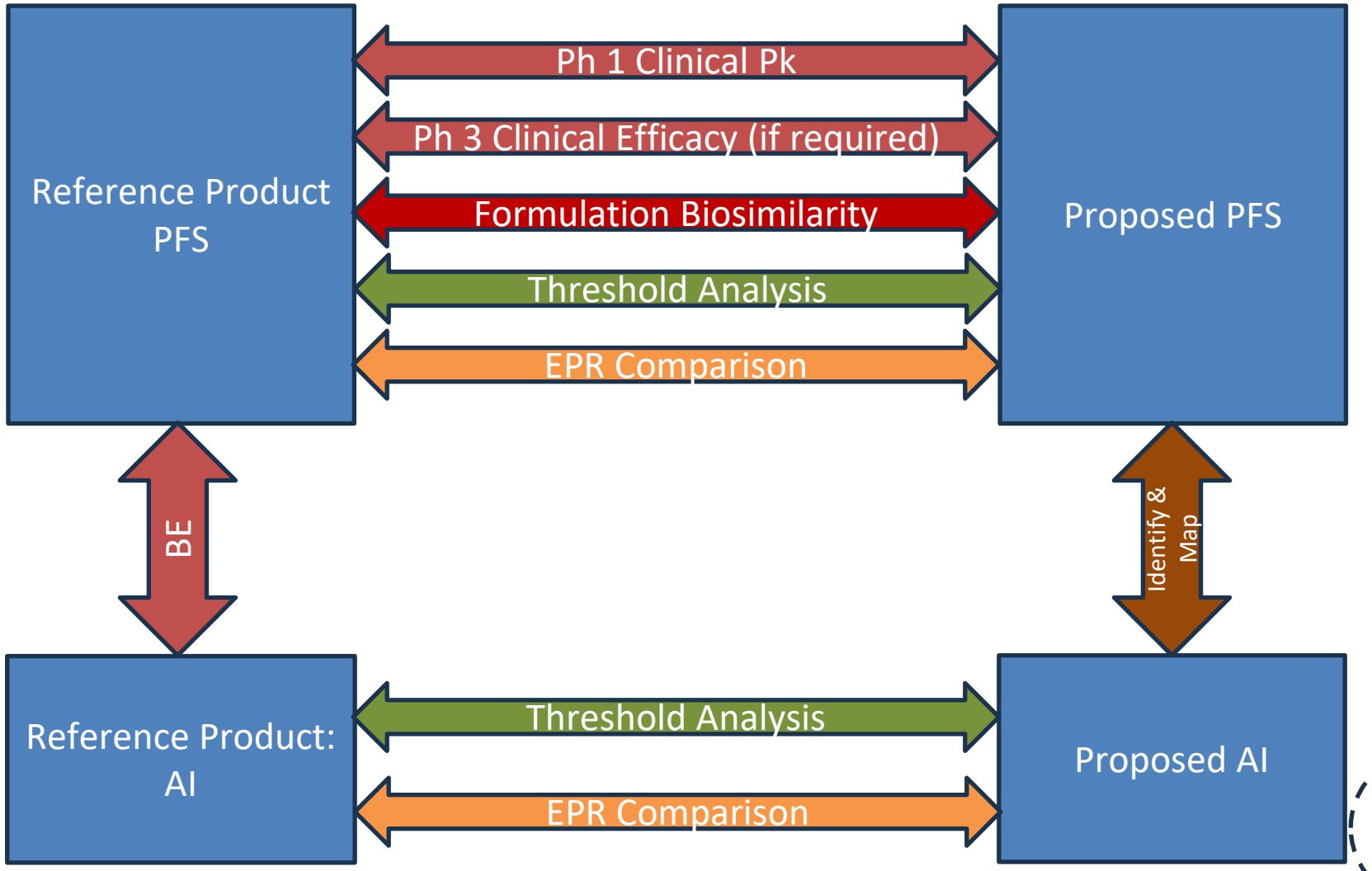
- Map each to potential effect (e.g. quality, purity, potency, safety, efficacy)

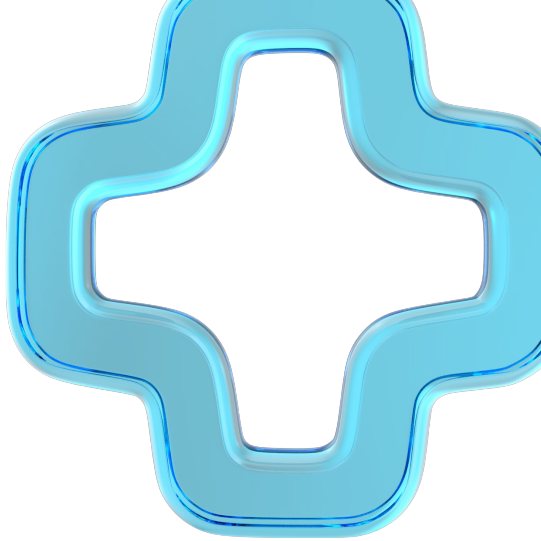
3

- Identify existing data to support proposed product and gather additional data as needed to address potential impacts listed above and provide data to demonstrate
  - Bridging data from other products
  - Referencing positive assessment of Reference Product data
  - Generating new data

Don't forget when bridging data from other products:
1. **Ensure you have right of reference**
2. **Any differences in those products are also considered**

Process Example: Additional RP AI BE Data

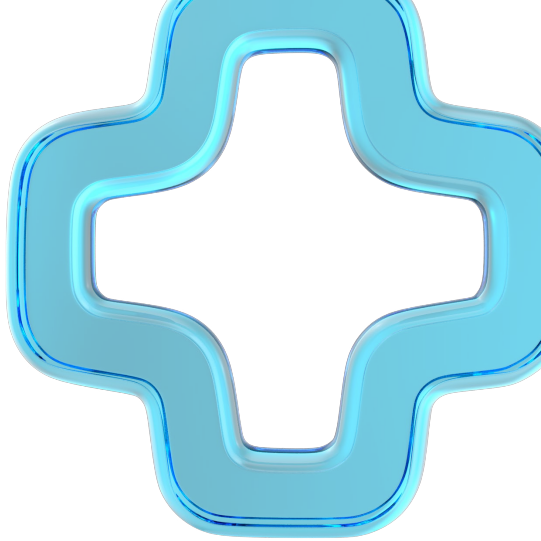


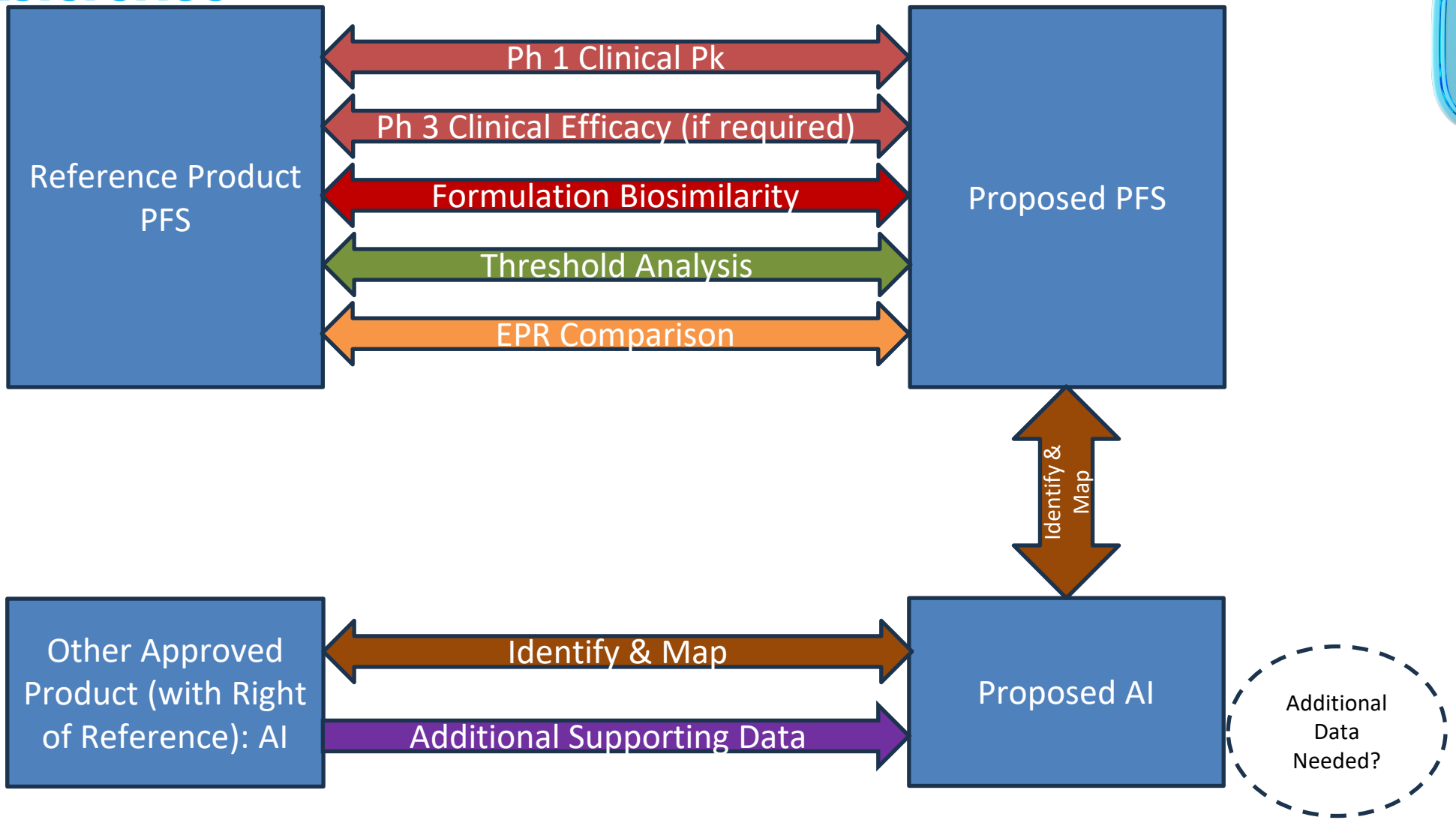


Lots of Assumptions including:

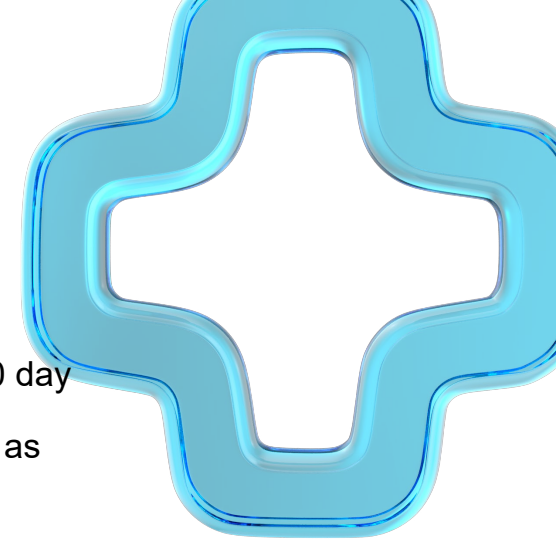
- no change to primary container/closure needle or formulation
- no potential impact from additional assembly/inspection operations
- successful TA/EPR Comparison

Process Example: Bridging to Another AI with Right of Reference





Opportunities for FDA Feedback



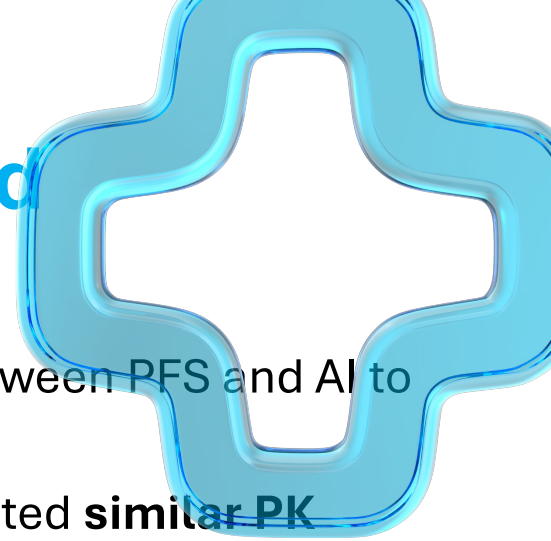
- BPD Meetings
  - Submit to IND
  - Various Types for different purposes:
    - Type 2 for specific issues and summary data (Type 2a: FY 2026 80% 60 day BsUFA Goal/Type 2b: 90% 90 day BsUFA Goal)
      - Walk through the process exercise and cover the differences providing justification or a plan for data as needed
      - Is the plan appropriate?
      - If clinical studies are required, is the basic design, analysis, etc. appropriate?
    - Type 3 for in-depth data and full report reviews (90% 120 day BsUFA Goal)
    - Type 4 for submission content and format (90% 60 day BsUFA Goal)
      - Cross-referencing applications (with right of reference)
      - Submission elements and location within BLA

TIP: Walk FDA through evaluation process step-by-step and provide rationale

- Intend to Market Sample Submissions/URRA/TA
  - FY2026 90% 60 day BsUFA Goal
  - Include specific questions and justification that a HF validation study does not need to be submitted.
- Human Factor Validation Study Protocol Submissions
  - If a HF Study is required, submit to IND with specific questions
    - Are study groups appropriate to represent intended users?
    - Are critical tasks appropriately identified?
  - FY2026 90% 60 day BsUFA Goal

BsUFA III Commitment Letter: https://www.fda.gov/media/152279/download

Case Study 1: RP has PFS & AI, pursuing PFS & AI biosimilar–clinical PK done with PFS not AI–Does AI need clinical bridging/what else is needed to support?



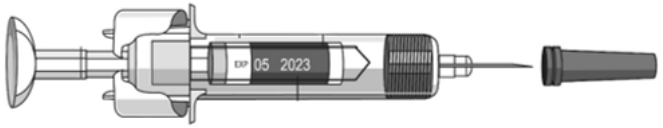
RP is approved in a PFS and an AI; The **originator** conducted a comparative PK study between PFS and AI to show no impact on PK (exposure)

- The proposed biosimilar used **PFS** for the comparative clinical studies and demonstrated **similar PK** (exposure) to the RP
- For AI development, the plan is to bridge to the proposed biosimilar PFS and demonstrate no impact on exposure
  - ➢ Same PFS is used for the PFS presentation as well as the AI, therefore primary container closure is the same, no impact on DP quality ; Assembly of AI is not expected to impact the DP quality
  - ➢ Critical factors that can affect the bioavailability when using AI are:
    - ❖ **Injection time**: Injection time is similar to RP; Added as specification for release
    - ❖ **Dose accuracy:** It is one of the important parameters that are evaluated and ensured that it is same as PFS
    - ❖ **Injection depth and angle:** a 90 -degree angle is standard for AI to achieve the correct SC depth; Injection depth is a critical part of the design and quality assurance process to ensure correct and consistent drug delivery
  - ➢ **TA required (**biosimilar AI Vs RP AI**); HF validation study if required**

If there are no uncertainties from the above, a comparative PK study should not be required

Case Study 2: RP has PFS only and pursuing PFS and AI interchangeable–what does that look like?

Pyzchiva (ustekinumab-ttwe) AI



Stelara (ustekinumab) PFS

Summary Review available at drugs@FDA: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2025/761373Orig1Orig2s001,761425Orig1Orig2s001CrossR.pdf

Approval Date(s) and History, Letters, Labels, Reviews for BLA 761373

Original Approvals or Tentative Approvals

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Action Date	Submission	Action Type	Submission Classification	Review Priority; Orphan Status	Letters, Reviews, Labels, Patient Package Insert	Notes
04/30/2025	ORIG-2	Approval		N/A	Label (PDF) Letter (PDF)	
06/28/2024	ORIG-1	Approval		N/A	Label (PDF) Letter (PDF) Review	

Showing 1 to 2 of 2 entries

Supplements

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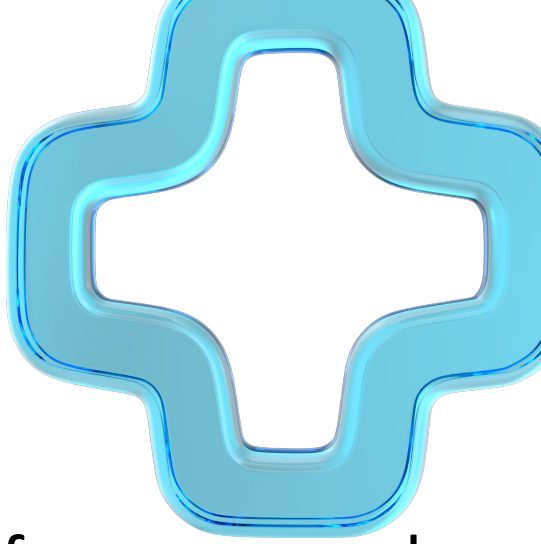
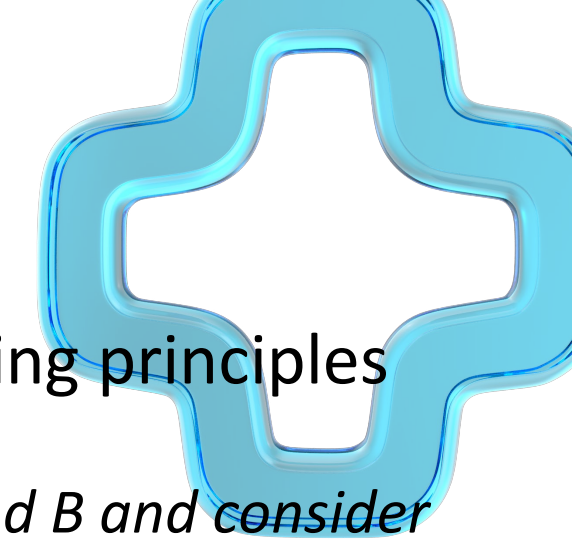
Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, P… Package Insert	Note
06/27/2025	SUPPL-1	Supplement	Label (PDF) Letter (PDF) Summary Review (PDF)	

Case Study 2: RP has PFS only and pursuing PFS and AI interchangeable–what does that look like?



1. Provided adequate product quality information including performance and compatibility data
2. User interface assessment
   - Conducted Comparative Analyses (formerly called Threshold Analysis) of user interface of proposed AI vs. RP PFS (physical, tasks, labeling)
   - Identified "*other differences*"
   - Leveraged their own HF validation study results from another product in same AI
   - Conducted CUHF study comparing proposed AI to RP PFS

Case Study 2: RP has PFS only and pursuing PFS and AI interchangeable–what does that look like?



3. Provided a justification for not conducting a PK study following principles in the Bridging Guidance (https://www.fda.gov/media/133676/download)
   - *Step 1: Identify all differences between Combinations Products A and B and consider the potential effect of the individual and aggregate differences*
     - Drug product quality aspects: viscosity
     - Device characteristics: needle length, injection depth, delivered volume
   - *Step 2: Identify existing information for Combination Product B*
     - PK study showing similarity between the proposed PFS and the Reference Product PFS
   - *Step 3: Identify how and why existing information on Combination Product A can be bridged and leveraged to support approval of Combination Product B*
     - PK study showing comparability between the AI and PFS for another approved product from the same applicant

A PK study was not needed to support approval of the proposed AI

Industry's View on Challenges with PFS Vs AI Clinical bridging Studies

- Takes longer to bring these patient-centric devices to market, thus preventing quicker access for patients
- Unnecessary exposure of human subjects to the drug
- High cost of conducting unnecessary clinical trials
- Generation of data that may not add additional value
- Other Health Agencies (EMA, HC etc) do not require PK bridging data for approval of AI
- No clear guidance is available on the data package requirements to waive AI bridging studies

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Thank you!
Q&A